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The Research Networks built by the MHR4 Programme

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THE RESEARCH NETWORKS BUILT BY THE MHR4 PROGRAMME

THE RESEARCH NETWORKS BUILT BY THE MEDICAL AND HEALTH RESEARCH PROGRAMME (MHR4) - RESUME

What do concerted actions build and produce?

Although the financing available is modest, MHR is still a major programme - involving more than 3000 teams - which has adopted an original approach to financing, that of the "concerted action". As it is not designed to fund research itself, there is no clear definition of what this form of public support for research can achieve, promote or produce. This report is intended to provide such a characterization, and as such, does not constitute an evaluation.

Three surprises as regards the characteristics of Concerted actions

Questionnaires were posted to all participating teams (more than 1400 replied). The results showed that on average the activities coordinated by the concerted action account for one fifth of each participating team's activities. This high degree of involvement is the first surprise. There is strong leverage, but for whom?

The second surprise was the composition of concerted actions : although seven out of ten teams consider research as their main activity, almost one in two includes clinicians, more than one in five is primarily involved in medical practice and more than one in three is a university hospital. These figures reveal the clinical emphasis of the programme and the interweaving of research and clinical practice : nine out of ten concerted actions bring together academics and practitioners.

What is the reason of such a mobilization? The results expected provide a first answer. In line with standard research practice, 70% of the teams will publish their results in journals with referees. For a third of them, the most important results will be "applied", the main output being by far new methods of diagnosis or care of use to clinicians. Most teams stress the importance of "new methods and new instruments for research": protocols or standards, new databases, new reference materials, new experimental facilities or new equipment. This surprise was confirmed when the exchanges were analysed. If, as expected, meetings (workshops, conferences, etc.) and visits are frequent and involve everybody, they are by no means the only form of interaction. More than 85% of teams also exchange data and protocols and nearly 70% are involved in the exchange of at least one of the following five support materials : biological samples, reference materials, reagents, prototypes and software.

This is far removed from the traditional exchange of academic results. The main emphasis appears to be on the collective construction of new data sources. This drives to a transformation in scientific approaches which has strong effects

on the harmonization of laboratory practices, and leads, within each project, to the coordination and sharing of tasks between teams.

The dynamics of concerted actions

This warranted more detailed analysis of the actions themselves, and this was done on the basis of existing documents and in-depth interviews with project leaders (more than one hundred interviews).

Three actions under the first MHR programme, ten or so under the second, thirty or so under the third, more than one hundred by the end of 1990, and virtually none of the actions has been completed. How can this dynamics be explained? We have shown that it could be described across six phases : initiation, assembly, structuring, implementation, processing and dissemination. However, not all actions follow the full path : some are based on pre-existing networks and begin at the implementation phase, others are limited to the initiation phase. In all cases, progress is far from linear : for example an implementation problem can lead to the introduction of new participants and hence a new structuring phase. In this résumé, we emphasize three points which we consider decisive for the future of this programme of Community research.

IMPORTANCE OF THE STRUCTURING PHASE

Each concerted action brings together an average of thirty teams belonging both to national systems with specific characteristics and to different professional environments. They need to get to know each other, to define a common language and to ensure that their data are comparable. These may appear to be simple problems, but they have major practical implications : harmonization of terminology and laboratory practices, setting-up of "common services" or "central facilities", etc. This structuring phase can take several years, and the time needed is almost always substancially underestimated. This goes a long way to explaining why actions are spread over several MHR programmes. Under MHR4, many actions (one in six of thoses studied) will end in budgetary terms just as the project leaders consider them to have become fully operational.

This is in itself worth stressing : the successful completion of the structuring phase not only leads to an exchange of knowledge but creates a new research actor, a *"research network"* (and not just so many collaborating laboratories). One must still ensure that this phase is successfully completed and give the new network the resources needed to prove its effectiveness, two questions with which the new programme is directly concerned.

SELECTION OF CONCERTED ACTIONS

Prior to the MHR4 programme, actions and project leaders were selected exclusively by the programme's advisory structure, the Management and Coordination Advisory Committee (CGC), its four "concerted actions committees (COMAC) and its two "working parties" (WP). By means of a wide-ranging invitation to submit proposals, MHR4 has more or less doubled the number of actions. Of the hundred concerted actions analysed, a quarter were already

operating before MHR4, a fifth were set up in direct response to the programme structure, and the rest came from the proposals submitted. In three out of four cases the proposal concerned the creation of a new network, but in one case out of four a preexisting network (linked to the WHO or a European association of specialists) was activated. The latter, still not particularly numerous, differ substantially from the others. Striking a balance between activating preexisting networks and setting up new networks is one of the problems facing those administering the follow-up programme, BIOMED.

THE DISSEMINATION OF RESULTS AND RESULTS "EMBODIED IN NETWORKS"

All concerted actions focus on a medical problem, whether confronted head-on (monitoring an illness, evaluating a treatment or technique, harmonizing a practice) or by means of a preliminary research phase, in which case a specialized scientific community capable of completing this phase must be first set up.

TABLE 1 : CONCERTED ACTIONS AND THEIR FINALITIES

*-**Surveillance services** (11 actions) concern regular monitoring of a medical situation so as to be able to make diagnoses, issue warnings, etc. There are two end results : a new scientific view of the situation plus a network capable of continuous collection of homogeneous, representative data throughout the Community.*

*-**Development and/or evaluation of medical treatment** (12 actions) corresponds to the production of validated treatment protocols, equivalent to "industrial development" in other economic sectors.*

*-**Development and/or evaluation of medical techniques** covers 14 actions aimed at developing new techniques, demonstrating their usefulness and ensuring the quality of diagnoses. The end result of these projects is presented most of the time in the dual form of recommendations and material intented to ensure that they are implemented.*

*-**Harmonization of medical practice** (19 actions) involves the use of the comparative approach to define best practices and make recommendations or produce tools promoting their dissemination to health professionals.*

*-**Forums** (15 actions) mark a change of register : the ultimate goal cannot be tackled directly. A scientific community must first be set up to study the problem. The sole objective of forums is to enable scientists working on the problem to meet and to promote the emergence of collective research projects.*

*-**Joint research facilities** (14 actions) are a quite different type of response involving the creation of a specific common service : a specialized instrument, a network for collecting samples, a production centre for viruses, etc.*

*- Between forums and joint research facilities, where the community of teams has been identified but the action to be taken remains to be defined, 13 actions aim at establishing **specialized research communities** by harmonizing language and practice.*

Table 1 shows that nearly 60 actions fall under the first heading. The question as to the dissemination of results arises where market mechanisms (which turn

interested users into customers and producers into industrial suppliers) do not operate. The public operator is then confronted to a new dilemna : how to ensure that the money spent is not wasted for lack of widespread dissemination of the knowledge accumulated? For example, how can you ensure that the hundreds of thousands of European general practitioners benefit from tools which can help them to make an objective medical decision about abdominal pains or jaundice? How can factors which guarantee the quality of electrocardiograms and of diagnoses be integrated into the rules on electrical safety? Of the thirty actions (or one in two) which were to end with MHR4, one in five would require support policies to enable them to actually produce their expected effects.

Eight concerted actions face a different problem : they have built up surveillance services (e.g. monitoring of congenital abnormalities, the epidemiology of Aids) or established services for the evaluation of treatments, techniques or practices (e.g. opportunistic deseases associated with Aids, costly pre-hospital treatment). The construction and validation of the network are the first result of the project, what we have termed "results embodied in networks" insofar we consider these to be a sustainable investment which a single project cannot bring to fruition. Should we rely solely on the teams to find the resources needed for the long-term maintenance of the infrastructure that has been created? This is a pressing question for the programme, as 12 of the 40 or so actions with a research finality are in this situation and two-thirds of the twenty or so concerted actions which will still be in the implementation phase when MHR4 ends (what support will they recieve from BIOMED?) will result in the establishment of such networks. In total, nearly one in three concerted actions raises the question of the long-term existence of a network which has proved its worth and can be applied to other problems (as some have already done, cf. the CA on tissue characterization). Instead of considering laboratories which are granted support or "associated" (to draw a parallel with the action of CNRS in France vis-à-vis university laboratories), the Commission is faced with the question of recognition and long-term support for "Community medical research networks" (with specific periodic evaluation mechanisms to decide whether or not to renew support).

The "delegation" of power at the heart of the success of concerted actions

This programme is also original in the results it produces : in part "operational" results which can be directly integrated into medical or clinical practice (which in other contexts would be termed "industrial" developments), in part new research structures. These results, obtained with what is after all only marginal funding from the Commission, are closely linked to the underlying philosophy of delegation of power.

CRUCIAL ROLE OF THE PROJECT LEADER

The programme involved a clear choice : full delegation would be granted to the project leader. He is the cornerstone of the concerted action system, as he bears full responsibility vis-à-vis the Commission and is the only recipient of

Community funds. In other words, he is fully responsible for the operational definition of the project, from mobilizing teams to disseminating results, for organizing the work and arranging the logistics of exchanges (often considered to be the strategic hub of concerted actions). As such, and this is one of the main difficulty for the external relations of actions, he is not granted a clearly identified status by the Commssion, and this limits his scope for action and also hampers the birth of new projects.

A TAILORED ADMINISTRATIVE APPROACH

This association of the driving role of an individual and the construction around a problem explains the differences between concerted actions. However, diversity does not imply dispersion of effort. Concerted actions have a number of common features : more than 80% of the actions fit into a framework defined by three types of composition, five forms of organization and four groups of exchanges (see attached tables).

Thus the specific features are the forms of assembly and the "technical" and "organizational" choices made. It must be stressed that the project leaders were in a position to combine technical and financial solutions[1]. The strength of the administrative approach adopted - the delegation of the budget together with the responsibilities - is that it authorizes this flexibility and, with it, the emergence of numerous organizational innovations which have enabled project leaders to progress towards their objective with modest financial contributions compared with the human and technical resources mobilized (less than 4% of the teams' budget on average). Many project leaders want to capitalize on this knowledge without thereby ending their capacity to innovate : rather than guidelines about what is and what is not permitted, this calls for a kind of "clearing house" for problems and solutions which enables the "philosophy" of concerted action to live on without becoming ossified.

TABLE 2 : TYPICAL COMPOSITION OF CONCERTED ACTIONS

What institutions do participatants in concerted actions belong to? We base our findings on the 76 actions for which we received at least five answers. Inspite of this relatively low number of participants, we found only 11 actions (15%) with exclusively "academic" partners : universities and university hospitals. All the other projects associate at least one "service" institution (general hospital or health service, 50 actions) and/or industrial partners (14 actions). The three dominant forms are : a) universities + university hospitals (9 actions, 12%), b) as (a) + service institutions (47 actions, 62%), c) as (b) + industrial partners (11 actions, 15%).

[1]This is not to neglect the numerous problems which remain to be solved and which file n°3 analyses in detail, particularly as regards the annual management of appropriations, the treatment of post-doctoral studies, etc.

TABLE 3 : ORGANIZATIONAL FORMS OF CONCERTED ACTIONS

*The **forum** (15 actions) is limited to the organization of conferences and the establishment of procedures for financial support for visits, exchanges or small seminars. **Outdoor laboratories** (3 actions), on the other hand, bring together small groups of peers which share the tasks and together produce a joint result. Between the two, there are "partitioned" and "star" networks. In **star networks** (31 actions), the action is organized around the project leader and his team, around whom gravitate providers of cases and users. In a few rare exceptions management is divided (the central core is expanded into a small nucleus of colleagues). **Geographically partitioned networks** insert another level of hierarchy between the project leader and the collection teams : the national coordinators. **Thematically partitioned networks** (35 actions) organize their activities into subnetworks coordinated by project co-leaders who, in most cases, form with the project leader a strategic "project management group".*

TABLE 4 : THE ACTIVITIES OF CONCERTED ACTIONS

*By looking at what is actually exchanged within the concerted actions, we can identify the activities taking place. There are four different groups according to the scale of exchanges. **Forums** (15 actions) merely arrange meetings between scientists to discuss their results. **Harmonization networks** (24 actions) add working groups and ad hoc exchanges of data and materials with a view to defining protocols making the data collected and produced by the different partners comparable. **Collection infrastructure** (28 projects) makes use of such protocols to collect data, which calls for the establishment of a "reference centre" to organize the collection process, manage the databases and take responsibility for data processing. The activities carried on in **instrumented networks** make use of centralized facilities (equipement, an equipped laboratory, a cell bank, etc.) which polarize or direct members' activities : members have to comply with rules regarding the supply of data and the accomapying materials, conditions of access, etc. This generally requires extensive logistical organization (in human, technical and financial terms) and is often the main cost of the project.*

In conclusion : one finding and two questions

Concerted actions are not just clubs at which scientists meet. In most cases the participating teams are heavily involved, resulting in a new scientifc workplace with harmonized practices. This is not brought about by chance, it is the result of an original combination associating the choice of a support procedure - concerted action - with the delegation of administrative responsibilities.

TWO CHALLENGES FOR THE NEW "BIOMED" PROGRAMME

MHR4 marks a turning point in the long adventure of Community medical research programmes. The change in scale (and it must be stressed that the

number of concerted actions is only an imperfect reflection of the level of demand shown in reply to the invitation to submit proposals) has not resulted in a change in management methods. The first challenge for the programme is to secure the means to back up, monitor and evaluate current actions. The second challenge is to determine the future of the "research networks" so far established, which prompted some of our partners to suggest that a NIH-style structure be established, i.e. that support should no longer be provided for projects but for structures which, unlike EMBO, do not involve the creation of new institutions.

WHAT FUTURE FOR CONCERTED ACTION?

We must emphasize the scale of the changes brought about in the Community research environment, while also noting the gulf separating these effects from the public perception, as witness the incredulity of those to whom we presented the results of the mailed questionnaire and the effort required to characterize the kind of work being done in these concerted actions. How can this gulf be bridged ? The question is all the more important as many other areas of Community research could take advantage of this method of granting public funding. But the message still has to be got across. We realize that is beyond the scope of a report of this type.

THE RESEARCH NETWORKS
BUILT BY
THE MHR4 PROGRAMME

SUMMARY
WHAT DO CONCERTED ACTIONS BUILD AND PRODUCE ?

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OCTOBRE 1991

CONTENT

THE RESEARCH NETWORKS BUILT BY THE MEDICAL AND PUBLIC HEALTH RESEARCH (MHR4) PROGRAMME SUMMARY

OBJECTIVES, METHOD AND RESULTS

In purely financial terms, the MHR4 programme is a "minor" Community research programme (with ECU 60 million allocated to it, spread over four years). However, it is the only one to have adopted the doctrine of support for "concerted action", i.e. which is designed to fund not the research but only the costs of bringing the teams together. The way in which this chosen approach has been implemented has three significant consequences for any analysis of the role and effects of the programme, the question which this report attempts to answer.

First consequence : there is no official definition of the activities and expenditure involved in this process of bringing teams together[1]. There is no yardstick against which to make comparisons. Consequently, a large proportion of this study is concerned with "characterizing" the concerted actions, i.e. with analysing what they entail. In a way, this observation alone gives firmer substance to the administrative concept of "concerted action".

Second consequence : the status of "participant" imposes no obligation. All the obligations are placed on the project leader, who bears sole legal responsibility for the action of which he is in charge and for the Community funding allocated to it. One practical consequence of this situation is the lack of any central record of the participants in the programme. Identification of the participants was, therefore, one of the first findings which added a new dimension to the programme. The 117 or so concerted actions[2] involve over 3500 teams. In terms of the number of actors involved, this programme is, therefore, one of the Community's largest.

Third consequence : since the programme provides no direct funding for research, how can scientific and technical results be attributed to it if it played no part in the financing? The only credible approach was to ask the teams themselves for their view of the role of MHR and of the effects which they expected it to have. To achieve this, the idea was to re-employ the method developed for other Community research programmes[3]. Questionnaires were posted to every team participating in the concerted actions to piece together an image of the programme based on the chief characteristics of the teams, their involvement, the results which they expect and their opinions on the programme, its value, its effects and its limitations[4]. After various difficulties, not least in tracking down the

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[1] The only, albeit very broad, definition found was in the presentation of the actions in the recent Biomedical and Health Research Newsletter n° 2/1990.

[2] Officially, mid 1990, the programme covered 141 actions, of whicch 16 were started after October 1989, 4 were classified as "studies" and 4 had submitted no list of participants, leaving 117 actions (cf. File 1).

[3] cf, interalia, the evaluations of the programmes on Non Nuclear Energy (1988), on materials (1989) and more recently on the COST actions (1991). See also the study on the Impact of Community research programmes on the French S&T fabric (Paris, La documentation Française 1990).

[4] At the same time an additional survey was conducted to attempt to identify more clearly the direct users of the results and, with the help of a second very bried questionnaire sent to them, the dissemination processes of the results. The experience proved highly constructive for pointing the way to a new method well suited to complex programmes such as MHR or the programmes on basic technological research. File 4 reports on the interesting results obtained.

participants, the survey was conducted from late 1989 to early 1990. Over 1400 of the estimated 3500 teams participating replied, enough to allow representative analysis.

The members of the evaluation panel[5] and the programme managers [particularly the members of the Management and Coordination Advisory Committee (CGC)] found the results set out in File 1 surprising and even provocative enough to warrant qualitative validation : consequently, the original plan to interview a few project leaders grew into a systematic survey of all the project leaders[6], no longer just to validate the information collected but also to reconstruct details difficult to pick out from the annual reports on the objectives, origin, progress, organization, work and exchanges connected with each concerted action (cf. interview guide in File 3). It took almost nine months, from May 1990 to January 1991, to organize these interviews and process the results. The files built up in the process were completed in June 1991.

A difficult choice had to be made between the need to maintain anonymity and the desire to produce information which would "say" something to the managers and actors involved in this programme, which is both extensive (if only by virtue of the number of teams involved) and original (by virtue of the guiding principles and procedures adopted). In the section on the managerial dimensions of concerted actions, the problems encountered and proposed changes in management of the MHR programme (File 3), there was no need to give examples to illustrate the analysis and conclusions. By contrast, it was impossible to characterize concerted actions (File 2) without giving examples. In so doing, there is a risk of singling out a few projects. Therefore, to avoid distortion, it was decided to be systematic and to classify all the sample in relation to each of the criteria applied. Since any classification exercise inevitably entails simplification, the authors have certainly classified some actions differently than the project leaders would have done. They accepted this responsibility since they felt that this was more conducive to opening up a dialogue which, as stressed in the analysis of operation of the programme, is still extremely limited, indeed embryonic.

To allow easier access to all the analyses, the data have been subdivided into four separate files:

File 1 : A quantitative approach to the networks set up

File 2 : Characterizing concerted actions and their dynamics

File 3 : Managerial dimensions of concerted actions and implication for the management of the MHR programme

File 4 : Analysis of the dissemination of the results of concerted actions : an experimental approach.

This general summary of the analyses in these four files is divided into eight sections:

1. Heavy involvement of the teams in concerted actions
2. More than academic results
3. What does this network seek to achieve? Seven finalities
4. With whom does it undertakes it? Heterogeneous networks with five main forms of organization

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[5] cf. The Evaluation report produced under the chairmanship of Pr. Maynard which has been published at the end of 1990.

[6] For practical reasons, only 106 interviews were conducted (cf File 3).

5. How is this achieved? Exchanges and intermediaries build four main groups of actions.

6. Where will we be by the end of MHR4 (1)? Concerted actions : a six phase dynamic

7. Where will we be by the end of MHR4 (2)? Probable scenarios and families.

8. Concerted action as an instrument for public intervention in R&D.

1. HEAVY INVOLVEMENT OF THE TEAMS IN CONCERTED ACTIONS

A total of 117 concerted actions involving over 3500 teams : what is entailed in bringing together an average of 30 teams in each action, a very high figure, particularly in the light of the conclusions of the evaluation of the ESPRIT programme, which recommended a limit of six co-contractors per action[7]? Where do these participants come from? In what way are they involved? Over 1420 teams replied to the questionnaire (response rate: 40%)[8], enough to underline three basic points.

HETEROGENEOUS ACTIONS ...

Some 43% of the respondents worked for "academic" institutions (universities 27% and government research organizations or foundations 16%), 34% were from university hospitals and 22% from "service institutions" (i.e. all institutions forming part of the health service: hospitals, health service departments and voluntary organizations). These figures reveal a significant orientation towards the clinical side; even though seven teams out of ten consider research as their main activity, more than half of them include clinicians.

TABLE 1: AVERAGE TEAM COMPOSITION

Source: Replies to Question 3 Note : res. = researchers ; clin. = clinicians.

Teams with	% of teams	average number res.	clin.	% of total res.	clin.
Research workers only	45	6,4	-	61	-
Clinicians only	12	-	6,4	-	30
Researchers and clinicians	43	4,3	4,7	39	70
	100	4,3	2,5	100	100

This mix between downstream and upstream activities, with a large sample of university hospitals to bridge the gap, is found in virtually every action (in 85 of the 95 CAs from which more than 5 answers were received). This clearly is the first dimension of these actions : even judging purely from the replies received, the concerted actions bring together a large number of participants (on average, 15). Although three quarters of the participants regard research as their main activity, they are drawn from different institutions, thereby enabling nine concerted actions out of ten to establish ties between researchers and the potential users.

[7] This by no means precludes the participation of subcontractors or associates in limited parts of the project.

[8] This response rate can be regarded as satisfactory, despite the variations between individual subprogrammes, with response rates ranging from close de 45% on BME (Biomedical engineering) and Cancer to just 34% on HSR (Health Services Research) and Aids.

TABLE 2: AVERAGE CA COMPOSITION

Source: Replies to Question 2

Notes: Teams from universities, government research organizations and foundations are classified as "academic". Teams from hospitals, health service departments and voluntary organizations are classified as "services". Only CAs from which at least 5 answers were received are included (37 actions started over one year ago and 58 "new" actions).

In terms of composition, the CAs fall into five categories: "academic" CAs in which all the teams are drawn from academic bodies and university hospitals; other government CAs carried out exclusively by teams from service institutions, some with a majority of academic teams, others with a clear clinical orientation and others with an equal mix of the two worlds. The fifth category contains all the CAs in which at least one industrial team participates.

Composition of CA	No of CAs	Participants (%) Acad.	UH	Serv.	Ind.	Total	Total
Academic	10	58	42	-	-	100	7
Government,							
with acad. orientation	27	69	16	15	-	100	16
with equal mix	21	42	38	20	-	100	24
with clinic. orientation	24	19	50	31	-	100	29
With ind. participation	13	48	33	11	8	100	24
Total	95	45	35	18	2	100	100

... WHICH FORGE NEW LINKS..

The second dimension concerns the wider circle of partners established as a result of participation in concerted actions. The number of partners with which teams work has doubled. Moreover, three out of four teams are highly enthusiastic about their new partners, saying that the CA "enables us to collaborate with the best scientific teams in Europe" and "will result in lasting relationships". Half of these new partners come from the team's own country and half from other Community countries. Consequently, the programme not only internationalizes the network of teams collaborating directly but also broadens the national base.

... AND HEAVILY INVOLVE THE TEAMS.

For 9 teams out of 10 their involvement in a concerted action is their only contact with the Community's research programmes (by contrast, the survey of the Community's cost-sharing programmes showed that over half the teams participated in several different programmes). This is reflected in the low level of financial support received by the teams: only one team in four receives Community funding, which, on average, accounts for just 3% of the participants' total budget.

For all that, these figures disguise the teams' human commitment. Six teams out of 10 rate their activities in these concerted actions as "central"[9]. However, analysis of the actions in progress for at least one year gives an idea of the teams' involvement[10]. On average half of their research and clinical potential works on the action in one way or another. This mobilizes one fifth of the teams' research

[9] All the answers to the questions in the survey confirm this finding : 63% of the teams consider that their work on the CA "is not a minor part of the team's work" and 72% reject the idea that the results of the CA will have "littel impact".

[10] See File 1 for details of the very conservative method used to calculate this involvement.

capacity. By way of comparison to stress the significance of this figure, a similar order of magnitude was calculated for the Community's cost-shared research programmes.

What lies behind this discrepancy between financing and involvement? The first answer which springs to mind is to draw a distinction between concerted action and traditional scientific exchanges with the aid of workshops and visits. How is it possible to spend such a proportion of research time on such activities? To attempt to obtain a clearer picture, the questionnaire and the replies looked at three further angles : the teams' activities on the concerted actions, the resultant exchanges and, finally, the results expected of them.

2. MORE THAN ACADEMIC RESULTS

MEETINGS AND VISITS: A KEY DIMENSION ...

Over 70% of the teams have participated in general meetings (in over 3 such meetings in the case of the 37 actions under way for over one year) and in smaller meetings (over 4 such gatherings on the same actions). Almost 6 teams out of 10 mentioned visits as one form of exchange and 1 in 4 referred to "exchanges of researchers". From the participants' point of view meetings and visits are an important part of life in these actions. Nevertheless, no more than 1 in 5 ranked them as the first priority amongst the forms of exchange in which they were involved.

...SUPPLEMENTED BY FREQUENT EXCHANGES OF DATA AND MATERIALS...

Instead, almost 85% mentioned exchanges of data or protocols (58% for data and 59% for protocols), while 80% exchange other forms of material support (almost 70% of the teams participating mentioned exchanges of at least one of the five following media: biological samples, reference materials, reagents, prototypes or software). The concerted actions are thus the scene of intensive exchanges of all types, centring around the development and implementation of protocols and heavily dominated by data collection.

... DIRECTED TOWARDS ONE MAIN ACTIVITY : THE CONSTRUCTION OF NEW SOURCES OF DATA ...

The same results are reflected in the activities performed in the course of the concerted actions (Table 3). Two thirds of the teams mentioned collection of data, over half the creation of protocols and one third clinical trials. In all, 9 teams out of 10 quoted at least one of these three activities and almost 60% ranked it as their main activity within the concerted action.

This intense flow of data and media requires preparation (hence, beyond a doubt, the importance attached to the creation of protocols) and organization. This could also explain the importance which the teams attach to organizational activities: "organization of CA work" (as distinct from "organization of conference") was mentioned by 4 teams out of 10[11] with one in four regarding it as their main activity on the action (although most of them also participated in data collection themselves).

[11] This fugure reflects a familiar bias in surveys of this type : only the participants showing the greatest interest reply. Whatever the bias, a group of some 600 teams, or roughly 6 per action, are heavily involved in its management, providing, therefore, a substantial active core.

TABLE 3: ACTIVITIES PERFORMED BY TEAMS IN CAS

Source: Replies to Question 31 ("old" actions) or 23 ("new" actions).
The teams were given a choice of 10 items and asked to give 2 types of reply, one yes/no answer to indicate whether or not they performed the activity, the other ranking it (is it a priority?)

Activity performed	Teams mentioning it	Teams ranking it as first priority
Collection of data	66%	26%
Creation of protocols	54%	18%
Clinical trials	33%	10%
Analysing data	35%	8%
Collecting and analysing data	88%	62%
Organization of CA work	40%	23%
Organization of conference	42%	4%
Feasibility studies	24%	2%
State of the art	36%	9%

... EXPECTED TO PRODUCE SCIENTIFIC RESULTS ...

What is expected from this flow of data and material? As mentioned earlier, 70% of the teams considered research their main activity. They took this to its logical conclusion, since over 70% of them expected to publish articles in refereed journals and almost all (85%) mentioned "new scientific knowledge" as one of the results which they expected, with one team in two giving it first priority (Table 4).

... NEW SOURCES FOR RESEARCH ...

However, these "academic" findings are not the only results. On average, the teams mentioned almost three other types of output (out of the 13 suggested). All in all, "new scientific knowledge" was quoted as one of the expected results in only one in four cases, whereas "new methods for research" scored 40%.

Over three quarters of the teams chose at least one of the five items in this subcategory (48% mentioned protocols and standards, 25% new data bases, 22% reagents or reference materials, 18% new experimental facilities and 15% new equipment). Exchanges of material combined with data and sample collection generate new knowledge and, at the same time, raise new research topics or open up the way for work which was previously inaccessible.

This is paralleled by the use made of the results. According to the teams, in one case in two the results generated will be used principally by scientists (themselves in half the cases and other scientists in the other half). The analysis of the flow of results (cf. File 4) highlights this significant result: the actors recycle a large proportion of the results in their own research activities before disseminating them to the usual users.

... AND APPLIED RESULTS.

Over one-third of the respondents mentioned the downstream operators, which almost 30% quoted as the major user. Although one third of the teams mentioned industry they themselves recognized that the results are too far from

the market for this to be considered the top priority output (only 5%) or to be quoted as the primary use (only 4%).

The picture is very different with clinicians and government departments. Over six teams out of ten considered that their results would produce new methods of diagnosis or treatment and would, therefore, be of use to clinicians. Over a quarter of the teams quoted this as the major use of the results and over 40% thought that either clinicians (29%) or health service departments (10%) would be the principal users of the results.

TABLE 4: EXPECTED RESULTS

Source: Replies to questions 33 and 34 (for "old" actions) or 25 to 27 ("new" actions).
Notes: The 13 items were classified into four groups. Three indicators were obtained for each of them: (a) the number of teams which mentioned each individual item; (b) the total number of teams ranking the items in each group as one of their priorities; (c) the number of teams quoting the items in the group as the principal output (first priority).

Expected results	Mentioned by	Chosen as first priority	Chosen as a priority
New scientific knowledge	85%	52%	24%
New methods for research	77%	20%	40%
Methods of prevention, diagnosis and therapy	61%	23%	24%
Commercial results	29%	5%	12%
Total		100%	100%

TABLE 5: EXPECTED FINAL USERS OF CA OUTPUT

Source: Questions 36 (for "old" actions) or 29 ("new" actions)

Expected user	Teams mentioning this type of user	Quoted as the major user
Yourself	65%	28%
Other CA teams	55%	12%
Other research teams	60%	13%
Clinicians	63%	29%
Health service departments	29%	10%
Industry	26%	4%
Others	8%	4%
Total		100%

This quantitative approach (of which only a few results are set out here) raises many questions for the observer. What are these networks which vigorously mobilize public teams of all origins with only marginal funding, which focus on the generation, exchange and collection of data and material support, which produce indisputably academic findings and yet attach great importance to the development of new research instruments, and, finally, where one third of the participants clearly label their activity as "applied" and falling within the area known, in conventional industry, as "development" or "innovation"?

Together, all these observations called for an in-depth survey, in which we met almost all the project leaders (106 interviews). This fascinating but time-consuming task taught two major lessons. The first concerned the details needed for an understanding or characterization of each concerted action taken separately. These can be subdivided into three further categories which, in practice, answer

the three questions most commonly asked about these actions: what does this network seek to achieve? With whom? And how? The second lesson deals with the dynamics of the concerted actions and echoes the other question which the members of the CGC asked us : where will we stand at the end of MHR4?

These four questions and the information collected on them (sections 3 to 6) define a limited number of markedly different scenarios (section 7) mapping out the broad path to be taken by the fifth version of the programme as recently adopted by the Council of Ministers of the European Communities (BIOMED) and, at the same time, highlighting the changes of direction needed in the current arrangements for management of the programme (section 8).

3. WHAT DOES THIS NETWORK SEEK TO ACHIEVE? SEVEN FINALITIES

FROM THE POLITICAL GOAL TO THE END RESULT : A COMPLEX TRANSLATION PROCESS

This question is not as simple as it appears at first sight. It mixes two different approaches. The first, political, defines the problem to be solved (for example, to treat insulin-dependent diabetes), while the second, scientific, describes the scientific progress sought (in this case, to obtain a supply of purified B cells which produce insulin). In this survey these two approaches have been designated the "**stakes**" and the "**end result**". The problem facing the programme manager is to decide how to pass from one to the other, i.e. the translation between the two. Drawing, once again, on earlier analyses it was possible to show that the addition of two further stages helped to place this translation from the political to the scientific on a more formal footing : the "**goal**" proposes a way for the research world to respond to the political stakes (transplantation of B cells) while the "**objective**" determines the scientific and technical choices made, namely to extract these cells from human pancreases. This provides, besides the scientific and technical end result sought, three other levels allowing closer definition of the different types of finality pursued.

Systematic analysis of the concerted actions showed that this duality between "stakes" and "end result" defines a limited number of pairs (seven) corresponding to two groups of actions : "purpose-oriented" actions which have a direct medical objective (four types) and actions which require, as a preliminary step, a specific structuring of the European scientific community (three types).

SURVEILLANCE SERVICES

Regular monitoring of a medical situation so as to be able to make diagnoses, issue warnings, evaluate preventive policies or medical practices, etc. is one familiar general goal of health policies. In this case, the objective is clearly defined : to construct and confirm the validity of the system used for observation. Consequently, there are two end results : a new scientific view of the situation plus a network capable of continuous collection of homogeneous, representative data throughout the Community. Homogeneous, representative and continuous are the three attributes shared by all eleven actions in this group, even though their subject areas or political stakes (AIDS, congenital abnormalities, osteoporosis, asthma, etc.) have nothing in common apart from the Europe-wide scale of the health hazard tackled. Another effect of this process of accumulation of previously unavailable information is to raise new research problems. Consequently, a number of actions started during earlier programmes have given birth to

"subsidiary" actions (six were counted) intended primarily to add to the knowledge of the problem and to fit into a wider surveillance network.

As was to be expected, these actions are shared between four different subprogrammes : two concerning diseases (cancer and, in particular, AIDS), the epidemiology subprogramme (on asthma prevalence and risk factors or on osteoporosis) and, finally, health services research (on the operation of health care systems : avoidable deaths and nocosomial infections in intensive care units).

DEVELOPMENT AND/OR EVALUATION OF MEDICAL TREATMENT

Since the present situation is unsatisfactory, these actions explore two complementary avenues: embarking on new paths (seven actions, including six on cancer) on the one hand and comparative analysis of the effectiveness of existing therapies on the other (five actions, including three on AIDS). In either case, the end results (validated treatment protocols) are comparable to "development" activities in industry.

DEVLOPMENT AND/OR EVALUATION OF MEDICAL TECHNIQUES

As in the previous paragraph, the situation is once again considered unsatisfactory. There are several possible ways of remedying this : develop a new technique (four cases, for example "forced respiratory techniques"), harmonization and recognition of emerging techniques (three cases, for example "biomagnetism"), ensuring the quality of diagnosis by developing standards, specifications or methods of assessment (four cases, for example, "quantitative assessment of bone quality"). Other actions concerned more with "methodology" focus on comparative analysis of how different countries proceed in the same situation (three cases). The end result of these actions is presented most of the time in the dual form of recommendations and material intended to ensure that they are implemented (example : CA on electrocardiograms). The BME subprogramme plays a central role, since 12 of the 25 actions serve this finality.

HARMONIZATION OF MEDICAL PRACTICE

The common denominator of these concerted actions is that they target on medical practice (principally, general practitioners and surgeons), or on the operation of subsections of the health service (hospitals, care for the elderly, etc.). Generally, they look at a clearly delineated problem. Half of them (eight CAs) focus on a comparative analysis of the situation, with a view to defining "best practices" and making recommendations on, for example, the "use of blood in surgery", the treatment of "head injuries" or "the referral of patients to specialists by general practitioners". The other half are generally smaller scale actions limited to taking stock of the situation [eight actions on, for example, the effect on children of maternal alcohol consumption (EUROMAC) or the use of diagnosis-related groups (DRGs)] or to disseminating methods which are already considered the "best practices" (three actions, including one on self-assessment in hospitals). Over half of these actions (ten out of 19) come under the HSR subprogramme.

FORUMS

Forums mark a change of register. The problem addressed or the political stakes pursued cannot be tackled directly. Before a product or service can be developed in response to it, a specialized European scientific community must be

set up to perform the task. All these actions have in common the fact that they are clearly defined in scientific and technical terms : "science knows nothing about...", "cellular biology offers new prospects...", "the specialist community is dispersed, it should be grouped together and encouraged to get down to work on joint actions", "all scientists are faced with this or that problem of analysis, sequencing, animal testing, etc what is needed is a joint facility which will resolve these problems and ensure complementarity between the work". These typical arguments point to three different approaches, forums being the first one.

Forums provide an opportunity for scientists to meet for seminars and informal exchanges which will gradually create a community from which joint actions will emerge on a decentralized basis, i.e. outside any specific programme. Half of the 15 CAs of this type focus on organizing small communities of specialists (for example, on "hearing impaired technologies"). The others, to borrow the image coined by the leader of the action on "breakdown in human adaptation" are "umbrella" activities designed to give birth to joint research actions on a new problem on the frontiers of existing disciplines.

JOINT RESEARCH FACILITIES

At the other end of the scale, the CAs dedicated to the creation of "joint research facilities" have clearly defined the path to follow. Researchers need a joint facility in order to acquire know-how commensurate with the problems addressed (e.g. to study AIDS, ageing or high blood pressure). These facilities take three main forms : centres (laboratories) specifically equipped and offering a specialized service unique in Europe (six cases, four of them under the AIDS programme, including one on sequencing of the AIDS virus); European networks for collecting the samples (five cases of blood banks, cell banks, etc.) required to obtain sufficient material (for example, "thyroid cancer genetics") or to investigate new research topics (for example, the "nutrition" and "thrombosis" networks) and, finally, production centres for viruses, peptides and adjuvants designed to target research (three cases relating to AIDS).

All three cases combine the dual function often allocated to large-scale instruments (such as CERN or the very large telescope), i.e. to open up access to new information and, with the aid of ad hoc committees for experiments and the control of access, to guide the scientific community concerned and foster complementary activities and joint ventures. However, one marked difference between them (to such an extreme that different terminology has been proposed) is the third specific dimension of these actions. The operator is a laboratory or network of laboratories pursuing research of its own via the service which it provides : the user who comes to the central facility for sequencing of a particular AIDS virus thus plays the role of a supplier of material for researchers interested in genetic variation of the virus.

SPECIALIZED RESEARCH COMMUNITIES

Between forums and joint facilities, there is a third group of actions likewise aiming at the establishment of a specialist research community. It goes beyond the forum stage since the scientists have been brought together. Their task is now to make progress together. Most of the time, the aim is to build up capacity for joint activities as a springboard for moving on to the operational phase (i.e. as defined in "purpose-oriented" terms). The practical end result expected from such actions is harmonization of practice and language. The distinctive feature lies more in the

approach chosen (working parties on specific subjects, circulation of gene probes, etc.) than in the definition of the scientific results to be obtained.

Analysing what CAs set out to achieve, produces a definition of seven types with very different purposes and expectations as regards results. What is the relationship between these seven types and the six subprogrammes of the MHR programme? It is not a question of specialization, since two of the subprogrammes include CAs of six different types, two more of five types and the other two of four separate types. Instead, it is fair to conclude that the subprogrammes can be defined by the mix used to attain the objectives set.

TABLE 6: SUBPROGRAMMES AND GENERAL GOALS

Note: ranking the CAs by various criteria, the number of actions fluctuates between 104 (total sample) and 96 (figure excluding six "secondary" actions concerning 2 monitoring networks and 2 other actions - OMDM (objective medical decision-making) and ENTA - which have been, each, the object of two CAs.

	BIO	CAN	EPID	HSR	BME	AIDS	Total
Surveillance services	1	1	4	4+1	-	1+5	11+6
Dev./Eval. of treatment	3	5	1	-	-	2+1	11+1
Dev./Eval. of techniques	-	-	-	3	11	-	14
Medical practice	1	-	4	10	1+1	2	18+1
Forums	1	1	-	2	6	5	15
European facilities	3	2	2	-	-	7	14
Specialized communities	3	-	2	1	5	2	13
Total	12	9	13	21	24	25	104

TABLE 7: RELATIONSHIP BETWEEN GENERAL GOALS AND COMPOSITION OF THE CAS

Note: Only CAs where five replies were received and the project leader was interviewed have been included, i.e. a total of 76 actions (the NQ column shows the CAs not quoted). This classification serves purely as a rough guide to the minimum scope of the action, as apparent from the replies only. The "types" refer to the institutions to which the respondents belong: type 11 = universities only, type 12 university hospitals only and type 13 both. Type 21 = type 11 plus services (hospital or health service departments); type 22 = type 12 plus services and type 23 = type 13 plus service. Type 31 = academic institutions plus industry and type 33 = academic institutions plus services plus industry.

	Principal types					
	13	23	33	Other	NQ	Total
Surveillance service	2	9	-	1(21)	5	17
Dev./Eval. of treatment	-	7	1	-	4	12
Dev./Eval. of techniques	2	5	3	2(11/12)	2	14
Harmonization of practice	-	7	4	1(31)	7	19
Forums	2	6	2	1(31)	4	15
Joint research facilities	3	5	1	1(31)	4	14
Specialized communities	-	8	-	3(21/22/31)	2	13
Total	9	47	11	9	28	104

4. WITH WHOM DO THEY UNDERTAKE THIS ACTION? HETEROGENEOUS NETWORKS WITH FIVE MAIN FORMS OF ORGANIZATION

HETEROGENEOUS NETWORKS

Quantitative analysis of the replies to the mailed questionnaires highlighted one clear result, despite the fact that fewer than half of the teams participating replied. Concerted actions bring together actors from very different backgrounds. Only two of the actions in the sample were restricted exclusively to universities and government research institutes ("academic institutions"). Under 15% involved teams from academic institutions or university hospitals alone. Consequently, over four out of every five actions involve teams from service institutions (hospitals or health service departments: two thirds of the CAs in the sample) or from industry (20% of the sample). This massive participation by downstream actors, the potential users of the results, in the concerted actions is one of the main features of these heterogeneous networks.

MULTIPLE ROLES

Which roles do these actors perform? Is it possible to keep to the official distinction between "participants" and "observers", where downstream operators (service institutions and industrial undertakings) are represented only to give them an opportunity to prepare to use the results generated? This is dubious, as the many examples in File 2 show. For example, many ***potential users*** also provide cases, data and samples (clinicians), apparatus, material, medicinal products, reagents or even specialized analyses or money (industry). Often these ***suppliers*** play a crucial role in the dynamics of the concerted action which is understated by the term "observer". Similarly, in a number of concerted actions some teams perform specialized scientific work (a specific type of analysis or treatment, for example). These ***special members*** provide specific resources for the action, without which reorganization or a change of approach would be needed. In addition, the commitment shown by the ***project leaders*** and their team plays its part in the success of the action. Yet this is not enough in itself: one in two project leaders delegates part of the responsibility to action ***co-leaders*** or to ***national coordinators***, i.e. to a small core of special members who, with the project leader, form an active "project management group" (PMG) to mastermind the CA.

FIVE MAIN FORMS OF ORGANIZATION

The existence or non-existence of an active PMG is the first sign of how a concerted action is organized : who takes the strategic decisions? Whatever the finality, a 50/50 divide is observed. This simple result shows that the organizational dimension of each concerted action is a factor to be considered in its own right. Like the finalities of the action, the forms of organization are also limited in number. Five main forms were found.

- The ***forum*** is both a finality and a form of organization. In the latter case, all it entails is organization of general conferences (usually once a year) and the establishment of procedures to support the programme of visits, exchanges or restricted workshops (generally a form to complete to obtain financial resources).

- In ***Outdoor laboratories***, a small peer group sets itself an S&T objective and shares out the work. Joint decision-making and allocation of tasks followed by

joint consolidation are the great strengths of this type of concerted action, which is characterized chiefly by the small membership. This form of organization is a reference model rather than a common occurrence since only three of the 104 actions analysed fit into this pattern (examples: HIV and tests on macaques). They provide a reference point in two ways : first because often they encompass the operations of the small core of teams which share the work on concerted actions with a masterminding PMG and, second, because they place the emphasis on the differences and specific nature of the results built up. They are less concerned with pooling equivalent resources and more with making complementary skills and products compatible and combinable.

- In ***star networks*** the concerted action is organized around the project leader and his team. In a few rare exceptions (just six out of 31 actions of this type), management is divided and this central core is expanded into a small nucleus of colleagues. Star networks cover two complementary situations.

In the first variant (16 actions) a group of "equivalent" members gravitate around this central core. They may include providers of cases (usually clinicians or general practitioners, for example in the case of the epidemiology of osteoporosis) or users (usually colleagues operating via the central facility, as in the case of sequencing of the AIDS virus). Consequently, this is a stable form of organization centring on the organizer and the resources which he establishes (eight of the actions are on the establishment of joint research facilities and five on the establishment of surveillance services). In one case out of three, a number of teams help the project leader with the tasks of the organizer : we are then facing "hybrid" star networks.

The other 15 actions are either short operations of limited duration and mobilizing only a small number of teams around a project leader (six actions on harmonization of medical practice) or recently started actions yet to be structured (particularly six actions on the establishment of specialized communities, for example the "neuropathology of AIDS" action).

- ***Geographically partitioned networks*** insert another level of hierarchy between the project leader and the collection teams. This comprises the national coordinators who coordinate the teams in their country or area. Primarily they are associated with two of the abovementioned finalities : surveillance services and harmonization of medical practice (16 of the 19 cases). These networks take three main forms, depending on the level of commitment by the basic collection teams.

In the first case, the national networks predate the action, which therefore focuses on standardization and centralization of the national data collected (three concerted actions including, for example, the one on the epidemiology of AIDS). The action consists of constructing the "reference centre" and is confined to the operators of the national networks alone, plus, possibly, specialized researchers.

The concerted actions on epidemiology which build up large data bases giving a representative image of the situation (nine cases) form a second group placing the emphasis on improvements in medical practice (example: care delivery systems) or on standardization of techniques (example: antenatal screening by ultrasound). In these cases, the national coordinators do most of the harmonization and all the collectors usually have to do is to complete questionnaires requiring no particular skills. Once the results have been obtained, these networks are dissolved in the dissemination stage itself.

This is not the case in the third category (seven concerted actions falling into four different finalities) where more complex collection infrastructure has to be set up to deal with the issue in question (harmonization of collection practice, logistics of transfers of samples, storage bases and banks, laboratories for specialized treatment...). Their organizers subsequently wish to see this infrastructure used for other actions (examples: objective medical decision-making and thyroid cancer genetics).

- ***Thematically partitioned networks*** are the commonest form of organization (35 concerted actions). In this case, activities are organized into subnetworks coordinated by action co-leaders who, in most cases, form with the project leader a masterminding PMG. Once again, there are three main variants, depending on the degree of integration of the subprojects.

In simple partitioned networks, the subprojects progress in parallel, usually with a few teams working on each. Apart from exchanges of information and results no integration is envisaged, except of a purely formal nature. Instead, the teams wait until completion of the individual subprojects before defining what, if any, further action to take. Alongside star networks, this is the other form taken by the seven projects which aim to establish specialized research communities. It is also the form preferred by the concerted actions on the development or harmonization of medical techniques (10 cases).

In the second form of partitioned network, several projects, whether or not in the same CA, simultaneously use the same collection infrastructure (nine CAs, for example "opportunistic illnesses associated with AIDS"). Once the initial star network has proved its worth, it can be mobilized for other purposes.

The third form - "integrated networks" - displays a fully-fledged project organization similar to the arrangements for complex technological objects, with parallel groups, meetings at each stage and further progress depending on integration of the results from the previous stage. This method is reserved exclusively for five concerted actions on the development of new methods of treating cancer [example : the BNCT project (boron neutron capture therapy)].

TABLE 8: ORGANIZATION OF CAS

Notes: Forums are excluded. Type 2 = outdoor laboratory; Type 3 = star network; Type 4 = thematically partitioned network; Type 5 = geographically partitioned network. "Shared" organization means that the strategic decisions are taken jointly by the project leader and a core of active teams, generally within the PMG. In all other cases, the organization is centralized, i.e. dependent on the project leader and his team.

	Type of organization					Centralized organization	Shared
	2	3	4	5	Total		
Surveillance services	0	6	2	8	16	6	10
Dev/eval.of treatment	0	2	9	1	12	5	7
Dev/eval. of techn.	0	1	12	1	14	9	5
Harmoniz.of practice	2	8	1	8	19	7	12
Joint research facilities	1	8	4	1	14	7	7
Special.communities	0	6	7	-	13	6	7
Total	3	31	35	19	88	40	48

This approach gives a second criterion for classifying concerted actions, not in terms of the teams participating since one of the major results is that the vast majority of the actions mobilize scientists and users (service institutions or industrial undertakings) at the same time, i.e. virtually all the networks are heterogeneous, but on the basis of the forms of organization adopted : forums, star networks, geographically partitioned networks and thematically partitioned networks, which are all very different ways for teams to come together and interrelate. Although there is no simple correlation between the finalities of the action and the form of organization chosen, there is nevertheless a strong link depending, to a large extent, on the factors which bond the teams together and on the degree of progress made with the work. This leads onto the third question : how is this achieved?

5. HOW IS THIS ACHIEVED? EXCHANGES AND INTERMEDIARIES AT THE CORE OF THE PROCESS

Rallying actors around one common purpose calls for numerous investments. First, the participants must meet. Next, a way must be found for them to exchange information. But what does a given result mean? How can one sample be compared with another? The first lesson to emerge from the analysis is that practices are extremely diverse and that it is extremely difficult for life scientists to ensure intercomparability of results, so that results obtained in one place can be passed on and incorporated in another. In the clinical research field in particular, this transition from local to general level calls for heavy intangible investment which, frequently, provides the heart, strength and originality of the work carried out on the concerted actions. To gain a clearer picture, the forms which this can take were analysed. These are so manifold that exhaustive description is difficult (even for just 104 concerted actions). It was therefore decided to subdivide them into three categories reflecting the different implications for the teams which they link.

MEETINGS AND VISITS

Meetings and visits lay the foundation on which the actions and communities are built. This truism is worth repeating once again here. Most CAs allocate the majority of their resources to this activity. It can take many forms. Exchanges of results - the favourite vehicle for academic meetings - is only one among many other means for scientists to keep others better informed about work in progress, to exchange views on laboratory practice (and to train each other), to harmonize data collection conditions, to organize joint activities, etc. This variety of objectives is echoed by the variety of membership (from small working parties to large-scale seminars open to the outside). Finally, the frequency of such events highlights their special role: "to manage the human resources", to borrow the fine phrase of one project leader "of this entity under construction which will become a concerted action". Meetings and visits are the cement which bind the individuals together and forge a collective identity. They, and they alone, provide a basis for contemplating changes of practice and making the compromises which allow CAs to bear fruit. No CA will succeed unless it lines up the actors behind a common objective and, in the process, changes their practices to allow Europe-wide

intercomparison and collection of data, to share tasks, to combine complementary skills, etc.

Consequently, meetings and visits, together with the reports and minutes they generate, are an indispensable medium. But however necessary they are to forming a common attitude, they alone cannot give substance to the action. In order to see what the teams produce together, it is necessary to take a look at the intermediaries. The examples given in File 2 illustrate their diversity and show that most concerted actions employ several sorts of intermediaries simultaneously. How do these fit together and in which way do they allow a clearer idea of the process for generating the scientific results expected?

CIRCULATING INTERMEDIAIRIES

Analysis of the intermediaries circulating between the teams provides an initial answer. ***Forms*** are central to most CAs: drafting, use and circulation of forms, followed by collection and processing of the data which they contain are all stages in the progress of the action towards its objective and milestones on the road to completion. With the aid of forms, local observations and representations can be exchanged, taken up by other teams and combined to piece together representative pictures of the phenomenon studied. ***Reference materials*** or ***phantoms*** perform the same role when ***samples*** are exchanged, rather than representations of the problem under study. These calibration instruments must be produced, the conditions for collection of the samples needed must be standardized and circulation and storage of the samples must be organized. Sometimes it is impossible to circulate the samples as such and either they have to be transferred onto ***animals*** or perhaps even the ***patients*** themselves must be circulated. In many cases, this harmonization of practices necessitates ***exchanges of equipment***. Systematic circulation of representations or samples of the phenomenon studied implies a method of organization ensuring that these representations and samples are comparable and, hence, combinable. Analysis of the concerted actions confirmed the major effort needed to achieve this result alone. Many project leaders stressed the strategic importance of the "***logistical details***" needed to reach this point.

FIXED INTERMEDIAIRIES

Circulation of representations and samples is rarely an end in itself (only a few CAs have set this specific objective and are concerned purely with formulation of the protocols needed to achieve this). Storage, accumulation, comparison and processing of such representations and samples are the means of attaining the objectives of the CA. To achieve this, many concerted actions have developed fixed intermediaries, often designated "centralized facilities". Three different types were observed.

The first type of fixed intermediary is like a "***common in-house service***". Ad hoc data bases on all the cases or samples studied in the course of the CA are the commonest form. Many cases concern specific therapies. Circulation of a blood sample limits harmonization between the teams to the data collection stage alone and guarantees that the analyses are comparable, by processing them at a single centre operated, in practice, as a common service. Sometimes, as in the example in File 2 (quantitative evaluation of osteoporosis), this common service depends on original equipment (in this case an automated X-ray plate reading system). At the same time as ensuring uniform analysis, common services of this

type are tangible proof of the link between the teams and, in the case of data bases, often secure their participation until results are obtained (otherwise the individual investment made would be lost).

The second category comprises ***fixed intermediaries which play a guiding role***. Sequencing of the AIDS virus, characterization of antiviral molecules and the breeding of transgenic rats are three of the many examples of the triple role of facilities of this type : (i) the unique service provided for researchers (often, they are the only means of access to a particular technology or product); (ii) via the access conditions, targeting of the themes and harmonization of practices within the scientific community concerned; (iii) acquisition of specialist knowledge (on, for example, the genetic variation of the AIDS virus) in the laboratory operating the fixed intermediary. This third point is particularly important since it confirms that the "facilities" are not equipment but a series of assets, including the know-how acquired in a laboratory pursuing its own research objectives behind the service it provides.

Fixed intermediaries which play a polarizing role are a very different case. They impose constraints which shape the structure of the CA and define the links between the teams and the timetable for meetings between them. The examples given illustrate their dual role, either within "projects" or to set up collection infrastructure. The Petten establishment is an example of the first type designed to devise a new method of treating cancer (BNCT). The "large number of cases" data base fulfils the same role in the evaluation of ultrasonic methods of diagnosis of congenital abnormalities. The centre for the production of B cells to treat diabetes follows the same approach : the fixed intermediary which polarizes the activities of this CA is itself one of the results and will remain so until they are put into practice. By contrast, other fixed intermediaries will continue in their current form but turn to other problems, as in the case, for example, of the colection infrastructure created to evaluate the clinical protocols on the opportunistic diseases associated with AIDS (see file 2 for its description). Many CAs are concerned with building up ***collection infrastructure*** of this kind, which entails heavy intangible investment, all the more so since most collect not only data but also samples, frequently combining extensive logistical organization with the establishment of common in-house services or of a ***reference centre*** which produces comprehensive results and acts literally as the life force and shopwindow for the concerted action.

FOUR CATEGORIES OF ACTIONS, DEPENDING ON THE MIX OF MEETINGS AND INTERMEDIAIRIES

Most concerted actions opt for a combination of several types of exchange. This combination defines the amount of effort which the teams put in to interrelate and at the same time serves as a yardstick for measuring their level of commitment. Observation of the concerted actions reveals a multitude of different combinations but nevertheless pinpoints practical thresholds for both the form of exchange and the amount of effort. This gives rise to a classification into four main categories.

In the first category, the teams are involved only in conventional activities, i.e. seminars and meetings. In some cases, they may have access to additional funding for occasional exchanges. This fits the definition of forums, which form a separate bloc within the programme, whichever approach is adopted.

In the second category, the meetings and visits are subdivided to form sub-groups on specific topics which focus on obtaining a consensus, usually in the form of a new protocol (for analysis, collection, etc.). In more than one in two cases this harmonization between teams entails exchanges of materials, whether equipment (example : gene probes for the action on "inherited polycystic kidney disease"), phantoms for testing apparatus (example : quantitative evaluation of osteoporosis), reference materials (example : heritable connective tissue disorders) or samples (example : multiple sclerosis), etc. In a way, the 24 actions in this second category correspond to a specific phase dedicated to the harmonization of points of view and practices. Not surprisingly, it includes most (11 out of 13) of the actions on the establishment of specialized scientific communities. The large number of actions on the development or evaluation of techniques (8 out of 14) is a sign of the recent start made or of major difficulties encountered with the work linked to this finality.

The third category focuses on collection of data, by means of the implementation of protocols. These data are collected by circulating representations of the phenomena studied. Consequently, the usual medium is paper in the form either of questionnaires distributed and returned (the most common situation encountered) or of treatment protocols distributed and medical reports returned (example : CAs on opportunistic diseases associated with AIDS). Within this category of 28 or so actions, there are wide differences in the method of initiation and the scale of the bases for data collection. Often these also reflect differences of finality.

A subcategory of 10 actions, nine of them on harmonization of medical practice, is defined by protocols which existed before the action started and by "ad hoc" data bases. At the opposite end of the scale, protocols formulated in the course of the action and "large number of cases" data bases are associated more with evaluation of treatments (five actions). Surveillance services are also heavily represented in this category (eight actions out of 11) because they all entail the development of large data bases (five cases; example : Eurocat on congenital abnormalities) or mobilize large-scale national bases to establish European reference centres (three cases; example : epidemiology of AIDS).

In the fourth category of actions, not only are the practices harmonized but also materials and samples of the phenomenon studied are systematically exchanged. All these concerted actions are linked with fixed intermediaries, which determine the progress or success of the action. The difference between this category and the others lies in the scale of logistical or technical investment required in order to analyse or circulate the samples. These investments take different forms, allowing subdivision of this category of 31 actions into two subcategories.

The first 17 CAs, like the third category, entail the establishment of collection infrastructure, though this time focusing on the collection and assembly of samples and, in one case in two, backed up by large data banks. There are actions of this type spread on six different finalities, though surveillance services (with four CAs; examples : prevalence of asthma or epidemiology of osteoporosis) and joint research facilities (five CAs; examples : ECAT on thrombosis or molecular cytogenetics) account for over half.

The other 14 CAs are organized around fixed intermediaries playing a polarizing or guiding role. The polarizing intermediaries are either equipment

(example : BNCT or the prototype in the CA on forced respiratory techniques) or production centres (examples : B cells and diabetes, joint research facilities to breed transgenic rats, to produce artificially aged mice or to make peptides/adjuvants). The four CAs with fixed intermediaries serving a guiding role concern analytical laboratories (example : HIV genetic screening) or test centres (macaques and primates).

In addition to the finalities, actors and forms of organization we are faced with a third dimension for characterizing concerted actions : the exchanges and intermediaries give a fuller idea of teams' involvement and at the same time, depending on which form this takes and on the tangible and intangible investment which it demands, of the solidity and durability of the networks formed.

This analysis sketches an initial outline of the relationship between finalities and types of exchange. The forms of exchange imposing the least constraints on the teams (which are accompanied by easily reversible networking) are generally associated with three finalities : forums, harmonization of practice and the development or evaluation of techniques. Conversely, the types of exchange which demand heavy involvement from the teams, and perhaps even changes in their daily practice, are strongly identified with two other finalities : the development of surveillance networks and the development or evaluation of treatments. Between these two extremes remain two other finalities - establishment of specialist communities and the development of joint research facilities - which entail the often complex process of aligning teams (by harmonization of their practices and/or guidance on their subject matter). However, apart from the BME programme, where the vast majority of the CAs entail the least binding forms of exchange, and the cancer programme, where each action requires heavy commitment by the teams, all the other subprogrammes cover the whole range of situations.

TABLE 9: TYPES OF EXCHANGES ASSOCIATED WITH THE CAS

Notes: This table defines the types of exchange in closer detail to give a clearer reflection of the differences between the finalities. Paper-based collection infrastructures (CI) have been subdivided into "ad hoc" and "complex" ones centring on the establishment of large data bases. The "materials infrastructures cover all the concerted actions, other than harmonization of practice, which have entailed establishing complex logistics for the collection, storage and dispatching of the biological material amassed. "Centres" includes reference centres (3CAs), fixed intermediaries serving a polarizing role (10CAs) and fixed intermediaries serving a guiding role (4CAs). The 8 "subsidiary" or "duplicated" CAs have been excluded.

	Mee-tings	Harmo-nization	-paper CI- Ad-hoc	com-plex	mat-erials CI	Cen-ters	Tot
Surveillance services	-	-	-	4	4	3	11
Dev./Eval. of treatment	-	-	-	4	3	4	11
Dev./Eval. of techn.	3	5	1	2	2	1	14
Harmoniz. of practice	3	1	10	3	1	-	18
Forums	15	-	-	-	-	-	15
Joint research facilities	-	-	-	-	5	9	14
Special.communities	-	12	-	-	1	-	13
Total	21	18	11	13	16	17	96

TABLE 10 : SUBPROGRAMMES AND TYPES OF EXCHANGES IN THE CAS

Type of exchange	Bio	Can	Epi	HSR	BME	AIDS	Total
Meetings	1	1	-	6	7	6	21
Harmonization	4	-	1	1	10	2	18
Ad hoc collection inf.	-	-	4	5	1	1	11
Complex paper coll. inf.	1	1	2	6	1	2	13
Comp.materials coll. Inf.	3	4	6	-	3	-	16
Centres	3	3	-	2	1	8	17
Total	12	9	13	20	23	19	96

6. WHERE WILL WE BE BY THE END OF MHR4? (1) CONCERTED ACTIONS : A SIX-PHASE DYNAMIC

INITIATION PHASE AND CHOICES MADE BY MHR4

Concerted actions often require a long gestation period. The first thing needed is a topic and a few teams acquainted enough to work on an action together (or to delegate one of their number to carry it out on behalf of them all). In the first three rounds of the programme, it was left entirely to the COMACs (Concerted Action Committees) to choose the subject matter and the future action project leader, who then gathered together a few experts to define the potential topic more closely and to prepare a preliminary workshop between the European teams interested in the subject. Generally, this was enough for an action to be entered in the programme and adopted. In some cases, several meetings or possibly even ad hoc studies were needed in order to complete this initiation phase. MHR4 marked a change of approach with the publication of an open invitation to submit proposals, which opened the way for decentralized initiatives in the form of statements of intent. Consequently, the process is now more complex with several different scenarios.

In 40% of the cases the initiative was still taken by the COMAC. Slightly over half of these actions followed up operations and/or studies started earlier while the remaining 19 CAs were initiated directly by COMACs and programme managers under MHR4 (direct contacts with future project leaders to encourage them to respond and to help them build up their action).

In other cases, the initiative came fully from the proposers, who submit fully-fledged projects in their declarations of intent. Most of them (15 out of 22) were based on activating preexisting networks, the majority of which were built around European associations (of clinicians or practitioners) and European branches of international organizations (principally the WHO).

Finally, in cases where several individual initiatives were submitted on the same subject, the COMACs and the programme managers reverted to the usual procedure, with a meeting of experts and a preliminary workshop for would-be participants. Over one third of the projects qualifying for support followed this path, which usually takes longer than a year.

TABLE 11: INITIATION OF CONCERTED ACTIONS

Notes: The data set out below were drawn from interviews with project leaders. Not all the replies could be classified as accurately as hoped, particularly those concerning "initiatives by researchers" (i.e. depending whether or not an informal network already existed beforehand). Initiatives by a Concerted Action Committee (COMAC) or Working Party (WP) were classified as "before MHR4" if there was a study or workshop on the subject before 1986. Initiatives under MHR4 cover proposals made directly by the COMAC (or by one of its representatives) to the project leader before the statement of intent was submitted. All other cases are classified as "initiative by researchers" whether or not they were subsequently brought together by the COMACs by means of workshops. Activation of a preexisting European network implies that the organized European groups which prepared the project already existed before the project was started.

	creation : initiative by COMAC/WP		researcher	activation via preexisting European Network	CA
	before MHR4	under MHR4			
Surveillance services	3	-	5	3	6
Dev./eval. of treatm.	2	1	8	1	-
Dev./eval. of techn.	3	3	7	1	-
Harm. of practice	3	6	2	8	-
Forums	5	4	6	-	-
Joint research facil.	3	3	8	-	-
Specialized comm.	2	2	7	2	-
Total	21	19	43	15	6

ASSEMBLY AND STRUCTURING : TWO PHASES UNDERESTIMATED ALL TOO OFTEN

Once the project has been accepted, the action starts. The first stage is to ensure that the teams previously contacted will actually take part and, often, to add names to the original lists (if only to fulfil the virtual obligation to cover every Member State). Often, this assembly phase is protracted by the fact that it must include acceptance by the teams of the organizational rules, particularly on their rights and obligations.

In practice, in many concerted actions the structuring phase is the crucial moment which determines the future of the project. It is the time to prepare the ground by reaching a consensus between the teams (usually enshrined by the adoption of protocols) and harmonizing practices. The section on exchanges showed the many forms which such harmonization can take, the complex procedures adopted and, hence, the long lead times entailed.

Not all projects have to pass through this phase. For example, most of the projects activating preexisting networks can capitalize on assembly and structuring work completed before MHR4. Equally, there are marked differences between projects requiring no specific skills on the part of the data suppliers (in most cases, questionnaires to complete or standard sampling) and others requiring training and harmonization of practice.

Ultimately, the relative duration of this phase determines the time-scale of the project as a whole because, in every case, once the teams have reached agreement and it is certain that the information collected will be comparable the ***implementation phase***, however complex, never lasts very long (except in the case of a few forward studies).

TRANSFER : TWO GROWING CONCERNS

As in any research, the ***treatment phase*** is usually a continuous process as the many intermediate results are generated during the implementation phase. It almost always has two dimensions: the knowledge acquired (or new findings which can be published) plus the new problems (and subsequent projects to which they give rise). These two outcomes, which are both familiar and well dealt with by managers of government programmes, are however far from the whole output of these concerted actions. The programme produces two other complementary outputs inherent in its very design.

Dissemination of results

The analysis of the finalities pursued showed that the programme goes a very long way in the attainment of usable results, since over 60 of the concerted actions are intended to generate information, protocols and material of direct benefit to users. The purely academic results are only part of the picture as regards the outputs of a programme which, in contrast to many of its cost-shared counterparts, can extend as far as the development of new treatments or recommendations for the best medical practices. This raises a familiar objection and question : what is the point of providing financial support for generating results without doing anything to ensure their dissemination?

Since dissemination of results is not governed by conventional market forces (with the potential users as buyers and the producers as sellers), government operators have to assume new responsibilities in order to avoid the investments running into the sand. The general rule of including potential users in virtually all concerted actions is both a guarantee that there are users interested in the project and a first step towards dissemination of the results. Consequently, the programme avoids the demonstration problems (cf. the energy field and heavy investment expended in the Community on this specific phase). However, it still faces the problem of general distribution. What can be done to make sure that the hundreds of thousands of general practitioners all benefit from the tools developed to assist them to make objective medical decisions on abdominal pains or jaundice? How is it possible to ensure that the rules on electrical safety incorporate clauses which guarantee the quality of electrocardiograms and of the diagnoses based thereon? What can be done to ensure that laboratories for diagnosing sero-positive carriers follow the recommendations made? Steps must be taken to make sure that the snowball effect enters into play. In a sense, work on the programme does not finish until the baton has been passed on, i.e. until the results have been taken up by the other government departments directly responsible for the users targeted.

Results embodied in networks

Since the funding is solely for the costs of networking the teams (and not to finance individual research), it is only logical that the programme should generate "networks". But once they have been set up, should they be of any further concern to the programme?

Economic theories on technical change claim that it is the cost of forming partnerships and the numerous preliminary trial and error stages which prevent the networking of individual actors, since no individual is willing to bear those costs. This justifies state funding, but at the same time sets a limit to it : once the network has been set up and has proven effective, the actors will have been able

to ascertain the value of such collaboration and of maintaining it themselves. In this respect, there should be no question of supporting a network which has proved its worth and is producing results. These conclusions, drawn from a study of cost-shared Community programmes, have only a slight bearing on the networks observed under MHR.

Although in some projects the network is intended to split up once the end result has been obtained (possibly to re-form in better shape to discuss any new questions raised, in which case it will not have to be set up once again but simply re-activated), this is not the case for a number of concerted actions which have developed joint facilities. With these, there are three different situations.

At one extreme, the facilities (and the network which supports them and is centred on them) are intended to last, albeit no longer in a research role but either as production centres (as in the case of the centre for extraction of B cells in the CA on diabetes) or as surveillance services (as in three cases at the end of MHR4, including the CA on congenital abnormalities).

At the other end of the scale, the programme has given birth to central research facilities (example: HIV genetic screening) or to complex collection infrastructure (example: ECAT on lung diseases) designed to provide a service for the scientific community. These make sense only over a far longer time scale than MHR4 (11 actions).

Between the two, MHR has facilitated the establishment of authentic services for the evaluation of treatment, techniques and practices. By the end of MHR4, these will have proved their worth on their first subjects, leaving the question whether to turn to other fields of activity (examples: hereditary diseases of the retina, objective medical decision-making, opportunistic diseases associated with AIDS or tissue characterization). In all, the future of over 20 networks will have to be reviewed at the end of MHR4.

7. WHERE WILL WE BE BY THE END OF MHR4? (2) PROBABLE SITUATIONS AND FAMILIES

THE FIVE PROBABLE SITUATIONS BY THE END OF MHR4...

This brings us back to the problems which the programme will face at the end of the current phase (MHR4). By subdividing progress on the concerted actions into six phases, starting with initiation and ending with transfer, five separate groups of actions can be defined, based on the stage reached in this process. The first group containing the "forum" actions will always be at the initiation phase, since this is also their ultimate objective. The second group (18 out of the sample of 96 CAs) expect to complete the structuring phase by the end of MHR4 and, hence, to be ready for implementation. The third group of 21 actions will be in the middle of the implementation phase by the end of their grant. The fourth group contains the 22 actions which will have attained their objective and be on the verge of the transfer phase while the fifth group comprises the 20 networks which will have proved their worth but, as shown in the previous section, leave the question of continuity open.

TABLE 12: PROBABLE SCENARIO BY THE END OF MHR4

Note: The classification is based on interviews with project leaders and on analysis of the files and reports available. It includes 96 actions i.e. excluding the "secondary" and "duplicated" actions)

	Initiation/ structuring	Implement. phase	Service in operation	Transfer	Total
Surveillance services	1	6	3	1	11
Dev/evaluation of treat.	2	6	2	1	11
Dev/evaluation of techn.	5	2	2	5	14
Harm.of practice	1	1	1	15	18
Forums	15	-	-	-	15
Joint research facilities	-	2	12	-	14
Specialized communities	9	4	-	-	13
Total	33	21	20	22	96

TABLE 13: SUB-PROGRAMMES AND PHASES REACHED BY EACH CA

Phase reached	Bio	Can	Epi	HSR	BME	AIDS	Total
Initiation	1	1	-	2	6	5	15
Structuring	1	2	-	2	10	3	18
Implementation	6	3	5	4	1	2	21
Service	3	2	4	1	3	7	20
Dissemination	1	1	4	11	3	2	22
Total	12	9	13	20	23	19	96

... GIVE BIRTH TO FAMILIES OF ACTIONS POSING VERY DIFFERENT PROBLEMS FOR MHR4...

With seven finalities, five forms of organization, five main categories of exchange and five probable scenarios by the end of MHR4 (not to mention three main types of composition), a set of indicators are now available for characterizing the concerted actions and their dynamics.

Simple calculation of the possibilities shows that there are very many combinations, however rarely some of them occur. It has been shown elsewhere[12] that networks are flexible arrangements which bring together actors from different backgrounds but look different depending on where the observer stands. Potential industrial users will not see the network with the same eyes as the researchers who change their practices. Government departments will take yet another view, since they are not directly interested in the results but, above all, in comparing performance in order to ensure better allocation of the incentives which they distribute. There is, therefore, no single perspective allowing a hard-and-fast, definitive classification of the networks.

Here the programme operator's point of view has been taken. What does this approach teach him? What expectations does it permit? What changes in practice does it suggest? This choice of perspective is all the more warranted by the recent adoption of the fifth round of the programme to follow up the fourth, which is nearing completion. Consequently, the programme operator faces a

[12] Des instruments pour la gestion et l'évaluation des programmes technologiqes M. Callon, P. Larédo & V. Rabeharisoa, in J. de Bandt et D. Foray (ed.), L'évaluation économique de la recherche et du changement technique, Presses du CNRS, Paris, 1991.

series of conventional but nevertheless difficult questions concerning the progress made so far, the quality of the output, the strategies to pursue, etc.

The starting point is, indisputably, the progress made with the actions. Which will be completed? Which transfer problems do they raise? Which will have reached the end of the structuring stage and how successfully? And what are the requirements of the actions which will be in the implementation phase? However, another side to consider are the implicit commitments made. Which networks has the programme built? Which can be counted as new research infrastructure? What can be done to ensure that they continue to operate and provide the services which prompted the programme to support or encourage their establishment?

The analysis set out below therefore focuses on the dual aspects of "progress" and "types of exchange". It takes stock of the situations and of the questions which they raise before the final section analyses the strategic and organizational implications for the operator of the MHR programme.

Forums : one ultimate goal of the programme?

Out of the 96 actions analysed, 15 are "exchange forums". Forums are a finality, a form of organization, a category of exchange ("meetings") and a specific output intended to help initiate joint projects all at the same time. The only output which they produce are summary records of the meetings (if any are kept) and the interest aroused amongst the teams. In this connection, the very high response rate to the questionnaires mailed to the teams participating is striking.

Most of these actions come under the two subprogrammes with the largest number of concerted actions: BME (6 actions) and AIDS (5 actions).

Some project leaders argue the merits of such an approach in two specific circumstances - for a small specialized community or for a new problem on the frontier of the existing disciplines. They feel that the managers of the MHR programme no longer give forums their rightful place but instead try to transform them into "pseudo-projects" on a specific topic or else put an end to them as soon as a project emerges.

If the programme chooses to maintain this dual form of activity, it will be faced with two strategic questions (which communities must be sustained in this way? Why these rather than others?) and two problems of assessment (has progress been made on the problem which generated all this activity? Is the form adopted still suitable?).

Structuring - often a heavy time consuming process

If all goes according to plan, 18 actions will have completed the structuring phase by the end of MHR4. In most cases, the effort required was grossly underestimated at the action definition stage. In one case it took two years to define a protocol, in another harmonization of practice entailed the adoption of reference materials, in yet another exchanges of equipment were limited by the competitive position of the suppliers, etc. All these situations cause delays and, frequently, force project leaders to conclude that by the time they will be ready to start the real work, their grant will have come to an end.

These actions centre mainly around two general goals. The first, as only to be expected, is the establishment of specialized research communities (9 of the 13 actions with this purpose). The inclusion of five actions on the development or evaluation of new techniques is a clear sign of the difficulties which the programme faces in this area.

These actions have two important points in common. They are almost all organized around the project leader and his team who run this difficult phase on their own (only four cases of shared management). This is matched by the choice of form of organization: either small, superimposed groups working in parallel (type 4) or a star network in which the teams gravitate directly around the project leader's team. The number of teams involved is often large and, in many cases, still unstable (many project leaders draw a sharp distinction between simple participants and "active members"). Three out of four of these actions, and this appears their second major common point, are in the midst of a complex process (based on multiple forms of exchanges) of aligning the teams to ensure that their output is truly intercomparable.

These two traits are evidence that these actions are recent. Nothing has yet been stabilized, neither the participants and methods of working together nor the action which the teams will be capable of conducting together. The finality of the action appears largely indicative, reflecting more the project leader's objective rather than the actual situation in the field. By contrast, the nature of the consensus reached, i.e. the practical result of the action by the end of MHR4, will give an idea of the potential dynamics of the action in question and, consequently, on any follow-up needed under BIOMED.

Finishing actions (1) : a limited number of dissemination problems

As seen earlier, MHR's responsibility does not end with attainment of the set objectives. To avoid wastage of Community funding, it must also ensure dissemination of the results. In view of the organization of health care systems, this can raise specific problems. What exactly is the situation?

By the end of MHR4, 22 actions, or less than one in four, will have reached the dissemination stage. The majority of these cluster around two finalities: evaluation of techniques (five cases) and harmonization of practice (15 cases). One in two of the actions comes under the HSR subprogramme.

These actions have three features in common. First, only limited investment is entailed, either because the actions are limited to meetings (six cases) or because protocols were already available when work on the action started and called for no specific skills on the part of the teams collecting the data (10 cases). This is reflected in the method of initiation, with half the actions activating preexisting networks developed by various European associations and the other half initiated by COMACs ("to gain a clearer picture"?). This is paralleled, second common characteristic, by a limited number of participants (on average 20) organized in a star network orchestrated by a project leader. And finally, the result usually takes the form of updating of information (example : Euromac), a situation report (example : mental health problems of deaf people) or information packs or publications to increase public awareness (examples : "HIV and oral problems" and "ICPC classification"). A few of these actions could open the way for future large-scale actions (examples : "use of DRGs in hospitals" or "head injuries"). A few rare examples raise the problem of formulation of recommendations which will have to be disseminated (example : "HIV serological methods").

The six actions which fail to fit into this pattern are all one-off cases presenting the programme with specific problems foreshadowing the others which lie ahead :

- the problem of generalization of the best practices, as in the case of "care delivery systems" or "self-assessment in hospitals". How can the results be passed on from the 100 or so hospitals "enlisted" to all hospitals in Europe?;

- the problem of maintaining ad hoc surveillance services tested in the course of specific operations (examples : the Eurosentinel networks of general practitioners tested in two separate concerted actions);

- the problem of the future of predevelopment actions, such as EULIMA (where the CA will have allowed completion of the "final conceptual design");

- finally, the problem of the incorporation of a quality standard in legislation (on diagnostics) in systems hitherto concerned solely with operator and user safety, as in the case of the action on ECGs.

Finishing actions (2) : question marks over the future of the "services" created

By the end of MHR4, 20 more actions will have attained their objective but will leave the MHR programme with another problem of their own : the future of the investments made.

At the end of an often lengthy process (most of the actions in question started under MHR3), these actions have built up fully-fledged services :

(i) surveillance services (three cases) as in EUROCAT on congenital abnormalities and the 20 or so regional networks set up from scratch or the "epidemiology of AIDS" action's reference centre for monitoring the spread of the disease in Europe;

(ii) services for the evaluation of treatment (two cases) based on the establishment of complex collection infrastructure for opportunistic diseases associated with AIDS (ENTA) and costly pre-hospital treatment (EMIP);

(iii) services for the evaluation of medical techniques (two cases), such as the CA on "tissue characterization" and the EUROSPIN test specimen packs which it developed;

(iv) service for the evaluation of practices (one case) for "objective medical decision-making" to follow up the achievements of the first two operations (methodology, material support and national networks);

(v) finally, research services, whether in the form of production centres (three cases), for example for artificially aged mice or transgenic rats, or of analysis centres (four cases) as for "HIV genetic screening" or collection infrastructure (five cases) as for ECAT (for lung diseases) or EURONUT (for nutrition).

Twelve of the actions which will be at the service stage by the end of MHR4 share the same finality : joint research facilities. By definition, this raises the question of their continuity. Can the programme rely solely on the teams' own capacity to raise the funding needed for them to continue? Possibly yes for most of the "centralized" facilities (seven cases). But it will be far more difficult for the collection infrastructure and the associated reference centres and logistics, as in the case of the five structures set up to evaluate treatments, techniques or practice. In these cases, the programme is approaching a turning point : how can it move on from encouragement for setting up such facilities to long-term support for the infrastructures developed as a result? LEBM-style "case-by-case" solutions no longer seem commensurate to the type of problems encountered.

Actions still in progress and the establishment of complex research infrastructure

By the end of MHR4, 21 actions will be in the midst of the operational phase. There are three main reasons why these actions were unable to complete the collection phase during MHR4.

Either the actions build up "large number of cases" data bases, usually backed up by banks of samples of blood, tissues, cells, etc. This applies

particularly to six of the 11 surveillance services (examples: "asthma prevalence" or "Eurodiab" on diabetes prevalence and complications) and to three of the actions on the evaluation of practice or techniques ("use of blood" and two actions modelled on the CA on ECGs with a view to standardization of techniques, namely "antenatal ultrasound screening" and "quantitative assessment of osteoporosis").

Or the activities are organized in projects, may they be centred around production centres ("B cells and diabetes treatment"), or "integrated". The CAs on BNCT or the "human stem cell project" are representative examples of these five actions on the development of new treatments which are organized as integrated partitioned networks.

Or, finally, harmonization has taken a long time, as in the case of four actions on the establishment of specialized research communities and there is little chance of completing this phase within the time limit granted for funding. It must be stressed that three of these four actions are expected, if seen through to the end, to culminate in services (two on the development of treatments - for chronic arthritis and for multiple sclerosis - and one on monitoring of dementia).

Consequently, the common feature of all these actions is that they rely on heavy investment (to harmonize collection conditions, to provide the logistics required for the large number of cases involved or to build up and use the often complex data bases and data banks). These investments are all the greater since often a large number of teams are involved (average around 40) and, in 15 of the 21 cases, shared strategic management was needed to implement the action. In essence, these actions correspond to three already mentioned situations which the programme will have to face : the establishment of surveillance services (six cases), the establishment of services for the development and evaluation of treatment (five cases) and the development of production services which can be transferred once the treatment has proved its worth (five cases).

Towards a Community form of National Institute of Health (NIH)?

Eventually 15 of the 21 actions still in the implementation phase at the end of MHR4 will probably raise the same question as the 20 or so actions at the service stage at the end of MHR4 : what is to become of the heavy capital and intangible investment generated in the course of the programme? Will the marginal financing which made it possible to make these investments still be needed to maintain them?

The future of the Community programmes on biomedical research will depend heavily on the (political?) answer to these questions since, in the final analysis, it is obvious that this programme produces three main types of result: (1) forums; (2) comparative studies taking stock of the situation; and (3) complex networks which raise the question of how to keep them in operation on a lasting basis. This last "output" gains more and more importance with the ageing of the Community intervention. Is the EC investment paid for by the initial scientific results? Should such new research infrastructures maintained on a longer period of time? These questions, and not those linked to financing research on a cost-shared basis as has been sometimes mentioned, give ground to the opening of discussions on a form of Community NIH.

8. CONCERTED ACTION AS AN INSTRUMENT FOR PUBLIC INTERVENTION

A PRIVILEGED AREA FOR APPLICATION WITH THREE DISTINCTIVE CHARACTERISTICS

All the analyses show that concerted actions focus on one special situation where, in order to advance knowledge, information never before accumulated and up to now incomparable has to be collected. As a result, multiple efforts are needed to ensure that the local observations are comparable and can be transferred, taken up by others and centralized. None of this harmonization of practice, standardization of laboratories, alignment of large numbers of actors from different places and institutions would be possible without heavy investment. This investment is marked by three distinctive features : it focuses more on manpower rather than funding, on organizational issues rather than institution ones and operational features rather than thematic ones. What does this imply?

The key to the success of the CAs lies in their capacity to rally teams (or at least the active core) behind the same objective, i.e. to make them progressively jointly define the terms for attaining it, with all the concomitant division of labour, loss of independence and even polarization of image. Investment of human resources is the decisive factor. This explains the importance attached to meetings, exchanges, visits, the flow of information or the image of the CAs (logos, newsletters, rules for publication, etc.). In a way, "management of human resources" is the lifeblood of any concerted action.

This comes before and accompanies the management of material resources. Here, once again, the striking point to emerge from the analysis of the actions is less the material dimension, i.e. the physical investment required, than the organizational side, i.e. circulation of data or biological material, coordination of the starting and finishing points, allowance for differences in the national legislation, checking the effects of the packaging, etc. Many project leaders stressed the strategic importance of these logistical "details" which hold the teams together and, in a way, give firmer shape to the organizational structure built up, just as much as any specific piece of equipment or joint service. But this by no means plays down the importance of the "facilities" set up. On the contrary, they are complementary and, beyond their intrinsic value, often serve as an anchor for the internal action and a reference point or means of projecting the identity of the action to the outside world (colleagues, parent institutions, national authorities providing the funding, etc.). Moreover, very often these facilities are closely involved in the logistical operations (storage and processing of samples, maintenance of data bases and data banks, etc.) for which they lay the foundation (the "reference centre" idea).

The third dimension of these investments concerns the implications for the teams. Despite their importance, the work on the concerted action is only a secondary activity for the teams (on average, one fifth of their activities according to the replies to the questionnaire). Consequently, the concerted action brings no major inflexion to the teams' priorities and fields. Instead, everything heightens the "operational" impact. The emphasis on intercomparability of data and on all the facilities to make this possible (i.e. to ensure that samples are taken in the same way, that the tests or clinical diagnoses are comparable, etc.) call for an alignment of experimental practice which has an impact felt beyond the activities on the

action itself and at the same time establishes a joint capacity to deal with other problems demanding similar approaches. Here the research approach and the resources and methods which it requires take precedence over the topics and subject matters themselves in the strict sense.

A CHALLENGE TO PROGRAMME MANAGEMENT

These three features dictate a long time scale. With their emphasis on management of human resources, organization of material relationships and alignment of laboratory practice, concerted actions gradually build up new spheres of communication. These are both irreversible (once practices have been harmonized, there will be no more difficulties with the flow of information) and flexible since they will not take shape unless the human and material organization needed to ensure this communication still exists in one form or another.

What are the conditions for the establishment and survival of these "quasi-institutions" which the networks set up by the concerted actions and their related infrastructure and organization represent? The survey clearly identifies them and, at the same time, pinpoints a number of management problems analysed in detail in File 3. Four main aspects play a decisive part in shaping the future of this original form of government support and, at the same time, questions the management choices of the MHR programme : delegation and its two counterparts, monitoring, programme visibility and strategic forward planning.

Delegation as a management principle and its consequences

The detailed analysis in File 3 on the structure and management of the concerted actions highlights the central role played by the project leader. Not only legally, as the Commission's sole contact bearing full responsibility for the funds allocated to the project, but also from the practical point of view as the person responsible for building up the network and for all the decisions to be taken (number of teams, terms of participation, Europe-wide cover, participation by industry, etc.). It is also up to the project leader to decide which matters are to be "concerted" and to define which to include or exclude. Finally, he represents the action and builds up links with the outside.

Many project leaders feel that they are ill-equipped and given little support in relation to the job which they accept. This applies at both the administrative and institutional level.

(a) They have not hesitated to devise a host of formulae to solve their problems. Together these constitute a genuine textbook on the financial and administrative practices involved in concertation. However, many mentioned that they felt that they were operating "outside the rules". Some even ruled out potential solutions (which others had adopted without their knowledge) because they thought that they were "not allowed". The administrative dimension pervaded all the interviews conducted. One of the loudest "demands" was to be informed about the methods, formulas, etc. adopted by others. Project leaders feel that the extensive delegation of administrative and financial responsibilities to them (beyond doubt, one advantage of this formula) should be matched by an improved flow of information and regular exchanges on the methods to be adopted, a sort of "***clearing house for management methods for CAs***"[13].

[13]There are a number of points which have been mentioned many times as requiring administrative improvements (e.g. the time taken and perverse effects of the annual funding allocations) or for which changes of funding practices would be desirable.

(b) Not only administrative duties are delegated. The project leaders are also responsible for publicizing their projects (the first full list of projects was not published until 1990) and for forging any links needed. This in turn poses problems, particularly two which were mentioned several times. Relations with industry often raise the question of access to results or data, of certain exclusive or prior rights or even of practical participation in the project (as in the case of at least 10 actions). The project leaders feel particularly at a loss on this point. Who are they committing when they sign or negotiate an agreement? On whose behalf are they acting?... The same problem recurs when they have to discuss exchanges of information and cooperation with outside partners (for example, the NIH institutes were mentioned in several cases). These two problems lie at the heart of the ***"status" of the project leader.*** Is he a straightforward contractor committing no-one but himself? Or should the project leader be given other recognition to facilitate his task? In practice, when the Commission of the European Communities entrusts the project leader with responsibility for a specific concerted action (and confirms his responsibility when the project is extended), it delegates to the project leader the task of activation of work on a specific problem.

This perhaps goes some way to providing a pragmatic answer to one question asked all too often : how can Community support be linked with national funding? How can the choices made by the authorized national representatives in Brussels be brought into line with the choices made in the Member States? Once again, many project leaders mentioned that they had been having problems, for example with teams that had had to withdraw for lack of national funding.

Monitoring of concerted actions and organization of the programme

Actions take time and many have to be extended. The report highlights the protracted length of the structuring phases and the unique forms which success can take (how is it possible to assess from litterature success in harmonizing sampling methods between 30 teams?). Nevertheless, outside observers of the progress of the actions are not left completely without guidance. The intermediate results are milestones in the life of the concerted actions and provide various pointers for assessing the rate of progress. The project leaders virtually unanimously stressed the unsuitability of the methods adopted by the programme. They feel that annual reports are not always appropriate and, what is more, rarely produce any feedback. The reviews by the COMACs[14] (ten minutes per year to report on the progress made on the action) were viewed dimly by the project leaders who had undergone them. They also felt that the role of the liaison officers appointed by the COMACs to monitor the projects was at least ambiguous. Monitoring of the concerted actions clearly raises two complementary problems : the first concerns objective reporting in order to characterize the project and assess the progress made (the means of analysis described here should help these efforts to achieve greater transparency), while the second relates to the scientific and technical choices and results. Many project leaders wished this

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For instance, proposals have been made to set aside part of the funds (and establish specific procedures within the programme) to support teams in the southern member states, to cover the expenses of postgraduates and to adapt the costs to the actual number of participants (to deal with a few cases of CAs run as closed shops).

[14] The COMACs or Working Parties were the only bodies referred to. No project leader, apart from those involved directly in the Brussels end of the programme, mentionned the CGC at any time. Similarly, it is unusual, at least judging from the other Community programmes we and our colleagues have been part in the evaluation of, to hear so little mention of the team managing the programme.

second dimension to be reinforced but, at the same time, felt that the changes in the composition of the COMACs and of the Working Parties leftthem no longer in a position to assume this task.

Programme visibility

One common strand running through all these problems is the lack of "visibility" of the programme. Countless project leaders said that they came across the MHR programme by chance. Many of the newcomers in particular said that the organization of the programme was an unknown quantity for them and its image confused. All concerned greatly appreciated the issue of a newsletter on the programme in 1990, the first publication to make everyone aware of the existence of the concerted actions. To know more about what the others are doing, to tell outsiders what is going on, to improve links with the national authorities (paradoxically, the survey showed that they were the group of potential users which knew least about the programme)... these are just some of the objectives mentioned by one project leader or another. But this effort to communicate will bear no fruit unless the programme is made more "transparent". Why the COMACs and the Working Parties? What do the six subprogrammes correspond to? Taking the reading given by the project leaders, particularly those whose proposals have been shunted from one COMAC to another, MHR looks like a "holding" of different programmes with practices, criteria and positions which are not always compatible. Communication is indubitably one of the immediate problems facing the MHR programme, possibly even a specific function to be created.

Programme strategy and the choice of problems covered by concerted actions

Finally, in over 10 years the programme will have given birth to 100 or so projects, fewer than half of which will have reached the completion phase by the end of MHR4. The transfer problems and the challenges which they pose for the programme and also, more broadly, for the Commission and the Council have already been discussed at length. The very concept of a Community "form of NIH" suffices to give an idea.

The number of actions appears small in some ways (what are 100 or so actions compared with a programme like BRITE for example) and large in others (if only because of the structural problems which it raises) and serves as a reminder both of the time needed to set up the networks and bring them into operation and of the difficulty of starting them. It is thus a strategic issue to define and select areas that are relevant to this "concerted action" approach.

The invitation to submit proposals has significantly increased the number of actions included in MHR4. But it has also triggered a change of approach : many of the new concerted actions support pre-existing networks which have already completed the harmonization phase at the heart of the establishment of new networks. This implicit strategic choice warrants further consideration : which balance must the programme strike between activation or maintenance of preexisting networks (including those engendered by the programme itself, cf. above) on the one hand and initiation of new networks on the other?

At the same time this calls into question the procedures used. Publication of an invitation to submit proposals every three or four years is out of step with the very long time taken for the initiation phase in many cases, one possibility being a "standing" invitation to submit proposals for the preliminary phases linked to the already existing practice of the programme for funding studies and preliminary workshops.

Above all, however, this raises the question of the strategic choices to make : on which fields to promote the creation of new networks? Now that greater experience has been acquired and more is known about the fields suitable for this specific form of public intervention, the programme is faced beyond any doubt with the question of "strategic forward planning"[15].

[15] as proposed by R. Chabbal in his report on the organization of evaluation by the Commission of the European Communities, Brussels, 1988.

FILE 1
A QUANTITATIVE APPROACH

RESULTS FROM THE QUESTIONNAIRE MAILED TO ALL PARTICIPATING TEAMS

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ANNEX 1 : METHODOLOGY USED AND PROBLEMS ENCOUNTERED

A QUANTITATIVE APPROACH

INTRODUCTION

The Medical and Health Research programme is a "minor" programme from the point of view of the amount of money allocated to it: 60 mECU, half the sum allotted to Non-Nuclear Energy for instance. It is the only programme dedicated to "Concerted Actions" (funding only the costs of "concertation") as all the other EC programmes are "cost-shared" programmes (which fund up to half of the research costs). Nevertheless, at the end of 1989, it brought together 4 to 5 times more teams than the abovementioned cost-shared programme[1]: 3 500 teams in some 120 Concerted Actions (table 1). It appeared very clearly, when analysing its role and effects, that the first point to assess was the effective participation of teams within Concerted Actions. We chose to address them directly through a mailed questionnaire which was sent beginning of 1990 to all participating persons or teams whose details were available to us. Annex 1 explains the methodology we used, the questionnaires we developed and the major problems we were faced with to organize this effort.

Sending a questionnaire without a clear view of what has to be addressed may make the whole effort unproductive. We thus had to make choices, which involved a fourfold process which needs to be explained here before analysing results obtained. The first, traditional way is to appreciate through interviews the main parameters of the programmes (who is concerned, what does it produce, how do people work together, what are the main issues at stake ...) : this was mainly done through lengthy and repeated interviews of EC programme managers. This was complemented by a systematic analysis of the content of annual progress reports (or projects for starting actions) of all concerted actions in order to obtain a glimpse of their objectives and activities.

We then capitalized on a recently completed survey (using a mailed questionnaire) on the impact of cost-shared programmes on the French S&T community[2] : after interviewing 80 senior French R&D decision-makers, we had developed a questionnaire which helped appreciating the activities of a "research team", its involvement in EC programmes, the results it expected out of it and its attitude about the role and effects of such programmes. We thus had experience of what questions needed to be asked and how to go about collecting usable responses, especially since our colleagues from York were specialists in health problems and the CSI team had been supplemented with a biologist. But we also knew we were missing a crucial dimension : how to appreciate the nature of the links between teams. We had to devise a completely new section about exchanges within CAs.

Initial testing of the questionnaire helped us to adapt to the specific population involved in health research. But it also gave us a first glimpse of the

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[1] For all comparisons with the NNE programme, see "L'évaluation des programmes publics de recherche, le cas du programme ENN de la CEE", PUN, Namur 1989.

[2] P.LAREDO, M.CALLON, L'impact des programmes communautaires sur le tissu scientifique et technique français, Paris, La Documentation Française, 1990.

problems we were going to face : very different realities depending on CAs and on institutional enrolment. Dealing with diametrically opposed attitudes towards the questionnaire obliged us to make formal choices : we did not choose to go for a simple, two page questionnaire which would have left out all items enabling us to "measure" an implication and to describe the nature of the links between teams. We chose to go for a complete 6 page questionnaire, knowing that we would get a far lower rate of response and even crude remarks about its content. We got the latter but, at the same time, were very much surprised by the final response rate (without using traditional means such as systematic phone calls 3-4 weeks after mailing to ensure an adequate return).

This first file presents the major results obtained against a simple canvas : Who took part? What are the human and financial implications of this participation? What activities are carried out under the CA? What exchanges result from them? What type of results are expected? and who are they suppose to interest (who are their future users)? This factual canvas was chosen on purpose, since these results (first progress report by May 1990) were looked at with much scepticism by some observers. It was then decided, with EC officials, that CSI would start a second more qualitative analysis to try to explain them : this was done by systematically interviewing virtually all Project Leaders (over 100 out of the 120 listed at the time); these interviews make up the core material used in the other files developing the arguments about the dynamics of CAs and thus explaining the quantitative "image" we arrived at through this mailed questionnaire.

1 - WHO ANSWERED ? ABOUT RESULTS RELEVANCE

Out of the 3500 participating teams (see table 1), over 1400 answered, giving 40,2 % coverage (see table 2). For such studies these absolute numbers and percentage coverage are considered good enough to provide representative results. Here the absolute number is such that one could limit oneself to the responding teams, making the asumption that only highly involved teams answered. If this is the case (but we have checked with quite a few PLs that it is too restrictive a hypothesis), then our description only applies to a core participation of 12 teams for each CA.

This coverage varies depending on subprogrammes: from 34% to 46%. No difference can be detected between older or newer actions. A completely new programme like CANCER has a similar response rate to that of an older programme like BME. What is interesting to note is that the lowest answering rates are with programmes with "extreme" participations : Biology officially has nearly 50 participants per CA while HSR and AIDS have 20 or less. Does this point up differences between subprogrammes? This is a question that will be dealt with at length in this study. One point we should make in relation to the answer to this question is that we see the basic explanation as being differences between CAs. And if programmes differ, it is in their mix of CAs.

When analysing the response rates per CA (table 3), one gets a clearer view of this situation. We have 22 CAs with fewer than 5 responses, half of them in the AIDS programme, which underlines, in this subprogramme, the contrast between CAs which responded and those which did not since overall the response rate is still over one third. The same analysis applies for HSR with 15 of the 21 HSR CAs having fewer than 10 responses and a 34% response rate. The size of the average CA in Biology is such that even with a low response rate, 9 CAs out of 12 provide more than 10 responses. Altogether the 95 CAs with more than 5 answers provide

96% of all responses received and their average response rate then amounts to nearly 45%, a satisfactory level of coverage.

TABLE 1 : MHR PARTICIPATION

Note : reconstructed data excluding "not yet started" actions and studies. The number of teams must be considered as an approximation.

Sub-programmes	number	number of teams	average of CAs	membership
Biology	(BIO)	687	14	49
Biomed. engin.	(BME)	1025	28	37
Cancer	(CAN)	330	12	27
Epidemiology	EPI)	621	17	37
Health Serv. Research	(HSR)	430	21	20
AIDS	(AID)	434	25	17
		3527	**117**	**30**

TABLE 2 : RESPONSE RATES BY SUB-PROGRAMME

Sub-programmes	number	answers of teams	coverage received
Biology (BIO)	687	254	37,0
Biomed engineering (BME)	1025	460	44,9
Cancer (CAN)	330	153	46,4
Epidemiology (EPI)	621	256	41,2
Health Servi. Research (HSR)	430	149	34,6
AIDS (AID)	434	149	34,3
	3527	**1421**	**40,3**

TABLE 3 : RESPONSES PER CA

number of CAs with	<5 answers	5 to 9 answers	10 to 14 answers	15 to 19 answers	20 and over answers	total CAs
Biology	2	1	3	1	7	14
BME	2	5	7	6	8	28
Cancer	0	3	5	3	1	12
Epid	0	6	4	3	4	17
HSR	5	10	5	1	0	21
AIDS	13	8	2	2	0	25
total	**22**	**33**	**26**	**16**	**20**	**117**

The analysis by institution shows another bias in our sample : "academic or academically related" teams tend to answer more while service institutions appear to be quite underrepresented in our sample. This applies to health service authorities and general hospitals. For the latter group, the large difference requires a specific explanation : it largely depends on the initial difficulty we had in classifying hospitals in categories, not in the global share of hospitals (45%) but by specialization hence the discrepancy observed. If we apply to the whole

population the correction rate we had with the answering population, we still have a significant under-representation of general hospitals. Given that health services and general hospitals make up, with private companies, the core of the potential users of MHR results, in all our further analysis, we will underestimate their direct presence in the actions.

TABLE 4 : RESPONSE RATES BY INSTITUTION

Note : characterisation of Hospitals and University hospitals in the total population is not reliable ; only global figures must be considered: 45,4 % on one side, 44,8 % on the other.

Institutions	total population percentage	answers percentage
Hospitals	22,3	11,9
University hospitals	23,1	33,9
Universities	28,9	26,6
Government research organisations	13,6	14,8
Health services	7,9	4,8
Industries	1,4	1,3
Foundations and voluntary org.	2,8	5,4
	100	**100**

2- THE DIFFERENT ORIGINS OF THE MEMBERS OF CA TEAMS

The first item of interest is what is the average composition of CAs. We will approach it through the analysis of participating teams: what institutions do they come from? what is their main activity? how are they composed? It will help us then to analyse the composition of CAs by answering the following question : to what extent are the teams from different origins and have different problems?

21. MEMBERS' INSTITUTIONS

Table 4 shows a two to one balance between "academic" institutions (universities, government research organisations) and "service" institutions (hospitals, health services, voluntary organisations). This is typical of most EC programmes, industrial companies being here replaced by service institutions. Even though their presence seems underestimated (see point 1), they still make up a fifth of the population of CAs. Potential users of results are thus quite strongly involved in the activities of CAs, creating from the start a relationship between the production and use of CA products. It may also be an indication of the kind of products CAs are interested in. More specific of this programme is the significant role played by "go between" institutions : 37% of teams are linked to such institutions, with industry having a very limited share[3] and a major role being played by university hospitals (34%). It may be worth noting that teams which have both clinicians and research workers represent over 40% of the total.

[3] even taking into account all pharmaceuticals, medical supplies or equipments industries.

22. MEMBERS' MAIN ACTIVITY

70% of teams consider research as their main activity. This is emphasized by the fact that more than 600 of the 900 teams which responded have no clinicians in their team. On the other hand, nearly 80% of teams qualifying their main activity as "clinical care" have no research workers (see table 5). These figures vary considerably between subprogrammes. The average figure reflects exactly the relative importance of the Biomedical engineering subprogramme (BME) and hides the differences between two groups of "opposite" subprogrammes. Biology, Cancer and Aids focus on the research end (80 % of research teams) while Epidemiology and Health Services Research sub-programmes get close to 50 % of clinical teams.

TABLE 5 : TEAMS COMPOSITION

Teams with	% of teams	average nber res.	clin.	% of total res.	clin.
Research workers only	45	6,4	-	61	-
Clinicians only	12	-	6,4	-	30
Researchers and clinicians	43	4,3	4,7	39	70
- mainly in research	(27)				
- mainly in clinical care	(11)				
	100	**4,3**	**2,5**	**100**	**100**

23 - TEAMS SIZE

Team size appears significant : on average 13, including 4 research workers and 3 clinicians. However, these figures are lower than those obtained for EC cost-shared programmes[4] (30 including 14 researchers). Even though some people seemed to have difficulties with our definition of the team (the people you work with daily), over 1300 answered, giving this information considerable importance, which confirms the finding about institutions : 1 team out of 7 has no full time researcher (mostly located in "service institutions") and 1 team out of 2 has an average of 5 clinicians (another indicator of the global orientation of the programme). These figures must be kept in mind when looking at MHR4 conclusions.

TABLE 6 : DISTRIBUTION OF RESEARCHERS

Number of researchers	% of teams population	% by team of total researchers (uniquely applies to teams with researchers)
1 to 5	67	32
6 to 10	25	37
11 and more	8	31
	100	100

[4] P.LAREDO, M.CALLON, op. cit.

Nevertheless, these figures underline the rather large proportion of teams with autonomous research capabilities (over 80%). These teams also provide typical figures for public research : equal shares for "small" teams (under 5 researchers), "medium-size" teams (5 to 10 researchers) and "large" teams (over 10 researchers). Obviously, this is the result of an unequal distribution with over 2/3 of small teams and less than 10% of large teams[5].

TABLE 6BIS : DISTRIBUTION OF CLINICIANS

Number of clinicians	% of teams population	% by team of total clinicians (uniquely applies to teams with clinicians)
1 to 5	73	37
6 to 10	20	32
11 and more	7	31
	100	100

24 - THE MAKE UP OF CAS

How do teams combine to make up CAs? Do we observe contrasting situations between, on the one hand, academic CAs and, on the other, clinical CAs. The results are very clear : the answer is no.

There is only one CA (out of the 95 analysed) with teams from Universities or Government Research Organizations (GRO) only and if one adds teams from University Hospitals, we arrive at ten CAs (table 7). These 10 CAs represent only 7% of the total responding population (table 8). All other CAs have clinicians and/or company researchers. Thus in nine cases out of ten we have "heterogeneous" networks with participants from at least three different "worlds" : academic (universities or government research organisms), service (hospitals and/or public authorities), and industry, not forgetting the specific "go between" role of University hospitals.

72 CAs present what could be termed a "public heterogeneity" combining academic institutions, University hospitals and service institutions. They split into three nearly equivalent groups as a function of the relative weight of each type of partner. There are 27 CAs with a majority of academic teams : 7 out of the 12 HSR teams analysed, while at the other extreme only 2 of the 26 BME teams belong to this group. There are also 24 CAs with a clear clinical orientation (over 2/3 of teams coming from service institutions or University Hospitals). They are spread over all subprogrammes with minimum numbers for CANCER and AIDS (only 2 such CAs per subprogramme). The other 21 CAs combine academic and university hospitals teams in equivalent numbers.

Industrial laboratories participate in 13 CAs, a figure that can be considered high considering the uncertainty as to how to deal with them (see file 3). Half these CAs are part of the BME programme while neither the Cancer nor the Epidemiology programme has any industrial participants. In these CAs, industrial laboratories generally represent one member out of ten and they tend to replace

[5] It may be noted that the same picture applies for clinicians in teams with clinicians.

other "service" participants rather than add to them. In 8 of these CAs, Academic teams constitute the bulk of participation.

TABLE 7: COMPOSITION OF CAS

notes: teams from universities, government research organizations and foundations are classified under "academic", teams from hospitals, health services departments and voluntary organizations are classified under "service". The present figures only apply to the 95 CAs which provided at least 5 responses (96% of total responses).

	Only academic teams	Only Public teams with ... academic orientation	mixt orient.	clinical orient.	including a private company	total
Biology	0	4	2	4	2	12
BME	4	2	7	7	6	26
Cancer	1	5	4	2	0	12
Epid.	1	6	5	5	0	17
HSR	2	7	1	4	2	16
Aids	2	3	2	2	3	13
total	10	27	21	24	13	95

TABLE 8: COMPOSITION OF CAS

note: see table 7 for the definition of the different items used in this table.

Types of CAs	total number	distribution of participants acad.	UH	serv.	Ind	(%)	total
total "Academic"	10	58	42	-	-	100	7
"Public" with							
-acad. orient.	27	69	16	15	-	100	16
-mixt orient.	21	42	38	20	-	100	24
-clinic. orient.	24	19	50	31	-	100	29
"with private participation"	13	48	33	11	8	100	24
total	**95**	**45**	**35**	**18**	**2**	**100**	**100**
Biology	12	49	36	14	1	100	18
BME	26	43	41	14	2	100	33
Cancer	12	54	31	15	-	100	12
Epid.	17	35	37	28	-	100	18
HSR	16	41	28	29	2	100	10
Aids	13	57	24	15	4	100	9

25- NEW PARTNERS

Collaborating with other teams is a common feature : 82% collaborate with teams in their own country, 75% with teams from EC countries and 52% with teams from other countries. The major effect of the Concerted Action programmes is thus not to initiate collaborative work but to enlarge its scope and enhance the partnership aspect : in older Actions, the number of partners with which teams

"work" now has doubled since the beginning of the CA (see table 9). The teams' opinion on these relationships are very positive : for most of them, they will result in lasting relationships and enable them to collaborate with the best scientific teams in Europe (see table 10).

TABLE 9 : NEW RELATIONSHIP

	OLD	NEW	
How many teams do you work with directly ?	5,9	9,5	How many teams do you expect to work with ?
How many teams did you work with before ?	2,5	4,5	How many teams do you work with now?

TABLE 10 : OPINIONS ON NETWORKING

Opinions	strongly agree	agree	disagree	strongly disagree
CA will result in lasting relationships	39	54	6	1
CA makes is possible to collaborate with best scientific teams in Europe	37	53	9	1
CA makes it possible to gain a position in the European scientific community	21	59	16	3

Who are these partners? Was a specific question asked for newly created CAs? It gives two complementary items of information on the composition of CAs (see table 11). The first deals with nationality : of the average five new partners they expect to encounter, two will come from their own country, two from other EC countries, one from another country. These figures point up two significant dimensions. CAs foster enlargement both at the national level and at the EC level, showing that MHR also promotes networking activities at the national level. They are also open structures since one new partner out of five will come from "other" countries, mainly COST countries (EC political arrangements seem to play a major role here).

The partnership spread is the second major item of information : new partners split equally between "academic" research (universities and government research organizations), health institutions (hospitals and health services) and university hospitals. As mentioned above, private companies constitute only a marginal proportion of expected partners (nevertheless some 13% in BME actions, reinforcing the feature previously mentioned). However, from one subprogramme to another, there are different emphases. Teams in the Cancer programme focus more on universities and research bodies. In contrast, teams in the Epidemiology and in Health Services Research (HSR) programmes expect to work more with hospitals and health services and, for teams of the Biomedical engineering (BME) programme, university hospitals and industries are of special importance. In all cases, the same factor is underlined : most of the time these new partners come from different institutional origins. One of the specific features of the programme is to attempt to facilitate and even promote encounters between teams otherwise rooted in very different or distant institutional settings.

TABLE 11 : NEW PARTNERS

note : answers to question 20 about new "expected" partners. Only participants in "newly created" concerted actions (less than one year of existence) received this questionnaire (765 answers). The letters relate to the different programmes (see table 8).

1- Country of new partners (average number of expected new partners mentioned) : 1,8 in their own country; 2,2 in other EC countries; and 1,0 outside EC

2- Institutions to which new partners belong

	% of mentions						
	total	B	C	E	H	M	S
"academic" institutions	38	40	49	37	25	33	43
University hospitals	28	32	27	27	21	31	26
"service" institutions	28	24	19	33	51	23	27
Industry	6	4	5	3	3	13	3
	100	100	100	100	100	100	100

First major quantitative result : 9 times out of 10 the make-up of the CA is "heterogeneous". CAs not only bring together academic teams (from universities, government research organizations or foundations), they also heavily involve teams from university hospitals which are both larger, have clinicians and researchers working together and represent 40% of total participation. Nearly one team out of five belongs to a "user" institution : a general hospital (3 times out of 4), a health service department or even a private company (1 CA in 7).
This explains why only 7 teams out of 10 classify research as their main activity and 1 team out of 5 declares no full time researcher. Such figures give an initial idea of both the orientation of the programme (it clearly has a major "clinical" interest) and the dissemination of results : "service" or "industry" teams (this second category being far less important) are directly involved in the production of results which one can suppose they will thus use.

3- INVOLVEMENT OF PARTICIPATING TEAMS

What do concerted actions represent for the participating teams? How much effort is devoted to such actions? What role do these actions play in the teams' European connections? These are some of the main questions we shall try to answer in order to better appreciate the role of the MHR programme.

31- A RECENT COMMITMENT AND MARGINAL EC FUNDING...

For over 90% of the teams, participation in the fourth MHR programme is their first and, in most cases, only link with EC actions (less than 10% of the teams participate in other Community research programmes). These figures contrast with results obtained for French participation overall in cost-shared programmes where half of the teams participate in at least two different research programmes. This recent and limited European connection is confirmed when looking at teams'

funding. Though this question appeared difficult to answer for some teams, more than 1200 teams responded fully, enabling us to get a unique picture of their budget. EC appropriations, which concern a quarter of the teams, represent only 3% of their total funds, half of what they receive from voluntary organisations and four times less than what industrial and pharmaceutical companies provide.

TABLE 12 : TEAMS AVERAGE BUDGET

Sources of funds	% of teams funds	% of teams mentioning such funds
Own resources	35 %	76 %
National public grants	41 %	76 %
Industrial funding	12 %	44 %
Other sources	12 %	
	100 %	
Specification of "other sources" :		
Voluntary organisation	7,4 %	26 %
EC funds	3,1 %	26 %
Other international funds	1,7 %	10 %

32-... COUNTER BALANCED BY SIGNIFICANT HUMAN INVOLVEMENT

For 56% of participating teams, the activity undertaken in the concerted action is considered as "central". This must be set against the fact that members with an active responsibility in CAs are strongly overrepresented : people participating in "Project Management Groups" (PMG) represent 40% of total answers while they make up only 19% of all participants; when asked about their role in the concerted action, only 54% consider themselves as "ordinary" participants and 32% as "special" participants. One must be conscious that this group of some 600 very committed teams boosts most of the following results.

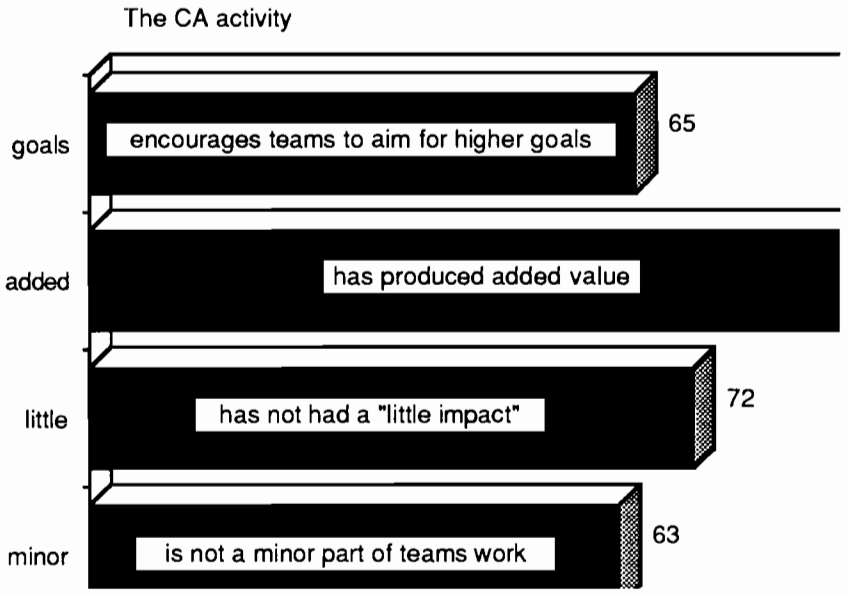
The analysis of concerted actions which have been active for more than one year enables us to assess, by team, the average number of researchers involved in the work of the CA (3,4 researchers) and the extent of their participation (on average 26% of their work). These figures[6], which have been calculated on a very conservative basis, lead us to believe that ***participation in MHR4 mobilizes a fifth of the research capabilities*** of answering teams which, again, are the most active.

A third, converging set of information, namely the opinion of the teams on the qualitative effect of their participation appears very positive overall even though the questions were phrased in such a way as to avoid predetermined results : 63% of them consider that their activity in the CA is more than a minor part of

[6] This figure is obtained through a comparison between the teams size (question 4) and participation in the CAs activities (question 30). There are 2 complementary ways to assess it : direct comparison in term of researchers involved (then nearly half of the research + clinical potentiel is concerned one way or another with the CA) or in term of research capabilities mobilized : which share of the activity is dedicated to CAs related activities. Out of the 650 such "old" teams, 400 have answered this question. Their total answers amount to 4400 researchers/monthes (r/m)while their average number of researcher is 4.6 per team (which multiplied by 12 monthes gives a theoratical capability of 16600 r/m). We thus arrive at a 26% involvement figure.

their research work and, for 72% of them, participation in the CA has had not a little impact on their main research activity.

FIGURE 1 : TEAMS OPINION ABOUT CAS EFFECT



Second major quantitative result : the MHR link is, for nine teams out of ten, their first and only link with EC activities. This explains the very limited share of EC funds in their budget (3%) which depends largely on national grants (over 40%) and to a lesser degree on industry funding (11%) and voluntary organizations (7%). This very limited figure must be contrasted with the importance given by teams to their activities under the umbrella of the concerted action they participate in : it is considered as a "core" activity for more than one team out of two and, for our sample of "older teams" (teams participating in CAs with more than one year of activity), it represents at least a fifth of their activity. This contrast is certainly one of the major quantitative results. It points up one problem which PLs will strongly emphasize (see File 3) : how to coordinate an activity defined within a CA and largely funded by national grants? It also clearly shows that participating teams are already engaged in "downstream" collaboration with industry and service institutions which may create problems when relating to other European teams (see the case of some BME actions, File 2) but which may also be a major advantage for future dissemination (see File 4).

4- TWO CORE ACTIVITIES : DATA CONCSTRUCTION AND CA MANAGEMENT

Is it possible to explain this paradoxical situation which sees a limited funding source, the MHR programme, drain and mobilize a large number of teams? Does it mean that the usual description of concerted action activities - the traditional pattern of scientific exchanges on the basis of workshops and meetings

- might be wrong and give a false image of the nature of CAs? To answer these questions, we have devoted a large part of the questionnaire to better characterizing the activities within the CAs. To get as complete a picture as possible, the questionnaire dealt with 6 complementary aspects : meetings, exchanges, the work of teams within the CAs, networking activities, R&D outputs, potential final users.

We suggested a large range of tasks which can be grouped under five main headings : management of the CA (3 items), preliminary activities (feasibility studies, state of the art : 2 items), data collection (creation of protocols, actual collection, clinical trials, database development and management: 5 items), development and/or management of new collective tools (1 item) and development or assessment of devices (prototypes or softwares : 2 items).

The answers give a very clear picture. CAs are first organized around all the necessary activities to create new sources of information : it is considered to be the first priority by more than 60% of all teams. Depending on how far the CA has advanced, the emphasis shifts from one activity to the other. Creating protocols (mentioned by more than 50% of the teams) is the first priority of one team out of five, while collecting data or conducting clinical trials (nearly all teams mention one or the other) is the first priority of a third of the teams. Almost one in ten of the teams considers its participation in the management of databases and the processing of the data as the first priority.

To these can be added the development or management of a "central" facility (mentioned by one team out of eight), the development or assessment of prototypes (mentioned by one team out of seven) or more often of softwares (mentioned by one team out of five). It is interesting to note that such activities are rarely mentioned as the first priority (probably only by those who do the development) as if they were complementary to comparative data collection or to the analysis of these data (File 2 will describe many such situations).

The enlargement of MHR4 has involved a number of new CAs, some of which are still in their preliminary stages, as shown by the number of teams concerned, at some point, with "feasibility studies" or "state of the art studies" (a third of them) but it is the most important activity only in one case in ten. This may well indicate the length of time involved in the creation process of a CA : we shall in fact see later (File 2) that a number of CAs have devoted their two years funding period under MHR4 to creating a common understanding of the topic they are working on and carrying out all the work (including feasibility studies) required to devise an active collective project.

Creating and managing a CA appears as the second very important dimension in tasks performed. An important feature to note is the sharing of these activities. Almost half the teams have been, are or will be involved in the preparation or organization of a conference or a meeting (see further chapter on meetings and exchanges). However, it is hardly ever considered as a major activity (most of the time ranked in third position). This is not the case of the "organization of the work of the CA" which is mentioned by 40% of teams and is ranked first by one team out of four. This is certainly connected with the bias in our "sample", since we also have 40% of teams which participate in PMGs or "ad hoc" CA committees. Nevertheless, it underlines an important point : to exist and produce, CAs require a significant managerial effort (which File 3 will describe in more detail). This in turn poses another question : is it worthwhile MHR4 funding? The answers lead one to believe that the members envisage a longer duration (and

a renewal of EC support). One is also tempted to consider such activities as an investment in a new infrastructure which is not reflected in buildings and equipment but in organizational and management structures.

TABLE 13 : ACTIVITIES PERFORMED BY TEAMS IN CA

Activity performed	teams mentioning it	teams ranking it as 1st priority
Data collection and analysis		
collection of data	66 %	26 %
creation of protocols	54 %	18 %
clinical trials	33 %	10 %
analysing data	35 %	)
managing data bases	20 %	) 8 %
		62 %
Management		
organisation of CA work	40 %	23 %
organisation of conference	42 %	)
network facilitation	15 %	) 4 %
		27 %
Preliminary studies		
states of the art	24 %	2 %
feasability studie	36 %	9 %
		11 %
Central facilities, softwares and prototypes		
development / management / assessment of ... (mentions only)		
- central facilities	12%	
- prototypes	13%	
- softwares	20%	

CAs devote most of their efforts to the construction of new European sources of information - this is the first priority of six teams out of ten and cover the whole range of activities related to it : creating protocols, conducting clinical trials, collecting and processing data, managing databases; it often requires the development or management of "collective" facilities, the development and assessment of softwares or prototypes. In order to achieve this, major efforts have to be made in the organization of the work of the CA, not only at the Project Leader level, since the burden seems to be largely shared, one in four teams underlining its vital importance for the existence of the CA. This second activity could easily be considered as a long term investment, building a new research infrastructure based not only on "hardware" but also on all the "software" linked to organizational and managerial structures, practices and skills. Such a description takes us far from the traditional academic exchange based on communications of already "codified knowledge".

5- EXCHANGES : FAR MORE THAN MEETINGS AND VISITS

What are the links that the teams establish between themselves? We have already seen that CAs enlarge the network of teams they directly collaborate with. But how do they collaborate? What is the importance of meetings and exchanges/visits? What other forms of exchange take place? Ten questions (representing over 100 coded items) were devoted to defining and rating them. We present here the salient features around three major aspects : the important role of meetings (of all sorts), the importance of visits and exchanges of personnel in establishing collaboration and the growing share of other types of exchange which File 2 will examine in detail.

51- MEETINGS : A COMMON FEATURE OF ALL CONCERTED ACTIONS

The figures here are overwhelming and do not require any comment. Over 80% of teams have participated in general meetings and smaller group meetings. In older actions (started before 1989), teams have participated, on average, in more than three general meetings and more than four smaller group meetings.

TABLE 14 : TEAMS PARTICIPATION IN MEETINGS

	teams participation %	average number of meetings (for "older" CAs only)
general meetings	70%	3.2
smaller group meetings	66%	4.1

Topics of discussion in smaller group meetings : % of teams mentioning		Type of output of these smaller group meetings (for "older" CAs only) : % of teams mentioning	
- present results	59%	- articles	42%
- discuss results in depth	61%	- internal documents	44%
- construct a common tool	39%	- reports	42%
- organize work	53%	- proposed standards	24%
- undertake training courses	20%	- books	25%

52- EXCHANGES : VISITS SUPERSEDED BY OTHER ACTIVITIES

We suggested 11 possibilities for the qualification of exchanges within the CA and, for participants in older actions, we asked them to rank them in order of importance. Some 600 answers relating to these older actions were received (Table 15).

They show that traditional features are still important : visits and exchanges of literature interest 60% of teams. While visits are numerous (three made and three received on average), they are usually short (nine out of ten last less than one week).

But it can also be seen that these types of exchanges represent the first priority in the CA for only 40% of teams. They have been superseded by other types of exchanges. Exchanges of protocols and data, mentioned by an equal number of teams and also ranked as their first priority in 40% of cases, clearly

underline once more the specific role of CAs: harmonizing and gathering relevant scientific information at European level. This is enhanced when more specialized exchanges such as those of samples, reference materials, reagents or software, in total another 20%, are added.

TABLE 15 : EXCHANGES PERFORMED IN "OLDER" CONCERTED ACTIONS

type of exchange	teams mentioning it	teams ranking it as 1st priority
Visits	59 %	19 %
Papers	64 %	20 %
Data	58 %	17 %
Protocols	59 %	22 %
Others	21 %	
	100 %	

Other types of exchanges (mentions only) :	
Researchers	27 %
Samples	25 %
Reference materials & reagents	18 %
Software	20 %

Exchanges tend to confirm what the analysis of activities told us. To build their new European information base, teams must do more than simply exchange results or visit one another. These ingredients are necessary and they explain the numerous meetings of various types the teams participate in; they also account for the visits made or received (mostly short term). However, this is not sufficient : the teams are required to harmonize their methods of collecting data (hence the numerous teams that exchange protocols and to a lesser degree software, reagents or reference materials) before combining the data collected in data bases or banks (hence the major role attributed to the exchange of data and to a lesser degree to samples).

6- RESULTS : MORE THAN ACADEMIC SCIENCE...

The results expected reveal an interesting pattern. To make a comparison of the results expected, we suggested 13 possible items grouped under four headings : new scientific knowledge, methods and instruments for research, methods and instruments for prevention, diagnosis and therapy, commercial results. We asked them to answer yes/no for each item and to rank them in order of importance. Over 1200 complete answers were received to this question. On average, teams mentioned 2,7 items. To analyse the results, we, therefore, have three series of data per item : the number of teams that answered yes, the number of teams that ranked it first, the total number of mentions this item received in the ranking process.

New scientific knowledge was, for example, expected by 72% of teams (answer given : yes), was ranked first by 52% of them, but only represented 24% of all results expected (total mentions). What does this mean? Academic results are

clearly important for the teams and are directly correlated to publications in refereed journals (also mentioned by 72% of them).

Nevertheless, almost half the teams do not consider it as the major output from its participation in the concerted action. Furthermore, 75% of output is aimed at something else. What? Two very different types of output are expected by teams :

- First, building a new basis for research through the production of protocols, standards, reference materials, databases and experimental facilities. These items represent 40% of all expected output even though they are ranked as first priority by only 20% of teams. It is worthwhile noting once more the central role of protocols and databases : 58% of mentions and nearly 70% of first priorities in this heading.

TABLE 16 : EXPECTED ARTICLES AND THESES

	theses	articles in refereed journals
Biology	39%	68%
Cancer	55%	70%
Epidemiology	36%	73%
HSR	44%	77%
BME	43%	74%
Aids	31%	63%
total	**38%**	**72%**

TABLE 17 : OTHER EXPECTED RESULTS

Note : letters refer to the different subprogrammes : B for Biology, C for Cancer, E for Epidemiology, H for Health services research, M for Biomedical engineering and S for Aids (sida in french!)

expected results	total	% of mentions B	C	E	H	M	S	% of first priority
new scientific knowl.	24	25	27	31	24	19	28	52
new methods for res.	40	42	37	38	37	39	42	20
methods of prevention diagnosis and therapy	24	24	21	26	30	24	20	23
commercial results	12	9	15	4	4	18	10	5

- Second, economic and social impacts are focused on clinical aspects. "Methods for prevention, diagnosis and therapy", indeed, constitute a major point of focus : they represent 25% of all mentions and, similarly, are the major expected output for nearly a quarter of the teams. They are equally split between "new" methods and "standardization" of existing methods. This is not the case with commercial results (covering all aspects from patents to new marketable products) which only receive 12% of all mentions and appear to be a rather long term objective since it is the first priority of only 5% of teams. This last aspect is the only major difference between subprogrammes : mentions received vary from 4% (Epidemiology and Health Services Research) to 18% (Cancer and Biomedical engineering).

Going further into the statistical evidence would not give much more information. The above results underline two major phenomena with regard to CA products or outputs. Production of "new" knowledge, which means recognized knowledge (through articles in refereed journals) is a professional necessity without which no researcher can survive for long (even more so in medical research as many bibliometric studies have shown). One is thus not surprised to see more than 70% of teams mention it as a future output. We put the question as to how many articles, and again we got a very stable response from programme to programme (nearly four articles by teams mentioning this output). But we did not ask : on what timescale? A crucial question for assessing the performance of CAs or at least their visibility as the evaluation considered this so important. In the near future? It can be assumed to be the case for the 52% of teams which mention production of "new scientific knowledge" as their first priority. But for the others?

The second phenomenon deals with the other kinds of output. They focus attention on the main directions followed de facto by MHR4 : new "infrastructures" for renewed research programmes, which also means that the path towards social and economic effects is not a short term one and requires further investments; clinical methods rather than products or processes for the health market, which poses the problem of their transfer once they are developed.

7- EXPECTED USERS

Innovation studies have shown than an invention becomes an innovation once it has found a market, i.e. a user ready to buy it. Here we have tried to assess whether teams had any idea of the potential users of the results obtained from CAs. We suggested seven potential types of users, on average the teams selected three.

Recycling of results within the scientific community appears as the first major use mentioned by teams. This will start with the teams themselves : for two thirds of them, these results will be useful for their future work and for a quarter of them, they will be the major users. Other teams in their CA will also benefit in the same proportion, as will other research teams : CA results not only "feed" teams participating in the CA, they are also disseminated (through the abovementioned refereed publications?). Altogether, this recycling of results within the research community is considered as the primary use for more than 50% of the teams. CAs first produce intermediate results to be fed into a further research process.

TABLE 18 : EXPECTED FINAL USERS OF CAS OUTPUT

	teams mentioning this type of user	quoted as the major user
Yourself	65%	28%
Other CA teams	55%	12%
Other research teams	60%	13%
Clinicians	63%	29%
Industry	26%	4%
Gov.departments	29%	10%
others	8%	4%
		100%

However, it also shows that, in one in two cases, the main benefit goes outside the scientific community. Industry, which is cited by a third of the teams (nearly one team in two mentions it in the BME programme) is ranked as the major beneficiary by only a marginal number of teams (less than 5%). Does this mean that the teams see industry as a user only in the long term? Nearly one team in ten considers that the primary users of their results will be government departments : programme bias is at its maximum here with HSR and Epidemiomogy providing twice as much evidence as the other programmes. However, the major non-scientific user is by far the clinicians : they are mentioned by over 60% of teams, a percentage common to all programmes (except for AIDS where this figure is down to 45%) and considered as the primary user by a third of them. Once again, the clinical orientation of MHR is demonstrated.

How do results circulate to the users? What does this recycling process mean and how long will it take to generate socio-economic benefits? How does the hetergeneous composition of CAs affect their dissemination and use? Using a sample of "direct" users of results identified by teams (over 200 of them mentioned such users), we tried an experimental methodology coupling a second very simple questionnaire and interviews. The results are presented in file 4. They show the multiple channels for dissemination, including teaching. They may also indicate that the hetergeneous composition of CAs is a powerful instrument in expanding dissemination, since it seems that privileged channels exist for circulating results : project leaders speaking more to government officials, university teams to industry and university hospitals to clinicians. They also may indicate the existence of an iterative process whereby intermediate results are taken over at the same time by a certain type of user and recycled within the community to start a new process which will produce another set of intermediate results... What is interesting is that the circles so described by users show a change in types of users over time as the Concerted Actions develop.

> *Concerted Actions appear as multifaceted producers which interest more than one type of user at a time. It is clear that CA results are first seen as "intermediate" results to be fed back within the scientific community, not only for the personal use of teams which produce them, but for similar use by other teams in the same CA and in broader terms by other teams to a similar extent : results, however intermediate, should not be confined to the inner circle of the CA but be widely circulated to other research circles. It is not because they are recycled within the scientific community that such results cannot be of use; on the contrary, most teams think that clinicians will be major users of their results and even the primary user for one in three teams. What these figures cannot say relates to the time span involved : will the two kinds of use be simultaneous or successive? The experimental analysis done (see file 4) tends to suggest an iterative process with different types of socio-economic users being involved at different times of the life of Concerted Actions.*

8- SUMMING UP MAJOR RESULTS

81- INTERESTS AND LIMITS OF A MAILED QUESTIONNAIRE

A mailed questionnaire is always a frustrating exercise for two reasons. First, it does not leave room for individual initiative, obliging the respondant to stick to pre-established responses (free spaces are not often filled in and are difficult to process on an equal basis[7]). Secondly, less than half the target population will respond, which means that the conditions of validity have to be very closely examined (which results are significant and which are not). This last exercise obliges the analyst to leave aside many aspects which, of course, are, most of the time, asked for by decision makers. But, on the other hand, it enables quantitative indicators to be established which cannot be assessed by any other method.

This is why, for a project as large as the MHR4 programme, about which, moreover, very different opinions exist, we chose to use this method in order to provide a minimal quantitative basis on participation, involvement, activities and results. We were then faced with a difficult compromise between relevance (enough questions to cover most aspects) and efficiency (make the questionnaire simple enough to maximise chances of return). We may have been wrong in focusing on relevance, asking quite a large number of questions and going into detail with some of them. We are conscious that in doing so we have devised a questionnaire which always had inadequate questions for any particular respondant. We wanted to cover most of the aspects we had picked up through an analysis of the written literature available on the 117 actions, through the numerous interviews carried out with the programme team and through some 30 face-to-face interviews with participants. Looking at the 1421 answers received and comments made, we would certainly change quite a few things in the questionnaire if it were to be done again ....

Nonetheless, we are fairly confident about the general results presented here, since, with a reference population of approximately 3500 teams, the return rate is over the 40% benchmark which is considered as proof of success in this type of exercise. Furthermore, this answering rate does not vary drastically when examined question by question : correctly answered questions amount, on average, to more than 1200 and, even in the worst cases, the figure does not fall below 1000. However, we must not give way to temptation and go too far in the analysis. With an average of 10 answers per CA, we cannot go into any analysis of the CAs and we shall not, for example, be able to cross subprogrammes with another criterion with more than 3 possible answers. This explains why we stick to global results and have gone further only in the qualitiative analysis (based on the 100 interviews done with Project Leaders). Even the overall results are numerous enough to shed a new light on the MHR4 programme and its achievements. We will summarize here the six results which appear to us the most challenging.

82- SIX MAJOR RESULTS WHICH CHARACTERIZE THE EFFECTS OF MHR

1- Even though not all 3500 teams are active, there is at least a core of more than 1000 teams actively involved which makes this programme one of the largest

[7] In fact, these answers are used more to adapt further questionnaires or help in the interpretation rather than as another quantitative source.

EC R&D programmes as far as participation is concerned. This participation is academically orientated and covers a wide range of health institutions : university hospitals represent over a third of participating teams and "service" institutions (health services, general hospitals) add up to another fifth, giving the programme a definite clinical orientation. Furthermore, this diversity is usually directly enshrined in each Concerted Action : *this spectrum of teams involved* constitutes one of the strengths of this programme and prepares the future dissemination of results.

2- Despite the limited financial support from the EC (less than 4% of the total budget), one cannot but be struck by *the size of teams' European involvement* which, on average, represents a fifth of their total scientific activities. This points up a potential problem of coordination with national authorities which, through national grants, provide more than 40% of the teams' average budget.

3- Concerted Actions are often linked with meetings, workshops and visits. This is also the case for the MHR4 programme. But while these three options are extensively used, they do not represent the totality of CA activities. The major focus is on *data collection* with all that implies, first in European *harmonization* (and protocol creation), and then, in "*central facilities*" management (databases but also, and more and more, cell, blood and tissue banks, and even collective facilities in order to provide a service not otherwise available). This means that MHR4 concerted actions not only produce scientific knowledge, they also pave the way for a complete new set of research actions which can be based on this new, unified and homogeneous information. This dimension must be taken into account when looking at results.

4- What exchanges and activities carried out in CAs show, is confirmed by teams when asked about expected results. On the one hand, teams emphasize that research needs to be assessed by colleagues : building up new scientific knowledge and *publishing in refereed journals* are, by far, the most frequently cited expected results (3/4 of all teams). On the other hand, for every other team, it will not be the major output and teams stress that there are other outcomes, three times as numerous as "new scientific knowledge", that spring from their activity.

5- The most important result relates to "*methods and instruments for research*", which clearly contributes to what point 3 underlined : the construction of new research "bases" at the European level. This type of outcome gets most mentions and is ranked by 20% of respondants as the most important one. This goes along with another important feature of the programme : the recycling of results within the scientific community, which constitutes the major expected user, not only because teams within the CA will use them for further work but also, teams think, because other outside research teams, in the same numbers as the CA teams, will also benefit from them. Instruments, methods, software, protocols, databases, fecilities are not only for the internal use of a "private" club, they are for wide dissemination.

6- This does not mean that CAs do not care about socio-economic outcomes. On the contrary, they are mentioned by a large number of teams and considered in nearly one case out of three as the major final result of the CA. Here again, as can be seen from the participation, there is *a clear emphasis on clinical*

dimensions (methods or instruments to prevent, diagnose or cure) : over 60% of teams mention this (divided equally between the development of new methods and the standardization of present methods) and a quarter consider it as the most important result the CA will achieve. Commercial aspects such as new drugs or equipment lag far behind as if they were only long-term prospects. Such results (clinical methods) do not build a traditional market with sellers and buyers. The dissemination of these results may be a concern for the future if the EC does not want its money spent in vain. The hetergeneous composition of CAs shows its full value here : it creates a first opening thanks to the interested users (economists would speak of "lead" users) who participate directly in the production of the results and will presumably be eager to use them.

83- A NEED TO GO FURTHER WIH OTHER INSTRUMENTS.

From this quantitative analysis devolves a major conclusion : while we can characterize global effects, it is difficult, even impossible, to understand how they are produced. Classifications by sub-programme, even if they give some limited clues, do not help to explain the dynamics of such a creation. And we do not have enough results per CA to do any relevant statistical analysis. This obliges the analyst to use complementary methods. Thus, for the term initially considered by the EC (summer 1990), we agreed with the EC management (both from MHR programme and from the Evaluation Unit) to undertake a complementary approach based on in-depth interviews of Project Leaders. The two following files will attempt, through the "eyes" of PLs, to enter the internal dynamics of CAs, testing the main issue we think this file brings forward : are we observing the emergence of a new setting for research work? In order to test this hypothesis, two complementary analyses have been performed : the first (file 2) focuses attention on the different parameters which help in characterizing a CA and which, by combining them in different ways, may lead to the definition of an initial typology of the research "networks" they constitute. The second deals with the organizational and managerial dimensions linked to the creation and development of this new "research setting" (file 3).

ANNEX 1 : METHODOLOGY USED AND PROBLEMS ENCOUNTERED

This annex presents the major choices made for this quantitative study (point1), describes the difficulties we were faced with in identifying relevant participants (point 2) and assesses the responses obtained (point 3).

1- THE CHOICE OF A MAILED QUESTIONNAIRE

The initial question put to us could be phrased as follows : are these Concerted Actions more than an expanded form of scientific meeting where results are exchanged and fresh ideas obtained and, following which, there is no further cooperation and a lone furrow continues to be ploughed? Or is there something different at stake? If so, what? Auditions previously carried out at Project Leader level had not answered any of these questions. The demand as such was for indicators which would help future evaluation panel members[8] to appreciate the effects and role of the MHR programme. Such demand built on two previous exercises, one dealing with an EC cost-shared programme (Non-Nuclear Energy 3) and a recent one dealing with the impacts of all EC cost-shared programmes on the French scientific and technical community. Thus from the start the idea was to address participating teams to assess the importance of their participation and their opinion about the programme and its effects on their activities. In order to avoid pre-sampling, we chose to use the method which had already been successfully used twice (and many more times for other evaluations but with a different approach). We shall not here reproduce all the reasons which explain this choice[9]. We shall simply underline the points with relevance for our study.

11- THE MAIN FOCUS ON "NETWORK CHARACTERIZATION"

The first point deals with limits : a mailed questionnaire only makes it possible to test hypotheses, since it only offers respondants a yes or no answer. Open questions and questions of the "other, please specify" variety are usually very specific : to understand the problems posed by a question (from which the next questionnaire but not the present study will benefit) or to help in the general interpretation. At this second level the use of "opinion questions" (testing the response to ready made sentences) is generally a greater help (especially when trying to make people react through negative forms). To construct a questionnaire, one has to make choices and choose directions. Here things were clear from the start : the focus was on characterization of the "network". EC programmes are supposed to foster collaboration. We had seen in our two previous studies that

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8 Unfortunately, for EC internal reasons, the timing of the MHR panel was moved forward so that panel members had to give their report while questionnaires were still flowing in. They only could get a glimpse at preliminary results.

9 We refer interested readers to a more detailed explanation in P. Laredo & M. Callon (op. cit.) and to a forthcoming article by P. Crance on the subject in "Le management de la recherche, vol1 : les programmes technologiques", Paris, Economica, Autumn 1992.

this is indeed the case, on an even larger scale than most officials thought. So the question was not so much to appreciate the extent of the networks but to characterize what was happening in these networks : with how many teams did participants work? What did "worked with" mean? What activities were carried out? What kind of exchanges took place? Did they only take place during meetings or were there other channels? How much were they involved in? What kind of results were they expecting? The basic questions were, therefore, known at the start of the action.

12- A "COMPLEX" QUESTIONNAIRE

The difficulty lay in the actual construction of the questionnaire and its adaptation to the MHR programme. The usual tools were used for this purpose : documentation (official documents, minutes from meetings, annual reports and proposals from PLs), interviews with Project Leaders. They enabled us to define the "universe" of MHR : different types of activities, exchanges and results. But the spectrum was large and the draft questionnaire had to be enlarged from 4 to 6 pages (nearly doubling the number of questions). This reflected the complexity of the task we were facing as well as our ignorance of the relative importance of the items mentioned. The test conducted on 30 participants did not help much : while agreeing on certain questions, they tended to consider others as irrelevant; but there was no way (apart from minor changes) to make their positions coincide apart from scrapping so many questions that we were back to a two page questionnaire which would have left out all items which might make it possible to "measure" an implication and to describe the nature of the links between teams. This clearly illustrated the need for such an effort to assess the relative weight of the different types of activities, exchanges, etc.

Thus, we did not choose the "simple" solution, but rather took the risk of going for a complete 6 page questionnaire, knowing that we would get a far lower rate of response and even crude remarks about its content. We got the latter but, at the same time, were very much surprised by the final response rate (without using traditional means such as systematic phone calls 3-4 weeks after mailing to ensure an adequate return).

13- A DELIBERATE FOCUS ON "TEAMS"

Another important point that our previous experience has shown up relates to the very different national institutional backgrounds which render comparisons very difficult as soon as one moves beyond the level of the "day-to-day" research group or team. Our notion of a team does not necessarily coincide with an institutional definition : the "team" is the group in which daily activities are carried out and scientific choices made. It thus can vary from one context to the next and requires respondants to make their own decision about what they consider as their team or the team they work with. This major choice always creates problems but at the same time qualitative tests undertaken tend to show that decisions with regard to descriptions, taken "just like that" by respondants, usually corresponded to the actual level of "scientific" decision-making (subjects, directions to follow, external competences needed ...). We therefore decided once more to address this level and focused on the identification of team leaders. Hence the first problems we were faced with (see point 2).

14- TWO COMPLEMENTARY QUESTIONNAIRES

A final point on the situation of MHR4. We had the choice of limiting ourselves to ongoing actions at least one year old (which would take into account only 40% of ongoing actions) or adapting the questionnaire for new CAs. We chose the latter and developed two complementary questionnaires for "old" and "new" concerted actions. They have in common a first section devoted to the characterization of the team (13 questions dealing with their institution, the size of the team, its budget, its current projects and their funding, its current collaboration...), a third section about expected results, future users (in the old questionnaire, participants are asked to give, if they wish, names and addresses of some of these future users) and general opinion questions. As regards involvement, they have in common the description of the CA and their role within this CA as well as common headings dealing with exchanges and activities. These headings are further expanded in the "old" questionnaire to characterize exchanges and to access the teams' involvement, and they are replaced in the "new" questionnaires by questions centred on new collaborating teams. Experience makes it clear that this choice was not entirely satisfactory and that other solutions will have to be found to ensure effective comparability.

2- SELECTION OF CONCERTED ACTIONS AND PARTICIPANTS' IDENTIFICATION

The difficulties encountered in creating a suitable "participants database" have kept us busy for far longer than expected. There were supposed to be around 3000 participants, but after two months of hard work we were faced with a list of over 4000 participants and a clear view of its unsuitable composition. In the end, trying to figure out whom we were addressing and what was the exact "reference" population ended up being the most time-consuming task and delaying the whole exercise.

21- SELECTION OF CAS

Data collection began in October 1989. At the time there was no initial list of CAs and participating teams available[10]. There were two reasons for this : (a) the programme was still in the process of selecting new CAs and many had only recently been selected (June 1989 CGC meeting); (b) the programme had expanded very rapidly and the programme managers had inadequate means, particularly in micro-computing, for dealing with such a large number of people. Thus at this early stage, there were two levels of uncertainty - exactly how many CAs were under way and how many participants were involved. Two devices were used to produce an initial list of participants. First, annual reports submitted by Project Leaders to the Commission were examined. Not all of the reports for the current year were available, so the previous year's report was used. Secondly, the declarations of interest for new CAs were used. For some CAs, no lists at all were available. Second, discussions were held with programme managers (around 20 over a two month period) to obtain data.

The objective of the study was to address the individual named participants in the programme directly to ascertain their actual participation, their assessment

[10] Since, in the first issue of the MHR newsletter (May 1990) was included a complete list of CAs with the title, the name of the Project Leader (and his address) and the number of participating teams split by country of origin

of the outcome and value of the programme. Particular emphasis was to be laid on the nature of the networks built up between participants. Therefore an exercise was conducted with programme managers to produce a database suitable for analysis. "Studies" (dedicated to assessing the interest of a research question) and "preliminary workshops" (dedicated to assessing the potential and interest of a common action) were omitted. All actions that were in the process of selection after October 1989 were also omitted. Table A1 below sets out the relation between the list of CAs recently published by the MHR programme (May 1990) and those CAs taken into account in this study.

TABLE A1 : CAS TAKEN INTO ACCOUNT

note : the actions listed refer to the official EC list published in May 1990, CAs are "newly selected" when they were not yet started at the beginning of autumn 1989, CAs are ranked with no list of participants only when no replies from PLs has been obtained (see further).

	nber of actions listed	actions included in study	reasons for exclusions newly selected	worshops & studies	no list of participants
Cancer	13	12	-	-	1
AIDS	29	25	1	-	3
Biology	17	14	3	-	-
Epid.	19	17	2	-	-
HSR	33	21	8	4	-
BME	30	28	2	-	
total	**141**	**117**	**16**	**4**	**4**

22- GATHERING THE NAMES AND ADDRESSES OF PARTICIPANTS

To gather the participants' names and addresses, we used either the CA's annual reports for "old" actions (more than one year of activity) or the proposal made for newly started actions. All addresses were entered in a "participants database". By mid-December 1989, lists had been obtained for over 100 CAs, but it was clear that there were deficiencies in the information. Therefore a letter was mailed to all Project Leaders asking them to check the entries corresponding to their CA. Less than two-thirds of PLs ever replied to the above request, so that for about one third of CAs, it was impossible to verify the names and addresses before the questionnaire was mailed. Where lists were checked, it was clear that in very few cases was our information completely correct. Many Project Leaders made minor amendments to their lists while some responses involved extensive additions and changes to the database. As a result of this process, a list was compiled which became the sampling frame for the questionnaire. It contained 4321 names.

23- ESTIMATING PARTICIPATION IN THE SURVEY

It is now clear that the process described above failed to identify some scientists who were currently participating in a CA while at the same time others who either had never been participants or who had dropped out were included. This situation reflected the fact that one third of the lists had not been checked

and that estimated participation (especially at the beginning) may not be correct or at least only in different terms from those initially considered. For these reasons it is necessary to reconcile the EC estimates of numbers of participants with the study estimates, i.e. the maximum number of individuals who might be reckoned on to return a questionnaire.

To estimate the latter figure, two adjustments to the gross figure have to be made : 1) an assessment of any over or under-estimation of the number involved in each CA, resulting from participants joining or leaving after the original list was compiled; 2) a correction for participants whose name appears on more than one list. Table A2 to A5 below demonstrate the major differences in the figures derived from the EC document and figures used in the study. In nearly 30% of the CAs (34/117) there are differences in excess of 10%. In 20 CAs the study figures are higher then the EC figures, which suggests that over 600 questionnaires were sent to non-participants. In 14 CAs the study figures are lower than the EC figures suggesting that some 500 participants were missed because their addresses were not obtained. These represent about 13% of the total number of participants estimated in Brussels and they cluster in three sub-programmes : Aids (five actions and 20% of total participation), HSR (five actions and 27% of total participation) and BME (three actions and 13% of total participation).

These considerations led to a "base number" of possible responses to the questionnaire which reflects the missing 500 addresses out of the EC population and removes the addresses for those individuals no longer considered as being in the programme by Project Leaders. A few (about 100) non participants answered the questionnaire, many simply to say they were non participants. They were excluded from the "base number". A further adjustment has to be made before it is possible to estimate the maximum number of replies it is reasonable to expect to the questionnaire. This is for multiple participation. Table A6 below sets the number of participants involved in more than one CA at 260. To obtain the best estimate of the number of different participants in the programme that the questionnaire reached, the "base number" has to be adjusted downwards by 336 (598-262 see Table A6) leaving a final figure of around 3200 (3191 exactly). The picture of a typical CA which this provides is thus a team of 30 participants of which only two participate in a second CA.

TABLE A2 : DIFFERENCES IN THE EC AND STUDY ESTIMATES. ANALYSIS PER CA

note: the difference is the absolute value of EC number minus "study gross number" related to EC number. A percentage higher than 100% means that gross value is more than double of EC value

	total number of CAs	nber of CAs with no significant difference	nber of CAs with differences from 10 to 25%	25 to 50%	50 to 100%	over 100%
BME	28	15	0	4	5	4
Cancer	12	11	0	1	0	0
Biology	14	10	1	1	2	0
Aids	25	17	0	3	3	2
Epid	17	15	0	2	0	0
HSR	21	15	0	3	3	0
total	**117**	**83**	**1**	**14**	**13**	**6**

TABLE A3 : CAS WITH DIFFERENT EC AND STUDY ESTIMATES

note : diffrences are taken into account only when they are "significant", meaning over 10% (see table A2)

	EC higher values	Study gross values higher	total CAs with significant diff.	% on total CAs
BME	3	10	13	46%
Cancer	0	1	1	8%
Biology	1	3	4	28%
Aids	5	3	8	32%
Epid	0	2	2	12%
HSR	5	1	6	29%
total	**14**	**20**	**34**	**29%**

TABLE A4 : EFFECTS OF SIGNIFICANT DIFFERENCES ON PARTICIPANTS DATABASE

note : only 34 CAs taken into account (see table A3)

	Individuals potentially missing		Questionnaires sent to non participants	
	total number	% / EC base	total number	% / EC base
BME	143	13%	387	34%
Cancer	-	-	14	4%
Biology	30	4%	44	6%
Aids	172	29%	68	11%
Epid	-	-	115	18%
HSR	167	27%	11	2%
total	**512**	**13%**	**639**	**16%**

TABLE A5 : NUMBER OF PARTICIPANTS. RECONCILIATION BETWEEN EC AND STUDY BASES

notes : gross number is the maximum number of individuals' addresses collected without any deletion (and therefore number of questionnaires sent); "base number" is the lowest figure between gross and EC figures.

	Gross participation number	EC number	"base number"	number of CAs	average per CA
BME	1435	1143	1025	28	37
Cancer	361	338	330	12	27
Biology	758	724	687	14	49
Aids	527	601	434	25	17
Epid	768	628	621	17	37
HSR	472	620	430	21	20
total	**4321**	**4054**	**3527**	**117**	**30**

TABLE A6 : NUMBER OF PARTICIPANTS INVOLVED IN MORE THAN ONE CA
source : computing from participants database

nber of participants in	2 CAs	3 CAs	4CAs&more	total
total number	210	38	14	262
total participations	**420**	**114**	**64**	**598**

3- ANALYSIS OF RESPONSES

Who answered and what type of analysis can we perform while sticking to the usual statistical rules? These are obligatory questions that any such study must address. In the following paragraphs we insist less on representativity since it has been emphasized in the main text (chapter 1 "relevance") than on the actual content of questionnaire.

31- RESPONSE RATES

Over 1700 answers were received of which 100 dealt with "non-participants" and around 200 were too incomplete to be taken into account. We were thus left with 1421 answers which have been coded and constitute our "sample". What does it represent and what are its biases? We shall now try to present the main points, leaving aside most of the quantitative assessments carried out to verify representativity.

The 1421 answers represent 40% of the total population. It is a good response rate for such questionnaires. But what is its significance? The first difference that can be observed is at the subprogramme level (table A7) : responses represent 34% for AIDS and HSR but 45% for the largest sub-programme BME and 46% for Cancer.

Are these response rates evenly spread over CAs? Not really. First, to be able to profile a CA, a minimum number of responses is required (Table A8). 22 CAs provide fewer than five responses : these 22 CAs only represent 4% of total responses (taking them out brings the total number of responses to 1365). As Table A8 shows, they are not evenly split since 13 are concentrated on AIDS and five on HSR, two subprogrammes with both lower rates and low absolute numbers (under 150 responses). Once these 22 CAs are omitted, the response rate is almost one in two, very near or over the 50% benchmark, and of the CAs under the 30% benchmark, most have very high numbers of participants (maximum noted over 200), which very often provide over 20 answers (we are thus able to obtain a good representative idea of their "core" members). Most CAs are well represented in this sample. While no processing can be done at the individual level, quantitative analyses can be undertaken for suitable groupings.

As we have different questionnaires, how do subgroupings within programmes behave? Firstly it is interesting to note that, although there are 47 "old" and 70 "new" actions, members split equally between both groups, pointing up a feature of some "old" CAs : their very high listed participation (7 with more than 50 participants and 4 with more than 100) and an average difference also due to the impact of the CANCER programme (20 participants on average). Response rates average 37%, varying between 28% (HSR) and 42% for "old" CAs while, for "new" CAs, it averages 43% ranging between 31% (AIDS) and 50%. Again, at the subprogramme level, we face quite large variations which make it impossible to

(6)

work separately on their sub-populations of new and old CAs. We thus chose to work on both populations at the same time, only taking one or the other for more specific analysis on the basis of questions dealt with only within one of the two questionnaires; we were unable to assess answers by subprogramme with a reasonable chance of being representative. Nevertheless, question-by-question comparative analyses have been done to assess variations between "old" and "new" participants. Significant differences are rare (see point 32).

TABLE A7 : ANSWERING RATES PER SUB-PROGRAMME

Sub-programmes	number of teams	answers received	coverage
Biology	687	254	37,0
Biomedical engineering	1025	460	44,9
Cancer	330	153	46,4
Epidemiology	621	256	41,2
Health Services Research	430	149	34,6
AIDS	434	149	34,3
total	**3527**	**1421**	**40,3**

TABLE A8 : ANSWERING RATES AND LEVELS PER CA.

note : though it is not representative, comparative analysis at the CA level has been conducted (for example about their composition).

	number of CAs with					
	< 5 answers	5 to 9 answers	10 to 14 answers	15 to 19 answers	20 and over answers	total CAs
Biology	2	1	3	1	7	14
BME	2	5	7	6	8	28
Cancer	0	3	5	3	1	12
Epid	0	6	4	3	4	17
HSR	5	10	5	1	0	21
AIDS	13	8	2	2	0	25
total	**22**	**33**	**26**	**16**	**20**	**117**

TABLE A9 : ANSWERING RATES FOR THE 95 CAS WITH MORE THAN 5 ANSWERS

notes : percentages refer to the number of treated answers compared to out "base number" (altogether 3500 teams).

	-----answering rates----------				
	<30%	<40%	<50%	>50%	total
Biology	1	3	5	3	12
BME	4	6	5	11	26
Cancer	1	0	6	5	12
Epid	1	2	4	10	17
HSR	4	5	1	6	16
Aids	2	2	3	5	12
total	**13**	**18**	**24**	**40**	**95**

TABLE A10 : "OLD" AND "NEW" CAS, ANSWERING RATES

note : "old" CAs are CAs initiated before 1989 (at least one year of activity when mailed questionnaire was mailed), "new" CAs are those initiatied before Autumn 1989.

	CAs composition			response rate		
	old	new	total	old	new	total
Biology	4	10	14	40%	35%	37%
BME	10	10	28	42%	50%	45%
Cancer	0	12	12	--	46%	46%
Epid	5	12	17	35%	49%	41%
HSR	9	12	21	28%	40%	35%
AIDS	11	14	25	40%	31%	34%
total	**47**	**70**	**117**	**37%**	**43%**	**40%**

32- THE CONTENT OF QUESTIONNAIRES

Our theoretical rate of response for any question is 1421 : 772 for "new" questionnaires and 649 for "old" questionnaires. How did participants respond to the various questions? None of the questions succeeded in getting responses matching the theoretical rate. Tests show "erratic" non-responses. Response rates differ largely as a function of the different sections of the questionnaire.

Section 1 on the teams sees the maximum average response with only 4% of non-responses to questions dealing with institutions and less than 10% for questions about team composition, main activity, collaboration or sources of funds (question 10). Team characterization can be considered as reliable since we did not use the few questions with lower response rates (22% non response in question 3 about budgets for instance).

Section 2 on the "involvement in the concerted action" and section 3 present similar pattern : an average response rate of around 80% (and a total of 300 non-responses). Most questions are thus dealt with on an absolute base of over 1100 responses (in 50% of cases the 1200 benchmark is exceeded). While this rather significant non-response rate is regrettable, the total number of expressed answers still gives a strong base for interpretation. The overall difference between "old" and "new" participants must be emphasized. On meetings, exchanges, tasks performed and expected results, the non-response rate is stable in both cases, but lies at15% for "new" answers and 25% for "old" questionnaires. It is interesting to note that the response structures do not vary significantly, except in a few cases where the total number of responses in each case does not add up to 100. Let us take a few examples of the variations : in tasks performed or to be performed, the first difference only appears with the fourth ranking item : "new" teams cite more "clinical trials" than "old" teams (42% against 28%), for all other items differences are less than 5%. For exchanges, the major differences do not lie in physical or data exchanges which are equally important in both case; "old" participants mention visits more (59% against 43%) while "new" ones focus more on exchanges of researchers (53% against 27%) and even technicians (22% against 11%). As one observer phrased it, newcomers may be more idealistic while older participants may be more pragmatic and realistic! These variations do not change the overall picture and have confirmed our overall approach. Just a note on specific questions used in the two questionnaires : questions on expected partners got the average non-response rate for "new" questionnaires, while questions about involvement

(for "old" participants) only got 400 answers (60% rate). Here the rough total number of answers has to be relied upon and precautions taken to be on the safe side and not overestimate the results obtained.

Overall, response rates have been satisfactory and always provided numerous enough a base for statistical evidence to be gathered from them, at least on the overall level we have employed in processing them. This does omit nearly nine potential results out of ten, and many which team leaders have asked for. But we do not consider them reliable and thus have chosen not to publish them.

FILE 2
CHARACTERIZING CONCERTED ACTIONS AND THEIR DYNAMICS

RESULTS FROM THE INTERVIEWS OF 100 PROJECT LEADERS

D. VINCK & P. LAREDO

JUNE 1991

CONTENTS

Introduction

Part 1 : six complementary approaches to the characterization of a concerted action

Part 2 : characterizing concerted actions

INTRODUCTION

I.WHAT IS THE REASON FOR THIS FILE ?

Why the interest in the various types of concerted actions? There are several reasons which have led us to devote a large part of our work to this question.

1. When the work began, we did not find a clear definition. Two things were certain : the concerted actions do not finance the research activities themselves, and the support provided for seminars and "meetings" is a key element in all of the actions. From the beginning, our few interviews with those responsible for the programme at the Commission and reading of the activity reports and/or proposals showed us that things were not quite so simple. On the one side were "central facilities" and on the other exchanges of materials. We were often far from the classical configuration of scientific interchange, namely peers meeting periodically to discuss their findings. Moreover, this was obvious from the only definition we found of concerted actions, which was so broad as to make it difficult for an outside observer to understand exactly what it meant[1].

The questionnaire sent out to all of the teams (see File 1) confirmed our analysis. The degree of involvement of most of the teams was far greater than normally found in exchanges of scientific findings : for the 1400 or so teams which replied, participation in the MHR4 programme was mobilizing on average one-fifth of their manpower. The eventual results bear little relationship to the kind of results normally expected in the academic world : to the new scientific knowledge, embodied periodically by publications in international journals, must be added numerous other types of results, first among which is the creation of European knowledge bases (a kind of broad platform on which to construct new comparable knowledge). The relationships in which the teams are involved have a variety of forms and are based on numerous material supports developed and used within the framework of concerted actions.

2. So how do we tackle this diversity? The problem did not arise when the programme covered a few actions which could be individually described and analysed (see the first two evaluations). Once over 100 actions are involved the situation changes radically. It is no longer possible to characterize the programme in terms of a sum of individual descriptions. Can it be described by the sum of the subject areas it covers? In some ways this is what the recent evaluation report did to some extent. However, seeing it in these terms raises a number of questions.

The first one is well known : what influence can one hope to have on the dynamics of knowledge as long as one is not financing the research activities? Will the lever effect of European coordination be enough to produce academic results which can be attributed to them?

The second stems from the survey findings : what academic results do you produce when you try to make data collected beforehand in different ways

[1] See supplement to Biomedical and Health Research Newsletter N° 2/90. It should also be noted that this is an "operational" definition concerning the practices actually encountered. See the "organizational aspects" file.

comparable or to construct a collective tool which helps, for example, in DNA sequencing or in carrying out animal tests?

3. This has led us to formulate a twin-track theory. First, concerted actions may only be suitable for dealing with (or at least taking account of) certain types of situation or problem. Secondly these situations fit into a limited number of configurations which all constitute "families" of concerted actions, which can be described. Linking the two should provide us with a tool which can be used both for monitoring (the output and status of the programme) and for strategic thinking (what other fields should be covered in this way). The purpose of this file is to present our conclusions.

II. MODUS OPERANDI AND CONTENT

To make progress on this difficult question, we decided, in agreement with those responsible in DG XII - although this had not been originally planned to enlarge on the information available by means of systematic meetings with the project leaders[2]. These interviews concentrated on a few major questions[3] and were often very complex (many of them lasting over three hours). From them we were able to gather mostly fresh information which placed the results already obtained in perspective. We have used the information in two main ways: to validate the twin-track theory of the role and the dynamics of concerted actions. The organizational aspects of the procedurally innovatory mechanism of CAs are analysed in another specific file.

This file is in four parts. In the first part, taking a particularly striking (but unrepresentative) example, we look at the problem of characterizing concerted actions. How should they be described? What information has to be gathered to be able to assess activity and progress? On the basis of this example we will then be able to look more systematically at the six headings under which the concerted actions can be characterized. We will see that the aims pursued and the results expected are limited in number and, similarly, that there are only a limited number of organizational forms most frequently associated with the actors involved. The richness and diversity of the concerted actions are due above all to the multiplicity of circulating and fixed intermediaries which interconnect the teams and often form the main basis for the organization of new research practices. Concerted actions take a long time to complete and go through a series of key stages. We have identified six stages which make it possible to follow the trajectory of the actions over time, realizing that each stage reflects different forms of association of the participating teams. The third part provides an account of the dynamic forces involved and the principal differentiation factors which we have observed. This leads us, by way of conclusion, to propose a tentative typology of concerted actions in an attempt to establish the relationships between the finalities, the organizational options and the time factor. The result is several families which, from the viewpoint of those responsible for the programme, seem to us to have very differing implications (duration, level of funding, follow-up arrangements).

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[2] More than 100 were visited out of the 120-odd concerted actions in progress in mid-1990. The fact that 15 % or so were not visited was due not to a delibarate choice but to problems of availability of project leaders and distance.

[3] Origin of concerted actions, teams involved, project schedule, main stages, exchanges and meetings, existence of central facilities and/or data bases/banks, rules concerning their operation, organization and logistics of excahnges, the "profile" of the project, progress at the end of the phase currently being financed, role of Community funding, relations with the CEC (programme team, COMAC, etc) and developments proposed.

PART I

SIX COMPLEMENTARY APPROACHES TO THE CHARACTERIZATION OF A CONCERTED ACTION

Rather than approach the subject in an abstract manner we chose to use an example to illustrate the difficulties encountered in describing the goals, the objective, the structure and the progress of a concerted action. This means bringing together a number of different elements which, because of the complementary insights they provide and the interconnections they create, enable us to gain a clearer understanding of what is involved in a given concerted action.

The choices made have been guided by three simple questions. What does this network seek to achieve? With whom is it to be achieved? What steps are to be taken to achieve it? These choices are based on a number of key concepts which have resulted from sociological studies of science.

The first question concerns the **finalities** of the action, i.e. the analysis of the process leading to the definition of the given scientific and technical objective. Between the latter and the socio-political stake, there is a whole series of changes involving a number of scientific, social, doctrinal and political choices which are often implicit. Formalizing this trajectory is the first step in characterizing the concerted action : what are the medical concerns? What links does the action establish between these concerns and the scientific choices made? For us this means distinguishing for each concerted action between the **stake** (or aim), the **goal** and the **objective** (the plural often being necessary even though most of the time the term applies to only one of the levels).

These choices are expressed in a series of concrete results : not just the desired end result, but also all of the results during the course of the action, the **intermediate results** which mark the (desired and actual) progress of the action.

Between words and aspirations on the one hand, and deeds on the other, there are those who act and the way they organize their activities. Concerted actions are based on one clear principle, which might even be called a prerequisite : the actions chosen are selected because the networking of individual actors is seen as the most appropriate way of solving the problem. To describe the networks, we need to know the participants, the actors involved : who are they and what is their involvement with the action? We must also look at how they are interconnected with each other. Earlier work has shown that, when making such an analysis, attention should be paid to the material devices which determine their collective output and which we shall call "**intermediaries**".

The term covers, first and foremost, the supporting mechanisms which form the basis for the interchange within the fabric of the network - exchanges of results, data, samples, etc. (e.g. when deep-frozen samples at - 70°C have to be moved from one point to another within 24 hours). They also include all of the common infrastructures which a concerted action may use and which the MHR (medical and health research) programme (see official presentation) refers to

generically as "centralized facilities" heavy equipment, a central data base, a centre for X-ray analysis, a monkey colony, etc. We shall refer to these as as "fixed intermediaries".

Finally, as in any independent entity, the structure of the concerted action, its management, the rules it adopts and the resources it uses to create its identity and set itself apart are all **organizational dimensions** which provide a measure of the strength of the overall action.

The following example will help to illustrate this approach and to show how it can provide a "standard" description of concerted actions which will facilitate intercomparison, which a recent evaluation of the programme has shown to be the key factor in the analysis. Each characteristic - the finalities, the results, the actors, the fixed and circulating intermediaries, the structure - is based on the example chosen and leads to a number of general conclusions (shown in italics).

1. FINALITIES

The **objective** of the concerted action (CA) chosen, i.e. what has to be done within the time agreed as set out in the proposal accepted, is to make available purified human B cells from the pancreas. These cells have to be tested to find out their characteristics. What do we know about the CA from this single objective?

1. The objective is "to make the cells available", i.e. at the moment they are not available (not yet, not enough, not where they are wanted, not there when they are wanted or not exactly the right kind of cells).

2. We are dealing with B cells, i.e. there are types of cells other than B cells. So why B cells and not others?

3. We are dealing with purified cells, i.e. normally they are not purified. Why are purified cells wanted?

4. We are dealing with human B cells, i.e. there are other types of cells (non-human). Why are human cells wanted?

5. "From the pancreas" means that the CA will in particular involve extracting the cells rather than, say, culturing them. It can be seen from this initial reading that the author of the proposal has made a number of choices. These choices are dictated, on the one hand, by general goal of a higher order and, on the other, by the constraints facing the author of the proposal. The declared objective is thus presented as a translation of a stake which transcends the framework of the CA, namely to use B cell transplants for therapeutic purposes. Let us call this level of finality the **goal.** This is itself part of an even wider purpose : the treatment of insulin-dependent diabetes. Let us call this level of finality the **stake**. There are therefore three different levels :

1. the stake, which is the treatment of insulin-dependent diabetes;

2. the goal, which is to transplant B cells as a therapeutic method;

3. the objective, which is to obtain purified human B cells from the pancreas.

There is not necessarily any link between these three levels, between the stake and the goal or between the goal and the objective. It is not because we want a method for the treatment of diabetes that we are obliged to choose to transplant these cells. To strengthen the interconnection between these two levels certain additional information, notably in the form of reasoned arguments, is needed. From the proposal for the concerted action and the interview we conducted we have learnt that diabetics have a B cell deficiency. Treatment therefore consists in compensating for this deficiency by transplanting new B cells.

Similarly, the translation from the goal to the objective made by the author is based on a series of arguments supported, as is the rule with scientific knowledge, by references to publications and tables of results. What do these tell us?

- In 1975 diabetes research was carried out on islets of Langerhans. These are heterogeneous as far as their cellular composition is concerned. Although most of them are B cells, the fact that a mixture of cells is involved creates a number of problems when interpreting the results. "Nothing can be concluded from heterogeneous tissue". This was the point at which the project leader decided to try to purify the B cells.

- A method of purifying these cells was developed which now makes it possible to obtain purified B cells from rats and pigs.

- Research was carried out on these cells, in particular on the effects of transplants. The results in rats showed that, unlike the islets of Langerhans, the B cells were not rejected. The question exercising researchers now is whether the same results will be obtained on humans and, if not, why not?

- If the results match up to the expectations, the ultimate idea - going beyond the research work - is to treat diabetes by transplanting B cells instead of transplanting the whole pancreas or the islands of Langerhans, which is not very successful.

Through the various stages, we therefore move from "availability of purified B cells" to "treating insulin-dependent diabetes". At the one end, we are dealing with a biology laboratory and, at the other, with a hospital. The author therefore links together, by means of a number of carefully crafted arguments, the laboratory and the hospital. He relates the research work which he wishes to organize as part of the concerted action to other work which, both in time and space, goes beyond that action. In the interview, he told us that he wanted to carry out "clinical research". Although this research primarily concerns research biologists at the moment, in the future it will principally concern surgeons and other clinicians. The stake and the goal are therefore outside the ambit of the concerted action and are in a different time and place, i.e. in the field of clinical medicine.

> *This example shows* ***the series of translations*** *which have to be gone through to pass from the "higher order" general goal to the actual goal of the concerted action. These are the translations which enable us, in a given case, to pass from cells to humans, from the laboratory to the hospital and from purification to treatment. We have described an analytical grid with three complementary levels : the* ***stake*** *is the economico-social problem to be resolved (in this case insulin-dependent diabetes); the* ***goal*** *describes the first translation and proposes a way of resolving the problem (transplantation of B cells) involving research; lastly, the* ***objective*** *determines the scientific and technical choices which are made, namely to extract purified B cells from human pancreases. This example also underlines the need for a formal structure. The links are not compulsory, they are the expression of strategic choices for two main reasons:*
>
> *(a) the translations involved are often indicative of subsequent social organization (in this case, the choice of a cell transplantation as a method of treatment, thus involving a specialized surgical operation and no doubt a complex distribution mechanism);*

> *(b) the scientific and technical options (in this case, to extract cells rather than culture them) will have a bearing on possible subsequent choices (economic studies of technological change clearly show the effect of initial choices made and therefore the differences in the accumulation of knowledge about the possible technological pathways).*

2. THE RESULTS

Looking still at the collection infrastructure, there is one dimension of the scientist's work which is missing. We know that a goal can be interpreted in a number of ways. When scientists say they want B cells, what do they mean? How, specifically, do they want to translate this objective into tangible form? In answering this question, we are moving from the finalities to the results.

What is meant by "making B cells available"? From reading the text of the proposal, it can be seen that, within the framework of the action, it involves setting up a production unit for human B cells and a bank in which to store them. Making them available also means that they will be accessible within a European distribution network. By trying to describe the concerted action in terms of the objective, i.e. what should be achieved at the end of the action, we have already started to look at it in terms of a concrete result : a production unit, a cell bank, a distribution network.

(A) THE END RESULT, THE NETWORKS AND THE SOCIO-ECONOMIC CHOICES INVOLVED

A production unit means that the concerted action will lead to an equipped site, installation, laboratory and team. The project leader says that "a group which does only that kind of work" is needed, that it is "feasible only with a specialized unit", and that there is "no question of duplicating an investment of that kind". To get the desired result major resources are required; "it remains to be seen whether the needs justified the resources". The unit needs a cell bank, i.e. a storage unit for the purified B cells, to permit further interactions without having to start purification all over again.

A production unit and a cell bank also mean an intersection or a point in a network (or subnetwork) which transforms the input (human pancreases) into output (purified, tested B cells). The production unit is not confined to one laboratory since, in order to characterize the cells, it is necessary "to bring together laboratories with complementary expertise". The production unit for "purified, tested B cells" will therefore be a sub-network within which purified B cells, purified and tested B cells and information will circulate.

This result, comprising the production unit and the characterizing sub-network, will be comparable to a centralized facility, a fixed intermediary in a new network. It is therefore not a conventional academic product. Furthermore, the result is an end result in the proper sense since it defines a stable network which continuously transforms human pancreases into B cells to supply researchers' and clinicians' networks.

This example shows that it is difficult and may even be impossible to speak about an end result without mentioning the networks which shape that result. Several other networks, apart from the network characterizing the purified cells, are included in this end result. The existence of a first network has to be assumed in order for the production unit to be able to operate, i.e. a network which drains

the pancreases. It is not mentioned in the results of the concerted action. Perhaps it has yet to be set up. Perhaps it already exists. Perhaps it will be superimposed on the B cell distribution network, in which case the people who send the pancreases will be those who receive the cells. The second network is the B cell distribution network. This has only been outlined, the terminal points of the network have only been vaguely defined (researchers and surgeons) and it has only been described in one direction, the direction taken by the cells. However, it is likely that there will be movement in the opposite direction, the form of which is not spelt out in the proposal. The project leader, however, visualizes the situation clearly : "Hospitals will buy the cells or grafts. This must be self-financing and generate money for research. A centre of this kind cannot be subsidized. The central unit must be paid for its products, but not for its existence as an institution. However, it must remain supervised by researchers and clinicians. There is no question of it being private. There are firms interested (in funding) but they want to fix the cost of the grafts. That firms should make a profit out of donors' cells is out of the question. This is ethically unacceptable." The project leader therefore turned down the private offers made and said he would even have refused them if there had been no money from the EC or Belgium. The similarity of views or of doctrine between the actors involved has led some of them (doctors) to join forces and line up against other actors involved (industry). In so doing, they make choices and produce standards which make some groupings easier and rule out others. Their joining together and the creation of a network therefore cannot be explained as a rational step taken on the basis of the objectives and results to be attained. The setting up of the network also involves the production of more or less explicit standards which shape the interactions.

> *The end result is therefore not only a scientific and technical result (being able to purify B cells which produce insulin), but also an operational device bringing a large number of actors together in a durable arrangement (what sociologists call a stable, "punctualised" network). Lastly, it is the vehicle for a specific social and economic organization of the health care system which will result from the concerted action if it is successful. The combination of the goal and end result therefore reveals both a scientific and a social side to the concerted action. In the second part, we shall see that this duality builds a limited number of typical situations.*

(B) INTERMEDIATE RESULTS : WAY-MARKERS ALONG THE PATH OF CONCERTED ACTIONS

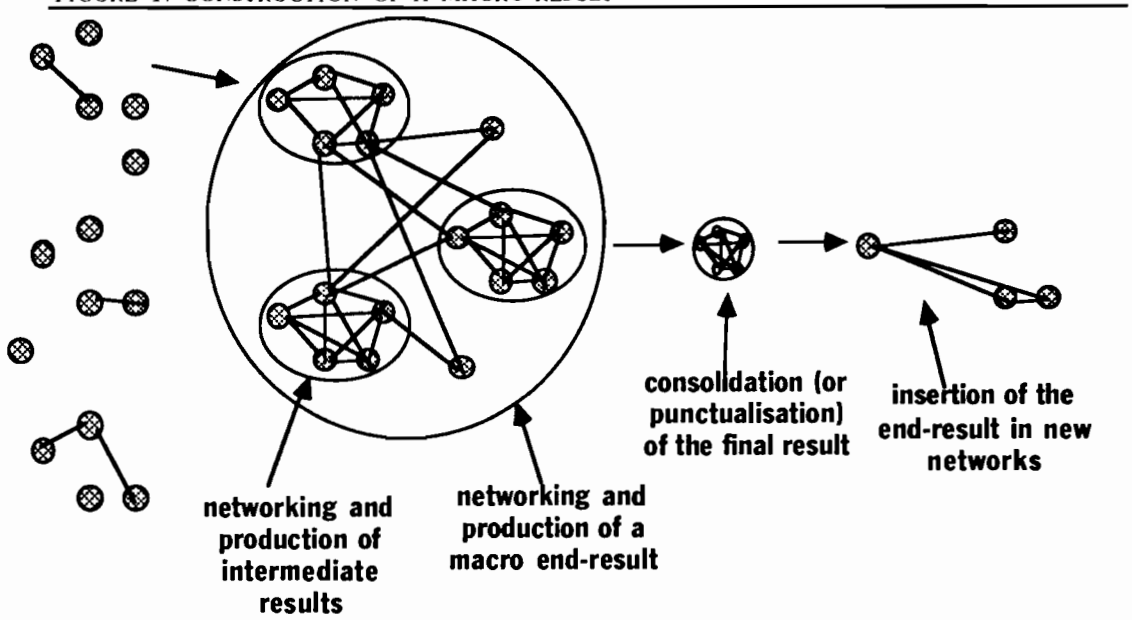
We have talked at length about the final result but said very little about the intermediate results. By contrast, these stand out like markers for the stages leading towards the construction of the final stabilized network. For example, the day on which the human B cells have been purified represents at the same time an intermediate result, a strengthening of the network and a marker in time. It will be the same when human B cells will be purified and characterized, especially B cells which actually produce insulin. A further intermediate result will be B cells which can be stored without deterioration. The B cells produced will be used. A action will test them on 50 patients. If the results obtained convince the researchers and clinicians, the network will be strengthened. They will also be distributed to scientific teams : "after five years, even if it does not work, there will be so many

actions in progress that a great deal of knowledge will have been generated". The action therefore has a guiding thread, but at the same time the very existence of the centralized facility will make it possible to perform a number of scientific and technical tasks which may also lead to other results. The purified B cells may very well have effects other than those expected.

> *This example seems to teach us a clear lesson. An objective may be attained in a variety of ways and analysis of the anticipated results makes it possible to analyze the one chosen, in this case obtaining cells not by culturing them but by extracting them. However, it is not enough for us just to look at the result. Attention has to be paid to the series of (expected and actual)* ***intermediate results*** *along the (forecast or actual) path of the concerted action. The intermediate results are milestones in the life of the network and mark the translation from one stage to another (for example, common terminology, followed by a data collection protocol and the corresponding forms, a data entry software, completed forms, a data base, raw results, a scientific publication, etc.). These markers act in two ways.*
>
> *First, the intermediate results often reveal a change in the state of the network (for example, until there is a protocol only a small number of teams are able to communicate. Once it has been written and distributed, the network may change in size and involve a number of partners who were previously excluded simply because their approach to the problem on which they were all working was different).*
>
> *Secondly, they build the time-frame of the network. Each result creates a "before and after" situation (standard example : the availability of purified B cells). On the one hand it is a culminating point which is the tangible expression of the agreement between the teams involved (a product, a protocol, an item of equipment, an article, etc.) and thus consolidates that agreement (the result, in a sense, "speaks" for all the teams involved in producing it). Yet, on the other hand it is also a new point of departure : it limits the scope for action, e.g. once a protocol has been accepted there are no longer 101 different ways to describe the object to which it relates, and it opens up new perspectives enabling those concerned to make intercomparisons which they were unable to make before. Of course, those involved have to grasp these opportunities, which is far from always being the case. A protocol published in a scientific magazine, however international and respected it may be, will be ineffectual if matters are left at that and, after its publication, the concerted action dissolves and the people involved each go their own separate ways. An adopted protocol, on the other hand, (aside from the fact that those who drafted it can be forgotten, which is typical of a consolidated network) creates a new network and a further stage in the life of the action.*
>
> *Each intermediate result helps in this way to test the strength of the concerted action, to make it more "irreversible" as economists would say. It can even be argued that the larger the series of tests, the more consistent the final result is likely to be, i.e. the more likely it is to be supported by a larger number of actors who endorse and make use of it. Identification of the intermediate results therefore makes it possible to*

follow the progress of a concerted action and to characterize its dynamics. Figure 1 illustrates this. Is it possible to find common types of pathway behind the infinite variety of intermediate results? The third part of this file will attempt to show that, once again, the number of stages, like the possible number of groupings, is limited.

FIGURE 1. CONSTRUCTION OF A MACRO-RESULT



3. THE ACTORS INVOLVED

Although we have a clearer idea of the shape of the concerted action, we know only a certain amount about the actors involved. What does the action mean for the project leader and his team? How many clinicians have agreed to remove pancreases and how are they integrated into the action? Who are the teams which will be performing the cell characterization? Which research groups are interested in B cells? It is essential to know who is taking part and the nature of their actual involvement in order to assess the feasibility of the action as described in terms of its general goals and results.

Let us begin with our main informant, the **project leader**. He is a doctor. After leaving the Medical Faculty, he went into research in the field of pancreatic cells, concentrating on basic research, in particular in the USA. He wanted to do clinical research. After returning to Belgium in 1975, he was frustrated by the fact that all research was carried out on islets of Langerhans, which have heterogeneous cells, and wanted to purify the B cells. The Belgian National Scientific Research Fund (FNRS) provided financial backing for his action, since at that time there was no method for the purification of such cells. In this way he received funding over a number of years without having to publish anything. Furthermore, the university to which he belonged had just moved to a new campus and a fully equipped laboratory had been built for his work. In the beginning the project leader was alone. Later on a few colleagues joined him. Now he has a large team of researchers and a method for the purification of the cells from pigs and rats. He manages a

number of research actions and cooperation schemes. In sum, as a doctor and a researcher he has been working on the subject of the CA for a long time. The CA occupies a central position in his research work. He has set up a laboratory and developed a method for rat B cells. He wants to do the same using human B cells. He understands the constraints involved in making this translation.

He has a **team** of 40. Two-thirds of the staff in his department are paid by the diabetology service and one-third by the pathology and biochemistry services. It is therefore a large team of biologists and in particular of doctors closely associated with clinical practice. They work mainly on B cells and have accumulated considerable expertise. The subject of the concerted action is therefore the team's main preoccupation. To avoid slippage, the project leader has decided to make a clear distinction between research and production : eight part-time staff have been taken on in the central unit for the purification of the human B cells.

The characterization and research teams : the project leader has mobilized various laboratories to characterize the cells and ensure quality control. These laboratories have specific, complementary responsibilities (molecular biology, immunology, etc.). He had to make these choices when recruiting the teams. He wanted to avoid the action becoming political and the teams competing. The question was whether it would be better to include strong teams, which would make it easier to obtain funds, or teams which worked well together. He opted for the latter, co-opting approach. On this basis he set up the project management group (PMG), through which he invited the teams which had responded (in particular those who had pulled political levers) to put forward research proposals. The research projects were selected by the PMG on the basis of two criteria, complementarity (seeking to divide up responsibilities) and the human clinical goal (not "pure research" but rather projects with a therapeutic objective). There was also a third criterion : the funds which the teams themselves had available. For the teams in southern Europe, the constraints imposed by the Commission led the PMG to adopt a specific mechanism, namely the proposal of training grants for outstanding, promising young research workers, excluding prominent diabetologists who were already established but whose laboratories did not have the dynamism the PMG was looking for. The concerted action is currently assisting young research workers in Greece, Italy and Spain to set up a high-standard laboratory in each of their countries (in Spain, the government has agreed to fund a laboratory as a member of the concerted action). The network of research teams involved in the action is therefore evolving continuously, with recruiting arrangements which have to adapt to the different national circumstances.

The surgeons : the Central Unit needs pancreases for the extraction and purification of the B cells. It therefore needs a network of surgeons to remove the organs from the deceased donors. Surgeons are used to removing pancreases, but normally they are for transplantation in patients who need them. It was therefore necessary to recruit a sufficient number of surgeons who would agree to donate pancreases to the research to be carried out under the concerted action over a period of five years. The project leader was afraid that surgeons would not go along with this because, in his words, "they think short term". He felt that surgeons would resent the project as being competition for the organs. In the event, there seemed to be enough pancreases and, since the results of pancreas implantation are not very good, clinicians prefer to look to clinical research for a solution. The search for surgeons is carried out by research laboratories taking part in the

project and are often attached to hospitals. There has therefore been a shift in and a strengthening of ties : the surgeons associated with the concerted action were already to some extent linked locally to the laboratories participating in the project.

The organ transfer network managers : a further group of actors is involved in the concerted action although it is not a member. These are the companies which run the transfer networks for human organs intended for transplantation, Eurotransplant, Francetransplant and Scanditransplant. These companies have set up systems to transfer organs from one hospital to another swiftly and safely, with centralization of supply and demand, training of specialized personnel, the availability of specialized equipment, organization of the transfers and coordination of the means of transport, etc. These networks are clinical only. However, they agreed to accept full responsibility for the transfer of organs, from surgical removal in a hospital to delivery to the central unit for the extraction and purification of the B cells. In so doing they add another purpose : the recipients are no longer only surgeons and the objective is no longer directly clinical. It involves clinical research, the outcome of which at best can be expected only in the medium term (in three to five years). This decision forms part of a wider development since, looking ahead to the expansion of grafts and cell exchanges, Eurotransplant has set up a specialized subsidiary (BIS) which already has developped bone-cell and cornea banks. This subsidiary will be responsible for the transfer of the B cells if the project is successful. The involvement of Eurotransplant underpins the laboratory work in progress and makes it into a strategic operation.

The sources of funds : researchers, surgeons and transfer network managers are not the only actors involved in the concerted action. Without the various agencies which fund the work of the CA in its various forms there would be no network and no B cells. First, there is the Commission (more specifically, the members of COMAC Biology who select projects for the Medical and Health Research Programme), which is funding one-third of the expenditure of the central unit. Then there are the Belgian Scientific Policy Programming Services which are providing a further third of the funds. The involvement of the latter is dependent on that of the former and vice versa: it was thanks to the money raised in Belgium during the years preceding the concerted action that the project leader was able to involve COMAC Biology, but it was also because the project was accepted by the Commission that the Belgian Scientific Policy Programming Services continued to provide funds.

In addition to these two sources of funds, the members of the concerted action have been able to raise funds in three other countries to cover the remaining third of the central unit's operating costs. The Eurotransplant network is covering its own transport costs and is also paying the hospitals around ECU 200 for each pancreas removed for the project. The project leader's university has made a site for the construction of the central unit (a sterile laboratory) available at no cost and the building work has been partly financed by donations. Lastly, there are grants provided by the Belgian National Scientific Research Fund for young researchers to come and train at the central unit. This situation is exemplary. It is because of the mechanism underlying concerted actions that the project leader himself has to organize these complex multi-source financing arrangements. The project therefore depends in part on the objectives and strategies of the various providers of funds. Although the Commission often acts as initiator, the method

of funding chosen often means that those involved in the concerted action are obliged to look for sources of funding other than internal ones for the research work associated with the project (work which very largely depends on their own priorities, as the quantitative survey has shown).

> *There are therefore a large number of actors involved, far more than tend to be allowed for in the proposal. They play different roles with differing degrees of involvement so treating them all in the same way e.g. by simply counting the total number, does not help in understanding the dynamics of a concerted action. There are two main lessons to be learnt from the analyses we have carried out :*
> *- The first concerns the* ***project leaders*** *: the life of the concerted action and even the possibility of setting up a network often depends on them. The CA must therefore be a major priority of the scientific and medical work in which the person who is made project leader is engaged. But this is not enough. The requirements are such that it is often essential for the project leader's research team to be closely involved. The existence of a structured research team associated with the project leader and having the same interests is therefore a second aspect to be taken into consideration.*
> *- The second lesson concerns the various categories of people involved. The concept of members and observers does not really reflect the nature of the involvement. There are many different kinds of involvement : on the one hand, there are* ***"special" members*** *who carry out specialized scientific work and need a special link with the project leader (in this case it is characterizing cells, in another project it may be setting up a data base, making phantoms but also taking part in a facility's* ad hoc *committee or acting as subject experts). On the other hand, there are the* ***suppliers*** *who agree to contribute now in order to secure results which will be useful for them later (in this case the suppliers of the pancreases, in others it will be those completing forms, providers of clinical cases, etc.). Usually there are no direct links between them. Everything goes via the project leader who may have to delegate by taking on* ***"correspondents"****, thereby introducing a third category of people involved - "national" correspondents who are often dedicated to monitoring the clinicians and practitioners who supply the data, and the "thematic" correspondents, who are often known as project co-leaders or sub-leaders. This division is often linked with the main activity of the participants (research, clinical work, medical practice) and the institution in which they work (research body, university, university hospital, general hospital, health care service, etc.). To these must be added all of the* ***actors with a logistical input****, such as the organ transfer companies specialized in the preparation and organization of exchanges, and the* ***direct potential users*** *who provide technical support as they are interested in the results of the project (typically the equipment supply industry). As they will be actively involved in future in distributing the results and in organizing the stages of the work after the concerted action has been completed, their role becomes especially important as the final phase approaches.*

Concerted actions rarely resemble meetings of peers at scientific colloquia. Most of the time the partners in such actions are ***heterogeneous*** *in terms of their main activities, their interests and their involvement. CA members reflect the whole gamut of experience from the most academic of research to the situations closest to the "market" and users, and include a large number of "prescribers", i.e. GPs, clinicians and surgeons. Paradoxically, it is the very richness of this mix which guarantees the future dissemination of the results. The more uniform the composition of the CA, the less chance the project will have of breaking out of its traditional sphere of activity and the less likely it is that innovation will result. This is ultimately the conclusion suggested by our work, showing once again that concerted actions are still a long way removed from the image of the 'laboratory without walls' which some would like them to be (and thus cannot be judged by the same academic criteria).*

4. FIXED INTERMEDIARIES

We have looked in turn at the finalities, the results and the actors involved, emphasizing in each case the importance of the exchange mechanisms. The example chosen is a good illustration and, even if not all concerted actions have this configuration, they are no less dependent on the movement of materials, information and people. The arrangements agreed on and the people to carry them out shape the action and are often the only material dimension specific to it. In our example, there are two different mechanisms involved - the materials (pancreases, B cells, etc.) and the circulation of information. However, the central feature of the exchange structure is the Central Unit in which the cells are extracted and purified. We shall call this a fixed intermediary. It is an intermediary because it serves as a means of bringing the actors - researchers and satellite laboratories, surgeons and organ transfer networks, funding agencies - together and because it provides spatial orientation for the networks. It is fixed because, unlike other intermediaries such as the B cells, it does not move and it is therefore the actors who have to move.

What is this Central Unit? We already know part of the answer. It is where the pancreases are transformed into purified B cells, the central node of the pancreas transfer networks, the project leader's laboratory, a specialized, equipped laboratory with an experienced research team. It is an expensive laboratory. "There is no question of duplicating this kind of investment", explains the project leader, mentioning the agreement concluded with the Canadians on the exchange of cells (the latter are to build an equivalent laboratory only if the project is successful). The laboratory is built in the university grounds near the teaching hospital. It is in fact a completely new, sterile laboratory (entrance chamber, special floor and wall coverings, etc.) which is well equipped in particular with special laminar flow hoods, an impressive array of microscopes and binoculars, and deep-freezes and centrifuges. The research workers wear medical gowns, caps, masks and special footwear.

"The purification of human B cells is a major logistical operation in terms of manpower and finance. It was not feasible without a critical mass of researchers and doctors. So everyone in the laboratory has to work on B cells to make the operation profitable." The Central Unit can therefore be likened to an item of

heavy equipment which, as in physics, partly structures the research work : "everyone has to work on B cells". The project leader has nevertheless taken care to distinguish in his laboratory between the tasks of his research laboratory and those of the Central Unit : "logistics and research applications are two separate things".

There are eight people working part-time in the Central Unit on the logistics side, several of whom are also doing research projects for their thesis. The laboratory works 18 hours a day in two teams and seven days a week. To work 24 hours a day, three teams would have been needed. The laboratory is structured according to the work stages, from receipt of the pancreases, their dissection, and breakdown of the encapsulated groups of cells by trypsin and another enzyme, to separation using a cell counter.

The centrepiece of the laboratory is the very piece of equipment which was modified by the team more than ten years ago to separate B cells from others. In the beginning, the cells were identified by means of a specific antigen-antibody reaction of the B cells using a fluorescent marker. The problem then was separation of the antibody from the antigen. They therefore tried to find an alternative : some constituents of B cells are naturally fluorescent and that reaction can be specifically coupled in the case of the B cells with metabolism of the glucose. They therefore kill two birds with one stone. They separate the B cells from the others without having to use immunological reactions and also avoid the subsequent step of separating the antibody. Furthermore, only the cells which react with the glucose - this being essential in view of their function after transplantation as regulators of the blood sugar level - are identified and separated by the cell counter.

> *In attempting to describe the Central Unit, we have passed through several stages which in our view characterize the "fixed intermediaries", of which there are a growing number within the MHR programme.*
> *- The team's expertise (extracting and purifying B cells) is translated into a process and equipment which are peculiar to it (or at least are difficult to obtain). Once a laboratory has been equipped, interest in a second facility diminishes considerably, at least until results have been obtained and the validity of the therapeutic method has been proven (see the position of Canada in this respect).*
> *- The centralized facility is more than the sum of its equipment or even of its logistical operations (which involve eight people). It only becomes meaningful if it involves the whole team. This ties in with what was said in relation to the project leaders' team. The situation is always the same, whether we are dealing with DNA sequencing, monkey colonies or BNCT (boron neutron capture therapy). There is a similarity across the board in the funding of the facility. The concerted action only funds part of it, often a small part.*
> *- Fixed intermediaries tend to polarize the organization of the concerted action. Everything has to relate back to them, in this case to carry out extraction, in others to standardize (processing of X-ray plates, analyses, etc.), for gathering (like the numerous data bases), to carry out tests (especially in the case of animal colonies) and to obtain suitable material (for example, transgenic rats), or to carry out treatment (cf. BNCT). The effects differ according to the functions to be carried out and the size of*

the facility needed : large-scale equipment such as BNCT or a "large-number of cases" data bank have a greater structuring and even constraining effect on participants than "small" items of equipment, such as a plate analyser, the main function of which is to ensure the intercomparability of one of the elements used to characterize a series of clinical cases. Similarly, some facilities provide researchers with a tool optimally suited to their work (saving them time, etc.) without directly affecting their projects e.g. monkey colonies, the AIDS virus sequencing laboratory, etc. Like CERN, their ad hoc *committees for experiments and their practices (for the acceptance of the material, for publications) help to standardize and give direction to the activities of a scientific community. Lastly, there are other facilities designed to have broader effects not confined to the members or the time-frame of the concerted action itself, namely to inform practitioners, carry out surveillance, etc. The wealth of contents and the number of examples have led us to propose, in the second part, illustrations of the four main types of fixed intermediary.*

- The last characteristic is the long time-scale applicable to a centralized facility. First, there is the time needed for designing it (though this is often outside the concerted action, pre-dates it or is a resource on which it capitalizes for its creation), then the time for building it (in the case of many CAs, this phase will just have been completed by the date specified for its completion), but above all it is the utilization of the facility which alone is able to produce the desired effects and makes the project leaders organize themselves "as though" the concerted action were going to continue over a longer period. Similarly, a number of facilities, in particular those associated with data bases and surveillance networks, tend to remain in place once their reliability and usefulness have been proven. Like the B cell purification unit, they are then no longer subject to the research funding process. How can it be ensured that the Community investment will not vanish into thin air? This, as we shall see, is one of major problems in the current organization of the programme.

5. CIRCULATING INTERMEDIARIES

The second, highly heterogeneous group of intermediaries are exchanges. In our example, earlier descriptions referred to several different types of exchanges, each of them resulting in different forms of involvement on the part of the co-exchanging teams. Similarly, the directionality of the exchanges (from all points to one, from all to all, etc.) provides a specific understanding of the structure of the CA and the durability of the links which are created (occasionally supplying a pancreas is not the same as depending on purified B cells to carry out research). Furthermore, in many concerted actions the material organization of the exchanges, their logistics, is the only area in which the CA has a specific financial involvement. Exchanges therefore determine the consistency of the network, so it is important to be fully familiar with them.

Let us take the example of the **pancreases** which move between the surgeons and the Central Unit. Normally, these only move between surgeons - the surgeon who removes the organ from a deceased donor and the one who

transplants it into a living recipient. In this CA, there is a deflection of part of the flow of pancreases exchanged. To make this deflection possible, it was necessary to convince the surgeons removing the organs. The argument is that in exchange for the pancreases they will, later on, receive **preparations for implants** of purified B cells initially for clinical tests and then for patient care. The problem was to motivate surgeons to provide pancreases over a period of five years without any return of implants during that period. "It is a mammoth task." The surgeons see nothing of the action except for some **information** about its progress. The project leader was also afraid that the surgeons would not go along with it, but "they understood and are motivated". The Central Unit receives about three pancreases a week.

It must be emphasized at this point that the exchange works both ways. For each organ donated, there is a counter-donation, for each exchange a counter-exchange, information and transplants in exchange for pancreases. However, the exchange and the counter-exchange are not simultaneous : pancreases are supplied now in return for information on the progress of the project a few months hence and transplants in three to five years if all goes well. Furthermore, the *quid pro quo* is general not individual. All the surgeons who have agreed to supply pancreases wherever possible will receive information, and that includes those who have not actually sent any organs. Similarly, it is not only the surgeons who supply the pancreases now who will receive the transplants in the future since the objective is to provide a new method of care for everyone. However, those who participate now do have one advantage : they can be associated with the clinical tests as soon as the transplant preparations are available. These exchange and counter-exchange arrangements are essential to stabilizing the relationships between teams and the network as a whole. "The teams receive something in exchange for what they give, otherwise it will not work", said the project leader.

In order for the exchange to take place, it has to be organized. For the pancreases, the CA uses the existing organ transfer companies. Their organization is such that they may be considered to be "black boxes" responsible for all liaison between the surgeons and the Central Unit. They are considered to be a reliable and even a transparent relay mechanism, but are they just conveyor belts? Far from it. For example, some of these companies offer the surgeons a modest sum (ECU 200) for each pancreas intended for the Central Unit, whereas one of the networks (Francetransplant) feels this is not necessary. Similarly, one may ask who decides when to divert some of the organs to the Central Unit. Does the surgeon decide alone or does he let the organ transfer network managers decide, as they have to balance supply and demand? Like the person providing the finance, the person organizing exchanges often plays an important part in a concerted action. Is it conceivable that the CA would not use the pancreas collection network to distribute the purified cells? The system used for the research operation predetermines the system that will be used in the future for the therapeutic activities.

Information is channelled back to the surgeons through local meetings. Two are held each year in Belgium to report on progress. Each country is required to organize the same type of feedback. There is a coordinator in each country and the national coordinators meet once a year. A newsletter is also sent out twice a year. This contains information on the work and serves as a letterbox for the members of the CA.

Outgoing, therefore, the form of the network is as follows : surgeons in various European countries > organ transfer networks > Central Unit. Incoming : Central Unit + PMG + CA members > national coordinators > local surgeons. The outgoing and incoming flows do not follow the same paths, chiefly because the items being carried are different. If the future incoming flow is added to this, we get : Central Unit > cell transfer network (BIS) > surgeons. When you change a circulating intermediary you change the path and the mediator.

A number of other exchanges take place within the framework of this CA, in particular the exchanges of **purified cells** between laboratories which have complementary expertise. We will not dwell on these in detail but simply point out two important aspects associated with them. First, the importance of the meetings and visits which enable results and techniques to be exchanged; this, in fact, is the only apparent cost to the CA. Secondly, in exchange for their contribution to the CA, the satellite teams receive (rat or pig) cells for their own research. The Central Unit takes responsibility for and organizes the transport (the transport arrangements are the same as for other types of cell : B cells simply require a suitable culture medium to maintain them for 10 to 12 hours). This process of active involvement is a basic feature in the dynamics of concerted actions : the teams need to have a feedback. Another illustration : some surgeons who send in human pancreases for the CA also have diabetic pigs for their own research purposes. They therefore supply the Central Unit with diabetic pig pancreases. Outside of the official CA, the Central Unit extracts the B cells from them, purifies them and returns them for the surgeons' own research purposes. This obviously does not come out in the CA report. It is in fact a form of feedback to those who are cooperating by supplying pancreases which is necessary to keep the exchange going.

> *The above example shows the extent to which details of the movement of intermediaries determine and affect the kind of interaction between the teams. During the 100 or so interviews carried out, we were able to measure the amount of time devoted to the management and organization of these exchanges. For a number of project leaders, the success of their project depends on these* ***technical and methodological "details"*** *which often constitute the most important strategic dimension of the CA. Following the paths of the moving intermediaries reveals the actors involved and the nature, intensity and strength of their relationships.*
>
> *This example also underlines a further dimension of the interaction created by the exchange : for each exchange (of pancreases, cells, information, etc.) there is a corresponding* ***counter-exchange*** *(even if it takes place later). As the project leader stressed: "There has to be a quid pro quo". This is the symmetrical basis on which CAs are built and which strengthens them. This state of affairs is often underestimated, in our view, in the creation of concerted actions which involve "suppliers" of material and cases and people who fill in forms.*
>
> *There are many types of moving intermediary. We have pinpointed* ***three main types of exchanges*** *: people, documents and materials. These represent three radically different situations : on the one hand, an exchange of representations of the object or the problem (data, results, etc.), on the other, movement of the objects themselves or portions considered to be representative (samples, cells, animals or even patients).*

Lastly, very often to compare these objects or representations, materials designed to standardize practices (equipment, reagents, software, "phantoms" and protocols) are used. The frequency of some of them has led us, as with the fixed intermediaries, to look specifically at two intermediaries which are common to all CAs : workshops and meetings and annual reports. Exchanges of samples, reference materials, phantom animals and patients will be illustrated by means of examples. Lastly, in view of their growing importance, particular reference will be made to exchanges of forms, illustrated by detailed analysis of a clinical protocol.

6. FORMS OF COORDINATION AND STRUCTURING OF THE CA

Finalities, results, actors, facilities and exchanges : each point has given us a better understanding and a clearer characterization of the concerted action under review. Organization of the scientific work and the network research involves the gathering and processing of texts and research results, the formulation of arguments, the choice of collaborators and their motivation, the organization of exchanges and counter-exchanges, the creation of laboratories and dynamic teams, etc. It has to be recognized that all of the details count and that project leaders devote considerable time to administering them. But how do they go about this?

In the example chosen, several features of this organization have appeared : (a) there is obviously an agreement between the organ transfer companies and the CA which provides a framework for relations between the Central Unit and the surgeons; (b) national correspondents have been appointed to report to surgeons on the progress of the action; (c) the project management group (PMG), the setting up of which is required by the MHR programme, is responsible for selecting the research teams which will receive the B cells; (d) a special procedure has been developed to incorporate teams from the southern European countries. An agreement, a team selection procedure which is also a system of access to a centralized facility, a delegation mechanism : to these points must also be added other factors concerning the signature of articles and/or mandatory references, monitoring of the work and the possible exclusion of teams which do not fulfil their commitments.

This example underlines two complementary dimensions which are specific to the structure of concerted actions.
*The first concerns the organizational forms encountered. As in a number of projects which share the use of equipment, there is centralization around the PL who delegates only some specific tasks. Here the PMG acts as a kind of "*ad hoc *experiment committee" and a special network of correspondents is set up. A second common form entails dividing the project into separate operations, each of which is run by a co-PL. The PMG in this case brings the co-PIs together for the purpose of overall coordination. A third form which is also fairly widespread is collective management (four/five teams similar to a PMG) of all of the teams simultaneously. It will be seen that the concerted actions are organized around a small number of models: forum, star network, laboratory without walls, networks partitioned by geographical or subject (thematic) area. These models do not always retain the same form over time and completion of a particular stage may lead to reconfiguration (e.g. a*

"laboratory without walls" attached to the creation of a protocol will become a "star network" when the protocol is implemented). This example shows the close link which exists between the actors involved and the organizational forms. The same organization is not used to involve a single colleague or a large number of case-providers. It also emphasizes the importance of the logistical requirements in the structuring of concerted actions. It is therefore possible in the organizational forms taken by concerted actions to see a form of synthesis of the possible types of "networking", a classification by "families". As a snapshot, this is true in a large number of cases : describing the organizational forms gives an overall picture of the state of the programme at a given moment. However, this photograph says very little about the dynamics of the actions and, by extension, about the programme.

The second dimension concerns the specific mechanisms for team selection, coordination of the work and the dissemination of the results. Is it necessary to have a formal procedure for the acceptance of teams into the network? Is it necessary to have contracts which set out in writing the commitments entered into by the teams? Is it necessary to have the power to exclude teams which do not carry out their share of the work and therefore endanger its progress? What can be considered to be the specific results of the CA? Who signs the results and what references are made to the CA? Who is able to conclude industrial agreements based on or connected with the work of the CA? Who has access to a centralized facility and under what conditions? In order to function, a concerted action is required as time goes on to adopt something like a set of ***"internal rules".*** *In so doing, it becomes a quasi-institution. As we shall see in the organizational file, this raises the question of the CA's status : is it a research operation like any other or a new form of delegating the management of European research.*

PART II : CHARACTERIZING CONCERTED ACTIONS

The case study has enabled us to show the various angles from which we need to view a concerted action to "characterize" it. The aim of this second part is to analyse how the concerted actions behave in relation to each of the characterization factors referred to : the objectives and the final results, the fixed and circulating intermediaries, the actors and the organizational forms. For each subset, we have adopted complementary approaches so as to avoid unnecessary repetition. The systematic classification adopted for the objectives and results is illustrated by a series of examples which, in our view, is a more effective way of explaining in practical terms what is entailed in the use of one type of intermediary or another. Similarly, although each organizational form is illustrated by means of examples to provide a better understanding of its contents, the main thrust will focus on a systematic analysis of their frequency and their relations with the actors involved and the principal configurations of actors.

1. CONCERTED ACTIONS, FINALITIES AND EXPECTED RESULTS

As we have seen in the initial example, a concerted action is first the creation of a complex relationship between a scientific, technical "project" and an ultimate social and medical goal. The relationship created is not automatic. It has to be built up and formalizing it helps us to understand better the "architectural" choices and the "technical" decisions made. The analysis has highlighted the various aspects of this process of translation : the stake refers to the socio-economic problem to be resolved, the goal represents the first translation by proposing a method of resolving the problem which is challenging the world of research, the objective determines the scientific and technical choices made and the final result describes the path which scientists choose to reach that objective. All of the concerted actions have been through this screening process and a specific data base has been set up to take account of the formal structure. What emerges from this? Two main points should be made in order to explain the reasons for opting for this approach.

(i) Certain stakes find expression directly at programme level : this is in particular the case when specific diseases (cancer and AIDS) are being tackled. However, in the other programmes aggregates are defined within which each proposer choses his own stakes, as with insulin-dependent diabetes in our previous example. The "socio-economic" stakes are therefore numerous, although they tend to fall into three broad categories : diseases to be treated, activities to be improved (e.g. hospitals) and techniques to be developed/evaluated (e.g. biomagnetism). Variety is therefore the rule here and the "stakes" can only act as guiding principles on the basis of comparable (or standardized) modes of expression. However, the data base built up emphasises the weakness of formal structures in terms of the expression (and a fortiori quantification) of these stakes.

(ii) Conversely, the final stages - the objectives and the end results hoped for are characterized by a limited number of types of structures. Despite the diversity of stakes there seems to be a limited number of shapes that European concerted actions can assume. They are at least as general as the finalities or purposes : establishing a surveillance network, developing and/or evaluating new treatments, developing and/or evaluating new products, harmonizing medical practices, and

structuring the scientific community. However, unlike the "stakes" the translation processes whereby they are expressed have at the same time determined conditions for the expression of the problems handled which specify them and, in our view, define five clearly identified aggregates. These conditions may be grouped together into two main categories. The first centres on the geographical dimension : the national setting is not relevant for the analysis on account of problems of representativeness, the fact that it is impossible to obtain an adequate number of cases, and the fact that it is difficult to assemble the necessary skills, etc. The second is based on arguments recently advanced by economists theorizing about technical change : the relationship between the size of the problem and the scale of the financial outlay to be made leads to cooperation between actors. The "European" approach is particularly relevant in two main scenarios : where the scale of the efforts to be made is such that no European country is in a position to cover it alone (as with microprocessors), and where the "base" market reaches an attractive scale only at European level (too small at national level to "interest" the actors).

As far as the objectives and end results are concerned, there are therefore a limited number of arrangements, which we shall now go through one by one before attempting to assess their relative importance to the MHR programme.

1. Surveillance services

The organization of periodic surveillance - regularly monitoring the medical situation from the viewpoint of a particular problem so as to be able to make diagnoses, issuing warnings, preventing epidemics, or helping to frame policies on disease prevention and assessing their performance, etc. - is a well-known dimension of health policies. The MHR programme adheres closely to this objective since 11 concerted actions have finalities of this kind (and six others are associated with them and deal with specific complementary aspects).

What form does this involvement take? The **objective** of a concerted action is always the same : to demonstrate the reliability and usefulness of a mechanism for the gathering, collection and processing of information. The **end result** therefore always takes the same form; on the one hand, an original scientific contributition relating to the situation in Europe as regards the problem studied, on the other, an operational collecting and processing structure often described as a "reference centre" and often also identified by its central function, i.e. the processing of data and the publication of results.

The **argument** for these projects is nearly always similar and may take two complementary forms : (i) The problem is a major one, e.g. foetal malformation or mother-to-foetus transmission of AIDS, but it is too specialized for representative data to be obtained at national level or for it to be possible to consider investment at national level alone in the infrastructure required. (ii) The national data collection methods in use are very different and give contrasting pictures. It is important to gain a clear picture and to ensure intercomparability of the data, in particular to know whether the differences observed are due to specific environmental factors or are the result of different policies whose effects could be compared. Ultimately the feature common to both of these arguments is that they emphasize the methodological difficulties which will be facing the project and, hence, the need for genuine research which will provide the opportunity for constructing the "collection network" and the "reference centre".

Scientifically, the **results** are similar to epidemiological studies and often take the same forms (in particular the European atlas). Operationally, the actions involve numerous clinical teams and often lead to the drawing up of national and/or regional "registers" based on a central team which manages the bases/banks, processes the data and publishes the results. Their compilation is often long and cumbersome.

The examples below underline the importance of the logistical aspects as well as the many different tasks and series of tests required to define joint collection methods, to identify and mobilize the data collection/ provision teams, and to organize the centralizing and processing of the data. This has three major effects on the MHR programme :

(i) The results are often long in coming and some of the value of the conventional intermediate "evaluation" is lost, which makes it more difficult to manage these operations over a period of time.

(ii) Very often the work and the results obtained give rise to further problems and lead to new requests for research which may either be directly included within the framework of the concerted action or result in new "subsidiary" CAs. The question of subsidiary actions is a dimension to be stressed in the management of the programme.

(iii) Nearly always, achievement of the objectives involves the creation of national and/or regional collection organizations and this leads to a third problem for the programme, this time at the end of the work once the CA has demonstrated its "scientific" value. How can the continued existence be ensured not only of the central data processing structure but also of the national/regional structures which are set up and run under conditions which vary considerably from one country to another.

An analysis of the 11 MHR actions of this kind (Table 1) shows the links between the objectives pursued and the end results hoped for. The table below sets out the main key words :

prevalence	<-->	management indicators
risk factors	<-->	early diagnosis (markers...)
		counselling (genetics, practices...)
identification	<-->	orientation of research
of problems		(identification of genes...)
		evaluation of treatments

How do these actions fit into MHR4? In the case of surveillance and identification it is logical that the epidemiology and HSR (health service research) programmes should occupy an important place, and similar actions are also to be expected for the two diseases covered by specific subprogrammes (cancer and AIDS). This is indeed the case :

- two concern cancer (registries in cancer survival, genetic studies in cancer families), one deals with the centralized processing of data on AIDS (supplemented by a series of specialized epidemiological studies which were set up as separate concerted actions), and one is designed to test the ability of "sentinel" networks (of general practitoners) to carry out surveillance;

- the others concern specific diseases (congenital anomalies, osteoporosis, asthma, diabetes) or the operation of health care systems (avoidable deaths, nocosomial infections in intensive care units).

TABLE 1: SURVEILLANCE NETWORKS

SP	Title of CA	Organizational principle	Dynamics of the CA and/or expected end result
S	CF for AIDS epidemiology	large data base aggregration of national data	supply management indicators and select relevant research hypotheses-->5 subsidiary CAs
H	Eurocare (cancer survival)	large data base aggregration of national data	see above (subsidiary CA in the pipeline for health care quality?)
H	Avoidable deaths	large data base aggregation of national data, "atlas"	see above --> subsidiary CA on quality of death certificates
E	Eurodiab (diabetes melitus)	establishment of national registries	tackling the problem by means of parallel approaches
E	Eurocat (congenital abnormalities)	establishment of regional registries large data base	a service (management indicators, alerts, relevant research hypotheses)
E	Osteoporosis epidemology	large data base CF (reading of plates)	see above
E	Asthma prevalence and risk factors	sample bank large teams' investment	large data base see above
B	Blindness prevention	reference centre blood bank	identification of genes, treatment validation and genetic counselling -> "Service to tackle successively 200 hereditary diseases of the retina" ?
C	Genetic studies in cancer families	establishment of national registries tissue bank	identification of markers & genes -> the register as a precondition for research orientations
H	Euronis (nocosomial infections)	large data base clinical evaluation	objectives: prevelance, surveillance and counselling -> extension from intensive care units to other places?
H	Eurosentinel	GP networks for clinical evaluation	objective : testing of GP networks for the surveillance of common diseases

This list underlines one last decisive point, namely that there is no common thread linking the subject areas. What it reveals instead is a series of compromises between different factors concerning the subject (and its interest), the kind of problems posed, the project proposed, the project leader and the participating teams. This has led to the spread we have observed and which cannot be addressed using a thematic approach, unless its terms of reference are wide

enough to embrace all health problems (which corresponds to a criticism often levelled at Community programmes and associated calls for tender).

2. Development and/or evaluation of medical treatment

This second subset of actions corresponds to a simple pattern and comprises two dimensions : the exploration, testing and validation of new treatments and the evaluation and comparison in existing treatments to determine more clearly their effectiveness and/or relative spheres of application.

The logic underlying these 12 actions (Table 2) is always the same, namely that the present situation is unsatisfactory. For the first actions, this means embarking upon new paths (seven actions of this kind, including five for the cancer subprogramme alone and one under the Biology subprogramme which also covers cancer treatment). The concerted action therefore sets out to explore a new avenue, such as cancer immunotherapy, but more often than not it focuses on the development of the key element of a proposed new treatment. The possibility of studying the benefit and value of the new treatment depends on the production of that element. The cancer programme has four actions of this kind, including two involving very large- scale equipment [BNCT and EULIMA (European light ion medical accelerator)] and two involving the setting up of a "service" (drug targeting) along the lines of the example we looked at first, with its central facility for the extraction of B cells to devise a new method of treating diabetes.

The other avenue focuses on comparative analysis of the effectiveness of existing treatments (five actions, three for the AIDS subprogramme and two on viral hepatitis and myocardial infections). In general, they are based on the creation of a network of clinicians throughout Europe, which is administered on a highly centralized basis as it involves monitoring the application of a clinical protocol. The initial objective which actions often set themselves is to create the necessary infrastructure to carry out comparative clinical evaluations at European level, using the specific problem as the reason for setting up the infrastructure which will eventually be used to tackle other problems. The issue is generally one that is difficult to tackle at national level alone, e.g. the opportunistic diseases associated with AIDS, and the choice is dictated by the need to interest the teams while at the same time demonstrating to the authorities the usefulness of the "service" thus provided.

These two configurations relate to actions which, if they concerned conventional industrial sectors and areas such as those covered by BRITE or ESPRIT, would mostly be regarded as falling under the heading of industrial development. This "downstream" nature, close to the "market" and the "end" use is reflected in the two-sided nature of these actions. To be sure, they give rise to publications (regarded by most of our interviewees as a "scientific" output) but they also entail the creation of an infrastructure designed to continue after the concerted action itself has finished.

In the first case, the infrastructure is intended to become integrated within the system of treatment which will be the result of the successful completion of the action and which is often largely determined by the choices made during this phase of "development/setting up" (see the earlier example of the centre for the production of B cells and, further below, the organization of the action involving

(8)

BNCT). The programme in this case does not confine itself to making scientific choices.

TABLE 2: DEVELOPING OR EVALUATING TREATMENTS

NT = Development of new treatment
CET = Clinical evaluation of existing treatments

SP	Title of CA	Organizational principle	Dynamics of the CA and/or expected end result
B	B cells and diabetes treatment	Production centre	NT: our initial example!
B	Human stem cell	Reference centre and division of responsibilities between teams	NT: a project to develop and demonstrate the feasibility of a new cancer treatment method
C	BNCT (boron neutron capture therapy)	Development of heavy equipment	A multidisciplinary action to develop and test a new treatment
C	Immunotherapy of cancer	Exploratory reserach	Focusing on a team with "the" technique
C	Drug carriers systems	Treatment protocol	NT : Treatment devel.b/validation (with animal and clinical testing)
C	Drug targeting	Treatment protocol	NT: see above for two molecules
C	EULIMA (European light ion medical accelarator)	Feasibility of an equipment design	NT: A action structure for the final conceptual design of the machine:
S	ENTA (opportunistic diseases of HIV)	Choice of treatment Large clinical protocol	CET: towards a permanent service (already used by 2 CAs)
S	PENTA	Choice of treatments	CET: towards a permanent service for reviewing treatments for AIDS-infected children?
B	EUROHEP (viral hepatitis)	Choice of treatment Large clinical protocol	CET: choice and performance of treatments (successive approach)
E	EMIP (myocardial infections)	Multicentre study	CET: towards a service for the evaluation of pre-hospital treatments
	"Major investments needed for evaluation borne by an industrialist"		

In the second case the MHR programme has to address the problem of re-using the research infrastructure created. Does the programme consider the cost to have been justified on the basis of the initial results alone or will it try to spread the cost over several operations? If this is the case, once its effectiveness has been demonstrated, such a structure becomes a tool which is truly specific to the European research effort and for which Europe must accept responsibility on a long-term basis. This is another way of asking whether there should be a European equivalent of the NIH, since it is not a question of incentives but of providing continuous support over a long period. These "European research structures" therefore represent a challenge to the programme and, in a wider context, to Community research activities. From the outset, they contain the fabric of a new kind of "joint centre" which is no longer organized around a fixed institutional structure (like the European molecular biology laboratory) but involves the networking of entities which retain their original status, while some of their work forms part of a new collective framework embracing concerted actions which, through their practices, have been instrumental in preparing the ground (see File 3).

3. Development and/or evaluation of new products

With a "biomedical engineering"(BME) subprogramme, it was to be expected that there would be a whole series of actions dedicated to hospital equipment and to analytical and diagnostic instruments. This is indeed the case since, out of 15 actions with this finality (see Table 3), 12 come under the BME subprogramme. The new products concerned are not drugs therefore. The actions are of two kinds : on the one hand the development or harmonization of new techniques, and on the other technology assessment and standardization.

What distinguishes the CAs concerned with new techniques from the earlier ones focusing on treatments is the starting point. In this case it is the technique as such which justifies the concerted action. It is a question of developing a new medical technique (three cases, e.g. forced respiratory techniques) or harmonizing and securing recognition for a new technique (three cases : ocular fluorometry, and biomagnetic and hyperthermic techniques). Most of the actions nevertheless involve technology assessment : (i) for the purpose of conducting comparative studies on the procedures used in the various European countries (three operations including two in the HSR programme), (ii) for breaking new ground in research (artificial hearts), or above all (iii) for guaranteeing the quality of the service to users and patients. Whether the actions concern electrocardiograms (ECGs), ultrasonic screening, quantitative assessment of bone quality or the use of tomography, the immediate objective is the same : to ensure the quality of the diagnoses made with the instruments used. This may involve the definition of "functional" specifications which these instruments must meet, the construction of reference bases or "phantoms" to verify the instruments' performance or even international standardization by the official bodies. However, the latter course comes up against the problem of the broad interpretation of the "safety" of these operations. This no longer relates to the safety of the patient during exposure to the instrument but the "safety" (i.e. reliability) of the diagnosis made using the instrument and the consequences of it.

TABLE 3: DEVELOPMENT OR EVALUATION OF PRODUCTS

TAS = Technology assessment and standardization
HVNT = Harmonization and validation of a new technique
NMT = New medical technique

SP	Title of CA	Organizational principle	Dynamics of the CA and/or expected end result
H	Health technologies economic appraisal	Comparative study	Methodology, "ad hoc" initiation work?
H	Health technologies regulatory mechanisms	Comparative study	Methodology: "ad hoc" initiation work?
M	Medical equipment comparative eval.	Comparative study of equipment	Towards a service for surveying and evaluating equipment?
M	ECGs	Large protocol data base	TAS: from the eval. of equipement to the eval. of interpretation software
H	Antenatal screening by ultrasound	Large protocol data base	TAS: moving towards standardization?
M	Perinatal surveillance	Clinical evaluation	TAS: evaluation of the value of the diagnosis/monitoring tests
"Dynamics: extension to other tests or focusing on the development of a test"			
M	Tissue characterization	Protocol approach	TAS: from MRI to MRS
"Towards a European service for the evaluation of new techniques in the area?"			
M	Osteoporosis: quantitative assess.	Large DB, phantoms...	TAS (& NMT via subsidiary CA centered on a new evaluation method)
"A CA which exists only because industrialists cannot reach agreement"			
M	Hyperthermy	Intercomparison of equipment	HVNT: technical validation through harmonization of instruments
M	Biomagnetism	Intercomparison of hard & software	HVNT: see above subproject to demonstrate value
M	Ocular fluorimetry	Clinical evaluation	HVNT
M	Electrical impedence tomography	Harmon. of conceptual framework (measures...)	NMT: a technique for ten years from now?
M	Forced respiratory techniques	Adaptation, new development	NMT: rethink spheres of application with new well-adapted tools
M	Heart: artificial heart	Clinical and technical assessment	NMT: survey and problems of uses with a view to defining a development?

The justification for these actions stems from two complementary sources : in many cases, it is necessary to construct very large reference bases (what we have called "large number of cases" data bases) and it is either impossible or very difficult to carry out this sampling nationally (it would mean mobilizing too many practitioners). However, the more important argument concerns the geographical dimension. What benefit is there in standardizing for a single country, in particular for products with a world market? For most project leaders the EEC is the right size : a market large enough for the recommendations of its health authorities to have an effect on decisions taken by industry (in some cases this argument has already been used), an area equivalent to that of the USA within which the development of joint operations stands a better chance of success than an international approach.

Once again, these actions present the programme with evaluation problems. How can the quality of the work be assessed if it is not yet at a clearly identified stage? What criteria can be used (relying on academic publications as the main basis for a judgment is far from ideal).

The end result of these actions is presented most of the time in the dual form of recommendations and material information intended to enable them to be implemented. Unlike the projects in the other two categories, these end-results close the CA which thus have a specified time-scale. Nevertheless they present the programme with a new type of problem, namely dissemination of the results. Recommendations can either be incorporated into regulations (standards, etc.) or used by purchasers (usually hospitals) in the light of the selection criteria used. In either case the results cannot be used as they stand and "conversion" operations are needed to turn them into acceptable rules, instruments to be included in the "clauses" of procurement specifications etc. Should the programme concern itself with this? And if it does not, what guarantee is there that the effort will be successfully continued "downstream"?

4. Harmonization of medical practices

The harmonization of techniques has its counterpart in the shape of the harmonization of practices. How can the quality of the health care systems themselves be ensured?

The common denominator of the concerted actions is their targets : doctors, hospitals and the health services. Several of the actions concern doctors, the way in which they make their diagnoses and the tools (expert systems) capable of helping them (what is known as "objective medical decision-making"), and practices with regard to referral of patients to specialists or "referral centres" which are able to carry out complex analyses (connective tissue). One concerns dentists and precautions against AIDS. A second set of actions focuses on the hospital, its practices (the use of blood, the handling of specific problems such as head injuries, etc.) and management (use of diagnosis-related groups, self-assessment of performance). The third group of actions concerns the health services, especially with regard to preventive policies (the appearance of stomach cancers, etc.) or care for specific groups (the hearing-impaired, the elderly).

TABLE 4: HARMONIZATION OF MEDICAL PRACTICES

SP	Title of CA	Organizational principle	Dynamics of the CA and/or expected end result
B	Heritable connective tissue disorders	Network of reference centres	Harmonize laboratory practices
H	Use of blood in surgery	Clinical evaluation Large data base	Change surgeons' practices
M	OMDM (abdominal pain)		
M	OMDM (jaundice)	see above	Change GPs' practices
H	Care delivery systems	Several coordinated epidemiological studies	Harmonize medical and clinical practices
H	Referral study	Large data base	Improve GPs' practices
H	Head injuries evaluation	Comparative Improve practices	Measure the scale of the problem
E	Exposure to cancer: evaluation methods	Harm. & extension of national surveys	Harmonization of retrospective evaluation methods
E	Gastritis and gastric cancer	Epidemiological study, DB and blood bank	Measure the scale of the problem
E	Euromac	Epid. study	Update information
E	Organic solvents: neurotoxicity	Development of a protocol	Measure the scale of the problem
H	Haemoglobinopathies	Epid. study	Measure the scale of the problem
H	ACRE (Age care)	Comparative study	Review the situation
H	Mental health pbs for deaf people	Comparative study	Classification criteria
H	Use of DRGs	Comparative study	Review the situation in hospitals
S	HIV: serological methods	Comparative study	Recommendations for the establishment of quality control
H	Hospitals' auto-evaluation practices	Survey of 100 hospitals	Disseminate a method
H	ICPC	publication	
S	AIDS and oral problems	Development of information supports	Inform dentists about risks and prevention

A second way of approaching this set of actions is to consider the end results sought rather than the sectors concerned (GPs, hospitals or the health service). Four main types of results emerge (see Table 4). By evaluating practices (and the large data bases usually set up), the objective is to help improve the practices of GPs (3 CAs), surgeons (3 CAs) and specialized laboratories (1 CA) or epidemiologists (1 CA). The objective of four concerted actions is to measure the scale of the problem (gastritis and gastric cancer, haemoglobinopathies...) through epidemiological studies, while four others are confined to comparative studies to review differences between European countries (use of DRGs, HIV: serological methods...). Lastly, three concerted actions focus directly on the dissemination of information or of practices (e.g. self-evaluation methods for hospitals).

Three features are common to all 19 actions in this large group. First of all, they are looking at a clearly delineated problem in order to make practical recommendations, suggest improvements and propose tools as an aid in decision-making. The second point they have in common is the importance attached to comparative approaches in the conventional meaning of the term : highlighting the differences between countries and, by analysing these differences, suggesting what might constitute "best practices". The third point they have in common is that they are generally carried out on a small scale - a few teams (often one per country) - for a short period. Most of the actions initiated under MHR4 come to an end once their budget has been used up. As with the earlier finality, there is still the problem of disseminating the results : what can be done to speed up the dissemination of an aid to objective medical decision-making? What can be done to ensure that the self-assessment approach to be tested is widely disseminated to all hospitals?

5. Structure of the European scientific community

In the case of the above four groups we were looking at an activity which, in an industrial context, would normally be known as "development", i.e. coming up with a product or a process which fulfils specific needs/demands and initiating the steps which will lead to its being marketed. It is true that the "market" in this case assumes different forms which are largely public and in part commercial, but it is a market nonetheless : practitioners who need a means of making a reliable diagnosis of abdominal pain, electrocardiograms we want to make comparable, opportunistic diseases associated with AIDS whose treatment we want to optimize, congenital anomalies whose rate of development we want to be able to monitor, and so on. There is a group of about 63 actions whose finality can be described directly in operational terms of this kind. The same does not apply to the 42 or so other actions about which we questioned the project leaders.

Those actions have a very clear factor in common, namely that they are defined in scientific and technical terms : "science knows nothing about...", "cellular biology offers new prospects...", "the specialist community is dispersed, it should be grouped together and encouraged to get down to work on joint projects", "all scientists are faced with this or that problem of analysis, sequencing, animal testing, etc. What is needed is a joint facility which will resolve these problems and ensure complementarity between the work". These are some of the standard arguments which are characteristic of the actions. What sets them so far

apart from each other after the initial action stage is the approach which they adopt. They can be grouped into three categories, each identified by a set of principal characteristics.

TABLE 5: THEMATIC OR DISCIPLINAY FORUMS

SP	Title of CA	Organizational principle and general goal
B	Breakdown in human adaptation	"Umbrella" CA : WSs and decentralized microprojects, which, if they work, will become autonomous
M	Medical laser applications	Organization to enable projects to emerge Visits by experts and exchanges as regards training
M	Chemical sensors	Follow-up of thematic WS & support for decentralized exchanges
S	Genomic variation	"exchange, identify, interest" ; role of initiation (CA, CF)
S	Immunology and AIDS	Spin a "spider's web" between teams to enable a specialized scientific community to emerge
C	DNA repair and cancer	Strategic (every four years) and thematic reviews: "specialized meetings on the participants' initiative"
M	Technologies for paralysed persons	Organization of a community on a thematic basis
M	Automated cytogenetics	Meeting place for isolated national specialists. Annual update and decentralized initiatives on specific topics
M	Technologies for the hearing-impaired : see above	
M	ISCAMI (medical images)	Exchange forum End result : a club of theoreticians
H	Distributive	Building a network of health economists via WS effects of cost containments
S	Math models for AIDS epidemiology	Meetings of European specialists every 18 months
S	Sexual behaviour	Organize a community of sociologists (using a common and HIV risks partial protocol)
S	FIV	Harmonization of small scientific community (15 teams) via WS & support for decentralized exchanges (persons, materials)
H	Clinical practice in hospitals : exchange of interns	

THEMATIC OR DISCIPLINARY FORUMS

The first category is the exchange forum. Scientists (often in small national communities) need help to come out of their isolation and to meet. This intermingling of disciplines will lead to meetings and, from them, joint actions. However, it is not possible to say who will be involved or what the subject matter will be, or even when they will come to fruition. These CAs are entirely centred on the seminars which they organize. As far as the concerted action is concerned nothing happens on a centralized level, although support is often given for decentralized exchanges and visits. In a word, what characterizes them is the absence of an identifiable output and they are defined only by their medium of communication, namely meetings. They may last only the length of one programme (MHR4) or they may be spread over several programmes (as in the case of the network on hearing problems) as they have no end in themselves. A meeting place is always needed and if it generates projects, why abandon it after the first project has been born?

Several project leaders strongly defended the principle of and the need for such "umbrella CAs" designed to prepare the ground for joint projects or identify the need for central facilities. They emphasized the role of such CAs if the MHR programme is to be able to take the initiative on subjects which are regarded as important but on which no groundwork has yet been carried out at European level. We have identified 15 CAs of this kind, mainly in the biomedical engineering (BME) and AIDS subprogrammes (see Table 5).

JOINT RESEARCH FACILITIES

At the other end of the scale, there is a second set of actions whose finality is quite clear : the creation of a "joint European facility". This concept merits explanation. The word "equipment" has not been used because it would be all too easy to associate the action with a heavy installation linked to complex machinery with a technical team and engineers but rarely with scientists. From these, the "facilities" retain the originality and the European specificity of such "equipment" : in most cases, as has already been seen with production centres linked to new treatments, a single installation in Europe suffices to meet all scientific requirements. They therefore reflect a two-fold situation : either their establishment can only be envisaged on a European scale or the economies of scale are such that a European entity is necessary on economic grounds. What differentiates these facilities to the above mentioned heavy equipment will be highlighted from an analysis of the three main forms : capital investments are often limited compared with all the investments which economists refer to as intangible.

Conducting trials on animals (primates, monkeys), carrying out DNA sequencing, producing artificially aged or transgenic mice, screening antiviral compounds, etc. define the first type of facility (six actions - see Table 6) : a centre (or laboratory) which is specifically equipped and offers a specialized service unique in Europe. It is generally the combination of a recognized expertise and a technique (which is difficult to master) which form the initial basis for such centres, which have often already achieved recognition long before the start of the concerted action. Such recognition is strengthened by the resources which the concerted action utilizes both to improve the service, the technique and the facility and to make it accessible to colleagues who will use it. Some of them are far more willing to take part if there is the joint management of access which is a

proven means of influencing the community, its areas of expertise, its priorities and even its organization[4].

TABLE 6: JOINT EUROPEAN FACILITIES

SP	Title of CA	Organizational principle	Dynamics of the CA and/or expected end result
B	ECAT (thrombosis) Protocol CF	Clinical research Angina pectoris, DVT, PTCA	Successive surveys
E	Euronut (nutrition and health)	Clin. research : protocol CF & blood bank	European centre for clinical research into the elderly?
E	Arteriosclerosis 1DB, 3 banks(blood,DNA)	survey with heavy logistics	"Biological" infrastructure usable for other cases?
C	Molecular cytogenetics of solid tumours	Tumour collection network Cell line bank	10 tumours: harmonize access to the equipment of others
C	Thyroid cancer genetics Harmonize scientific approaches		2 banks (tissue, blood)
B	Eurage	Aged mice CF : a facility to structure the research community	
B	Transgenic techn. & cardio-vascular res.	CF transgenic rats with hypertension	See above
S	HIV: genetic screening	Laboratory CF & ad-hoc essay committee	A service (sequencing) linked to genetic variability research
S	New antiviral compounds	Laboratory CF	Screening of 20 000 molecules a year
S	Aids research in primates	Test CF & ad hoc essay committee	Chimpanzee CF in Europe (political choice)
S	Monkeys CF	CF network	Intercomparison of results
S	Immunogenetics of AIDS Finding a genetic link		DB on HLA typing
S	HIV protein and cell membrane interaction	CF : production of peptides lipids and antibodie Sofware exchanges	Targeted research: understand interaction with a view to a vaccine
S	EVA (European vaccine against AIDS)	CF buying & distributing products (viruses peptides, adjuvants)	Targeted research via Call for proposal and selection of projects

[4] We shall look later on this point which was largely covered in connection with the effects of large-scale equipment such as that of CERN.

A centre is not the only form of joint facility developed under the projects. There is a second one which has already been touched on in the context of the studies on the assessment of treatment : the European data collection network. Five actions have this objective, which also often focuses on the creation of cell banks or banks of other samples. The nutrition and thrombosis networks are typical of this second type of European facility. It took many years to teach a very diverse group of teams to design a protocol together, to construct a common framework of practices for the collection of data, etc. Networks of this kind are created around a given scientific problem which they resolve or for which they provide the researchers with fresh resources (typically a cell bank, blood samples, clinical cases, etc.). Often, as soon as the end of a "study" is in sight, the network seeks another point of interest. What struck us, and what the examples in the following chapter will show, was the scale of the investments which have to be made and the time which this takes. Unlike networks set up for the clinical assessment of treatments, the main goal of the actions here is to improve scientific knowledge and to provide fresh bases which will lead to new approaches or new issues.

A third group, very specific to the AIDS programme, uses the joint facilities to carry out what the project leaders refer to as targeted research. The centralization of resources (which are subsequently redistributed over limited and defined actions) should speed up the process of accumulation of knowledge and the resolution of the problem. An extreme form of this is the EVA which operates as a programme which is based on an invitation to submit proposals and on project selection and has as its attraction the "products" which it distributes (viruses, peptides, adjuvants) and of which it organizes the production, guarantees the quality and ensures the distribution.

CREATION OF A SPECIALIZED EUROPEAN SCIENTIFIC COMMUNITY

A third group, consisting of 13 actions (see Table 7), may be subtitled the "creation of a European scientific community". These actions have in common a clearly identified theme, which is generally new and interdisciplinary. Most of the time this entails the involvement of a few teams in each country, teams which are often isolated or not very well known in their own national community, teams which generally know each other (at least through colloquia and publications). The concerted action sets out to bring them together to address a clearly defined problem. It is not, as in the first example, a matter of allowing joint projects to emerge in random fashion but rather of encouraging teams to join forces to tackle a problem which is defined from the outset. The problem may be very specific or targeted (e.g. techniques for the characterization of biomaterials), it may concern a subdiscipline (e.g. the neuropathology of AIDS) or it may focus on a disease which is causing problems (such as chronic arthritis, multiple sclerosis or evaluation and treatment technologies related to brain damage).

When comparing these actions, virtually all of which were initiated under MHR4, with the actions initiated under earlier programmes, the feeling you get is one of describing a transitional phase, namely the genesis of a genuine working group which takes shape gradually as the problem to be dealt with is defined. It is almost as if it takes the life-span of a concerted action to implement the second stage of the translation process described above : how can the objective to target,

the desired end result and the path to be followed be clearly defined? Concerted actions of this kind are therefore something of a transitional stage leading towards another form which the action might take if it is successful and is renewed.

TABLE 7: CREATION OF A SPECIALIZED EUROPEAN SCIENTIFIC COMMUNITY

SP	Title of CA	Organizational principle	Dynamics of the CA and/or expected end result
B	Chronic arthritis	Organization in subprojects	Immunology directed towards hospitals (bringing rheumatologists together)
B	Inherited polycystic kidney desease	Gene probes as vector	Clinical molecular biology
B	Multiple sclerosis	Support for thematic harmonization (DB, software, epid. studies, vocabulary, harmonization of lab practices)	
M	Clinical applied analytical cytometry	Subgroups with protocols field tests & harmonization of lab pratices	Towards a community of cytometry clinicians
	"From automatic machines and technologists to expert systems as aids to analysis and to clinicians"		
M	Brain-damaged patients: assessment & rehabilitation	8 subprojects with precise objectives & material support. Pool of equipment	Structuring of community as initial phase (next phase = harmonization)
S	Neuropathology of AIDS	6 subgroups, atlas of images Exchanges of samples	Creation of a community of neuropathologists
E	EURODEM (prevention of dementia)	Collation of all studies (prevalence, retrospective) to prepare forward study	Better understanding of scale and nature of phenomenon
	"One project over 10 years with virtually all the European teams in the area"		
E	Homocystinemia & cardiovascular disease	Clinical survey link	Towards the demonstration of a
H	Mentally ill Community care	State of the art Field survey	Comparison of different institutional approaches
M	Sleep wakefulness analysis	Task groups, functional specifications, towards DB?	ECG CA as a model?
M	Eurobiomat (biomaterials and haemo-compatibility)	Survey of methods, Common reference materials for tests	Network of test centres, moving towards standardization
M	Technology and blindness	Identification of teams & set of mini-projects	Creation of thematic community with the objective of developing new products
S	AIDS: preventive strategies	Subgroups by risk population or problem	CF epid model for risk factors

6. The MHR programme and its finalities

What is the breakdown of the seven groups we have identified in the context of the MHR programme? What are the relations between them and the six subprogrammes making up the MHR programme? The summary table below relates to the 105 CAs whose project leaders we managed to interview. It does not, therefore, cover all the activities under these programmes and must therefore be regarded as indicative. It nevertheless reveals strong trends, in our view.

While none of the subprogrammes covers the entire range of general goals, the two most targeted ones in terms of finalities ("Cancer" and "BME") cover four of them, ranging from the structuring of the European scientific community to the pursuit of more directly operational objectives.

TABLE 8: SUBPROGRAMMES AND FINALITIES PURSUED

	Biol.	Cancer	Epid.	HSR	BME	AIDS	Total
Surveillance network	1	1	4	4+1	-	1+5	11+6
Dev./eval. treatments	3	5	1	-	-	3	12
Dev./eval. products	-	-	3	12	-	15	
Medical practices	1	-	4	10	2	2	19
Forum	1	1	-	2	6	5	15
European facilities	3	2	2	-	-	7	14
Specialized community	3	-	2	1	5	2	13
Total	12	9	13	21	25	25	105
(CAs in postal survey)	14	12	17	21	28	25	117

The profiles of the various subprogrammes differ considerably. Three focus half their efforts on a single "operational" finality : new cancer treatments, harmonization of medical practices for HSR (health service research) and the development or standardization of techniques for BME (biomedical engineering), while the other subprogrammes divide their efforts between a wider range of finalities. Similarly, the overall impact of the three finalities primarily concerned with the creation of a European scientific community differs considerably from one subprogramme to another : very slight in the case of HSR, secondary in the case of cancer and epidemiology, strong in the case of BME and primary in the case of biology and AIDS.

> *This preliminary analysis of finalities therefore brings out the different ways in which each of the subprogrammes operate. There are certainly not one or two forms of CA for each of them which are supposed to translate the priorities set and/or the state of the community to which they are addressed. On the contrary, given the thematic and scientific categories covered, the subprogrammes have been conducted in such a way as to develop complex strategies adapted to the many situations encountered, as a result of which (in the light of the stakes) they have adopted different mixes of finalities (e.g. building a community via a joint facility, mobilizing clinicians around the comparative evaluation of treatments, etc.). While some programmes are strongly targeted, they have*

nevertheless always been required to pursue multi-faceted approaches. For a better understanding of the choices and the actual lines of action it is therefore imperative to take a look at the CAs involved.

Analysis of some 105 concerted actions has led us to distinguish between two groups of actions : "purpose-oriented" actions, which have a direct medical objective, and actions for structuring the European scientific community. We have pointed out the existence of four principal type of "purpose-oriented" actions which concern the creation of surveillance services, the development and assessment of medical treatments, the development and assessment of medical techniques, and the harmonization of medical practices. Similarly, the "structuring" actions involve the creation of new joint research facilities, forums for meetings and interchange or "specialized" scientific communities.

Different arguments are put forward and there are different end results for each of these finalities. As far as MHR4 is concerned, these can be grouped in three separate categories:

(i) scientific end results disseminated by means of the conventional processes of publication,

(ii) recommendations regarding changes in practices, raising the problem of their rapid dissemination and legal incorporation,

(iii) networks which must be maintained on a lasting basis whether the programme accepts the cost of funding them on a longer term basis or whether it passes on that responsibility to others.

II. CONCERTED ACTION AND "INTERMEDIARIES"

In characterizing concerted actions we emphasized the wealth, importance and multiplicity of interactions between teams. We also stressed the importance of circulating or fixed intermediaries which underpin and give substance to the interactions. This section seeks to illustrate the wealth of interactions and is concerned with the types of intermediaries most frequently encountered. Unlike in the previous section, concrete examples are preferred here to an abstract presentation so as to make the ramifications of each main type of intermediary more perceptible with regard to the durability of the end products.

Let us first of all examine the "non-circulating" or fixed intermediaries. Physics has taught us the importance of "large-scale equipment" in the organization of a discipline, a programme or an institution. The concept of large-scale equipment is threefold : there is a financial aspect (a team, an institution, or a country cannot afford the equipment on its own), an ineluctable element (this type of equipment has to be used in order to carry out a particular operation) and recognized uniqueness (only one of its kind in the country or in Europe, very few or none at all in the rest of the world).

Sociological studies of science indicate two complementary types of effects : (i) a polarization of teams for the design, construction or operation of the equipment; (ii) a strong impact on the thematic approaches and practices of the user teams. Effects of this kind are also apparent with MHR despite the much smaller scale of investment involved. However, they tend to be disjointed. Polarization effects are observed more in the case of actions dedicated to the development of a therapy based on the use of large-scale equipment (e.g. BNCT) or of a laboratory playing this role (case already mentioned of B cell extraction).

This is also the case with "large number of cases" data bases and registers, two examples of which will be presented. Orientation and alignment effects are apparent more in the case of facilities dedicated to a given stage in a research process (virus sequencing, animal testing) : in that case the actual organization of access to the facility (ad hoc experiment committee, preparation of samples, rules concerning the publication of results, etc.) or access to its products (e.g. transgenic rats) is what counts.

The example of large-scale equipment by no means exhausts the range of centralized facilities encountered in MHR. Two other types may be observed. "Small-scale" equipment acts as a "common in-house service" by ensuring the intercomparability of data (e.g. plates for osteoporosis); the same applies to the numerous ad hoc data bases created for the duration of the CA which will disappear with it (e.g. the forward study on children born of seropositive mothers). In several concerted actions these "common services" constitute a result (if not the result) of the CA which will be widely used in the outside world by the entire scientific and/or medical community concerned : reference bases and banks, reference centre networks, surveillance and/or monitoring networks, registers. The question then arises of their "transfer" and their funding from other financial sources.

The analysis of exchanges and of the circulating intermediaries underpinning them will be based on a twofold approach. The first aspect concerns something to which concerted actions are all too often reduced - meetings and transfers of paper. An attempt will be made to indicate the importance they actually have in the gradual coordination of the network of actors involved in the concerted action. They represent to some extent what manpower management and communications organization represent for an industrial company : a means of establishing themselves and developing as an effective entity before being products as such which express its existence and dynamism. With paper, it is a question of transferring representations, "literary" translations of problems and of objects studied. Concerted actions are not confined just to that, they also provide a space for the exchange of the very essence of the objects studied, so as to encourage the replication of analyses, allow specialized processing, and compare instruments and practices. These exchanges take many and varied forms : samples, reference materials, equipment, phantoms, animals and even patients. It will be seen from the examples given of each of these types that what they have in common is that they impose on the concerted action a strong logistical component which almost always occupies a central position in the activities of the concerted action and helps to strengthen the action, and make it more "sustainable".

1. Three examples of the "polarizing" role of fixed intermediaries

THE CA ON "BNCT" (BORON NEUTRON CAPTURE THERAPY) AND THE PETTEN REACTOR

In 1982 interest revived - following the setbacks in the United States in the 1950s and the 1960s - in cancer therapy based on boron neutron capture (BNCT). Various countries were interested in this promising avenue, notably Japan, the United Kingdom, Germany and Switzerland. Research scientists in this area, few in number at that stage, gradually got to know one another, forming an embryonic informal network. They exchanged ideas and staff, but their scientific cooperation ended there. There was no research coordination as such. However, the Petten

establishment of the Joint Research Centre (JRC), an offshoot of the Commission of the European Communities, was looking for an alternative use for its nuclear reactor. A British team was aware of the situation and of the invitation to submit proposals under the MHR4 programme, and persuaded the teams in the small informal network to put together a proposal based on several components, the main one centering on the joint use of the Petten reactor.

This reactor is fitted with peripheral tubes through which neutron beams from the nuclear fission reaction can be channelled. One of these tubes was placed at the disposal of the concerted action. However, since the installations were already used very intensively, especially for tests on materials for nuclear power stations, the HB 11 tube was only available for medical research during the summer months. The teams therefore had to coordinate their work so as to fit in with the time schedule dictated by the operation and management of the installation.

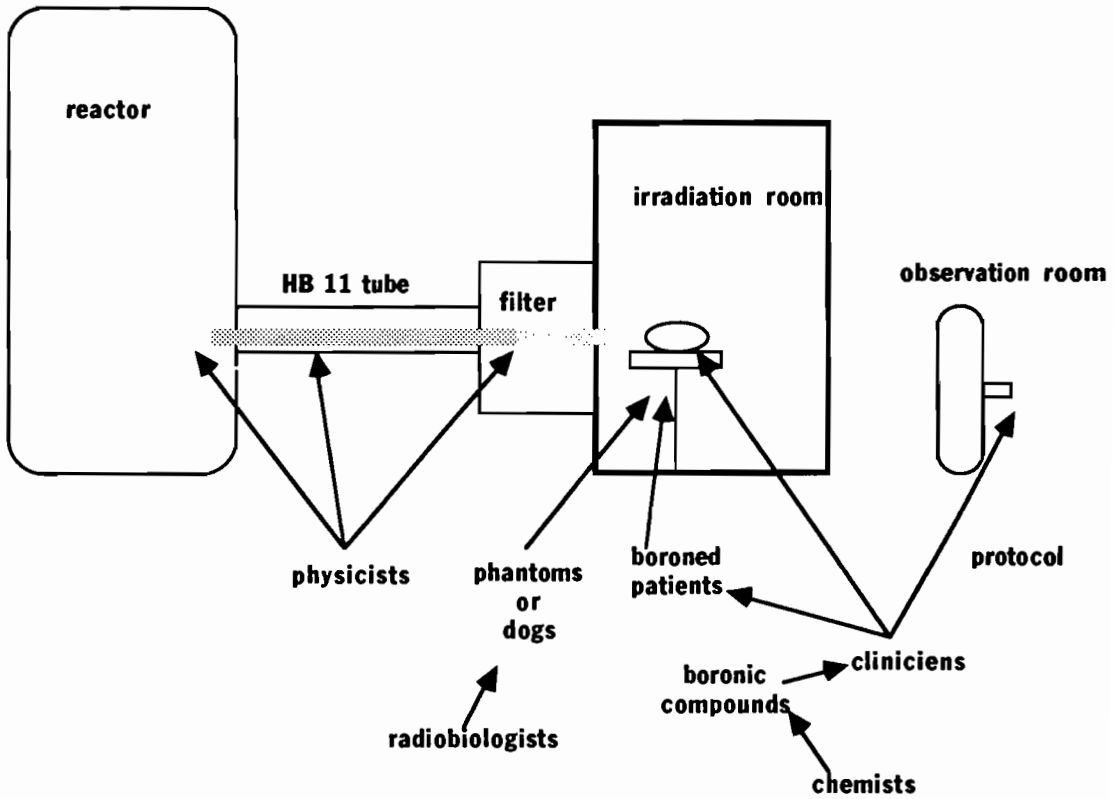
The neutron beams entering the HB 11 tube contained, among other things, thermal neutrons, epithermal neutrons, fast neutrons and gamma-ray photons. Only the first two types are of value for therapy. The others are harmful. Consequently, one of the first tasks of the research scientists was to design a neutron beam suitable for their purposes. What they needed was a beam which could penetrate the body, without causing unnecessary damage, and interact with the boron compounds targeted at the tumours to be destroyed. Previously the researchers had used thermal-neutron beams with a kinetic energy of around 0.025 eV. These were captured by a boron compound absorbed by the cells which disintegrated immediately and released high-energy particles locally to destroy the tumours. A very small amount of boron compound was needed to obtain an intensive reaction locally. Unfortunately, in view of their low kinetic energy, the thermal neutrons were arrested by the human body and never reached the boron compounds. The researchers therefore abandoned them and attempted to harness epithermal beams. These are much higher energy beams (between 1 eV and 10 keV) and penetrate the human body better. However, the boron compounds did not capture them. Fortunately, although they were very energy-intensive they lost a great deal of energy through collisions in the human body, so that they fell to the values of thermal neutrons. Thus, they were transformed as they advanced into biological tissue.

The problem was therefore one of designing, defining and producing an epithermal beam going from the reactor to the human body. The researchers divided up the work, each according to their particular expertise; the physicists studied the reactor and the beam leaving it while the clinicians studied the biological tissues and the beam penetrating them. However, the beam with which they were concerned did not have the same significance for both sets of researchers; the former defined it primarily in terms of its kinetic energy, which was of no interest to the latter who were particularly interested in the way in which neutrons interacted with biological tissues. On the basis of two definitions and classifications of beams, the teams succeeded in defining and constructing an interdisciplinary neutron beam. The mutual interest of physicists and clinicians was strengthened as a result.

The beam coming from the reactor therefore had to undergo transformation before entering the human body. The task was hence to design filters for the HB 11 tube. Given the limited accessibility of the tube, the design and production of the filters had to be carried out during the year in such a way that they could be installed on the day on which the equipment was reserved for

them. Initially the researchers were able to use an existing filter available at Harbor. This 1 m by 50 cm filter was transported to Petten in liquid nitrogen. In addition, at the end of the beam, where one day patients would come to undergo radiation treatment, it was necessary to build facilities for receiving them. The teams therefore had to coordinate very precisely the various tasks to be performed, divide them between the laboratories and enter them in a tight planning schedule. The coordination of this research network was therefore more akin to the carrying out of complex engineering work than exploratory research.

PETTEN INSTALLATION FOR BNCT



To achieve the final objective, there was also a need for boron-treated human bodies. That was another task for clinicians in hospitals. They had to determine the doses to be absorbed and study the distribution of boron compounds in the body. They took part, along with the physicists, in the simulation of the effect of treatments using this therapy. The physicists produced information about the irradiated regions; the clinicians determined the boron concentration. The two types of information should make it possible to evaluate the targets and surrounding damage. However, the researchers were not yet in a position to send patients to the Petten installations. In the meantime, they sent phantoms. These were made of plastic and comprised equivalents of biological tissues. They were manufactured in accordance with the ACRU standards (International Radiobiology Commission). Although they were easy to make, one team took on the task of producing them for the others. The phantom was more or less the size of a head. It was easy to transport. There would be three or four of

them for the first rapid experiments. They were fitted with detectors to measure irradiation. The phantoms had to be ready at the right time since it would be necessary to proceed quickly during the irradiation experiment. They would be used in Petten initially but also in a laboratory in Essen. After use they are neither destroyed nor activated. It is therefore possible to reuse them. The phantoms would be used above all to carry out measurements.

After the phantoms and before sending patients, the researchers considered sending animals to the installation. Once again there arose the problem of comparing and coordinating the results. The ideal solution would be for all the teams to use the same type of animal. The dog would be the ideal standard animal to follow the phantoms. 20 or 30 dogs would have to be bought, several of which would go to Petten. While there are scarcely any problems involved in sending phantoms or dogs to Petten, the situation is quite different in the case of patients. There are several problems : the funding of travelling and hotel expenses, insurance cover and accompaniment. For example, an Italian patient sent to Petten in the Netherlands would have to be accompanied because of language problems. How could it be ensured that psychological damage caused by the journey did not outweigh the benefit provided by BNCT?

There was one final element in this complex set-up, namely the boron compounds. Several teams used them in order to produce the information needed to prepare the Petten experiments. In order to ensure optimum coordination of teams and results, a team took responsibility for the central distribution of the compounds. It brought the products and distributed them to the others, which could not pay for them out of national funds. Operating in this way, the network addressed itself to a single supplier and at the same time standardized the products. There are few producers of these boron compounds anywhere in the world; furthermore, they have different purity criteria and charge very high prices. Hence, after contacting American and Japanese producers, the project leader turned to European manufacturers. One of them agreed to begin producing a boron compound for the concerted action. The CA network is at present its only client, but the order is sufficiently big. Its market is the European BNCT research network. However, the manufacturer in question has undertaken to contact other potential clients, in particular to "plug" the probable results of the research in progress. If the results obtained by the BNCT network are favourable to the development of this type of therapy, the quantities of boron compounds needed for the treatment of patients (8 000 to 15 000 patients a year) will be much greater than those needed for research purposes. The future market of this manufacturer is very closely tied up with the success of the European research project.

The concerted action was complex because it was necessary to coordinate the installation, the beam, the filters, the boron compounds, the human bodies treated with boron and the orchestration of the entire operation in a clinical protocol which was effective as far as the tumours are concerned and safe for the surrounding tissues. The protocols also had to be designed in such a way that comparisons could be made between treatments and between patients. Equipment was needed to test the medicaments and devise the protocols. Animal experiments and tests will make it possible to combine work on the equipment and work on the medicaments. Not until then (and the end of this CA) will it be possible to make a start on clinical tests with a view to the complete validation of the clinical protocol for the treatment of cancer patients with a glioma (between 8 000 and 15 000 die of one each year).

On the basis of the ultimate objective, the researchers broke the problem down into the different work stages. They identified tasks and found people to work on them. The tasks were allocated and planned. The physical measurements had to be carried out at Petten, which was not the case with either design or simulation. The teams worked in parallel; there were four design teams, two metrology teams and three test teams. They met group by group to discuss calculations, designs and measurements in order to build a consensus on each point. To avoid coordination problems arising from existing demarcations between disciplines and the division of tasks, those in charge of the concerted action organized overlaps between the groups in order to make for translations between the disciplines and between the tasks : some teams were members of several groups in order to encourage the exchange of information. Thus, alongside the planning and distribution of tasks involved in achieving the complex objective, another means of coordination by consensus-building had taken root at the level of each task.

> *This rather exceptional concerted action (like the initial example chosen concerning B cells and diabetes) illustrates the importance a fixed intermediary may have in the building of a research network. It shows that the equipment and its adaptation are only part of the action and that its size, the investment entailed and the use constraints it imposes strongly influence the shape of the project : all the tasks and the specialists from the different disciplines which carry them out have to meet at fixed dates for the experiments (on phantoms, then dogs and then patients) which mark the progress made with the CA. As emphasized in the outline, the teams' roles and interactions are to a large extent dictated by the installation.*

THE "SCREENING FOR FETAL MALFORMATIONS" CA AND ITS "LARGE NUMBER OF CASES" DATA BASE

The next concerted action is directed towards a cost-effectiveness assessment of the systematic detection of fetal malformations using ultrasonography. The idea stems from COMAC-Epidemiology; while its members were debating the epidemiology of congenital anomalies, they wondered whether it might be a good idea also to examine the effectiveness of diagnostic methods. Researchers specializing in ultrasonography were therefore contacted to carry out a feasibility study. The main goal was to develop a methodology for a larger-scale study. Since the study was designed to result in a concerted action, the results were never published. When the concerted action (large-scale study) was proposed, COMAC-Epidemiology, the composition of which had changed in the meantime, rejected it. Some of the teams involved in the feasibility study did not want to leave it at that, and reacted by seeking alternative funding; after contacting the management of the MHR programme, they submitted the proposal to the COMAC-Health Services Research. In so doing, the proposers decided to modify the project to bring it into line with the presumed interests of their new interlocutor. Two complementary aspects were added. It was no longer simply a question of assessing the epidemiological effectiveness (sensitivity and specificity) of ultrasonography but also of making a cost-effectiveness assessment since it seemed logical that the COMAC-Health Services Research would be interested in this aspect. The drafting of this part of the proposal was delegated to another,

more specialized member of the concerted action. Similarly, following discussions within a foundation for handicapped persons to which the project leader belongs, a "psychological impact" section was added to assess the positive and negative repercussions of knowing whether a child will be normal or abnormal and then trying to translate them into financial terms (cf. compensation awarded in US courts). The concerted action was therefore aimed at contributing towards the assessment of the systematic detection of malformations by means of echography (of which many speak highly but whose value has never been proven). The new proposal was accepted outright by the COMAC-HSR but only for a period of two years. Two years seems a very short period to the project leader since he is dependent on pregnancies which last nine months.

The difficulty of the action lay in the fact that, for one thing, fetal malformations are relatively rare, and, for another, there are many types. This means that each type of defect is very rarely encountered. If sensitivity (few false negatives) and specificity (few false positives) is to be assessed, the study has to be carried out on the basis of a very large number of situations. In this case, the action aims to gather data on 75 000 births a year.

The protocol for the project was devised during the feasibility study. However, only now do the difficulties inherent in the protocol emerge. On the one hand, there was a great deal of enthusiasm for the action, but this dwindled when it came to the questionnaires. Also, health systems differ from one country to another. The pilot study concerned France and Belgium, whose health systems are similar, but the differences in the other countries are greater. In Germany, there are only referred patients (i.e. patients are sent to the echographer by another doctor); there is no systematic and routine echography. In Belgium and France three-quarters of all echographs are done without prior selection. In Denmark the situation is comparable to that in Germany; screening is authorized in only one or two centres. In Sweden hospitals see everybody; doctors cannot perform echographs outside hospitals. If the protocol was too rigid, only ten teams in Europe would take part, with the result that at most 50 000 births a year would be covered. Another difference concerns the time when the echographic examination should be carried out; it was difficult to require carrying out the examination in the twentieth week of pregnancy, so a range of a few weeks was proposed. Similarly, it was impossible to require a second screening because in certain countries, e.g. the United Kingdom, that is quite simply not allowed; a second examination is authorized only in specific cases. Consequently, a flexible protocol was needed. The difficulties would be overcome when the data were analysed.

The teams participating in the action were recruited from the personal network of the project leader in several countries. They in turn recruited others. According to the project leader, the teams take part out of scientific interest, for the pleasure of it or for the honour of taking part in a Commission concerted action. However, to keep them, support them and stimulate them, he has to engage in a considerable amount of correspondence, make a lot of telephone calls and pay a lot of visits on the spot. Also, it is possible to answer the teams' questions at meetings organized by the national representatives. One of the difficulties of mobilizing the teams concerns the question of local funding. For example, to support his Portuguese representative, the project leader had to send a letter to the relevant Minister. The same applies in the United Kingdom. Apart from these sustained contacts, there is little feedback to the teams. The project

leader would like to pay them something as a recompense for the work carried out, e.g. a small fee per questionnaire completed. However, either the amount is ridiculously small, or the cost involved is too great.

The data to be collected are standardized through a series of one-page questionnaires in all languages. Not all the births are recorded; only those with anomalies are taken into account. Where an anomaly is detected during the echographic examination, a questionnaire is completed. At birth, another questionnaire (No 2) is also completed. If the examination does not reveal any anomaly, no questionnaire is completed. However, if at the time of birth a defect is found which has not been suspected a No 3 questionnaire has to be completed. The No 1 questionnaire ensured that clinicians do not correct themselves after finding an unsuspected anomaly during the echographic examination at the time of birth. Pessimistic clinicians send a lot of No 1 sheets; consequently, they will have many false positives, causing an extra burden, in particular of a psychological nature, for the parents. Optimistic clinicians consider small anomalies insignificant and send few No 1 sheets; they will have many false negatives.

The data are transmitted on paper because there are too many incompatibilities between computerized systems. They are encoded so as to build up a large data base. All the questionnaires received are encoded, whether they are from countries where screening is systematic or countries where the examination is carried out only for referred patients. The latter are recorded only to serve as a comparison between the two systems and in order to understand why patients are referred. The data base is then split up; part of the file is processed by the Toulouse team for the epidemiological side. Another file is generated and sent to the Lille team for the cost-effectiveness analysis. Psychological aspects are not covered by the questionnaires; a team is given the responsibility of contacting patients and carrying out its own survey since it seemed out of the question to cover the psychological aspects in a questionnaire. Analyses will be carried out on the data base(s) of the echography concerted action; even through there may be a shortage of data, these analyses will have to display the rigour hoped for initially. The size of the base will be unique : several non-EEC countries (Japan, Israel, Yugoslavia, Argentina, Canada) wish to be able to take part in this project to increase the number of cases and to compare the screening systems.

> *The polarizing element in this case is the infrastructure that has to be established to assemble the cases. Even though the initial project had undergone a prior feasibility study, it had to be changed considerably, and adapted to the different national institutional contexts, and a follow-up (national representatives) and awareness-raising set-up had to be created. Like the phantoms or the dogs at Petten, sub-bases circulate to enable the specialized teams to carry out ad hoc processing. The base constitutes both a culmination and a starting point. Faced with such a configuration, the analysis often tends to obscure the first dimension, the collection infrastructure put in place. Does it pay for itself as a result of the sole operation carried out? This question is all the more important since several other "large number of cases" data bases have been encountered in this programme.*

AN EXAMPLE OF A REGISTRY : THE CA ON CONGENITAL ABNORMALITIES

Registries constitute a variant of the "large number of cases" data bases. A registry is a data base which is supposed to be updated regularly as and when certain events occur, e.g. every time there is a birth. Several concerted actions have been devoted to setting up such registries, e.g. the CAs on avoidable deaths in Europe, viral hepatitis, central data bases for the epidemiology of AIDS or the data base for the monitoring of a reference population of patients suffering from sexually transmissible diseases. As for the "large number of cases" bases, the registry is the focal point of the network; all the flows of circulating intermediaries converge on it or stem from it.

It is perhaps no coincidence that the oldest concerted action concerns the establishment of a registry. That is the one that we have chosen to illustrate the polarization resulting from this centralized facility and also to raise the question of the future. In 1971 the present project leader was invited by an EC expert group on chronic bronchitis. In 1973 he was asked to consider the possibility of a European medical research programme. It was a question of identifying and selecting a few research subjects which might arouse the interest of the medical community. A research project of the project leader, funded by the Belgian Medical Research Fund had recently come to an end; this was a study on congenital anomalies in Hainaut. The topic of congenital anomalies fitted the bill. After the Thalidomide affair, nobody could turn it down, despite the suspiciousness of doctors about epidemiology (problem of secrecy). The project leader was given a grant to travel around Europe and see what was being done in terms of registries of congenital anomalies. A report was drawn up on the various practices and problems encountered; it was a contribution in itself since at the time nobody had suspected the scale of the standardization problems. On the basis of this a concerted action was launched. This was the first and only concerted action of the "Epidemiology" sub-working group. With the passage of time, the chairmen and the acronyms have changed; what was the sub-working group has become the COMAC and what used to be called the COMAC is now called the PMG.

Epidemiological monitoring on a European scale was impossible at the time; it was first of all necessary to speak a common language and carry out a data-validation study : what was recorded in each of the registries? After several years of work, the registries reaped the benefits of cooperation. For a number of years now they have formed a network which makes comparisons possible between countries or regions. They have demonstrated that monitoring was possible. They have also shown that the transfer of data from one country to another is possible without infringing confidentiality. Some years ago, for example, a German television team came to take a look at the central registry to find out "what was done with the data on poor little German children suffering from congenital anomalies". At the time there was an opinion campaign against medical statistics. However, the reporters were won over; the researchers showed all the security measures and the precautions which were taken to ensure confidentiality. Contrary to their intitial intention, their broadcast showed that it was possible to preserve confidentiality. This was a very favourable development for the concerted action. At present 23 regional centres each record data concerning about 20 000 births per annum. Overall that corresponds to around 350 000 births a year. The regions were selected on an informal basis following visits by the project leader assisted by one or two colleagues. The liaison officers for these registers are three epidemiologists, six paediatricians, four geneticists, five public health specialists

and three people with multidisciplinary training (e.g. in epidemiology, genetics and embryology). Training in the recording of data and local data handling has been organized. Publications and course notes have been printed. The encoders from the different centres meet regularly with the project leader's team. Data transmission is mostly via an electronic mail network which has gradually developed between the centres with the support of the concerted action. The data gathered by the centres (diagnoses and questionnaires) are centralized in the project leader's team which has computer equipment and qualified staff to carry out processing and interpretation (determination of artifacts, analysis of trends, identification of specific problems to be studied ...). The teams can process the data and publish them quite freely if their own country is involved. If, on the other hand, all the countries are involved it is first necessary to obtain the agreement of all the members. Provision is also made for the possibility of replying to external requests. In that event, anonymous data are provided so as to prevent comparisons between countries. This is the case, for example, with a research project on mongolism and seasonal variations (Down's Syndrome).

The stage in progress is aimed at setting up alarm mechanisms to identify whether environmental factors are involved. For example, this network was the only one able to assess the impact of the Chernobyl accident in terms of congenital anomalies. The investigation of alarm mechanisms, and their genesis (early warning systems) will be one of the main developments of work in the future. To this end, a user's manual for new methods of alarm mechanism investigation is to be prepared for the centres.

The users of the results obtained from this network of registries are mainly the public health authorities and doctors. While relations with the Belgian health services are good, they are not particularly well developed. Thus, within the Commission itself, another Directorate-General wanted to take action following Chernobyl and was completely unaware that DG XII was already doing something. The action's visibility has improved considerably since it has published its own two- page newsletter. An important objective is to pass on the message to doctors, paediatricians and gynaecologists. Information meetings are organized, and summaries and articles for the layman are published. A considerable amount of work is needed vis-à-vis users, in particular to answer their questions; this has been done in Glasgow with paediatricians. However, in general, the clinicians do not use the data produced by the network. Doctors and clinicians should first of all be trained in clinical epidemiology, so as to demonstrate the value of such analyses for clinical testing, the definition of syndromes, etc. Lastly, there is a specific collaboration with industry on a research project on retinoic acid.

The network was built up with few resources. The project leader found additional funding in his country. The concerted action pays for coordination, travelling and computer costs but, apart from that, the 24 centres have to operate their registry on their own (secretary, validation by a clinician, ...). Some registries are adequately funded, others operate with volunteers and there is one registry that is in a bad way because the money has run out. It is difficult to help it and to exert pressure at national level because the links between the COMAC and the national authorities are weak. This is an unentended effect for the informal approach adopted which appears to the project leader to be the only possible way of proceeding since it makes for direct collaboration with people at the grass-roots level.

This third example of polarizing fixed intermediary of which, as we have indicated, there are many in the MHR programme, highlights a major problem. A lengthy, cautious research operation which was based on interested partners (and was hence informal) was needed to establish a series of regional or national collection systems, organize data comparability, and build a reference centre capable of encoding, storing and processing large quantities of information (some 350 000 cases a year). However, once its value has been demonstrated two questions arise :

(i) The question of durability. If there is to be continuous monitoring, ways will have to be found to put on a lasting basis not only the central unit but also the networks on which it is based. This raises the problem of coordination with the national authorities, a problem which is especially delicate in that in several countries the situation regarding these networks is unstable.

(ii) The question of achieving an "industrial scale". The example given showed just how much needs to be done to make the information available to all those for whom it is of value, to make it more user-friendly, and to have a forward impact (early warning). By not confining itself to "fundamental" research and by paving the way for constructive answers to the questions raised, the programme will increasingly be confronted with the problem of "exploiting" these answers, a problem which is all the more difficult given that the "markets" in question are rarely commercial ones.

2. Three examples of "guiding" fixed intermediaries

In the cases described above the intermediary "polarizes" the teams towards a common goal; there is another type of set-up which, like the CERN, provides a unique working tool for a community of researchers, enabling them to have a facility they did not have before or to carry out an operation which was difficult for them to do before. It is worth noting that in all the cases we encountered this service does not simply boil down to the title often given to it, namely the provision of heavy equipment. On the contrary, the centralized facilities comprise a package of equipment, which is perhaps neither unique nor rare, and knowledge and skills accumulated and incorporated in research workers, procedures, a laboratory set-up and publications. While none of the individual items may actually be innovative, the way in which they dovetail turns them into a special whole which functions as an obligatory passage point. The following three examples illustrate this.

A CENTRALIZED FACILITY FOR SEQUENCING THE AIDS VIRUS

Established in the old, renovated laboratories of the famous chemist Paul Ehrlich in Frankfurt, a research team forms the core of a concerted action dedicated to the genetic analysis of the AIDS virus. Between 60 and 70 people are working in this team, including 30 to 40 on DNA sequencing. The laboratory is comparable to other molecular biology or biochemistry laboratories if only because it contains a sterile area and automatic sequencing equipment. Such equipment exists in other laboratories and is therefore not unique. There are two types : that of the European Molecular Biology Laboratory (EMBL) and that of private companies (more and more automated sequencing instruments are coming

onto the market). So why, if this equipment is so readily available, set up a concerted action organized around a laboratory set up as a centralized facility for sequencing the AIDS virus?

Some laboratories carry out by themselves the sequencing they need. This is not, however, true of all laboratories, in particular the smallest ones. In the survey carried out before the concerted action was launched, it emerged that three-quarters of the teams said that they were unable to have their material sequenced. It was therefore important to organize these laboratories' access to sequencing facilities and to establish a European network of competent teams. To this end, it was necessary to organize links between teams, and enable them to train themselves and learn to master the technique in the best laboratories and improve the sequencing techniques. In this way one laboratory becomes a centralized facility for others, e.g. ones that are too small and do not have the means to carry out the work themselves. However, it is not only the small laboratories that are interested in such a centralized facility; even larger laboratories have expressed a need for one. In fact, sequencing techniques are evolving very quickly and it is important to have teams who can keep up with developments. Although certain laboratories can carry out sequencing by themselves, they turn to this centralized facility because not only does it have good instruments but also the best accompanying know-how. It is not just a question of having ad hoc instruments available, sometimes it is important to mobilize high-level technical skills.

Lastly, other laboratories with state-of-the-art instruments and high-level technical skills are also turning to the centralized facility. Although they know how to sequence they are in fact less interested in the genetic variation of the virus than the Frankfurt laboratory is. Knowledge of the subject is vital to guide investigations and interpret results. The skills and knowledge built up in Frankfurt are such an original combination that the laboratory represents a resource for all the other teams. Thus, it is not enough to have efficient instruments at one's disposal or even know how to make use of them, the important thing is that knowledge and skills should be built up in such a way that the whole becomes a preferred passage point. There are automatic sequencers but the virus is so variable, for example, depending whether it comes from the blood, nervous tissue or a culture, that knowledge of it is as important as knowledge of the equipment. Prior to 1984-85 the Frankfurt team had in fact never carried out sequencing but had considerable expertise in viral biology. They therefore added sequencing to their repertoire. As a result, they now have virtually unique expertise and know-how. The centralized facility is therefore not just a repository of innovative instrumentation but here provides a device, namely the laboratory, which lines up instruments, researchers, procedures, and inscriptions of various kinds, including literature.

Since the centralized facility is a passage point par excellence, part of the work of the Project Management Group is to manage access to it and the use made of it. Thus in February 1990 a first meeting brought together all the high-level teams involved in sequencing to decide on the general rules and priorities (see box). Although the service is at the disposal of the teams which wish to make use of it for the purposes of their own research projects, very precise guidelines have been adopted, so that a selection and probably also a redirection of projects is carried out through the use of this intermediary. Attention has focused on two areas of the virus genome. The first is a loop which is genetically very variable. It comes into contact with the cell receptors, e.g. of a human being. It has therefore been decided to focus on this part of the virus envelope i.e. the sequence of 600

base pairs out of the total of 9 000 which the envelope contains. In making this choice, the teams are giving preferential attention to the analysis of variations in the virus and its interactions with the cell attacked. The other area on which attention is focusing generates immune reactions and therefore has a protective function. It is important for the study of the development of resistance to anti-viral chemotherapy. Through the organization of the centralized facility, one of the finalities emerges: knowledge of epitopes (where the virus is most differentiated) and the preparation of anti-viral therapies and vaccines.

RULES AND PRIORITIES FOR THE CENTRALIZED FACILITY

For example:

- it has been decided to announce the launching of this concerted action in Nature in order to ensure maximum "visibility" and to reach the teams which might wish to avail themselves of this opportunity;
- rules have been adopted for the selection of the sequences - DNA fragments - proposed. Thus, if material is proposed by a committee member, he will withdraw during the discussions. Voting will be by secret ballot;
- the sequencing results will be kept a secret between the proposing investigator and the centralized facility until they are published or presented at a scientific meeting. They will not even be discussed by the group of experts of the concerted action before publication or presentation;
- for decision-making purposes communication will be by telefax. Meetings will be organized as and when required, possibly on the initiative of one of the members;
- clones will be jointly owned by the centralized facility and the investigator. They will be accessible to the entire scientific community following publication;
- there is no general rule concerning publication; agreements will be prepared on an ad hoc basis between researchers;
- there is no general rule regarding patents. The Commission has no patent rights;
- the results will be evaluated by the PMG,
- project selection criteria have been adopted : the investigator proposing a fragment to be sequenced will provide information on the project for which sequencing is proposed. In addition, only viral sequences will be analysed and certain areas of the genome are regarded as having priority, precedence having been given to human problems. The material also has to be presented in certain special forms.

The centralized facility will sequence some 200 000 base pairs per annum for the network. This represents about half of the sequencing to be carried out in all the laboratories inside and outside the concerted action (estimate based on work published in scientific journals). The centralized facility is aimed primarily, but not exclusively, at Europeans. Prior to the concerted action, the Frankfurt team sequenced, solely for its own requirements, 40 000 base pairs for AIDS and 100 000 base pairs for cancer. To move from 40 000 to 200 000 base pairs five times as many staff and more sophisticated equipment will be needed. That is why one of the tasks of the central team is to improve the technique in collaboration with industry. Recommendations have been made with a view to improving the equipment; the new, improved equipment should be available in the next few years. However, the technique has not yet been fully mastered. Apart from equipment, other components of the process will have to be improved : the starting material proposed by the teams, the enzyme used in the reaction, reaction efficiency and software.

With regard to the material analysed, the centralized facility needs virus fragments from different laboratories. Part of the work of the Frankfurt team is to organize the transmission of viruses. To do this, specifications have been adopted concerning the vector : sample of infected blood, cloned fragment, etc. Also, each country has laid down its own rules concerning the carriage of infected blood : test tube in a container itself placed in another container (in case there is a plane crash). Transport is expensive, costing approximately DM 200 per sample. The carrier has to be informed and this entails a lot of formalities, especially as there are differences between the rules in the different countries.

Sequencing quality depends to a large extent on the quality of the material analysed. Consequently, the central team not only lays down rules for the preparation of the material but also undertakes to train research workers proposing a sequence, so that gradually the practices of the proposing teams are improved. Quality and purity are major problems. Researchers will be sent from Frankfurt to the other teams to assess how the work is carried out and to help them. Quality control will be organized internally within the analysis procedure, thus subjecting the sequence to two reactions in opposite directions. Discrepancies between the results will make it possible to assess the quality of the material submitted.

While the actual organization of exchanges is a time-consuming exercise for the central team, it is recompensed by the information and material received. By placing its knowledge and skills at the disposal of the other teams, it can build up even more knowledge and skills regarding its main research topic : the genomic variability of the virus - its users are thus transformed into its suppliers.

> *This example indicates the threefold role of such facilities dedicated to a stage in the research process, in this case DNA sequencing. The first is obvious : the facility is an instrument at the service of the teams to enable them to tackle this stage more easily and more reliably. The second concerns access conditions which help to gradually guide the community of users : first by focusing the work on only part of the pairs of the envelope, and then by improving and harmonizing laboratory practices (for the preparation of samples). By bringing their viruses for sequencing, the users are also suppliers of a team specializing in the genetic variability of the virus, which as a result continually increases its knowledge and skills : this is the third role. This example clearly shows the three simultaneous effects produced : the service rendered to researchers, the focusing of topics and the harmonization of practices, and the accumulation of specific knowhow (in this case the genomic variability of the virus).*

A CENTRALIZED FACILITY FOR RESEARCH INTO ANTIVIRAL MOLECULES

A second example of a laboratory set up within a network as a centralized facility concerns the design, synthesis and evaluation of new anti-viral compounds. In this case, the attraction of the laboratory lies mainly in skills and knowledge built up rather than in special instrumentation.

Although the service offered is methodological in nature, namely the systematic testing (screening) of molecules presumed to be potentially active against the AIDS virus (primo-infection), the main reason why it is such a preferred obligatory passage point is that it provides support for the tests as a

guide to the deliberations of the partners. It is therefore as much an actor - jointly responsible for orienting the work of its partners - as an intermediary, a service screening the molecules submitted to it. Seen as a centralized facility the laboratory is an intermediary which gives substance to the interactions - perhaps the only interactions - between research teams providing their own molecules. However, it is also an actor which transforms the network of laboratories seeking anti-viral molecules by impacting on the flows of circulating intermediaries, i.e. the publications it co-signs and the molecules it agrees to test.

The laboratory work had begun well before the concerted action, with research into other anti-viral molecules. The institute where it is situated carries out microbiology research for its medical faculty. It was set up by a rector who had been the director of a pharmaceutical company which had donated a building to the university provided that the research conducted there was of benefit to it. There was therefore a close link between the university and this company. The link has since been broken but the traditional connection between fundamental research and applications has persisted; the department of pharmaceutical synthesis has in fact been very successful. A member of this laboratory, a colleague of the current concerted action leader, has been interested in anti-viral molecules for a long time. However, there has been less success than with antibiotics, since unlike other microbes, the viruses do not have general action mechanisms. It all happens in the human cell; the difficulty lies in the fact of having to act on the mechanism which is both the most suited to the virus and the least suited to the cell. It has been a challenge for 20 years. Only two or three molecules have proved successful, in particular against herpes, meriting a Nobel prize. This research colleague has quite a reputation; chemists and pharmacists like to work with him. Later AIDS was added to his work. In 1984 one of his molecules was tested by the National Institute of Health (NIH) and became the first anti-viral molecule against AIDS. However, it turned out to be too toxic. The laboratory then started to analyse systematically a large number of molecules analagous to nucleosides in order to identify ones which might have anti-viral properties against AIDS. In this connection, the laboratory had already contacted many others which wanted to have their molecules examined and to determine whether they might be active against the AIDS virus. The proposals sent to the laboratory were in all cases discussed by the proposing team and the laboratory. The latter carried out a selection on the basis of the assumed merits of the experiment. The tests were carried out on the basis of ad hoc scientific collaboration; there was no question of payment.

The laboratory considered charging for this service. The NIH in the United States did in fact try to do so, but its scheme proved unsuccessful. This experiment showed that with an automatic screening service researchers lose all motivation. Neither competence nor remuneration is sufficient to operate such a laboratory as a centralized facility. Fundamental research is vital to keep alive the interest of competent researchers. The project leader's laboratory therefore decided to avoid any system of automatic screening against standard charges. It preferred instead to go in for collaboration between scientists with fundamental research interests. It made it a rule always to choose its partners and its molecules. It is therefore not simply a centralized facility at the disposal of the other teams but a partner.

Part of the competence of the laboratory lies in the fact that a very sensitive test was developed by it. With this test researchers identify "lead" molecules active

against primo-infections which they subsequently modify to make them active against persistent infections. In fact, according to the project leader, the modification of the lead molecules is the heart of the matter. The objective for the laboratory is therefore to be able to test a growing number of molecules without losing its ability to act with discernment, to be able to operate in accordance with a certain routine while being driven mainly by questions of research. The present concerted action has made it possible to establish a certain routine in the work carried out and broaden both the collaboration and the spectrum of molecules. This laboratory differs from ones offering similar services in that it considers a broad spectrum of molecules whereas the others mainly focus on a molecule which they are trying to vary. Competitors are, moreover, not particularly interested in carrying out genuine screening. Instead of being confined to screening, its endeavours are more concerned with providing guidance for research projects. In this way it exerts significant influence over the direction of the work of the teams proposing molecules. Some have changed molecule in the light of the results obtained by the central team.

In the concerted action all the teams are on an equal footing, whether European or not, whether public or private. "The molecule makes all the difference." This also means that the membership list is not exhaustive; it depends on the proposals. Moreover, the network confines itself mainly to a series of independent links between proposers and the central team. As a result of concerted action and Community intervention, the number of molecules tested has doubled even though funding represents only 10% of the laboratory's resources. It has 15 scientists and 20 to 25 technicians. In selecting the collaboration to form the basis for the network, the central team also takes account of the quality of the applicant and the research project concerned by the test application. At present 25% of collaborations concern the pharmaceutical industry. This figure may seem rather low but it is explained by the lack of certainty with regard to patent law. Many manufacturers have molecules pending but are hesitant about taking the plunge. The value of concerted action for the central team consists in increasing the number of its publications and co-signing texts with teams which submit molecules. Between 1986 and 1990 a hundred or so articles were published, 41 of which acknowledged the Commission's contribution. The NIH does not have as many. Most of the articles are written by the laboratory.

> *This example of concerted action illustrates a second aspect of this type of central facility; its strength lies less in the uniqueness of its technical set-up than in the competence and experience built up; this cannot be maintained easily, it is necessary to achieve a compromise between users of the facility and the scientists who operate it. This results in the selection of molecules directly by the facility and joint publications. It is less a question of guiding a community than of providing a service and of performing an advisory role for user teams with very different interests and problems. This process of accumulation of expertise and knowledge strengthens it as a resource and guide for its research partners.*

THE CA ON CARDIOVASCULAR RESEARCH AND TRANSGENIC RATS

Another exemplary case concerns the production of material tailor-made for users of the facility. This is the case with the concerted action aimed at

introducing a new cardiovascular research technique, namely the production of rats carrying genes which are not part of their normal genetic pool - transgenic rats.

Transgenic rats could be a new medium for investigating biological mechanisms and certain pathologies. Thus, by cloning (in the rat) the gene responsible for an illness it will be possible to study the development of the illness. Researchers would have an experimental model. The transgenic rat production technique is of recent origin, it is fairly expensive and the skills involved take a long time to acquire. Only a few teams in the world have mastered this technique.

It is a known fact that the rat is a better model than the mouse for the study of hypertension. The rat also has an added advantage since it is easier to fit a catheter to it. That is why the present project leader had the idea of proposing a project aimed at applying the transgenic rat production technique to cardiovascular research. It would therefore be a question of cloning the hypertension gene in rats.

There are two methods of producing transgenic rats : traditional microinjection - the cell nucleus is bombarded with DNA - and the embryonic-cell technique - DNA is added to the cell culture containing an embryonic cell. Two member teams of the concerted action are skilled in the first method but the feasibility of the second has not yet been demonstrated. With microinjection the genetics of the animals is known over two to three generations. The advantage lies in the fact that several animals can be bred in the same place and distributed; there is therefore standardization of the material used and control over the genetics of the animals. This standardization will be all the better when it is possible to move on from "outbreeding" to "inbreeding" techniques. In parallel with the production of transgenic rats by microinjection and the development of the embryonic-cell technique, to get round the absence of a breeding facility some teams are endeavouring to develop a method of freezing rat embryos. These embryos will easily be sent to all the teams, but "the teams have to be prepared". They have to send a technician to the central team for two or three days to learn how to defreeze the eggs and reimplant the embryos. At full capacity there may be several hundred embryos but that will depend on the types of transgenic rats requested. With outbreeding, it is difficult to produce many embryos. With inbreeding, once an embryo is obtained it is easy, with hormone treatment, to obtain more than 100. However, to meet the needs expressed at present it is unnecessary to resort to these techniques or freezing.

The concerted action network revolves around the production of transgenic rats. The outlying teams are of two types : ones with experience in molecular biology will be interested in the genes to be cloned while the others will study the transgenic rats and use them as models. The former provide genes to the central team which clones them and supplies rats to the latter.

All the teams that want to receive rats can submit a request. However, priority is given to the ones which supply genes. Thus, if a team has cloned a gene for several years it will receive rats carrying this gene on a priority basis. Members of the concerted action have agreed that teams outside the project should also have access to this facility. If a team, even an industrial team, asks for rats for a research project it will be given them provided that collaboration ensues. For this reason, applicant teams are asked to give details of their projects, the goal being to ensure that the rats are not produced unnecessarily : effective use, relevance and

prospects of success for the research project are pre-requisites, and there must be no duplication with other actions. As of June 1990, 20 requests for rats (each for between 6 and 30 animals) had been made, including six for specific genes. Where possible, the central team tries to accept all requests.

While not actually calling for unique equipment, the production set-up does call for specific and comparatively expensive equipment for the production of transgenic rats : micromanipulators, camera microscopes for DNA injection, microinjectors, CO_2 incubators, binoculars, including one specially designed for rats (bigger than the binoculars generally used), freezing equipment with microcomputer, a special binocular for eggs etc. Among the reagents, allowance has to be made for costly hormone reserves. The rats are produced on request. It takes three to four months. To transport the rats a cage is needed and there are special formalities depending on the countries involved. With frozen embryos, frontier and health problems will be avoided. The transport of genes, on the other hand, is simpler; preserved in pure solution or in the form of precipitates, they are easily transported in small flasks.

When many teams have transgenic rats, the network will be able to produce reference material and organize intercomparisons. To do this, the teams will have to set up a group with joint research projects. At present this is a distant prospect. The network consists of 20 or so teams which did not know one other before the action began and which each have their own individual projects apart from a few *ad hoc* collaborations. Those in charge of the action are keen to develop contacts between the teams but consider that the time is not yet ripe. Before organizing networks around research topics they feel it necessary to establish a "hard network": a larger number of interested teams, technicians trained in the freezing and reimplantation of embryos, reliable methodologies and above all transgenic rats. The teams will then ask themselves new questions, and their perception of the mechanisms of arterial hypertension will change as will the way in which they formulate the problems. The existence of a hard network and new techniques will have an impact on the general direction of the researchers' questions. That is already the case following an article published by the project leader in Nature.

> *The centralized facility, by changing the models on which work is carried out, seeks to transform research topics in this area. The approach chosen is a gradual arousal of interest by distributing an original and specific material. This is regarded as another way of rethinking and structuring a topic at European level. These three examples show to what extent these centralized facilities which combine techniques and competence can play a decisive role in the organization and structuring of a speciality. They do not seek, as with BNCT or the B cell extraction unit, to produce a new "treatment" directly, they are primarily concerned with organizing a scientific community and its work on a European scale. The service they provide is part and parcel of their scientific advisory and guiding role.*

3. Two examples of "common in-house services"

The distinguishing features of all the facilities looked at so far have been their uniqueness and originality : they are compulsory passage point not only for CA members but for scientists in general wanting to work on these questions. The facilities described below are different. They are perhaps ordinary by comparison,

but their purpose is to ensure intercomparability of the output of the teams and to make use of this output to achieve results. Their primary task therefore is an in-house contribution to a course of action which they do not define.

CA ON OSTEOPOROSIS AND THE CENTRE FOR X-RAY PLATE ANALYSIS

Osteoporosis is a disease which is increasingly attracting the attention of the medical profession, firstly because it is affecting a growing proportion of the population through ageing and, secondly, because of the appearance of new instruments to measure bone density. The economic stakes are high for both the equipment industries and the pharmaceutical companies (hormone treatment). Through this concerted action researchers are seeking to improve their knowledge of the prevalence, risk factors and impact of osteoporosis. A research protocol has been prepared and some 50 medical teams recruited to gather the relevant data. The protocol was issued in the form of a questionnaire to be completed for each patient. Doctors must attach two X-ray plates to each questionnaire. All data are collected by a central team which encodes and processes them.

The requirement to append X-rays resulted in a fall in the response rate to around 60%. While the Project Management Group is prepared to accept some loss in scientific precision in order to increase the numbers taking part, it is nevertheless determined to maintain the requirement to attach two X-rays. Similarly, as regards the reading and interpretation of plates, the same concern to find a solution which would extend participation while maintaining a very high level of scientific quality prompted the PMG to standardize the work. Knowing that some 40 000 X-ray plates would have to be read and analysed, the PMG could have asked each team to carry out the work on its own plates on the basis of an agreed protocol. This approach was rejected since the composition of the teams varies from one country to another, but above all because one member of the concerted action was determined to develop an automated plate reading system.

The machine is an image analyser linked to a computer developed for the project by one of the teams belonging to the PMG, in collaboration with the Siemens company and with financial assistance from the German Government and the Commission. It cost some DM 2 million. The machine does not need to rely on the skills of the teams involved in order to ensure a high quality output for the overall network; in other words, it assumes that the teams have no knowledge of how to read X-ray plates. Without the plate reader, this action might have followed the same pattern as some other actions, with local practices being changed to meet a new quality standard but with some loss of overall scientific quality. In this case the opposite happened. Relying on the machine to ensure a high level of overall quality avoids the need to change the teams' habits. Furthermore, centralizing the machine-reading of X-ray plates limits interaction between the teams : information meeting and initial discussion of the project with the teams, distribution of questionnaires, collecting of questionnaires and plates. The network has a "star" structure, so apart from the subgroups which initiate and organize the work the data-gathering teams are linked to the central team and have little contact with each other. Without the plate reader to ensure a high level of quality it would have been necessary, for instance, to organize more meetings to prepare and train the teams, to harmonize their practices and to ensure the necessary feedback.

The setting-up of the analysis centre and the development of the plate analyser avoided the need to go through the lengthy process - experienced with other subsequent projects - of harmonizing the wide variety of training experience and practices in the different teams. The action benefits in terms of time-saving and size (it was able to recruit a large number of teams), but on the other hand it has no standardizing effect on practices and does not generate any new space for collective research.

AN EXAMPLE OF AN AD-HOC DATA BASE

The number of data bases developed for the in-house needs of the CA is increasing. They require premises, a team, data-gathering facilities but, unlike the previous case, data bases are usually just one of the resources which oil the wheels' of the project without having a profound influence on its direction. This is illustrated by the following example.

A small European network of epidemiologists, paediatricians, obstetricians and virologists was set up to carry out a forward study on children born to seropositive mothers (AIDS). It comprises 11 teams working chiefly in hospitals. Following a pilot study on pregnancy infections conducted by a number of teams as part of another concerted action, it became apparent that no forward study had been made of the transmission of AIDS from mother to baby. It was this observation, together with the experience gained by certain teams on forward studies, that gave rise to this concerted action. Their aim is to assemble information on the rate and circumstances of virus transmission by studying a set of factors liable to influence transmission from mother to baby.

The teams working on the concerted action have to mobilize local resources to monitor children over a period of six to seven years. This duration is considered the absolute minimum because of the latent period in the development of the virus and the disease. It is necessary to monitor the children's growth and to find out what happens to them. An epidemiological questionnaire was prepared to provide local guidance for data gathering and to harmonize the data in order to make them comparable and combinable. It also sets out the conditions of participation in the study, in particular the commitment to monitor the children for seven years. These strict parameters limits the sample to some 600 children. However, even though the sample is small, it could never have been assembled using only local resources and it would be impossible to compare the results of individual studies.

The questionnaires completed by the teams are returned to the project leader. His team enters the results in a data base, monitors each case individually and, each month, asks the "registration centre" teams to monitor the child and document its development. The data base is located in the computer system of the project leader's university. It is anonymous in order to ensure confidentiality of the data on the children monitored. The teams belonging to the project have access to the data; a diskette can be forwarded to them regularly with changes and updates. In practice the teams do not ask for such information on diskette because manipulation is too complex. The project leader hopes nevertheless that the teams will use the information once the data base has established itself. In any event his own team will process the data in order to provide information to be used in education and by the public health services concerned; the World Health Organization is also interested in this study for the purpose of making comparisons with the situation in Africa. The results of the study on transmission

factors will be published in scientific publications under the auspices of the concerted action.

> *In this case the data base is the medium which enables the forward study to produce results. It confines itself to recording standardized data on the children and reminding the individual teams of their obligations. The participants are held together by their reliance on statistics, but there is no need for interchange or joint activities after the initial meetings to set up the project. This is a different kind of "common in-house service" whose intermediary function is both clearly defined (a specific task which is executed without real interaction) and for a finite period of time (once the task is completed the purpose has been served). It performs a service function for the concerted action, facilitating the work without altering or going outside the scope of the action. It should be stressed, however, that it can only come into being once practices have been harmonized and a common protocol has been established : such ad hoc data bases therefore signify the transition to another stage and (through all the associated arrangements for gathering the information) constitute a concrete expression of progress towards the end result.*

4. Traditionnal scientific and technical interchange

To the outside observer centralized facilities are like major architectural achievements in the sense that they attract the gaze and command attention. Their other advantage in the context of this programme and the stereotyped images which it all too often creates is that they stand out and typify the concrete achievements of the programme. A concerted action does not fit snugly into the traditional model of academic interchange, i.e. conferences, reports, articles, visits, etc. However, these forms do play a key role in the building of concerted actions. They are the most common forms of interchange. It is necessary to know what other people are doing in order to consider working together and it is necessary to meet in order to organize the pooling of preoccupations and plans.

Meetings and reports are commonplace. Yet our study of 100 or so concerted actions has underlined for us the extent to which their material organization, their outcome and the dissemination of results influence the appeal and the visibility of the concerted action. As with a company, human resources management and communications are tools which are essential to the performance of concerted actions. We therefore felt that it would be useful to present a brief, if incomplete, summary of the traditional forms of interchange and scientific and technical collaboration.

MEETINGS OF RESEARCH SCIENTISTS

Virtually all concerted actions organize meetings, seminars, workshops or colloquia. All these activities bring together the researchers belonging to the network and also, depending on the case, other research scientists, clinicians who may wish to use the results, industrialists, politicians, etc. By bringing people together in a single place, an interaction takes place which is more or less intimate or formal depending on the respective amounts of time devoted to papers, discussions and informal exchanges. On such occasions individuals chiefly exchange papers and documents (texts, layouts, data, business cards), but also

equipment, samples, computer media, etc. Often a number of such meetings are organized during the life of a concerted action; they set the tempo of its development. They generally mark turning points in the work : initiation of the project, approval of the protocol, discussion of findings, general presentation of the project results.

Not only are meetings organized for all concerted actions, but most of the teams involved have attended one or other of these meetings. In fact, 80% of those replying to the postal survey[5] said that they had taken part in such meetings. What is more, it is an important activity since the teams whose actions began before 1989 attended on average three plenary meetings and four meetings of restricted working groups. As far as the CA budgets are concerned, the organization of meetings and corresponding travel expenses for research scientists generally account for over half of Commission funding.

TABLE 9 : TEAM ATTENDANCE AT MEETINGS

	team attendance	average no. of meetings ("old" CAs)
plenary meetings	70%	3.2
restricted meetings	66%	4.1

TABLE 10 : TEAM ATTENDANCE AT RESTRICTED MEETINGS

purpose of meeting	attendance by teams
presentation of results	59%
detailed discussion of results	55%
preparation of joint instrument	39%
organization of work	53%
training	20%

TABLE 11: RESULTS OF MEETINGS

nature of results	referred to in teams' answers
articles	42%
internal documents	44%
reports	42%
standards	24%
published works	25%

Not all meetings are necessarily the same. Plenary meetings include both those which involve only the members of the network (initial meeting, annual meeting) and those which are open either to a number of invited observers or to the scientific community or to an even broader audience. Restricted meetings can be devoted to work organization (these tend to concern the Project Management

[5] It should be borne in mind, however, that the teams who replied are those most closely involved int he programme.

Group), to the preparation of a joint instrument (often a protocol), to the training of participants (e.g. to harmonize data gathering) or to detailed discussion of results. These meetings sometimes generate an end product, which in most cases is a text.

One type of restricted meeting deals with the preparation and organization of work. This task generally involves the Project Management Group, but often other subgroups are set up for specific tasks (for example, the drafting of documents for a plenary meeting at which they are to be discussed) or for tasks which will run throughout the life of the concerted action. In the network on heritable connective tissue disorders, for example, three specialized committees have been set up : a laboratory committee to harmonize methods and procedures, a clinical committee and a data-management committee. A number of these subgroups meet quite regularly, between twice and six times a year depending on the project, in contrast to plenary meetings, which are held at least at the beginning and end of the action and at most once a year. A number of our informants stressed the importance of this systematic joint activity, which helps to create the habit of common working practices going beyond the framework of the action.

Many of the meetings devoted to preparation and work organization involve discussing work protocols, which generally speaking are working documents which have been prepared in advance. In some cases discussions have to end in a consensus at the meeting. In other cases the organizers take note of the discussions and reword the protocol accordingly, which is then either discussed again at a future meeting or implemented as such after being amended by a team or a subgroup. In any event, the purpose of these discussions is to arrive at a consensus and/or to secure acceptance of a joint protocol. Sometimes these meetings are open to people unconnected with the concerted action, in particular where their approval may make their subsequent involvement easier. The October 1990 plenary meeting of the concerted action on the quantitative evaluation of osteoporosis was a case in point. Industrialists were invited as observers to inform them of the process of consensus-building in the network. Their comments were taken into account in the discussions and those taking part adjusted their positions so as to encourage subsequent active involvement of the industrialists concerned. In another concerted action on abdominal pain, the consensus-building process also brought in people from outside the network, in this case the national scientific societies. The aim here was to arrive at a consensus on terminology. A consensus on a protocol is often of such strategic importance that rigorous procedures are implemented, such as the systematic drafting of minutes setting out the arguments advanced by the various parties. This was the case with the ENTA network protocols.

The task of forming a consensus is sometimes delegated to a specialized committee, as in the case of the concerted action on thrombosis which set up a committee to harmonize difficult cases. In certain instances this produces very specific forms of organization. In the concerted action on the diagnostic performance of ECG computer programmes, for instance, a meeting of cardiologists who had taken part in the cutting up of tracings was held. Using a modified Delphi procedure they were sent the tracings and had to mark the point where they would cut between the waves. The data gathered were processed to determine the average and extreme positions for each plot. The tracings with large deviations were sent back to the cardiologists with the previous positions marked;

they were invited to reposition their marks. The results were processed and a third round was organized for those tracings on which a consensus had not yet been reached. At the end of this procedure there were a few tracings (3%) on which no consensus had been reached. At that point the cardiologists were convened to discuss the remaining tracings until they reached a consensus for each.

Meetings are often deliberately open to specific partners, such as the national scientific societies or industrialists in the two cases mentioned. On a more general level they are geared to colleagues who are not actively involved in the network. In the concerted action on heritable connective tissue disorders, plenary meetings of the network are organized systematically in conjunction with the international meetings in this field in order to ensure that the work of the network enjoys the highest possible visibility.

Apart from the discussion of protocols and the consensus-building process, a number of meetings are devoted to the presentation of findings, detailed discussion and comparison of hypotheses and exchanges of ideas. Such meetings are central to the organization of a number of concerted actions. A number of working groups are set up in such cases, corresponding to the individual subprojects. For instance, in the network on problems of the hearing impaired, four subgroups have been set up, starting and concluding their work with plenary meetings. In the hyperthermy network, a series of 15 meetings are planned for the five subprojects as a whole; the main purpose of these meetings is to exchange ideas. In the chronic arthritis network, the members of each of the seven subprojects, each comprising two to three teams, meet four times a year. In the concerted action on DNA repair restricted meetings and plenary meetings are held, chiefly for the exchanging of ideas and results.

In certain cases, meetings are more explicitly aimed at training members of the network to ensure that they are using comparable practices. Under the concerted action on the epidemiology of congenital anomalies, some of these meetings are aimed at the operators of local registries and amount to training courses.

REPORTS AND MINUTES

The meetings and get-togethers give rise to reports and minutes which are often widely circulated within and beyond the concerted action circle. They serve both as a vehicle for information and as a chronicle of intermediate or even final results - final report on the concerted action, workshop proceedings, annual progress reports, etc.

The content and structure of the annual progress reports, which provide the key information to those responsible for the programme, have been specified by the secretaries of COMAC and therefore annual progress reports generally contain the following nine headings :

— preliminary information : title, project leader, membership of project management group, project start date

— status : summary of objectives, scientific and technical status

— activities undertaken: meetings (meetings of the PMG, workshops, symposia), trips by the project leader, exchanges of staff and equipment, publications

— collaboration : members of the concerted action, collaboration outside Europe and with international organizations

— relations with industry

— difficulties encountered in the form of scientific and management problems
— scheduling of meetings and exchanges
— financial information: total budget, expenditure for the period under review
— benefits for European research, for the European Community and for the teams involved.

This kind of report demonstrates the variety of connections established : between teams (activities), with research objects, with the Commission of the European Communities, and with scientific partners (teams outside Europe, scientific organizations), and industrialists, etc. The report, which runs to between 20 and 50 pages, is generally a relatively dry document.

Not all annual reports necessarily conform to this pattern. In the case of the concerted action on common standards for quantitative electrocardiography (CSE), it takes the form of a bound 16 x 24 cm publication of around 300 pages. These progress reports already represent quite a collection, with the ninth being published in 1989. Typically the document consists of:
— a cover page with the title of the concerted action and the name of the organization on whose behalf it is being carried out (concerted action II.1.1.2., Medical and Public Health Research Programme, Commission of the European Communities), the name of the project leader, the volume and year of publication of the document and the logo,
— acknowledgements
— a table of contents
— a brief general introduction (two pages)
— the organizational structure of the concerted action and the position of the various participants in the overall scheme (two pages)
— the minutes of the last annual workshop and the preparatory report for the next workshop
— synopsis of articles already published or soon to be published and the conference proceedings setting out an overall view of the work carried out under the concerted action
— a set of texts connected with this report, already published scientific articles and correspondence between the members of the project about the various tasks and subprojects. They describe the state of progress, work protocols, results obtained and comments, as well as future plans (including reference to standardization bodies in the last annual report).
— a list of doctoral theses using the network data
— a list of the names and addresses of the members of the network
— a list of members' publications during the past year, identifying those which are directly connected with the project
— conclusions (a few pages).

This type of "circulating intermediary" helps to stabilize the network, consolidate it by building on its achievements and lend it a high visibility. Typically the publication of intermediate results marks the various stages of the life of the network.

> *Visits and meetings are the very lifeblood of concerted actions, providing as they do an opportunity for participants to get to know one another, establish joint projects, and harmonize their practices. The examples given demonstrate the variety of forms encountered, the diversity of subjects covered, and the vital role of the consensus-building procedures. Reports*

are generally the medium of written expression, especially annual reports which, in various shapes and sizes which are often specific to the CA, are milestones in its long journey from the cradle to the grave, in many cases constituting a genuine "intermediate result". Meetings, visits and paperwork are the main CA human resources management tool, setting the tone for the project.

5. Exchanges of forms at the core of numerous concerted actions

Of the conventional modes of communication, forms have a particularly important role. They have two distinguishing features. They structure the collection of information between a recipient and a sender to whom the form is supposed to be returned completed and they reflect a situation of "unequal" exchange between one sender and a number of recipients which is deemed to be so large as to rule out the possibility of an unstructured exchange (and the probable follow-up). It therefore lends a particular character to the network. Forms are found in virtually all networks but their circulation varies from one network to another. Sometimes they are sent to a subgroup, sometimes to all members, sometimes to the project member networks (where the members of the action are in fact responsible for local and national epidemiological surveillance networks), and sometimes to people outside these networks (where the questionnaire is used as part of a postal survey of a specifically targeted and/or sample population). In a number of concerted actions, forms - prepared and drawn up by a sub-working group - are used as a means of collecting data. They are filled in by scientists (e.g. as part of the standardized assessment of equipment or to gather information on users' needs at a centralized facility), by clinicians (e.g. whenever the clinician meets a patient whose characteristics correspond to those defined for the project), by general practitioners (in the case of epidemiological surveillance or "sentinel" networks), by correspondents taking part in a survey (as in the case of assessment of the quality of care in intensive care units), by patients (in such cases the questionnaire is submitted by clinicians taking part in the project) or by selected individuals as part of a postal survey. From the layout of the form and its appendices (accompanying letter and protocol or instructions for use) it is generally possible to identify the authors, the issuing and/or transmitting bodies, the recipients of the blank forms (or at least a profile), the recipients and forwarders of completed forms and the end users responsible for processing them.

What happens to these forms from their conception to their processing will vary from one concerted action to another. In some cases they are sent without amendment or intervention by the authors directly to the individuals who are required to complete them. In other cases they go via an agent, often a national correspondent, who receives several tens or hundreds of copies and is responsible for distributing them in his particular network. In other cases the forms undergo major changes, notably when they are translated into the languages of the various countries taking part in the survey. In such cases the questionnaires sent from the drafting working party to the national correspondents are not the same as the questionnaires sent by those correspondents to the survey teams and respondents. National correspondents often take charge of translating the questionnaires and adapting them to national circumstances. However, such are the

changes resulting from translation that some networks have introduced other coordination mechanisms, e.g. (1) questionnaires are translated directly and/or under the supervision of a single central team; (2) alternatively they are translated by the national correspondents and then returned to the central team to check conformity with the original text; they are then photocopied and distributed by the national correspondent; (3) questionnaires are translated from English into the language of the country by the national correspondents, then returned to the central team which translates them back into English and compares the final English version with the original English version; (4) the questionnaires are translated by the national correspondents but printing and distribution is the responsibility of the central team (this situation is found in particular in cases of concerted actions where the project leader stresses the need to have a single-page layout for the purposes of encoding the results, whatever the language and despite variations in the length of the questions depending on the language in which they are written).

The changes which are made when the questionnaires go through the hands of the national correspondents are sometimes far more significant than just matters of translation. In certain concerted actions the joint questionnaire is intended to be incorporated into national surveys. Each of these has its own priorities and specific features. Certain questions are added, there are differences in layout and administrative procedures, etc. In some cases national correspondents are not even obliged to incorporate the whole of the joint questionnaires and, in other cases, only a common denominator is given for guidance while the actual wording of the questions is left up to the national correspondents. This applies in particular to those concerted actions where the project leaders experience considerable difficulty in bringing their partners into line either because there is too great a variation in the resources available to those partners or because they are expected to adapt the well-established procedures of certain countries which are difficult to change (for example, the use of protocols of the "informed consent testing" or "anonymous unlinked testing" type is closely connected with national tradition, parliamentary debate, or the sensitivity of the media and public opinion), or because the partners are reluctant to march in step.

The questionnaires also vary considerably in terms of content, form and target group. Just reading the questionnaire is enough to give a partial picture of the concerted action network, specifying the objectives of the project, the actors involved, instruments, working procedures, etc. There is also the matter of who is to complete the questionnaire : individual respondents, a specialized researcher, a clinician surrounded by instruments and colleagues, etc. All these connections can generally be seen in the texts. The layout of the forms also has its part to play : it may be presented as a typewritten half page, a double page properly presented and printed, a 25-page brochure on paper of different colours depending on the purpose of the survey, NCR paper for the production of a number of duplicates, etc. Such details have been the subject of voluminous treatises on methodology and numerous debates between members of concerted actions. They affect the response rate, the accuracy of the information, errors of transcription and the organization of checking and validation procedures, the quantity of work done by the encoders and thus the breakdown of the action budgets, the reliability and scientific credibility of the results, peer recognition, the genesis of new research programmes, etc.

The fate of the questionnaires once they have been completed can vary as much as the questionnaires themselves. Sometimes they are sent directly back to the issuing body, sometimes to a specialized team. Sometimes they are sent via the national correspondents for dispatch in bulk to the central team, other times they go no further than the national coordinators. The coordinators' task is sometimes simply to forward the questionnaires, in other cases to check and validate them, and sometimes even to encode them.

> *This preliminary analysis underlines the number and variety of the cases encountered. Clearly, for MHR, forms are one of the main tools, possibly the main tool, for circulating information. The following example illustrates the extent of changes in practices which can be brought about as a result of these techniques, as well as the scale of the coordination required.*

EXAMPLE : CA ON THE OPPORTUNISTIC DISEASES ASSOCIATED WITH AIDS

These are two networks which have drawn up protocols for the clinical evaluation of the treatment of opportunistic diseases connected with AIDS, in this case toxoplasmosis (ENTA4) and tuberculosis (ENTA5). The protocols are devised and implemented jointly. The ENTA 4 project leader's team acts as the coordination centre and the PMG of ENTA 4 plays a key role in the organization of both operations. A "chief investigator" is responsible for the operation of each of the protocols. The chief investigator for the ENTA 5 protocol is also the project leader of this second concerted action.

The head of the ENTA 4 project is a clinician. Having returned from the United States with an interdisciplinary, global and integrated model for the care of AIDS patients, he has set up his own clinical unit - the only one in Belgium - with 20 beds and an outpatient department. In his view, delivering quality care involves carrying out rational clinical research into treatments. He therefore set about finding other clinicians in Europe to determine with them what could be done in this area. He met up with an existing group of clinicians practising clinical research. American researchers belonging to this group expressed considerable interest in the study of toxoplasmosis as an AIDS-related opportunistic infection which is widespread in Europe but rare in the United States. A meeting was organized in Genval paid for by the group's own funds, bringing together clinicians from America and Europe, some of whom were already taking part in the Commission's MHR programme. Following that apparently constructive meeting, these members suggested to the future project leader that he join a project being prepared by the PMG on AIDS. That group, made up of 22 to 24 members appointed by their respective ministries, was at that time the equivalent of the current Working Party and was directly responsible for initiating operations, since the call for tenders procedure had not yet been used in the MHR programme. The change of structure and the move to a Working Party were to lead to fresh appointments including that of the future project leader as representative for Belgium. The new Working Party is subdivided into PMGs. One of these deals with the treatment of AIDS (ENTA - European Network for Treatment of AIDS) and our eventual project leader became its chairman. Initially, therefore, the ENTA was not a concerted action in the current sense of the word; it was a subcommittee responsible for coordinating research on treatment. Once the new procedures had been put in place the ENTA became one of the concerted actions. However, because of the dynamism and experience of its PMG, the European programme

managers gave it the task of evaluating the new CA proposals. In this way those responsible for one CA were required to take decisions on other CAs. The PMG for this concerted action thus performs three functions : selecting new proposals submitted to the Commission; organizing its own concerted action, in this case the development of the ENTA 4 protocol on toxoplasmosis; coordinating multi-centre clinical studies on the treatment of AIDS. There are currently two such studies, the first under this CA and the second part of another CA involving the implementation of the ENTA5 protocol on tuberculosis.

The choice made in this programme demonstrates the desire to achieve optimum coordination of clinical research in Europe into the treatment of AIDS. The question is : does a structure of this type have the institutional capability to succeed? The following two examples appear to suggest that it does not. The ENTA had a third protocol in its clinical test portfolio : pneumocystosis, which chiefly affects homosexuals in the countries of northern Europe. The implementation of this protocol has met with competition from the American programmes. Similarly, the member countries are keen to develop their own clinical evaluation programmes and want to have the prerogative of implementing them, particularly where any new treatments might be concerned (especially those directly concerning the HIV virus). This does not apply to toxoplasmosis and tuberculosis, for which treatments already exist. These two AIDS-related infections are essentially found in the southern countries. They are not studied in the United States since they occur less frequently there. The European programme therefore provides an opportunity, in a complementary and non-conflictual context, to convince Member States of the value of this kind of coordination, and it is the wish of the PL for the ENTA to be recognized as the vehicle for such coordination.

The ENTA network consists of a coordination centre in Brussels, a centre for processing results - also in Brussels - main investigating centres for each protocol and several dozen clinical investigation teams. The coordination centre has two secretaries, a doctor and a nurse. It organizes the implementation of the protocol, collects, validates and corrects data and returns them to the teams. The computer centre is part of the EORTC (European Organization for Research and Treatment of Cancer). It registers and analyses the data. Two full-time members and one half-time member of the EORTC staff are attached to this project. The chief investigators' functions differ from those of the coordination centre; they are responsible for evaluating the scientific benefits of each project. The coordination centre brings together the scientists responsible, examines all files, sends information letters to investigators and so on. However, it is the chief investigator for each project who presents the scientific papers. A French team holds the scientific leadership for the toxoplasmosis action and a Spanish team for tuberculosis. Between 30 and 40 centres are permanently playing an active part in collecting data from hospitals, mainly from the southern European countries.

Protocols are drawn up and improved by a technical group next to the coordination centre. The CTEG (Clinical Trial Expert Group), chosen from among the members of the PMG, consists of approximately eight clinicians and has drawn up the protocols for toxoplasmosis and tuberculosis. The new protocols are now due to be prepared, this time with the assistance of biostatisticians. They are approved by the PMG. Once a protocol has been defined by clinicians it is implemented by the coordination centre which has the main responsibility for managing paper flow. This whole procedure is orchestrated by a nurse, known as

the Clinical Research Associate. Apart from being trained as a nurse, she has studied epidemiology, statistics and data processing. She has worked at the EORTC, the NIH and in a pharmaceutical company, preparing other clinical evaluation protocols. Within the ENTA she is responsible for the production and circulation and filing of the various types of paperwork used ("circulating intermediaries"). Her office is attractively decorated with everything in red and blue - files, folders, filing cabinets, etc. However, this is not simply for aesthetic reasons. Since there are two protocols to administer, all paperwork concerning ENTA5 on tuberculosis is in red and everything relating to ENTA4 (toxoplasmosis) is in blue. In this way it is impossible to mix up documents or files. There is no chance of any piece of paperwork being misdirected. The colours differentiate between two paperwork systems, in other words two networks of clinicians. The data produced by the clinical investigators can be neither lost nor confused. The reliability of the results of the two sets of clinical tests is a function, among other things, of the colour of the files.

There are no papers lying around, everything is filed in a separate filing cabinet according to whether the document is entering or leaving the office or has to be amended or read by other people. The flow of paperwork is controlled by a network of filing cabinets, folders and ring-binders. The office is normally kept locked so there is no chance of a passer-by creating disorder. It is also a means of ensuring the utmost confidentiality; the credibility of the ENTA depends on this lock.

Everything entering and leaving the office is dated. Everything entering and leaving the office is on paper (letter or fax). Only written replies are considered, the purpose being to make interactions irreversible so as to be able to reconstitute the various steps in cases of doubt and demonstrate the successive layers of entries in the event of a dispute over results. Everything is on paper, everything is filed, everything is kept. However, the fact that everything is on paper does not mean that all those involved have to painstakingly draft long handwritten documents. There is a form for each item. There are forms to inform, to request information, to correct and to accompany other documents. There are forms for the coordination centre, forms for EORTC and forms for those in Spain or Portugal who have to give or request information. The teams receive a supply of forms; the level of these supplies is continuously monitored by the Coordination Centre, so that the investigating teams receive new forms even without having to request them. This applies at least to the observation books; there are special forms for faxes, there are also model forms to cover patients who die or withdraw from the trials.

Let us take a look at the ENTA5 protocol for tuberculosis. The first stage is to recruit teams of clinicians to conduct the investigations. The PMG proposes a list of centres to be recruited. The Coordination Centre writes to these centres and all those who have contacted the network on their own initiative asking them for additional information on their structure and interests. Only the written declarations are taken into account. On the basis of the replies a list is drawn up and regularly updated; the date of the last update appears on the document. Each document is allocated a composite number : protocol number/country number/ centre number/patient number. The file of the centres taking part even include those countries which are not taking part, with a record of their reasons for non-participation. The particulars of the investigator responsible for each centre and those of the contact person in the field are recorded together with the

approximate number of patients anticipated. In this way the nurse at the Coordination Centre can say at any time how many active centres there are, in each country, for each protocol, and with how many patients. For instance, as at 15 May 1990 there were 49 centres for tuberculosis, mainly in Spain and Italy, three centres in Greece and three centres in Portugal. Only 26 of them were active, i.e. actually returned observation records. These centres monitored a total of 154 patients. This figure was higher than anticipated at the start of the project. An updated mailing list is constantly available so that information can be sent to the investigators.

The observation record book is designed in such a way that any document is automatically copied in triplicate. This reduces errors by avoiding the need for re-transcription. The investigator, the Coordination Centre and the EORTC are thus sure to have the same information. There are two different observation records depending on whether the treatment is being administered for acute or for routine cases. Two treatments are compared in the protocol. The inclusion of a new patient in one or other course of treatment is determined by the EORTC computer (randomization). The operation works as follows : The investigator announces the inclusion of a new patient. The EORTC determines the group to which the patient is to be assigned and sends a fax to the investigator who then confirms the assignment. There are special fax forms for the various types of correspondence between the investigator and the Coordination Centre. Once a week the EORTC brings out an updated list showing which treatments are covered by the study and for which patients. An anonymous file is created for each patient. The patients' files are kept together in the folder for the corresponding centre. These folders are categorized by country. All documents are read and validated by the nurse and the doctor at the coordination centre, and subsequently by the chief investigator. No correction is made without the written agreement of the investigator. Files are kept on every aspect, including discussions of the protocol with references to the arguments of the various participants, the various versions and the time limits for preparing the protocol. All correspondence is also filed, particularly the letters explaining why a centre is or is not taking part in the study, etc. By administering the flow of paperwork the Coordination Centre becomes familiar with the teams and gains an exact idea of how they work. They know, for instance, who tends to be late, who is disorganized, who has been well organized since the start of the study and so on. A newsletter is published for the investigators. The coordinating nurse regularly reports to the PMG on the state of progress of the studies.

The situation is slightly different in the case of the other protocol (on toxoplasmosis) since it has to be possible to administer emergency treatment to the patient. The investigator therefore cannot wait for the details of the assignment of the patient to be faxed to the Coordination Centre and for the EORTC to inform him of the treatment decided upon by randomization. Randomization is therefore done by envelope in this case. The centres receive a number of sealed envelopes in advance and open them after having made their diagnosis and before starting treatment. They must inform the Coordination Centre of the treatment and the particulars of the patient using a standard fax form. These cases call for greater confidentiality than the other protocol; the teams must not open the envelopes in advance. As our informant told us, this is also one way of spotting investigators' errors (of which a record is kept). This protocol also includes a supplement on neurology, making this study unique in the world. This supplement was added after

the start of the project but includes the original patients. As at 24 April 1990 there were 42 centres working on toxoplasmosis, of which 28 were active, with 162 patients. That figure had already risen to 192 by 15 May 1990.

> *This example illustrates one of the strengths of the protocol, in that the form representing it is merely the tip of the iceberg. It amounts to a military operation which has to anticipate every possible situation from the outset, prepare the steps to be taken and the relevant paperwork, keep records of all events, and organize permanent inspection and validation procedures. The way in which the various documents circulate in the ENTA network reveals its nature : who is involved, what they do, the gradual accumulation of tangible results, the structure of the network and the way it is coordinated. It is possible to give a complete description of the network simply by analysing the paperwork on which every operation is recorded. This example shows the extent to which the cohesiveness, rigour and stability of a scientific project are dependent on the niceties of organized paperwork. It explains the strategic importance many of the project leaders interviewed assign to the physical organization of their CA.*

SOME COMMENTS ON OTHER TRADITIONAL FORMS OF INTERCHANGE

Telephone and fax

A concerted action brings together participants from various countries who must be coordinated, involved, etc. Many PLs have stressed the importance of the telephone or the fax in this connection. These items often account for a considerable proportion of the budget of concerted actions. Although the telephone lends itself to informal conversations it often comes up against language barriers, problems of availability and the absence of any written record. The fax makes up for this without any loss of speed. For many PLs concerted action would not be possible without these instruments. In many cases they underpin the coordination between the members of the PMG, who have said that they do everything by telephone because meetings cost too much and take up too much time. The use of electronic mail - encouraged at one stage by the programme - encountered a number of difficulties, as in other areas, and has been largely abandoned except by those CAs which regularly exchange large quantities of data.

Headed paper, logos and newsletter

Similarly, headed paper, logos and newsletters are becoming increasingly popular means of ensuring recognition and visibility for CAs. This is unique to the MHR programme. There are very few actions which make use of such media under the shared-cost programmes. It is an additional sign of the special position of CAs in the Community research system, as they are neither specific programmes under the Framework Programme nor individual research projects.

Visits and exchanges of research scientists

Visits and exchanges of research scientists often provide an opportunity for transferring and comparing know-how. The best way of learning techniques is to visit the teams specializing in the relevant protocols, according to several project leaders who spoke to us. In the case of MHR and many concerted actions, exchanges of research scientists also serve another purpose, namely to ensure

balanced participation by all European countries by encouraging the incorporation of the southern European nations. The two other traditional functions, namely post-graduate training and periods spent in central facilities for the purpose of experiments (BNCT, central facility for AIDS research in primates), etc. need no further mention. In many concerted actions there is a particular type of visit that falls into a different category from visits and exchanges of research scientists; these are visits by project leaders or their assistants. These tend to take place regularly between three and five times in a year per CA as a means of getting to know a team better, for restricted working meetings, for harmonizing certain local practices, supporting teams that are encountering problems in their area, and so on.

Scientific publications

Naturally, scientific publications are a preferred vehicle for communication and recognition. There is much truth in the old saying that a person's worth is reflected in what he publishes. Our conversations showed that this aim is espoused by all project leaders : they conduct research but research only exists to the extent that it is recognized by their peers. However, it is sometimes difficult to see the wood for the trees. For example, what part of the teams' activities qualifies as research related to the concerted action? How can the recognition of a CA be organized in a publication? Reference could be made to the financial support received, as in the case of funding from the NSF, but a CA is not a research agency. Co-signature by the project leader might be another option, but this could involve a risk of excessive individualization. How does one make allowance for the often long waiting periods prior to the publication due, for instance, to the length of the case gathering period. Other questions are also sometimes raised about the minutes of meetings : should they be published in journals (and their supplements) etc? This lengthy list of questions is indicative of the diversity of strategies which CAs employ with regard to publication : it is certainly necessary but the publication medium and schedule depend on actual progress with the action.

> *Visits and publications are the two most familiar forms of scientific interchange and, like meetings, they are part and parcel of the daily round of CAs which always spend a substantial proportion of their budgets on them (all too often the cost of publications is glossed over in the rhetoric on the subject). Other, less vaunted instruments, also have a big role to play in the life of a CA, e.g. the fax machine - as emphasized by many project leaders. In addition to this interpersonal communication process, there is increasing evidence of an identity-seeking process based on special logos and especially newsletters. They raise the profile of CAs vis-à-vis the outside world and bring to the fore their special characteristics - they are neither "specific" Commission programmes nor individual research operations.*

6. Exchange of materials

We have seen the importance of direct interchange and exchange of paperwork of all kinds in the construction of the networks. These are far from being the only exchanges observed. We have already quoted some examples, such as pancreases and B cells, boron-treated compounds, transgenic rats and dogs,

molecules for screening, DNA for sequencing, etc. These exchanges are different in two respects. Firstly, it is no longer a representation of the object or the problem under review which is being circulated, but actually part of it. Secondly, the organizational model of paperwork movement of which the ENTA and its clinical research associate are the prototype generally no longer applies. Material problems abound. How is the physical distribution to be organized? How are these materials to be transported? How are they to move between countries with such varying legislation? How are they to be stored and not suffer loss of quality? Logistical problems are often of crucial importance, as our initial example on pancreases showed, and increasingly call for the use of specialists.

Differing aims and specific organizational problems : the organization of a CA is often like a vast opera where there are very few skilled operators to work the stage machinery and they must be treated with kid gloves. The following examples illustrate the various types of exchange of materials we encountered under the MHR4 programme, with apologies for any omissions.

EXCHANGES OF REFERENCE MATERIALS

When teams want to make their results comparable they try to make their laboratories comparable : same techniques, same procedures, common protocol, exchange of research scientists and/or technicians to carry out ad hoc transfers of know-how. Sometimes, efforts to align laboratories go even further, involving the use of the same reagents and sometimes the same lab equipment. Only a small number of reagents are involved, namely those which differ the most according to the laboratory or firm producing them, or those which are most critical or most strategically important for a particular technique. There are many examples of the range of different situations encountered. In the concerted action on thrombosis, reference reagents (particularly coagulation factors) are distributed to the teams who use them as part of jointly defined research projects. The reagents are produced by a reference laboratory or bulk-purchased from a private company at a substantial discount. In all cases the project leader centralizes the reagents before distributing them. One consignment of reference materials is dispatched on average each week. The circulation of these reagents defines the shape of the network within which the research results will become comparable. It is a method of coordinating the work in its most practical aspects.

Similarly in a specific subproject of the CA on chronic arthritis and immunotherapy, a laboratory supplies reference materials to other teams for the standardization of methods in preparation for future clinical trials. In the BNCT network reference samples are prepared by a single team so that they are standardized. These are samples obtained by surgery (boron-treated tumours).

In a concerted action on viral hepatitis the reference material is not distributed systematically to the teams on the basis of a jointly defined scheme. It is simply held available for teams which wish to use it to test gene probes. Here, too, the aim is to make results comparable but in this case by using a standard material to which research scientists refer to calibrate their own equipment.

In the concerted action on the creation of an animal model (macaque) for the study of AIDS, the selection and distribution of the reference material is a very sensitive issue. In addition to the distribution of reagents from the best laboratories, virus strains are a strategic reference material. There are many different strains and in order for the results to be comparable all teams have to work with the same strains. The strain actually chosen depends on the success

rating during testing by the teams. However, there are so many different strains that research workers lose track. Therefore it is not enough to choose one strain and distribute it; that strain needs to be precisely identified, i.e. sequenced. Moreover, the HIV virus is so flexible that its transformations have to be monitored and it has to be re- sequenced after one or two years. The virus strains are kept in tubes in liquid nitrogen. Transporting them poses few problems. Researchers rely on the postal distribution networks, but the fact that postal regulations vary from one country to another and make this process more difficult. The German postal authorities, for instance, will no longer transport strains of the AIDS virus. Teams therefore have to make use of private carriers.

Sometimes the reference material is a form of currency. In the network on prevention of kidney failure caused by inherited polycystic kidney disease, the project leader makes his DNA probes available to the teams in exchange for data on the major families. In this way he ensures homogeneity in the group and provides an opportunity for new scientific collaboration.

By pooling the purchase of reference materials the teams are able to make substantial savings. In the case of thrombosis the price reductions are between 30 and 40%. Sometimes, as in the concerted action on drug targeting, private companies agree to provide reagents free of charge, in this case expensive cytotoxic drugs, in return for direct access to the results of the research and for being acknowledged as suppliers. Quite apart from these substantial price reductions, collective purchasing is sometimes the only way to obtain costly reagents for collaborative work which is difficult to justify under national research project budgets. A case in point is the use of boron-treated compounds in the BNCT network. Purchases of reagents account for nearly one-third of the budget for this concerted action. The volume purchased is such that a European private company has agreed to start producing this substance to the purity specifications defined by the BNCT network. The success of this action will mean the opening-up of a new market for this company.

> *The effects of the circulation of reagents and reference materials are felt in two distinct stages : during the concerted action it creates an area of intercomparability which provides a new opportunity for generalizing the research results. In a second stage, after the concerted action and the dissemination of its results, new market prospects are opened up for the suppliers of the reference materials, which will lead users gradually towards the standardized application of results.*

EXCHANGES OF SAMPLES

Unlike reference reagents, which have the generalizing effect described above, samples are specific local and unique entities. The circulation of samples leads to the mobilization and meeting of entities which are by definition local. The value of this interchange lies in the opportunities created by these circulating intermediaries. There are several different types of situation.

Situation No 1: a batch of samples is sent to be tested in various laboratories. In the thrombosis network, for example, one team is responsible for preparing a batch of plasma every three months and sending it to the network laboratories. They carry out the various agreed tests on the samples received and send their results to the statistical team, which processes them and compares them with the results of the reference centres. If deviations are observed, the laboratories are

contacted by telephone in an effort to clarify the reasons for the differences and change the practices concerned so as to ensure standardization. In this way the samples are used as a means of gathering data on the laboratories in order to bring them into line. If the deviations persist and a team does not fall into line, it is eliminated. This serves as a quality control. In the same way, for the same network, blood samples are collected, stored, divided and redistributed to different laboratories but not, in this instance, to test the laboratories but rather to test the new methods of analysis coming onto the market. In both cases a known group of samples is used to obtain data on the research facilities, in the first case the laboratories and in the second case the analytical apparatus.

Situation No 2 : In the two examples given above the samples were known and were used to obtain information on some other aspect. In many other situations samples are collected and gathered together as representatives of particular situations. Frequently samples are collected in a single location where one team analyses them all. This single analysis ensures standardized results. In the neuropathology of AIDS network, fresh brain sections are exchanged either on coloured slides (classic neuropathology technique) or frozen in liquid nitrogen (modern neuropathology). The aim of this exchange is to get around the difficulty researchers have in obtaining fresh brains. The system of exchange has been so devised as to ensure that the sections are grouped by speciality. Readings are made by only one person in order to ensure reproducibility of the conditions of analysis.

In certain cases the samples collected in a single site are distributed to a number of reference laboratories whose methods have already been harmonized. In the case of the thrombosis network, for instance, blood samples are collected and redistributed to analytical centres. This procedure, like the one described above, focuses attention on the standardization of the material and the collection of samples. The central team sends apparatus to the clinical teams responsible for taking the samples. It also distributes a manual of procedures and trains the teams' technicians in the taking and standardized preparation of blood samples. Because the only aspect which needs to be standardized is the taking of samples, it is easier to recruit clinical teams who do not necessarily have to have a suitable laboratory. Where this is not the case - for example where samples have not been circulated and only the results of the analyses are sent out - the network has to institute other procedures to ensure comparability of results. In many cases much work has to be done to harmonize methods of analysis unless it is possible to rely on equivalent knowhow.

Situation No 3 : Samples are collected or exchanged locally to be compared, characterized, studied and/or selected. In the network on viral hepatitis, for example, 18 clinical teams plus industrial firms collect data and samples. These are centralized by the coordination team which redistributes them to a dozen research groups, which process them and send the results back to the clinical centres. In addition, all teams are asked to provide the specific antibodies in their possession to build up a reference serum panel for subsequent redistribution to the clinical teams. These antibodies will then be compared and the results standardized to identify the antibodies most suitable for diagnosis or screening of patients. In the network on the extraction of B cells from the pancreas, the B cells are circulated for characterization by teams with differing expertise. In the network on heritable connective tissue disorders, skin or intestine biopsies are sent from one team to another to be characterized. In the hepatitis network teams

are asked to keep the blood samples they have in order to set up blood banks. Other teams can obtain these samples for intercomparison purposes subject to prior agreement of the team concerned. In the concerted action on chronic arthritis and immunotherapy, antibodies are exchanged between three teams for comparison, the aim being to select the best antibody in preparation for a double-blind clinical study. In the concerted action on the screening of anti-viral molecules, molecules are sent to the central team, which characterizes them for the team supplying them. The same applies to the sequencing of the AIDS virus. In the network on DNA repair and cancer, cell lines and DNA repair genes are exchanged for comparison to verify that the genes found by the different teams are actually involved in the process and perform the same function.

Situation No 4 : The samples constitute the raw material on which the teams can begin to work. This happens in the case of the human pancreases under the concerted action for the extraction and purification of B cells. In another action the genes are sent to the central team which uses them to produce a strain of transgenic rats.

The exchange of biological samples often raises specific problems and the way in which these are solved determines how the network of research scientists operates. The main problems lie in the preparation of the sample and the method of transfer. Preparation depends in particular on the material and how it is used and transferred. The brain samples used in the concerted action on the neuropathology of AIDS, for example, are exchanged either in the form of coloured slides or slides frozen in liquid nitrogen, whereas in the BNCT network they are prepared in the form of homogenized and frozen suspensions. In the first case the tissue has to be examined visually, in the second case it has to be analysed. In both cases it is dispatched by express package. In the network on heritable connective tissue disorders the samples are sent in the form of cell cultures either at 37°C in a thermostatic flask or, more frequently, deep-frozen in an Isomat block. In the BNCT network tumours are placed in suspension and frozen for transfer by post or by a private company. In the immunotherapy network they are transported simply in the sterile container supplied to the clinicians or grafted onto NUDE mice. In both cases the tumour must be accompanied, i.e. a technician or a research scientist is responsible for taking the sterile flask (for short distances) or the cage with the mice (between Paris and Brussels for example). Genes in the arterial hypertension network are transported in the form of a pure solution or precipitate. In the AIDS sequencing network they are most often either cloned in a host organism or whole in the blood sample in which the virus was detected.

In fact one of the areas where certain concerted actions have experienced difficulties has been the conditions of preparation of the samples. Where the samples have to be used as a reference, a single team is responsible for their preparation. In other cases a great deal of work goes into ensuring standardization of collection and preparation, as in the case of blood samples in the thrombosis network. The problem in the case of the centralized facility for the sequencing of the AIDS virus is less a matter of standardizing the preparation of the material but rather of improving its quality given the possibilities and constraints of the methods of analysis. Consequently, the team from the centralized facility resorts to working individually with the teams to the extent of sending the researchers to the laboratories to see how the preparations are made. Since the quality and purity of

the source material are the major problem, there is a need for a gradual transformation in laboratory practice. Moreover, in-house quality control will also be organized involving two reactions carried out in opposite directions, the idea being to obtain the same response for the two reactions. If the material is of poor quality this will show in the result.

Once the sample has been prepared and correctly labelled and addressed, it then has to be packaged and dispatched. Packaging is rarely considered as a problem by the project leaders, at least as far as the contents are concerned : a cardboard package for precipitates, "fragile" express parcel for histological slides, thermostatic flask in a reinforced packaging for cell cultures in suspension and test tubes for samples of infected blood, etc. in an inner container within an outer container. The exterior of the package, on the other hand, causes considerable difficulties. Transport has to be organized in such a way that the material can be carried rapidly and in accordance with the regulations. There is the problem of coordinating transfer at the airport, flight and package gathering, enclosing the special paperwork required, informing the shippers, completing *ad hoc* formalities and so on. Even that is not sufficient. The German postal authorities have now refused to transport the AIDS virus and regulations differ from one country to another. This means that there are many situations where research scientists prefer to use alternative methods : private carriers, combining exchanges of materials with exchanges of research workers or the organization of meetings. This type of exchange is more difficult, however, when the material has to remain frozen. In any event, the packaging of the material and the administrative formalities represent a considerable and expensive part of the work of coordinating the teams' operations. The transfer of infected blood, for example, costs around DM 200 per sample. Sometimes formalities are quite simply counterproductive; there have been cases where it has taken one week to recover a biological sample from the customs.

> *By exchanging samples, and especially by centralizing them in blood, cell and tissue banks, CAs have three transforming effects. First of all, there is the set of mechanisms and measures to be put in place to ensure that the samples are comparable (some do in fact serve to verify that laboratory practices are standardized). To circulate them it is often necessary to establish a complex and time-consuming logistical set-up which, as well as giving the action its own individual identity, gives rise to a collective expertise - a point often made by the PLs. Exchanges of samples also forge permanent links simply by virtue of the number of cases built up, to which the teams can refer (via the banks or the analysis results) : local situations are put into perspective, teams can have access to complex analyses, the proliferation of cases makes it possible to identify genes, etc.*

EXCHANGES OF EQUIPMENT

Exchanges of equipment are far less frequent than exchanges of samples. Where they do occur, they generally contribute to a change in practices. There are therefore considerable underlying economic implications, which perhaps explains why exchanges of equipment are limited. The concerted action on hyperthermy is a good illustration of the nature and scope of the problems which can arise with such exchanges.

For several years international meetings have been organized by international organizations, in particular the ISHO (International Society for Hyperthermy Oncology), on this technique, which may be used as a back-up to anti-cancer therapies. These meetings are attended by clinicians and physicists, including certain Danes and Britons familiar with the MHR4 programme. Four requests on this subject had been made and MHR4 held a preliminary meeting, thereby increasing the number of teams and incorporating engineers. Hyperthermy is not highly rated internationally. It is a complicated method which is labour-intensive. Clinicians do not like it because it complements radiotherapy. The only randomized trials have been carried out on terminal patients. The marginal position of this method has engendered a movement of solidarity between the research scientists developing it. The clinicians treating hyperthermy are trying to find ways of obtaining a large number of *ad hoc* patients quickly. They support the physicists because they need standardized and sophisticated apparatus. The main thrust of this concerted action is to study the technical problems involved in clinical applications.

Five priority areas have been identified and meetings have been held to exchange ideas. These are not research projects. Their aim is to evaluate the method to ascertain whether it is worth continuing to develop it and to present a sufficiently strong scientific case in its defence. One priority area deals with the preparation of a clinical protocol, while the other four concern physics. The interaction between physicists and clinicians takes place both at the level of each subproject and within each team in the radiotherapy departments.

In the subproject on heat emission there are two competing methods, one using ultrasound and the other electromagnetism. The aim is to deliver the energy in the right place, namely to the tumour. The problem is both physical and biological since vascularization determines thermal diffusivity and tolerable temperature limits. Each team has thermal emission equipment, the main difference between the teams being the antennae used to direct the energy emission towards the body. The objective of the CA is therefore to evaluate the antennae. Each team should be able to evaluate the others' antennae, notably by exchanging them. Since the energy generators are standard the antennae are easily interchangeable. While it may be difficult sometimes to move the antennae around (there are six different basic models) this is not a function of their size or compatibility, but of the fact that the teams are closely linked with industry, which does not take kindly to being obliged to change direction. For the time being the teams prefer to exchange researchers rather than antennae. This collaboration should also make it possible to characterize the antennae and to make recommendations to industry, whose representatives may attend the working meetings. In any event industrialists are showing a willingness to collaborate at local level. They defend their equipment and reject competitors' solutions.

> *This example is a typical situation, where exchanges of equipment and comparative evaluations have economic and business implications which sometimes go beyond the remit of the concerted action. The example of software for electrocardiogram interpretation shows that, with time and appropriate Community support, these objectives can be attained.*

EXCHANGES OF PHANTOMS

Generally phantoms are substitutes for human beings or parts of a human being, such as the head or an arm. They are manufactured and circulated for the evaluation of therapeutic instruments and to compare diagnostic instruments.

In the concerted action on hyperthermy, for instance, comparison of equipment is undertaken not only by exchanging antennae but also by producing and circulating phantoms. A first phantom was developed by an Amsterdam team, which circulated it to a number of other teams in the Netherlands and Germany. The phantom, carried in a suitcase, is always accompanied by a member of the research team. It simulates a patient from the point of view of electromagnetic radiation. It is transparent and contains detectors and light-emitting diodes. It is used to evaluate energy distribution, particularly the hottest point. It does not generate any measurements. It is used to evaluate multi-antenna systems and to monitor the movement of the hot spot in relation to combinations of thermal emissions. A second phantom - this time made of paper - is being circulated among the modelling teams. These are actually tomographic sections of an imaginary patient with a tumour, plus data on the theoretical antenna. These paper phantoms are used to test computer models of energy density per point.

In the BNCT network the phantoms are made of plastic and contain the equivalent of biological tissue. They are prepared in accordance with the ACRU international standards (International Radiobiology Commision). They can easily be made with gelatine. The project leader's team is responsible for this task since it is easier to produce phantoms in one place and then circulate them. The phantom is more or less the size of a human head and is easy to transport. For the first set of trials three or four will be made. Detectors are placed in these phantoms, which are to be used for irradiation experiments. Initially they will be used at Petten but eventually they will also be used in other teams. Since they are neither destroyed nor activated they will be re-used for carrying out measurements.

In the Concerted action on the quantitative evaluation of osteoporosis, other phantoms specific to each family of instruments have been defined by the working groups, fabricated by specialized teams and discussed at a workshop. The aim of this action is to standardize methods and instruments. Although teams used to exchange their results, intercomparisons were not possible since the instruments produced diverging data. Four industrial firms agreed to harmonize their equipment, but their attempt to do so failed. The teams involved therefore opted for the solution of standardization by the users, in particular by defining, producing and circulating phantoms. Companies are interested in this exercise and strongly aware that any common standard will concern them directly. They are taking part in the discussions as observers and express their opinions on phantom design. Depending on the type of phantom defined and the measuring criteria adopted, certain instruments are likely to have an advantage over others, and therefore industry is following these discussions very closely.

Before the last workshop a measurement protocol was drafted and sent to the teams for their comments. It was debated in conjunction with a presentation of the phantoms. There was considerable debate about the actual characteristics of the phantom. It is a whiteish block containing an area of a different type, the shape of which represents a human vertebra. The phantom is a section of hydroxyapatite which is supposed to be equivalent to a section of the human torso. Photographs reconstituted from the measurements taken on the phantom show in detail the form of the hidden "vertebra". This prompted discussions on the quality of the

contours and the concentration of hydroxyapatite in the various parts. Some participants queried the dimensions, others would have liked the phantom to contain fat. The industry representatives had some reservations and steered the discussion towards the inevitable definition of the regions to be measured. It appeared from these discussions that the adoption of such a phantom would mean that certain measuring equipment software would have to be modified. The industry representatives pointed out that the software was not designed to measure everything, but only human bones. The question of whether the phantom is equivalent to the patient was the nub of the debate. Which is the best reference : a patient, a phantom or the patient population?

A frequently recurring question is that of the reproducibility of results. First, each team will need its phantom. How can we be sure that every team has the same one? Is the method of fabricating the phantom sufficiently reproducible? This would appear not to be the case. The solution would be to produce a single large, homogeneous phantom and then to cut it into sections. The phantom would also be documented (size, composition, manufacturing procedure) for the teams. Secondly, again in connection with reproducibility, we must ask whether the results from a particular instrument are reproducible in the long term. How are we to know? Are patients a good reference? Are their bones stable? But the main problem is how to get normal patients to return a number of times over a period of several years. Patients appear to be very difficult to get hold of. Some prefer to resort to phantoms. This simply reopens the discussions of whether phantoms themselves are stable over the long term. Do they not age? Does hydroxyapatite not undergo changes with time? There were no answers to these questions and the issue had not been resolved by the end of the meeting. Has the phantom had its day?

EXCHANGES OF ANIMALS

This example underlines the difficulties which often surround the use of materials simulating humans. A well-known method of avoiding this problem is to work on animal models. A number of concerted actions have opted for this approach. We have already discussed the case of dogs for the BNCT network or the use of transgenic rats to transform research on arterial hypertension. We could also mention the exchange of aged mice. The problems here are less to do with the movement of mice than with organizing their "production" so as to ensure intercomparability or suitability for the problems under study (transgenic rats, for example).

Virtually all of the examples described point to the parallel need for centralized facilities which we have already described and which introduce an additional organizational dimension; the situation is made especially complicated by the fact that national regulations on the movement of animals vary considerably from one Member State to another (see the section on samples).

EXCHANGES OF PATIENTS

Finally, where no model or simulation is available, or alternatively in the final stage before the validation of a treatment, it may be necessary to use patients. Even though a number of concerted actions have plans to make use of patients, to our knowledge there is only one which actually uses patients, namely the action on cancer immunotherapy.

This network is made up of two groups. One works on plasminogen activators, with researchers exchanging results and standardizing methods of analysis. The other group is attempting to apply new immunological findings to the treatment of cancer. It is in this latter subnetwork that patients are exchanged. There is occasional collaboration between laboratories, according to research needs. The project leader avoids expecting too much from this type of collaboration but he does underline the need for it. There are many types of cancer and research scientists with knowledge of each type are dispersed. The culture of cancer cells is particularly difficult and requires joint efforts and the pooling of know-how, for instance between a hospital with knowledge of a particular type of tumour and a laboratory equipped to work on cancer cell cultures. This network consists chiefly of a laboratory with its own in-house skills and a number of surgical teams who remove the tumours. The tumours removed from patients (since the surgeons would have to remove them anyway, it is easier to secure their participation) are then grafted onto NUDE mice, without immune systems, and then transferred to the central laboratory which takes care of the cell culture. Far from being a detour, the stage of grafting onto NUDE mice makes subsequent culture easier. The cancer cells being cultured are used for essentially exploratory purposes even though they are human cells. After a number of years of experience with mouse tumours, the project leader felt that it was time to move on to human tumours to continue the investigation into new potential applications of immunotherapy. This is a research action where "search" is the operative word. We are a long way from the clinical trial stage which would entail a rigorous evaluation of a new treatment. The aim here is to discover that new treatment. The principle of this approach is to remove a tumour, culture it, subject the cells to chemical mutagenesis, reculture the surviving cells and then irradiate them before reinjecting them into the patient in the hope that this will provoke an immune reaction in the patient against his own cancer. Two types of tumour are considered - colon cancer and skin melanoma.

In the main, patients are exchanged with the Curie Institute in Paris which is particularly specialized in cancers of the colon. The team at this hospital was informed of the action and adopted the patient selection criteria proposed by the project leader. They take the appropriate tumours and graft them onto NUDE mice. The two teams then get together to discuss the patient. If the patient satisfies the criteria used by the laboratory, someone goes to collect the mouse in Paris and bring it back to Brussels. The tumour is then removed from the mouse and cultured. If the tumour comes from a neighbouring hospital it is taken directly to the laboratory in a sterile container provided by the laboratory. There it is cut into two parts of which one is grafted onto a NUDE mouse and the other is cultured.

Cancer cells are very difficult to grow. Their doubling time is between 30 and 60 hours. Consequently, a tumour requires several months in order for the culture to take. After six months, if the culture has taken in the laboratory, the team contacts the surgeons again to inquire about the patient's condition, whether he is still alive and so on. If all is well, the next phase is initiated in which the cells are subjected to chemical mutagenesis. In general 0.2% of the cells survive, and some of these must be presumed to have mutated. The survivors are cultured and then separated into 20 to 40 clones. Between 5 and 10 of these are chosen for re-injection into the patient. At the appropriate moment the cells are irradiated so as to avoid any risk when they are re-injected into the patient. Some of the cells, before irradiation, are kept at -80°C. In this way it is possible to treat the patient

over a period of years. This second phase lasts between 3 and 6 months, which means that the first re-injections take place between six months and one year after the removal of the tumour.

Once the mutagenesis phase is initiated, the clinical team sends the patient's complete dossier to the laboratory and there are further telephone conversations. The patient is called in to give informed consent even if that has already been obtained by the clinical team. During this first meeting with the patient a blood sample is taken to make a genetic fingerprint to ensure that there is no mix-up of patients and to avoid the consequences of possible errors in culture or sample-taking.

When the vaccine is ready, patients are called in again for immunotherapy. This is a very minor operation (intradermal injection) which has no after-effects. The patients visit the outpatient department once a month for four months and thereafter at longer intervals. The concerted action pays for their travelling and, in some cases, hotel expenses, which, as the project leader explained, helps to "oil the wheels". The patient is then monitored by the clinicians who have taken over his case; the only member from the laboratory team involved is the immunotherapy technician. However, there are regular exchanges of information between the teams to keep abreast of the patient's development and the effects of the immunotherapy. Exchanges of information embrace both exchanges of patients and tumours, to the point where the project leader considers his concerted action as an intellectual network.

At present the laboratory does not need many tumours as it is still working on a small scale. In order to have five patients per year at the end of the process, between 30 and 40 tumours are needed at the beginning, which means over 100 potential patients. In practice, the Belgian network of surgeons could be sufficient at this stage. France's involvement in this network is due in fact to an initiative taken by a Parisian patient who came to Brussels of his own volition. He was treated here and then the team contacted his doctors in Paris. Cooperation was a gradual process requiring considerable commitment from the partners involved. Other teams regularly come forward but take the matter no further when they realise the scale of the investment required. The whole process has to be started afresh for each patient. Ultimately it is hoped that this work can be avoided by having vaccines that are suitable for different patients.

> *So exchanges of patients do not occur in isolation. They are accompanied by a series of other exchanges including telephone messages, patient files, tumours in sterile containers or grafted on NUDE mice, people transporting the tumour and, in some cases, the patient. However this will be replaced by the circulation of vaccines. The patient is more than just an intermediary, since he at least has the responsibility of giving informed consent.*

OTHER EXCHANGES OF MATERIALS

The above is not an exhaustive list of the materials circulating between teams. There are at least two others which should be mentioned : pictures and magnetic media.

The concerted action on the neuropathology of AIDS is a good example of the importance of pictures. There are few specialists in this area and virtually all of them attended the preliminary meeting. The aim of the project is to list and

characterize the lesions due to AIDS so as to have the necessary resources and data available to constitute a field of scientific research. This is based on the collection, classification, definition and designation of images which will be connected with the clinical conditions and stages of the disease. The final result of the concerted action is to be an "atlas" to which each team will contribute its best pictures. In order to prepare the ground for fresh research the action focuses on the pooling of documented images.

Exchanges of computer media involve chiefly data bases (including computerization of ECG graphs), and software. In most cases the software provided is for data storage and is distributed to the local teams or national correspondents. Sometimes this software is also designed so that the teams to which it is distributed can carry out some processing of their own data. This slight difference means that some teams are able to channel their local efforts to greater effect and often leads to new initiatives. In a concerted action the data storage package includes an introduction explaining about the MHR programme, the COMAC responsible for the project and the aims of the action for which the teams are invited to collect data. Physical problems of compatibility or capacity often affect the development of such exchanges. Several project leaders have stressed that they would consider a move towards harmonization of equipment in the context of the concerted action as a useful step.

Intermediaries : supporting and marking the dynamics of CAs

It has nearly taken 50 pages to give an account of the multiplicity of intermediaries, and even then only a select few of the many possible examples have been given : what better testimony could there be to the wealth and importance of exchanges which take place in the context of CAs? What points have we been endeavouring to make in the course of this lengthy discourse? There are three main factors which we shall briefly summarize before going on to see how they fit together to form four principal groups of activities with regard to exchanges.

MEETINGS AND VISITS

Meetings and visits lay the foundation on which the actions and communities are built. This truism is worth repeating once again here. Most CAs allocate the majority of their resources to this activity. It can take many forms. Exchanges of results - the favourite vehicle for academic meetings - is only one among many other means for scientists to keep others better informed about work in progress, to exchange views on laboratory practice (and to train each other), to harmonize data collection conditions, to organize joint activities, etc.

This variety of objectives is echoed by the variety of membership (from small working parties to large-scale seminars open to the outside). Finally, the frequency of such events highlights their special role : "to manage the human resources", to borrow the fine phrase of one project leader, "of this entity under construction which will become a concerted action". Meetings and visits are the cement which bind the individuals together and forge a collective identity. They, and they alone, provide a basis for contemplating changes of practice and making the compromises which allow CAs to bear fruit. No CA will succeed unless it lines up the actors behind a common objective and, in the process, changes their practices to allow Europe-wide intercomparison and collection of data, to share tasks, to combine complementary skills, etc.

Consequently, meetings and visits, together with the reports and minutes they generate, are an indispensable medium. But however necessary they are to forming a team, they alone cannot give substance to the project. In order to see what the teams produce together, it is necessary to take a look at the intermediaries. The examples given illustrate their diversity and show that most concerted actions employ several sorts of intermediaries simultaneously. How do these fit together and in which way do they allow a clearer idea of the process for generating the scientific results expected?

CIRCULATING INTERMEDIARIES

Analysis of the intermediaries circulating between the teams provides an initial answer. *Forms* are central to most CAs : drafting, use and circulation of forms, followed by collection and processing of the data which they contain are all stages in the progress of the action towards its objective and milestones on the road to completion. With the aid of forms, local observations and representations can be exchanged, taken up by other teams and combined to piece together representative pictures of the phenomenon studied. *Reference materials* or *phantoms* perform the same role when *samples* are exchanged, rather than representations of the problem under study. These calibration instruments must be produced, the conditions for collection of the samples needed must be standardized and circulation and storage of the samples must be organized. Sometimes it is impossible to circulate the samples as such and either they have to be transferred onto *animals* or perhaps even the *patients* themselves must be circulated. In many cases, this harmonization of practices necessitates exchanges of *equipment*. Systematic circulation of representations or samples of the phenomenon studied implies a method of organization ensuring that these representations and samples are comparable and, hence, combinable. Analysis of the concerted actions confirmed the major effort needed to achieve this result alone. Many project leaders stressed the strategic importance of the "logistical details" needed to reach this point.

FIXED INTERMEDIARIES

Circulation of representations and samples is rarely an end in itself (only a few CAs have been set for this specific objective and are concerned purely with formulation of the protocols needed to achieve this). Storage, accumulation, comparison and processing of such representations and samples are the means of attaining the objectives of the CA. To achieve this, many concerted actions have developed fixed intermediaries, often designated "centralized facilities". Three different types were observed.

The first type of fixed intermediary is like a "*common in-house service*". Ad hoc data bases on all the cases or samples studied in the course of the CA are the commonest form. Many cases concern specific therapies. Circulation of a blood sample limits harmonization between the teams to the data collection stage alone and guarantees that the analyses are comparable, by processing them at a single centre operated, in practice, as a common service. Sometimes, as in the example linked to quantitative evaluation of osteoporosis, this common service depends on original equipment (in this case an automated X-ray plate reading system). At the same time as ensuring uniform analysis, common services of this type are tangible proof of the link between the teams and, in the case of data bases, often secure their participation until results are obtained (otherwise the individual investment made would be lost).

The second category comprises *orienting fixed intermediaries* which play a guiding role. Sequencing of the AIDS virus, characterization of antiviral molecules and the breeding of transgenic rats are three of the many examples of the triple role of facilities of this type : (i) the unique service provided for researchers (often, they are the only means of access to a particular technology or product); (ii) via the access conditions, targeting of the themes and harmonization of practices within the scientific community concerned; (iii) acquisition of specialist knowledge (on, for example, the genetic variation of the AIDS virus) in the laboratory operating the fixed intermediary. This third point is particularly important since it confirms that the "facilities" are not just equipment but a series of assets, including the know-how acquired in a laboratory pursuing its own research objectives behind the service it provides.

Polarizing fixed intermediaries which play a polarizing role are a very different case. They impose constraints which shape the structure of the CA and define the links between the teams and the timetable for meetings between them. The examples given illustrate their dual role, either within "projects" or to set up collection infrastructure. The Petten establishment is an example of the first type designed to devise a new method of treating cancer (BNCT). The "large number of cases" data base fulfils the same role in the evaluation of ultrasonic methods of diagnosis of congenital anomalies. The centre for the production of B cells to treat diabetes follows the same approach : the fixed intermediary which polarizes the activities of this CA is itself one of the results and will remain so until they are put into practice. By contrast, other fixed intermediaries will continue in their current form but turn to other problems, as in the case, for example, of the collection infrastructure linked to the opportunistic diseases associated with AIDS. Many CAs are concerned with building up *collection infrastructure* of this kind, which entails heavy intangible investment, all the more so since most collect not only data but also samples, frequently combining extensive logistical organization with the establishment of common in-house services or of a *reference centre* which produces comprehensive results and acts literally as the life force and shopwindow for the concerted action.

FOUR CATEGORIES OF ACTION, DEPENDING ON THE MIX OF MEETINGS AND INTERMEDIARIES

Most concerted actions opt for a combination of several types of exchange. Consequently, the combination chosen defines the amount of effort which the teams put in to intercommunicate and at the same time serves as a yardstick for measuring their level of commitment. Observation of the concerted actions reveals a multitude of different combinations but nevertheless pinpoints practical thresholds for both the form of exchange and the amount of effort. This gives rise to a classification into four main categories.

In the first category, in practice the teams are involved only in conventional activities, i.e. seminars and meetings. In some cases, they may have access to additional funding for occasional exchanges. This fits the definition of forums, which form a separate bloc within the programme, whichever approach is adopted.

In the second category, the meetings and visits are subdivided to form subgroups on specific topics which focus on obtaining a consensus, usually in the form of a new protocol (for analysis, collection, etc.). In more than one in two cases this harmonization between teams entails exchanges of materials, whether equipment (example : gene probes for the action on "inherited polycystic kidney

disease"), phantoms for testing apparatus (example : quantitative evaluation of osteoporosis), reference materials (example : heritable connective tissue disorders) or samples (example : multiple sclerosis), etc. In a way, the 24 actions in this second category correspond to a specific phase dedicated to the harmonization of points of view and practice. Not surprisingly, it includes most (11 out of 13) of the actions on the establishment of specialized scientific communities. The large number of actions on the development or evaluation of techniques (8 out of 14) is a sign of the recent start made or major difficulties encountered with the work for this purpose.

The third category focuses on collection of data, by means of the implementation of protocols. These data are collected by circulating representations of the phenomena studied. Consequently, the usual medium is paper in the form either of questionnaires distributed and returned (the usual situation) or of treatment protocols distributed and medical reports returned (example : CAs on opportunistic diseases associated with AIDS). Within this category of 28 or so actions, there are wide differences in the method of initiation and the scale of the bases for data collection. Often these also reflect differences of purpose. A subcategory of 10 actions, nine of them on harmonization of medical practice, is defined by protocols which existed before the action started and are based on ad hoc data. At the opposite end of the scale, protocols formulated in the course of the action and "large number of cases" data bases are associated more with evaluation of treatments (five actions). Surveillance services are also heavily represented in this category (eight actions out of 11) because they all entail the development of large data bases [five cases; example : Eurocat (congenital anomalies)] or mobilize large-scale national bases to establish European reference centres (three cases; example : epidemiology of AIDS).

In the fourth category of actions, not only are the practices harmonized but also materials and samples of the phenomenon studied are systematically exchanged. All these concerted actions are linked with fixed intermediaries, which determine the progress or success of the action. The difference between this category and the others lies in the scale of logistical or technical investment required in order to analyse or circulate the samples. These investments take different forms, allowing subdivision of this category of 31 actions into two subcategories.

The first 17 CAs, like the third category, entail the establishment of collection infrastructure, though this time focusing on the collection and assembly of samples and, in one case in two, backed up by large data bases. There are actions of this type on all six finalities, though surveillance services (with four CAs; examples : prevalence of asthma or epidemiology of osteoporosis) and joint research facilities (five CAs; examples : ECAT on thrombosis or molecular cytogenetics) account for over half.

The other 14 CAs are organized around fixed intermediaries playing a polarizing or guiding role. The polarizing intermediaries are either equipment (example : BNCT or the prototype "forced respiratory techniques") or production centres (examples : B cells and diabetes, joint research facilities to breed transgenic rats, to produce artificially aged mice or to make peptides/adjuvants for the three CAs for research targeted on AIDS). The four CAs with fixed intermediaries serving a guiding role concern analytical laboratories (example : HIV genetic screening) or test centres (macaques and primates).

Consequently, in addition to the finalities, actors and forms of organization there is a third dimension for characterizing concerted actions : the exchanges and intermediaries give a fuller idea of teams' involvement and at the same time, depending on which form this takes and on the tangible and intangible investment which it demands, of the solidity and durability of the networks formed.

TABLE : TYPES OF EXCHANGES TAKING PLACE WITHIN CONCERTED ACTIONS

Note : This table comprises 3 groups. The first one gathers the CAs centering on meetings and on harmonization : thematic groups correspond to the existence of subgroups designed to build a consensus between teams on a specific matter (usually the preparation of a protocol); material back-up is linked with exchanges of reference materials, samples, etc. to achieve this harmonization. The second group corresponds to "paper" collection structures. Two criteria enable classification of the CAs : the need for an harmonization phase (CAs are "latent" if the protocol predates the start of the CA and "created" if a harmonization stage is needed before collection can be started), the size of the data base : they are regarded as "ad hoc" in the case of a limited number of cases where virtually individual processing of case providers is possible or "large" where they are so big as to require substantial logistics to be able to handle all situations. The third group corresponds to "sample" collection structures (based on the gathering of blood, tissue,... samples) and to Cas with fixed intermediaries.

1. Meetings and harmonization

finality	Meetings	Harmonization		Total
		Thematic gps	Material back-up	
Dev./Eval. techniques	3	1	4	8
Harm. practices	3	-	1	4
Forums	15	-	-	15
Specialized research communities	-	6	6	12
Total	21	7	11	39

2. Paper collection structures

Finality	Latent		Created		Reference	
	ad hoc	large DB	ad hoc	large DB	centres	total
Surv. serv.	-	3	-	2	3	8
Dev./Eval.treat.	-	-	-	5	-	5
Dev./Eval.tech.	-	-	1	2	-	3
Harm.pract.	8	1	1	2	-	12
Total	8	4	2	11	3	28

3. Sample collection structures & fixed intermediaries

finality	Collection structure		fixed intermediaries		
	Large DB	Other	Polarizing	Orienting	total
Surv.serv.	3	1	-	-	4
Dev./Eval.treat.	-	3	3	1	7
Dev./Eval.tech.	-	2	1	-	3
Harm.pract.	2	-	-	-	2
Joint res.fac.	3	2	5	4	14
Spec.res.comm.	-	1	-	-	1
Total	8	9	9	5	31

III. THE ACTORS AND THE COORDINATION OF CONCERTED ACTIONS

Who takes part in concerted actions? How are they organized? What does it take to get teams working in a network and how does one go about it? All the project leaders told how the experience is both fascinating and frustrating, there being no reference model to help them make choices. Yet these questions are crucial to concerted actions : how should they be organized, what is the best strategy to mobilize and interest the teams, how should relations be managed and what communications are needed? Analysis of intermediate results has shown these considerations determine the eventual performance and success of the quasi-business or quasi-institution which is the CA. Two other features bear this out : the set of collective rules which actions have to adopt as they go along (governing the inclusion or exclusion of members, access to joint resources, publications, relations with industry, etc.) and decision-making processes about the organization of work.

The special nature of the problems involved and the ingenious solutions hit upon by researchers dealing with this unusual situation have led to a proliferation of organizational approaches. Nonetheless, all of these follow one of two definite patterns : centralized or collective decision-making, the individual, collective or distributed organization of work. They fall into five main organizational families : the forum, the outdoor laboratory, the star network and thematically or geographically partitioned networks.

Before looking at these in detail, we should stress an essential feature of the composition of concerted actions : their *heterogeneity*. File 4 on the dissemination of results will return to this point. We do not have a reliable statistical picture for each of the concerted actions, but the replies to our postal survey have enabled us to establish the minimum scope of the concerted actions. The table below attempts to define this scope by looking at the institutional backgrounds of the teams taking part in the concerted actions which replied to the survey. Of the 77 CAs for which we got more than 5 replies, only two have purely "academic" teams (from universities and/or government research institutes) and only nine involved a mixture of teams from academic institutions and university hospitals. All the other actions, i.e. 85% of the total, include at least one service institution (hospitals or health service departments : 62 actions, i.e. 80% of cases) and/or private business involved in health (15 actions, i.e. one case in five). The table shows clearly the predominant set-up : 48 concerted actions (i.e. six out of 10 in our "qualified" sample) include "academic", university hospital and service institution teams. It is not surprising, then, that this combination should be the most common in each of the finalities being pursued. The conclusion is obvious : as a general rule, concerted actions involve potential users of results, even if only in the capacity of "observers". As has already been stressed, this participation has two complementary effects : it means that future users can be interested at an early stage in the changes which the results will bring about in their practices; it also gives impetus to the action in that, through the interaction it generates (see the description of industry's participation in the concerted action on the quantitative assessment of osteoporosis), it encourages reciprocal adaptation, which makes the dissemination of results simpler and more likely.

There are many ways in which future users can participate, but a common feature is often that they are directly involved in obtaining results : many clinicians

collect data or cases or supply materials (e.g. the pancreases in the concerted action on diabetes), industry supplies equipment, even at the prototype stage (e.g. the CA on biomagnetism), or products (e.g. the CA on myocardial infections) or its analytical capacity (e.g. Euronut), while general practitioners fill in logbooks to help define tools to assist in objective decision- making, health service departments provide data, etc.

TABLE 12 : RELATIONSHIP BETWEEN FINALITIES AND THE COMPOSITION OF CONCERTED ACTIONS

Notes:
- Only CAs where five replies were received and the project leader was interviewed have been included, i.e. a total of 77 actions. This therefore forms a subgroup of the 95 actions looked at in the previous File (the NQ column shows the number of CAs not quoted).
- This classification serves purely as a rough guide to the minimum scope of the action, as apparent from the replies only.
- The "types" refer to the institutions to which the respondents belong : type 11 = universities only, type 12 university hospitals only and type 13 both. Type 21 = type 11 plus service (hospital or health service departments); type 22 = type 12 plus service and type 23 = type 13 plus service. Type 31 = academic institution plus industry, type 32 = industry plus service and type 33 = academic institution plus service plus industry.

	Principal types					
	13	23	33	Other	NQ	Total
Surveillance service	2	9	-	1(21)	5	17
Dev./Eval. of treatment	-	7	1	-	4	12
Dev./Eval. of techniques	2	6	3	2(11/12)	2	15
Harmonization of practice	-	7	4	1(31)	7	19
Forums	2	6	2	1(31)	4	15
Joint research facilities	3	5	1	1(31)	4	14
Spec. research communities	-	8	-	3(21/22/31)	2	13
Total	9	48	11	9	28	105

1 - The forum

A project leader endeavours gradually to guide individual peers towards common interests; such, in simplified form, is the picture of the first type of organizational set-up. It has been seen that of the 105 concerted actions there were 15 actions of this type, 11 of which were concentrated in the two largest subprogrammes (in terms of the number of actions) : biomedical engineering (BME) and AIDS. They correspond to two slightly different case scenarios.

In the first, as set out by several project leaders, the concerted action plays a specific role : focusing on a new field, which, at the frontier of the known disciplines, is having problems establishing itself. Its function is to bring together interested teams, indeed, to stimulate the interest in the first place. Such meetings need to remain informal if links are to be established, and the first and foremost result of these encounters is the emergence of joint projects, the pinpointing of common requirements, in short, the outlining of new concerted actions, whether these involve actions as such or the construction of "central facilities". There are five CAs of this type, developing forms of support for various individual initiatives.

For instance, the CA on "breakdown in human adaptation", defined as an "umbrella" concerted action and involving almost 70 teams, encourages the decentralized creation of micro-projects as a spin-off of limited and informal thematic meetings at which the teams come together to discuss their projects. The concerted action on "immunology and AIDS", on the other hand, is an organized effort to set up a network between the fifteen or so European teams interested in the project : regular meetings, visits, support for exchanges of researchers and materials are organized to this end.

In the second case, the scientific Community already exists. Yet while it may already be defined, its problem is its small size, the isolation of the teams and the absence of scope for dialogue and brainstorming. The CA serves to fill this gap and clear the way for exchanges. The rhythm of these CAs is marked by large annual meetings, which form the main work of the project leader (and indeed of those working with him). The CA on technologies for the hearing-impaired is a long- standing example of this type of action, soon to celebrate its tenth birthday and involving at least a hundred participants. In addition, some concerted actions support decentralized initiatives by the teams : exchanges of people or materials (the "FIV" CA) or the organization of small workshops on specific subjects ("automated cytogenetics" or "DNA repair & cancer"). There are nine concerted actions of this type, which, if the reply rate to the postal survey can be considered indicative of the teams' interest in the concerted actions, are clearly meeting a need.

2 - The outdoor laboratory

A small group of peers sets itself an S&T objective and shares out the work. Joint decision-making and allocation of tasks prior to joint consolidation are the great strengths of such concerted actions, which are characterized chiefly by their small membership.

Take, for instance, the case of a concerted action involving five research teams. These come together to prepare a joint project, determine the research protocol, standardize their methods and share out the work. Each team carries out more or less the same tasks. Macaques are contaminated with AIDS viruses and the results from the various teams and from individual animals are compared and any differences assessed. One team, however, plays a more central role, managing the budget and allocating it among the teams according to the number of macaque-months represented by their work under the jointly established plan. This team is also responsible for distributing the same strain of virus to all the teams, thereby precluding any risk of discrepancies deriving from different strains. Lastly, this team sets up and manages a data base of the study's results, which puts it in a special position. Publications are joint.

There are only three concerted actions of this type, the other two concerning the harmonization of medical practice ("exposure to cancer : evaluation methods" and "mental health problems of deaf people").

There are two advantages to maintaining this type of category. Firstly, the organization of a lot of concerted actions is two-tiered, with a large number of teams gravitating around a small core whose operation is that just described. This precludes the need to provide individual descriptions, for each category, of the operation of the central core, often found within the PMG (project management group) and which figures largely in File 3 on the organization of concerted actions.

The table below shows that just over half of all concerted actions enjoy joint management, or at least joint decision-making.

Secondly, this type of category makes it possible to underline the real meaning of "effects of scale", a feature commonly sought in concerted actions : it is only rarely a question of pooling equivalent resources to arrive at a "critical scale". Most of the time the aim is to bring together complementary skills for the execution of a action or to set up new bodies (which often become permanent) or to help subject- or discipline-based communities set themselves up and gain recognition. These different finalities call for various complex forms of organization: star networks, thematically partitioned networks and geographically partitioned networks. The table below analyses the incidence of these forms of organization and the way in which they relate to the finalities.

TABLE 13 : ORGANIZATION OF CONCERTED ACTIONS

Notes : Forums are excluded. Type 2 = laboratory without walls; Type 3 = star network; Type 4 = thematically partitioned network; Type 5 = geographically partitioned network.
"Shared" organization means that the strategic decisions are taken jointly by the project leader and a core of active teams, generally within the PMG. In all other cases, the organization is centralized, i.e. dependent on the project leader and his team.

	-type of organization-					- management -	
	2	3	4	5	total	centralised	shared
Surveillance services	0	6	2	8	16	6	10
Devpt/eval of treatment	0	2	9	1	12	5	7
Devpt/eval of techniques	0	1	12	1	14	9	5
Harmonization of practices	2	8	1	8	19	7	12
Joint research facilities	1	8	4	1	14	7	7
Specialized communauties	0	6	7	-	13	6	7
Total	3	31	35	19	88	40	48

3 - The star network

The concerted action is organized around the project leader and his team, around whom there gravitate "equivalent" members : "providers of cases" (usually clinicians or practitioners) or "users" (usually colleagues operating through the central facility). There are more than 30 concerted actions of this type.

Even though the creation of a PMG has become virtually compulsory, very few concerted actions of this type endow the PMG with strategic decision-making capacity : only six out of 31. The star network may therefore be considered hybrid, since it is operated not from a single central point but by a core of laboratories making joint decisions on its form and future. Instead, and in the great majority of cases, the PMG is at best a committee which meets once or twice a year to discuss any problems which have arisen, leaving the project leader and his team with the task of arbitrating and orchestrating. This type of organization encompasses two scenarios.

THE STAR NETWORK ORGANIZED AROUND A FIXED INTERMEDIARY

A known scientist backed up by a highly competent team gathers around himself (and possibly around the nucleus of colleagues backing him up) the other

teams working in the field (or some of them, at least) so as to effect a change of scale and, with the help of the community, set up a quasi-institution.

Most of the concerted actions with a "central facility" follow this model. For instance, eight of the 14 joint research facilities, the three actions involved in targeted research and four of the six "central facilities". The concerted actions on HIV antiviral compounds or on virus sequencing (HIV genetic screening) dealt with earlier are good examples of this and illustrate the two forms of organization : the first operates solely according to the internal decisions of the team operating the facility (which will only screen compounds it is interested in), while the second places great importance on the "experiments committee" which makes decisions and establishes practices.

A number of "collection structures" also display this star structure around a "reference centre" which organizes gathering and is, in this case, synonymous with the project leader's team. Take ECAT, for instance, which brings together 21 regional networks in the epidemiological monitoring of congenital malformations. In concerted actions of this type the organization of data collection is usually associated with complex processing tools often belonging to internal facilities : e.g. "epidemiology of osteoporosis" and the image reader, "prevention of blindness" and the tissue bank, "arteriosclerosis" and the tissue, blood and DNA banks. Several "thematically partitioned" concerted actions are organized along similar lines but with several actions being managed in parallel (thus Penta - type 3 - closely resembles ENTA - type 4 - in that two protocols are managed in parallel).

All in all, 16 concerted actions take the form of "star networks around a fixed intermediary", all of them long-term : eight "joint research facilities", five "surveillance networks" and three concerted actions relating to the evaluation and development of "treatment" ("B cells & diabetes", "Penta") and "techniques" (ECG").

STAR NETWORK AND INITIATION

A second grouping includes CAs of identical origin and organization but which, initiated only recently, are often still at the structuring stage. This is the case for six of the 13 concerted actions aiming to set up "specialized communities" (e.g. "Eurobiomat" or "neuropathology of AIDS") and for two CAs relating to the harmonization of practices ("haemoglobinopathies" and "use of DRGs in hospitals").

This grouping also includes six concerted actions relating to the harmonization of medical practices and displaying special features : a small number of participants (at the limit of the "laboratory without walls", as far as scale is concerned), focusing solely on obtaining information at European level and of limited duration (disintegration once a picture has been formed). Take, for instance, Euromac (maternal alcohol consumption) or the CA on oral problems relating to AIDS. Typically, this is a form of organization adapted to short-term concerted actions or those which get off the ground and determine their organizational set-up at the same time as defining their objectives.

Thus the star network corresponds to two very different but complementary situations :

- on the one hand, a stable form of organization centring on a fixed intermediary and in which the manager or organizer (when he works between several laboratories) is in fact the leader of the concerted action. In a third of all cases joint decisions and/or task-sharing produce a "hybrid" star network;

- on the other, a short-term set-up reflecting the one-off nature of the project (forming a picture of the situation in Europe) or the recent nature of the concerted action. In the latter case this form of organization indicates an individual initiative which has to "prove itself" if it hopes to set up a community and work with it to determine a course for the long term plus the necessary back-up.

4- The geographically partitioned network

In contrast to the star network, the geographically partitioned network includes a hierarchical level separating the project leader or the central nucleus of teams and the individual participants. This level comprises national correspondents coordinating the teams within their country (or area).

A good example of this is the action on the way general practitioners refer their patients to specialists. A data collection protocol is drawn up by a small working party and is then discussed with 12 national representatives. Once the protocol has been approved the central team creates data collection logbooks for the general practitioners involved in the study. The logbooks are translated and, after any corrections have been made by the central team, distributed by the various national representatives. Each representative sends this material to the doctors in his network. Having filled them in, the doctors return the logbooks to their national representative, who checks them and sends them to the central team, which then enters them into the data base and has them processed. Feedback to the doctors on work progress and results is the responsibility of the national representatives.

This is the model for 19 concerted actions, 16 of which are associated with two finalities : the setting-up of surveillance services (8 CAs) and the harmonization of medical practices (8 CAs). Yet if we look more closely at the details of the logistical organization (and the strategic importance of detail has already been stressed on a number of occasions), we find that there are almost as many variants as there are actions : relays may be operated through national representatives or otherwise; such relays may be with ad hoc networks, existing networks (e.g. the epidemiological monitoring networks of general practitioners, ("sentinel" networks) or quasi-institutions (national or regional registries); relays may or may not carry out certain data processing (e.g. translation, shaping, incorporation into national projects, quality control, intermediate data base, local sifting of intermediate results, etc.); it may or may not be the case that only information moving in one direction will pass through the relays; the protocol may be common or there may simply be a few common indicators to be incorporated into the various national procedures; the CA may comprise a single project or a number of subprojects organized according to this model; the teams may or may not have access to the central data base; the importance of the joint work can vary (e.g. establishing terminology and language); data may be analysed locally by the collating teams or exclusively by the central team; data collection may be specifically for the duration of the study or more permanent, like a service; the central team may or may not develop and supply data entry software, etc.

Amid this great diversity, which needed to be contrasted with the organization of the star networks, three forms of organization may be discerned.

- The first is confined to the setting-up of a central structure whose function is to gather and process the data collected through independent and pre-existing

national networks. This is the case in the concerted actions on the epidemiology of AIDS and on "avoidable deaths" (with specific secondary projects which validate and enhance them). This type of CA usually has few participants : simply the representatives of the national data collection networks and a few epidemiological specialists assisting the "reference centre" team. The primary collectors work solely with the national systems, which are coordinated at the second level, that of the harmonization and pooling of data.

- The second group, and by far the largest, is that of the "epidemiological" CAs, which build up large data bases. The aim is to create representative images of practices and help individuals, operators and systems to locate themselves (the "secondary" CAs stemming from the first group can often be likened to this type). These structures are not intended to be long-term; set up to meet a specific requirement of the participants, they are destined to break up during the dissemination process which will help improve practices or standardize techniques. Examples include the concerted actions on "antenatal ultrasound screening" and, especially, "care delivery systems", "hospitals auto-evaluation practices", "HIV serological methods", "use of blood" and "head injuries".

- Concerted actions in the third group, working with reference to the problem they are tackling, set up long-term collection structures based on what is generally a two-tiered form of logistical infrastructure : national representatives who organize and sustain the networks of collectors, and a European collection centre, the nerve centre of the system (usually the project leader's laboratory). These concerted actions are distinguished in part by the arrangements made for national collectors, who are directly organized with an eye to European analysis in the knowledge that national analysis is often unrepresentative (through lack of cases).

The two concerted actions organized around general practitioners ("Eurosentinel" and "GPs referral study", outlined above) are examples of this, as are the CA on nocosomial infections ("Euronis") and, especially, the CAs on objective medical decision-making ("OMDM"). As regards the last two cases, the two project leaders want to combine their projects to encourage the creation of renewed projects on other illnesses but making use of the intricate and original procedures developed during the first two experiments. The other two CAs ("EMIP" and "thyroid cancer genetics") have set up "complex" networks, which include a third tier of laboratories specializing in complex treatment or analysis (their specific nature often tends to confer on them the status of "joint research facility"). Although they are organized with reference to a specific problem, these two concerted actions will, if successful, be extended and focused on other problems : the first as a service for analysing costly pre-hospital treatments and the second as a molecular biology service.

5 - The thematically partitioned network

The last major form of organization and the most widespread (35 concerted actions) are the thematically partitioned networks. Work is organized in subnetworks coordinated by joint project leaders. Project management groups generally correspond to the groups of joint project leaders. These networks fall into three main categories according to the way the work of the subnetworks is synergized within the framework of the concerted action.

SIMPLE PARTITIONED NETWORKS

In these networks work is not synergized (or only at the end of the project). The CA's task is to split up the problem or phenomenon under study into subproblems to be tackled in parallel by individual groups guided by the joint project leaders. These groups are usually small (five or six teams) and will produce an identified output (a protocol for the cytometric analysis of such and such a cancerous tumour, the comparative evaluation of x hyperthermic installation units, the clinical evaluation of such and such a perinatal diagnosis, etc.). What distinguishes one CA from another is the way the output is mobilized and whether or not it has been provided for at the current stage within the framework of the CA. Such is the case, for instance, for the protocols on clinical immunology for chronic arthritis, which are being drawn up in parallel and the test for which is already being prepared (by specialized subgroups), or the stocktaking of the technical clinical problems affecting artificial hearts to help find a working definition of a new type of artificial heart. Nonetheless, the most common form involves the piling-up of independent results, often with the project leader alone in a position to synergize them.

Take, for instance, the concerted action on heritable connective tissue disorders, in which the work is split up between specialized subnetworks (sub-working groups). However, these are linked together by the wide dissemination of results organized by the project leader. For instance, one task is to draw up an annotated directory of laboratories specializing in the diagnosis of connective tissue disorders for subsequent widescale distribution to clinicians. Another subgroup, this time of clinicians, is responsible for establishing diagnostic flow charts for publication in a major medical journal. A third subgroup, of laboratories, is asked to organize the comparison and standardization of methods and draw up a reference manual for laboratories. It also has to establish a tissue bank. Lastly, another subgroup deals with the setting-up of a data base of patients suffering from these diseases with a view, ultimately, to offering genetic advice. The teams shares out the work by subgroup; results are given wide dissemination via the project leader.

The concerted actions adopting this form of organization are concentrated around two finalities. It is the course adopted by project leaders for setting up specialized scientific communities, given that they do not centralize everything around their own teams or around the small core of instigating teams (seven CAs). It is also the most common form of organization for concerted actions on standardization of the development of new techniques (10 out of 14 CAs). It is interesting to note that none of the concerted actions is currently at a stage where it can bring together the various outputs, as the ECG action can.

INTEGRATED NETWORKS

This type of network can be compared to a genuine project structure. The subnetworks correspond to allocated tasks in a project where those tasks have been defined so as to speed up progress and exploit the presence of complementary expertise in the network. In these networks, the gathering of results for the compilation of a final integrated result is already clearly defined and in fact constitutes the real objective of the network. Subnetworks are no more than a passing stage in a network's career. Five concerted actions on the development of new cancer treatments are built on this model. The extreme manifestation of this type of network model has already been seen : the BNCT

action. Or take, for instance, the succession of cycles (each cycle requiring complex organization of activities, sometimes in parallel, sometimes in sequence) to improve the purification of stem cells (human stem cell action). Similarly, the two concerted actions on drug targeting and drug carriers organize the selection of target/vector pairs, their production and the carrying-out of animal and then clinical tests. Lastly, a particularly good example is the Eulima project, which is organizing its work to arrive at a final conceptual design for the new clinical instrument to be developed for improved cancer treatment.

PARTITIONED NETWORKS AND FIXED INTERMEDIARIES

Although central facilities are often set up in a star structure, some of them are to be found in partitioned networks :

- Four are organized in surveillance networks with registries (Eurodiab, Eurofap) or are aiming to set up a service for the evaluation of techniques relating to problem diagnosis (tissue characterization, perinatal surveillance).

- Five others, of fairly long standing, are mobilized simultaneously by several projects. Such is the set-up of the two concerted actions on AIDS-related diseases. A central core of teams organizes the work. Tasks are allocated very carefully among those teams. Thus one of them is responsible for overall coordination and for the day-to-day implementation of the protocol. Another deals with all statistical and data processing relating to the protocol, viz. chiefly the random selection of therapies and data processing. A third team, different for each disease, is responsible for sifting the scientific results. The others help draw up the test protocol and take part in the discussion of the results. Around this nucleus are several dozen teams assisting in the implementation of the protocol. These teams comprise clinicians who have become involved in the study and have undertaken to apply the protocol. They have no contact with each other, but deal solely with the coordinating team.

A further example is provided by the concerted action on thrombosis, in which the division into subnetworks is the work of a team which organizes a vast network of logistical support for various research projects. First, it organizes the standardization of methods of analysis by setting up one or more reference centres, where appropriate and depending on the subproject. It then organizes the logistical support (definition and distribution of reference material, organization of quality controls, drafting of recommendations, training of laboratory technicians). In addition, it was set up a committee to harmonize decisions on difficult cases. Lastly, data bases and materials banks (serum and blood samples) has been set up. These should serve to standardize work throughout the duration of the action, even if available analytical methods are changed (appearance of new diagnostic kits, etc.). This vast organization takes account of the various needs of subprojects. The three subprojects themselves are headed by three associated project leaders, who base themselves on the standardized working methods. In this instance, scientific work is coordinated through the management of work tools.

Thematically partitioned networks associated with fixed intermediaries, and more particularly with collection structures, thus reflect a project's development over a certain period. Initially set up in star form, they are gradually transformed into partitioned networks capable of managing several projects simultaneously. At the same time they become long-term, which requires a new response from MHR and its procedures.

6 - Types of organization, actors and finalities : special relationships

Concerted actions which are almost always distinct in composition and which include future users of their results; concerted actions organized according to three main models - in star form or as thematically or geographically partitioned networks; concerted actions which are as often as not managed jointly. These are the principal features thrown up by this analysis. Is it possible to go further and seek out the relationship between actors, organizational forms and finalities? The analysis does give several guidelines.

TREATMENT/TECHNIQUES AND THEMATICALLY PARTITIONED NETWORKS

Most of the CAs whose finalities are the evaluation or development of treatments and techniques are organized according to the "thematically partitioned" model. This is no doubt because to focus on a treatment or a technique requires approaches from a large number of angles at the same time. These concerted actions assume three additional forms depending on the degree of integration.

- Most of them split up the work into a series of problems to be solved in parallel (in the hyperthermy project, for instance, delivery of heat, measurement of its distribution, patient modeling and clinical protocols for radiotherapy association). This division is then structuralized in subgroups of participants led by joint project leaders and the strategic management of the CA becomes joint, as happens in 50% of cases, when the group of joint project leaders meets regularly to make decisions on the project's course. A great many concerted actions, faced with the size of the problem and given their current state of progress, are as yet unable to envisage the collection of the various results with a view to producing a working result. This integration phase, even when drawn up (e.g. animal and/or clinical testing of finalized protocols) remains formal or latent and cannot be fitted into the current framework of CA funding.

- A second group, peculiar to the subprogramme on cancer, includes five CAs which are genuine "projects" for the development of new treatments, whether focusing on the use and adaptation of heavy equipment (BNCT) or calling for firm cyclical sequential organization (human stem cell action).

- The third and final group, encompassing very few CAs, uses the evaluated treatments or techniques to help develop long- term evaluation services : in the clinical treatment of AIDS (ENTA), for tissue characterization techniques and even for perinatal surveillance techniques. All three take the form of "collection structures". These concerted actions are somewhat larger than the previous ones (50 participants or more, compared with 30 or less, many cases) and have a different make-up : outside the organizing core they usually use clinicians as collectors. The other concerted actions generally bring together scientists and engineers, with only occasional recourse to clinicians for a clinical evaluation subproject (e.g. Viral hepatitis or "Heart").

N.B. : Of the 26 concerted actions in these two finalities (evaluation of treatment or tehcnique), 21 use this form of organization, demonstrating clearly the close link. Five CAs have nevertheless chosen a different form of organization. Analysis of these five and their differences gives a better understanding of the logic behind the choice of the predominant form of organization. For one of them, in

star form (Penta), it is clearly a transitional validation stage before setting up, like ENTA, as a collection structure for AIDS treatments for use on children. For another (Diabetes and B cells), the project, focusing on the activity of the "production centre" is maintaining a star form, though development of uses will in all likelihood transform it too into a partitioned network. Two other CAs, in order to evaluate the effective application of a technique (antenatal screening) and a treatment (EMIP), have set up major networks of collecting clinicians and, in order to manage them, adopted the geographically partitioned form (one of them, EMIP, considers that it has in this way set up an original service for the evaluation of costly pre-hospital treatment). The last action (ECG), now in its final phase, foreshadows what will probably happen with a number of CAs once they get to the results integration stage : reconstruction of a star network around a "reference centre" (or a "laboratory without walls") which will consolidate and operationalize the first network's achievements.

GEOGRAPHICALLY PARTITIONED NETWORKS AND HARMONIZATION OF PRACTICES

In order to characterize what are essentially widely disparate practices prior to harmonization, a large number of clinicians and practitioners need to be assembled and strict rules on geographical coverage enforced (so as to allow for historical and organizational differences in health services). Hence the frequent use of geographically partitioned networks and the importance which is often attached to this form of organization, which sets up national joint project leaders who will channel first the mobilization and then the dissemination (e.g. the CA on objective medical decision-making and acute abdominal pain). Eight out of 19 concerted actions display this form, though most of them do not include national collectors in the list of participants. Although in one case (the CAs on objective medical decision-making, which the project leaders want to merge to tackle other diseases posing diagnostic problems) this structure is intended to be long-term and establish itself as a service, it is otherwise temporary and will last just long enough to produce the results needed to form recommendations.

This type of concerted action therefore belongs with the very large group of small-scale CAs targeted on a specific problem, where the aim is either to take stock of a situation (e.g. maternal alcohol consumption and its effects on pregnancy and child development, or the mental health problems of deaf people), or carry out a comparative study (e.g. use of DRGs in hospitals, or age care research) or to prepare targeted information (e.g. the book on the "International Classification of Primary Care", material informing dentists about oral problems relating to AIDS). These CAs, which are more like studies, generally take the form of a star network around an initiating project leader with sole responsiblity for ensuring the final consistency of the results. For some of them success will mean transformation into a geographically partitioned network in order to look more deeply into a particular aspect (e.g. CA on haemoglobinopathies). This change in organizational set-up over a period of time reflects standard diachronic development in the pursuit of this finality : initiation usually by the programme, and more specifically the HSR COMAC ("the stake is important and something needs to be done"), a mandate given to a recognized scientist (who must then assemble the necessary teams) usually after a number of workshops have been set up, followed by genuine comparative research into practices (which is what requires the introduction of geographically partitioned

organization) and the finalizing of recommendations and the development of instruments (e.g. software to assist diagnosis) whose dissemination must then be ensured (or even taken over), failing which all this effort will go to waste.

N.B. Only one concerted action adopted the thematically partitioned form of organization. Its aim was to set up a network of reference laboratories to which general practitioners can turn for analyses of heritable connective tissue disorders. In a way the CA is aiming, through a series of parallel operations (aimed at diagnostic cards, clinical practices, etc.), to establish a quality label and introduce recognized specializations at European level. This synergization, which must ultimately be self-sustaining, raises two important points affecting the national health systems: (i) professional standards need to be introduced at Community level; (ii) since, for a number of highly advanced genetic analyses there is no need for each country to have a specialized laboratory, how will it be possible to turn to the "right" laboratory if each country does not have one? The difficulties emphasized by this example no doubt explain why very few CAs have launched into this type of harmonization.

ON-GOING SURVEILLANCE AND GEOGRAPHICALLY PARTITIONED NETWORKS

As has been seen, harmonizing practices means gaining an overall picture of the situation and thus organizing the gathering of information from a large geographical area. Since the aim is no longer to gain a "snapshot" picture of the situation at a single point in time, the action heads towards the setting-up of "surveillance networks", one of whose main functions, along with monitoring over time, is to evaluate the effect of health policies and to set off "alarms" (in the event of hiccups or unexpected events, such as the Chernobyl disaster). It is not surprising, then, to see a large degree of organizational continuity between the two groups.

- Three concerted actions bring together existing national networks (AIDS epidemiology, avoidable deaths and Eurocare: registries in cancer survival). Their core is therefore the reference centre, which gathers, processes and disseminates this data. In the process, all three throw up new questions and prompt new research intended to supplement the surveillance. In two cases the projects have given rise to "secondary" actions (with the same steering group), which typically adopt the organizational form of the CAs dedicated to the harmonization of practices, with the reference centre taking charge of dissemination.

- In order to operate, the other concerted actions have to start by setting up gathering networks. In five cases the chosen model means setting up regional (Eurocat) or national (Euronis, Eurofap, Eurosentinal and Eurodiab) networks, data from which is centralized in a reference centre. How symbolic that most of these networks have adopted acronyms preceded by "Euro", as if, even at programme level, there were a desire to proclaim the durability of the concerted action programme. What these five projects have in common, along with the equivalent projects dedicated to the harmonization of medical practices, is that they do not count collecting clinicians as participants; logically, therefore, the only members are partners active in organizing the collection or processing of data.

- In the three other cases, on the other hand, the collecting clinicians are fully-fledged members of the concerted action and enjoy direct links with the core of teams constituting the reference centre. The CA takes the form of a "hybrid" star network. There are always sound reasons for this choice : the difficulty of

gathering useful samples for "prevention of blindness", the existence of a joint facility for the analysis of X-rays for "epidemiology of osteoporosis", the major investments which collecting clinicians need to make for "asthma prevalence".

- Unlike the three "reference centres" of the first group, a feature of a number of recently initiated networks (which got off the ground under MHR4) is that they combine the setting-up of a surveillance network with the pursuit of research objectives within a single concerted action : identification of markers and genes in Eurofap (cancer families and familial adenomatous polyposis) and "prevention of blindness", which is tackling the two most common heritable disorders while at the same time taking organizational steps to treat them all in turn; dealing with complications for Eurodiab ("diabetes mellitus").

CREATING NEW SCIENTIFIC COMMUNITIES : ORGANIZATIONAL CHOICES REVEALING VERY DIFFERENT SITUATIONS

In view of the large number of concerted actions pursuing this broad finality (over 40 out of our sample 105) we have already had to break them down on the basis of the strategy adopted : establishment of forums, guidance through the development of a "fixed intermediary" which is often unique in Europe (which we have termed "joint research facility"), and coordination through the harmonization of practices and the gradual establishment of a project. These strategies are implemented through very different organizational forms.

The forum is a form in its own right, which is specific and limited in terms of the involvement on the part of teams. It is nevertheless a valued tool, going by the interest shown by the teams in taking the effort to reply to a mailed questionnaire as complex as the one sent to them! The fact that a small specialized community has been given access to the traditional media of academic exchanges (meetings, visits, ad hoc exchanges) is bound to have an effect on the dynamics of this community (e.g. "technologies for the hearing-impaired", and "automated cytogenetics"). Other examples of finalities pursued through the instrumentality of such an organizational form and strongly supported by several project leaders are the assistance to the emergence of projects in new areas on the frontiers of established disciplines (e.g. "breakdown in human adaptation"), and assistance with the recognition of common needs ("genomic variation of HIV").

All the other actions aimed at structuring a specialized scientific community take the form either of a star network (around a project leader, more rarely around a core of teams, 14 CAs), or a thematically partitioned network (generally involving task-sharing between laboratories and joint management of the project, 11 CAs). Only 2 CAs organized around joint facilities do not fall into this pattern, one being a "laboratory without walls" for five animals (monkeys) test centres, the other organizing a geographically partitioned network for the collection of tumours for genetic research into thyroid cancer.

Of the 14 CAs organized around a joint facility, nine are centered on the development of a "fixed intermediary". With the exception of one case where the existence of a centre for the production of aged mice is linked to the development of autonomous subprojects (Eurage), all of them take the form of a star network whether a "laboratory" (as for "HIV genetic screening" or "HIV antiviral compounds") is involved or a production centre (like EVA or "HIV protein and cell membrane interaction"). In every second case an "ad hoc experiment committee" PMG is associated with the facility and organizes access conditions and user selection. Special mention should be made here of the role of the AIDS

subprogramme which has given birth to seven of these. The four other CAs build "collection structures" which are organized directly at European level and, except for a more recent case, are simultaneously mobilized in several parallel actions (e.g. "Euronut: nutrition and health" or "ECAT: thrombosis and disabilities").

The 13 other actions take one or other form depending whether the activity is centralized around a project leader and his team or else organized in a set of parallel subprojects. A feature they all have in common is that they are at an early stage in their development and there is therefore a considerable degree of uncertainty about their future path.

PREFERENTIAL ASSOCIATIONS WHICH ALTER OVER TIME

The linkage between finalities and organizational forms adopted makes it possible, therefore, to pinpoint preferential subsets : development or evaluation of treatments or techniques goes hand in hand with the establishment of thematically partitioned networks; harmonization of medical practices and surveillance networks are often associated with geographically partitioned networks or, where the problem is more specific, with "hybrid" star networks; central research facilities are propped up by star networks, while collection structures are often simultaneously mobilized by several projects, thus taking the form of a thematically partitioned network.

At the same time, this analysis shows that these relations transform over time, witness the transition between star network and thematically partitioned network observed in many cases. It highlights, for one and the same finality (in particular harmonization of medical practices or creation of specialized research communities) organizational transformations bound up with the very development of the action, the results obtained or the experience acquired.

PART III : THE TIMING OF CONCERTED ACTIONS

Parts I and II have shown the various elements which characterize a concerted action. Part II included a systematic analysis of three groupings : finalities, objectives and end results, exchanges and intermediaries (circulating or fixed), and actors and organization. The result was a map indicating five "finalities", four main forms of organization all based on a large number of meetings and exchanges, three main types of fixed intermediary and a wide variety of circulating intermediaries, the logistical constraints on whose movements often have a major influence on the setting-up of concerted actions. It has also been seen, through numerous examples, that concerted actions evolve as time passes, undergoing changes in composition, exchanges and organizational set-up. Is each case specific unto itself? Are we obliged, in this respect, to look at projects on an individual basis or can we distinguish standard paths and common constituent phases? It seems that we can. We shall try to show that the vast majority of actions follow a similar time-scale, punctuated by peaks of activity which we have grouped into six phases : initiation, assembly, structuring, implementation, processing and transfer. This type of linear presentation is of course an over-simplification : phases often overlap, their duration can vary greatly from one action to another, the problems encountered often make it necessary to repeat a phase which has supposedly been completed, some phases may be taking place or have taken place outside the concerted action framework, etc.

The value of this approach is threefold. Firstly, it allows us to compare actions. Secondly, it has the advantage of providing a means of monitoring the progress (both that anticipated and that actually achieved) of actions (interviews have shown that the approach provides a valuable framework for deliberations by project leaders and a useful basis for planning a course of action and for forward analysis of problems to be dealt with). Lastly, it makes it possible to determine more accurately the necessary lifespan of a action. This will depend largely on the degree of preliminary existence of the network and on the nature of the objective chosen. It will vary according to whether the network has to be built up from scratch or whether it already exists in "latent" form. Similarly, the objective to be attained at the conclusion of the concerted action can vary greatly, from the completion of a phase to the completion of the entire process. Nonetheless, a concerted action can be properly understood only with reference to this final objective and the path leading to it.

I - A COMMON PATH FOR CONCERTED ACTIONS

At the outset, all networks are built up around a small number of teams, usually between three and six. These teams often know one another before engaging in the action. In some cases, the project promoter brings in a number of foreign colleagues with whom he has already had occasion to work; in other cases, a small network already exists, often on a relatively informal basis. These teams then get together at meetings or by telephone to prepare a joint project. This

initiation phase generally corresponds to the preparation of the proposal for concerted action. Under the MHR4 procedure, with the launching of the call for proposals, this gets under way with the preparation of a statement of intent. Occasionally, the founding teams already form a small group prior to the statement of intent. The next stage is a meeting of experts, to which a number of additional specialists are invited. Following this, a large number of teams likely to take part in the project come together at a "preliminary meeting" to prepare the ground for the concerted action. The aim is to reach a consensus on the project so as to mobilize a sufficient number of competent teams. The project is put forward, illuminated by various contributions, e.g. on the state of the art, and is then discussed and reworked.

This meeting often becomes a sort of scientific symposium on the project's subject matter and is considered to be an important result of the concerted action : it marks the completion of the work to assemble teams which have never before had the opportunity of taking part in a scientific meeting on this subject. The assembly of teams at this meeting is often more than just an extension of the initial core since, when the Commission of the European Communities has received several statements of intent on related subjects, the programme managers invite the proposers to get together and prepare for a joint meeting which should normally lead to a unique concerted action. Thus the assembly of the teams is sometimes a little forced; in certain cases preparation of the project involves a degree of bargaining between subgroups which are already more or less set up. In addition, the project management group and the project leader are usually elected at this meeting.

The *assembly phase* generally ends with this preliminary meeting. Once the resultant proposal for a concerted action has been approved, the project leader has merely to activate the newly created network. However, this is not the case for all concerted actions. In some of them, active recruitment begins at the same time as the project gets under way. This applies, for instance, for certain centralized facilities (sequencing of the AIDS virus, screening of antiviral molecules, experiments on chimpanzees, production of transgenic rats, etc.). It applies also for networks in which the implementation of a protocol calls for the recruitment of a large number of local teams for the collection of data. In some concerted actions assembly ends with team selection. For instance, following a two-stage selection procedure (assessment of team quality and of conditions of participation), the 82 teams which came forward in the project on heritable connective tissue disorders were whittled down to around 50.

Once the assembly phase is over, the dynamics of the networks diversify considerably. Some appear to maintain stability of form throughout the project. This is the case for the star networks around centralized facilities. New branches are formed while others disappear. One might say that although the star twinkles the network always retains its shape and could do so indefinitely. Other networks, meanwhile, appear to evolve quite considerably. They extend and are transformed. One can usually distinguish a *structuring phase* in which the work is prepared and organized, tasks are allocated, various coordination mechanisms are set up, and common languages and tools are established, etc. The duration of this phase varies from network to network, ranging from a few months to several years. Some concerted actions appear to be devoted entirely to this structuring phase, while for others it is the following phase which constitutes the core of the work.

In networks with open-ended forms of coordination, the stage which follows structuring is the *implementation phase*. However, this general term encompasses a number of quite different realities. It is very often a question of implementing a protocol. Once again, this operation can take very many forms, ranging from the incorporation of a common denominator into very different local practices to central organization and management of every last detail. In other concerted actions implementation is more a division and allocation of tasks among teams or among groups of autonomous teams.

After the implementation phase comes the results *processing phase*. Once again, this term covers a wide variety of practices. Sometimes it means the processing of results by an isolated team or a subgroup; sometimes it is a general discussion of results; sometimes integration of results; sometimes this phase is omitted.

Lastly, concerted actions end with a *transfer phase*, which is designed to make the transition from the project itself to the application of its results. This phase may take various forms : publications, symposia, preparation of a standard, setting-up of a service, development of a prototype, renewal of research projects, etc. Clearly, only the last of these can be carried forward under MHR. The question arises of how to deal with the others; a tricky question given that, in a lot of cases, traditional market mechanisms do not come into play.

This, then, is a standard path, with all the unknowns it can encompass. In the following paragraphs we shall underline the main features which serve to distinguish the networks from one another : (a) depending on the way the programme chooses to initiate the networks, two extremely different types of action will be implemented : creation of new networks or activation of "latent" networks; (b) the duration of the phases (which must not be confused with the duration of the approved funding) varies enormously depending on the type of network, this variation being linked largely to the importance of the structuring phase; (c) the duration of the phases is closely linked to the gradual mobilization of the actors interested in the stakes, of which the intermediate results and their application are the chief markers; (d) results are transferred differently according to the project and in a lot of cases this leads back to new forms of public funding.

II - THE TWO INITIATION AND ASSEMBLY SCENARIOS

Where did the idea come from? How did it develop? How did it become a concerted action, i.e. the networking of teams from the various European Community countries? The interviews pointed to two main courses corresponding to different strategic choices by the programme. The first entrusts this responsibility to the COMACs (Concerted Action Committees) or to the Working Parties set up for each of the subprogrammes (the term COMAC will subsequently be used to designate both types of structure), while the second places it de facto in the hands of those who reply to the call for proposals.

COMAC initiatives

Initiation by the COMACs was the spur, if not for all, then for the great majority of projects begun up until 1988. The COMAC would form an opinion on the expediency of looking at a particular problem, e.g. the relationship between

nutrition and health. The next stage was to find someone enjoying sufficient recognition at European level to attract competent teams from the various countries. COMAC members played a crucial role in the choice of project leaders, and there are grounds for wondering whether there was some connection between the activities of certain members and the large number of project leaders from the same countries (UK, B and NL). Sometimes it was the COMAC member concerned who was directly entrusted with the task of setting up the action.

Once an initiator had been found his task was to put together a proposal. In our chosen example, the project leader to whom the approach was made contacted two other colleagues and drafted a proposal. This was then used as the basis of a "preliminary workshop" funded by the Commission on a subject which was not yet that of the eventual concerted action (diet & nutrition). Some 30 teams from the various countries were contacted and attended the meeting, most of them at the invitation of the COMAC. The project leader and his team prepared the ground for the meeting and, in addition to the written project, produced a preliminary draft protocol for discussion. This type of meeting produces a range of results.

- First of all, the teams express their interest. The future project management group is usually formed at this stage. In this case the COMAC imposed a geographical representation : originally comprising six members, the project management group has now grown to 12.

- The teams then confirm the project leader's status. This particular mode of election is employed in almost every case. Sometimes it results in a change of leadership (as in the concerted action on automated cytogenetics, for instance).

- The discussion of the project often leads to a compromise, which the project leader has to draft (the compromise often involves the addition of related projects in order that a sufficient number of teams can be mobilized and proper geographical cover achieved).

- Lastly, this type of gathering often gives rise to a report. In our exemple, it was published as a book by the Oxford University Press, as the future project reports will be. This is an important element in the concerted action's external, or indeed institutional, visibility.

These preliminary workshops mark a step forward in the setting-up of a concerted action : a project leader has been singled out, the first teams have been interested in and have discussed a specific subject, and an initial course of action has been determined. Most of the elements needed to set up the project are already to hand. Until recently, the COMACs' initiative went even further : "in the beginning, both the teams and the subject matter were dictated by Brussels; nowadays, all I have to do is ask for approval of my own list of participants," said one project leader, underlining the direct involvement of the COMAC in the life of the action.

MHR4 marks a turning point in that it makes a broad appeal to the scientific and medical communities in Europe by means of a call for proposals. This has meant a change in the function of the COMACs : instead of taking initiatives, they are now, as those in charge of shared-cost programmes often say, "in the hands of the respondents." This leads to two complementary situations, depending on the nature of the responses obtained : either the respondent offers a "complete package" covering the full range of project translations and defining the course of action (on his own initiative), or he merely expresses his interest and offers his services (statement of intent). In the latter case, the statement is usually goal-

oriented : "this stake is very important because..., this is what we have done and this is what we know, so what we have to do now is..." In a sense, the initiative then returns to the COMAC, which in this way identifies potential project leaders. It can once again apply the "preliminary workshop" formula and bring together all those respondents interested in a certain subject (for which there are many examples, artificial hearts, for instance). Such responses are selected only where there are no proposals for networks which have already been set up. As in the initial scenario, then, the situation requires the exploration of new networks. Several project leaders, acquainted with Community organization, have stressed the active role of the "mark 1" COMACs in selecting subjects from virgin territory (virgin to Europe, or even worldwide) and building up networks from scratch.

Respondent initiatives

The picture is quite different when the COMAC receives a complete proposal. Before looking at the effects of this development on the programme content, we would like to indicate two findings of the research into the mechanism of the call for proposals.

- The many analyses of project peer reviews have shown that the "academic" quality of a project almost always prevails over the originality of the subject matter and that it is difficult to make a group agree to take risks, especially when the large number of projects means that selection is going to be tough. Despite the material problems involved in launching this first call for proposals, MHR4 received a great many proposals.

- Secondly, thematic coverage. Our work on shared-cost Community programmes has underlined the decisive importance of defining the call for proposals and its capacity clearly to advertise a number of priority subjects compatible with the size of the budget. This is rarely the case for Community programmes[6], which read more like subject catalogues. This inevitably results in "conservative" thematic coverage in that it tends to be a faithful reproduction of the strengths and interests of the targeted scientific community. Any positive action will depend on the initiative of those responsible for programme administration and on direct contact with teams likely to tackle subjects truly considered to be of priority. The small size of the administrative team restricts its scope for action, a considerable investment in terms of man-hours being needed before the contacted team is in a position to give an answer.

It is not surprising, then, to see a significant change of emphasis in the projects selected by MHR4. A number of them concern existing networks, either operational (CA on the International Classification of Primary Care) or "latent", like the many which have emerged from European medical societies (patients as well as general practitioners or specialists) and from the European committees of the World Health Organization (WHO Europe). These international organizations have stepped into the initiatory role played by the COMACs : identifying potential project leaders (specialists who are often already in charge of specialized groups), locating teams active in the field, determining focuses of interest and common goals. The nature of the proposal changes accordingly : rather than attempting to break new ground in a potential concerted action, the aim is to define a targeted

[6] We shall not expand on this aspect here, which we have already shown to be linked largely to the functioning of the CGCs and the reaching of compromises between Member States. We even stressed that these national committees (whatever their form, title or official purpose) should provide themselves with the wherewithal to carry out proper "forward strategic analysis" as defined by R.Chabbal in his report on the organization of evaluation in the EC.

"scientific and technical operation" with a clearly defined objective, specific final results, known participants and an established work programme. Thus defined, it can be slotted into the new financial frame of the programme : an initial undertaking restricted to two years.

Creation of networks as opposed to activation of "latent" networks : how to strike a balance?

TABLE 14 : INITIATION OF CONCERTED ACTIONS

Notes: The data set out below was taken from interviews with project leaders. Not all the replies could be classified as accurately as hoped, particularly those concerning "initiatives by researchers" (i.e. depending on whether or not an informal network already existed beforehand). Initiatives by a Concerted Action Committee (COMAC) or Working Party (WP) were classified as "during MHR3" if there was a study or workshop on the subject before 1986. Initiatives "at the start of MHR4" cover proposals made directly by the COMAC (or by one of its representatives) to the project leader before the statement of intent was submitted. All other cases are "initiatives by researchers" with a distinction between those with "indirect input" by COMAC (through an already existing CA or by bringing together "individual answers" or declarations of intent by means of workshops) and those cooresponding to the activation of a latent European network.

	COMAC direct input		COMAC indirect input		activation of
	during MHR3	at the start of MHR4	via an existing action	thanks to individual(answers	preexisting or "latent") networks
Surveillance services	3	-	6	4	4
Dvt/eval of treatments	2	1	-	6	3
Dvt/eval of techniques	3	3	-	6	2
Harmoni. of practices	3	6	-	1	9
Forums	5	4	-	4	2
Joint research facilities	3	3	-	8	-
Specialized Communities	2	2	-	7	2
Total	21	19	6	36	22

What is the split between initiation by the COMACs and activation of "latent" networks? The table below shows that the COMACs played a direct role in 40 proposals out of the 104 concerted actions examined, while the primary initiative for 60 others came from outside. The introduction of the call for proposals has therefore brought about major changes in the way project leaders are recruited and concerted actions initiated. Closer analysis of each of the categories will show the nature of these changes more clearly.

- The COMACs have not abandoned initiatives altogether : of the 40 CAs they initiated, 21 result from initiatives dating back to MHR3 (CAs initiated during that programme, past studies or workshops already set up) and 19 are linked directly to the implementation of MHR4. This means that the project leaders of these 19 concerted actions consider their projects to be the result of a direct initiative by the COMAC or one of its members, an initiative taken before the project leader submitted any statement of intent. Most project leaders even felt that without the

COMAC initiative they would not have applied, most of them having been unaware of the programme.

- To these may be added some 6 CAs which directly derive from existing ones (the "daughter" CAs mentioned above linked to surveillance services).

- Of the 58 CAs from outside sources, only 22 came from existing networks, 15 of these from European associations of specialists or international organizations. More than 35 concerted actions therefore derive from initiatives by individual researchers or a small nucleus of teams. So the COMAC often finds itself playing a stimulatory role, bringing teams together, supporting preliminary workshops to check the foundation of the proposal and the interest it prompts.

Expansion and a change in practices have brought about a significant alteration in MHR's strategic choices. The programme, in fact the COMACs (see File 3), are no longer confined to giving rise to concerted actions in areas they consider to be of sufficient priority to warrant direct intervention. They have two complementary roles : (a) supporting decentralized, indeed individual initiatives and (b) backing up and putting into operation the work of international institutions and academic and professional societies already collaborating at European level. Was this balance in fact sought? Is it satisfactory? What direction should it take? This radical transformation observed in MHR4 requires comment from the programme leaders. Their remarks will determine the image of the recently adopted MHR5.

III - THE DECISIVE IMPACT OF THE STRUCTURING PHASE ON THE DURATION OF CONCERTED ACTIONS

The period between the assembly of the teams and the transfer of results may be only two or three years or may be more than ten. In our view this depends largely on the initial state of the network. Short timescales generally correspond to latent networks activated by an "initiating respondent". In such cases the actors involved already speak more or less the same language, have similar equipment, employ equivalent working methods, are developing common interests, etc. Their working guidelines are often similar even if there has been little contact between them. In the other cases, however, the bulk of the action work consists in harmonizing teams interests and practices by developing common tools and languages. This work can often take many years.

Let us take the example of a concerted action to implement clinical test protocols for the treatment of thrombosis (ECAT). Set up at the beginning of the 1980s, this concerted action has gradually built up a logistical network comprising reference centres, materials distribution centres and materials banks as a basis for the planning and execution of clinical research projects in the field of haematology. The project leader is responsible for overall coordination, including management of the budget. He is assisted by associated project leaders, each of them responsible for one of the four subprojects. The main object of the concerted action has been to set up this logistical network.

Between 1982 and 1984 efforts went into structuring a logistical network designed to support a survey on angina pectoris. The teams designated certain laboratories to serve as reference centres. These were responsible for editing and

publishing recommendations for the other teams in a special brochure. Reference centres were thus set up for the analysis of anti-TDA (for the platelets subproject), anti-protein C (for the fibrinolysis subproject), anti-prothrombin III and Factor VIII (for the coagulation subproject). Technical training was also organized (eight courses with ten students per class) for the members of the clinical teams.

In addition, reagents - either bought in or manufactured by the reference laboratory - were distributed to the teams taking part in the survey. Where commercial products were involved, bulk purchases were negotiated by the project leader with a view to obtaining price reductions. In any event, all reagents were centralized in a distribution centre, which organized their distribution. In this instance, it was the project leader's team. One person working half-time was needed to deal with the centralization and distribution of the products, which involved administrative formalities, storage of reagents, postal consignments, etc. There was on average one consignment a week. A quality control mechanism was set up. This involved a quality control team preparing a batch of plasma once every three months and sending it to all the clinical teams and to the reference laboratory. These then carried out various tests on the samples and sent the results to the statistical centre, which compared them with a view to ensuring greater standardization. Any problems encountered were dealt with either by telephone or by a visit to the premises by a technician. If in spite of all this the problems persisted, the team was expelled. In addition, an Assay Committee brought together representatives of each subgroup and technicians to coordinate the practical aspects of the various biological analyses.

From 1984 to 1987 the logistical network was maintained primarily thanks to the distribution of reagents and of quality control samples. An Executive Committee was set up, including experts on epidemiology and statistics. The Committee found that, as it stood, the network of ten teams was too small and had not yet reached the critical mass for carrying out clinical studies. It therefore had to be expanded, and ten new teams were recruited. Like the first ten, these had to be trained and made equivalent. A large part of the structuring work having by then been completed, the alignment of the new teams could then be pursued more rapidly.

The Executive Committee, now in a position to make use of the network, drew up a research protocol and prepared a questionnaire to be given to each patient. In drawing up the protocol the Committee held discussions with the NIH (United States), following which it made improvements to the protocol. The questionnaire was sent out to the clinical teams at the end of 1984. The aim was to gather data on some 3 000 patients. The completed questionnaires were returned to the statistical centre, where a data base was set up. The samples were analysed in the biological laboratories of the clinical teams and the results were sent along with the questionnaire to the statistical centre. Also around this time, the project leader created a half-yearly information bulletin for the teams taking part in the study. Recruitment of the 3 000 patients was completed at the end of 1987. The monitoring of the patients then began, this phase lasting two years.

However, methods of analysis changed between 1984 and 1987. New tests came onto the market. The people in charge of the action felt that the 3 000 subject-patients should benefit from this progress. To this end, it was planned that each clinical centre would conserve, at -70°C, blood samples from each of the recruited patients. The project leader then took one sample per patient and divided it up into ten tubes. In this way he obtained some 30 000 samples, which

were conserved in a serum bank. This could be used only with the permission of the project leader. To make allowance for the seven or eight new tests which had appeared on the market, he forwarded some of the samples to five reference centres. The logistical management in evidence here is more centralized than that used in setting up the basic logistical network. Lastly, with a view to validating infarction diagnoses, an End Point Committee was required to give consensual and standardized opinions on cases of infarction. The study is due to end in 1991. A congress will be organized for the presentation of the final results, which will also be published for the benefit of the scientific community and clinicians.

DEVELOPMENT OF THE NETWORK FOR THE ANGINA PECTORIS SUBPROJECT

	80	82	84	86	88	90
Assembly	---------> initial recruitment of 10 teams	-------->		recruitment of 10 more teams		
Structuring		---------> equivalency	---------->	integration of new methods of analysis		
Implementation of protocol		---------->	recruitment of patients		monitoring of patients	
Processing of results					---------->	
Transfer						-----> congress publications

In 1987 a second logistical network came together for another study, on deep-vein thrombosis (DVT). It brought together 14 clinical teams aiming to recruit some 1 000 patients between 1989 and 1991. Centralized logistical management was chosen for this subnetwork. Samples were centralized by a team which redistributes them to the reference analytical laboratories referred to in connection with the previous subproject. This approach enables emphasis to be placed on the standardization of the methods and equipment used to collect blood samples : consignments of small-scale equipment, provision of a manual of procedures, training of technicians to take blood samples and prepare them according to standard methods. The advantage of this method lies in the fact that it is easier to recruit clinical teams if they are not required to provide a good analytical laboratory. A quality control mechanism similar to that employed in the previous subproject has been set up. In addition to this, a mobile venography centre moves between the centres to read the images in batches of at least 50 cases. It is this centre which makes standardization possible. Lastly, a bulletin is published for the clinicians.

A third subnetwork is organized along the same lines. It brings together ten clinical teams which have to fill in a standard form for 600 patients. One team is responsible for gathering samples and redistributing them to the five reference centres. Another team centralizes the reading of the angiograms. Each patient's

angiographic film is sent to this team and returned to the clinical team after the reading. Lastly, a consensus procedure has been introduced for difficult cases : twice a year, the cardiologists meet at the reference centre to read the angiograms.

This concerted action illustrates how important the structuring work can be, explaining the time taken to attain the objective (over eight years). At the same time, we now have an operational network which can be easily activated for other operations. Indeed, that is what its developers are now doing with the newly initiated studies, whose timescales are far shorter thanks to the established collective infrastructure. The question which immediately occurs to an outside observer concerns the future. Does the mere acquisition of improved knowledge of angina pectoris justify the cost involved? Should we not be assessing the value of this logistical infrastructure for other operations of the same nature? We shall return later to these questions affecting the future of the programme.

Of the 104 concerted actions in our sample, 18 (not counting the 15 forum actions) will have got no further than the end of the structuring phase by the time MHR4 funding ceases, while 21 will be in the middle of the operational phase, i.e. still carrying out work originally planned to be financed entirely by MHR4. These figures stress the importance, the length and the problems of this phase, whose ultimate purpose is to enable the teams to work together.

TABLE 15 : PROBABLE SCENARIO BY THE END OF MHR4

Notes : The classification is based on interviews with project leaders and on analysis of the files and reports available. The table comprises 4 parts : analysis of all 104 CAs, of CAs already in action at the start of MHR4 (21), of "activated" CAs (initiated before MHR4 but by initiatives outside the MHR programme, 21) and of "newly created CAs".

all CA	structuring phase	operational phase	service phase	in transfer	total
Surveillance services	1	6	3	1+6	17
Dvt/eval of treatments	2	6	2+1	1	12
Dvt/eval of techniques	5	2	2	5	14
Harmonisation of practices	1	1	1+1	15	19
Forums	15	-	-	-	15
Joint research facilities	-	2	12	-	14
Specialized communuties	9	4	-	-	13
Total	**33**	**21**	**22**	**28**	**104**
recently created CA					
Surveillance services	1	4	0	0	5
Dvt/eval of treatments	2	6	0	1	9
Dvt/eval of techniques	5	1	1	3	10
Harmonisation of practices	0	1	0	7	8
Forums	10	-	-	-	10
Joint research facilities	-	2	9	-	11
Specialized communuties	7	2	-	-	9
Total	**25**	**16**	**10**	**11**	**62**

CA activated by MHR4	structuring phase	operational phase	service phase	in transfer	total
Surveillance services	-	2	-	1+6	9
Dvt/eval of treatments	-	-	1	-	1
Dvt/eval of techniques	-	-	-	1	1
Harmonisation of practices	1	-	0	7	8
Forums	-	-	-	-	-
Joint research facilities	-	-	-	-	-
Specialized communuties	-	2	-	-	2
Total	**1**	**4**	**1**	**15**	**21**
CA initiated by MHR3					
Surveillance services	-	-	3	-	3
Dvt/eval of treatments	-	-	1+1	-	2
Dvt/eval of techniques	-	1	1	1	3
Harmonisation of practices	-	-	1+1	1	3
Forums	5	-	-	-	5
Joint research facilities	-	-	3	-	3
Specialized communuties	2	-	-	-	2
Total	**7**	**1**	**9+2**	**2**	**21**

IV - THE ROLE OF THE INTERMEDIATE RESULTS

How should we follow the action phases? How are transitions effected? What are the indicators of progress or success? The course we have outlined is punctuated by the production of intermediate results : drafting of the protocol, approval of the protocol by the participants, manufacture of phantoms, development of data entry software, editing of the reference work, standardization of analysis procedures from one laboratory to the next, training of technicians, purification of cells, setting-up of materials banks, completion of the data base, etc. These mark the work stages and also make the course of the action less and less reversible. Thus the network is no longer the same once a joint research protocol has been approved by the participants : the latter are no longer seeking a common denominator; they are now ready to align their work. They progress from a situation in which, although wishing to work together, each of them orientes his work, to a situation in which the teams undertake to follow the protocol. In principle, a team may always contest the protocol, but in doing so it risks being excluded from the network, which has now found its course and has little wish to deviate from it.

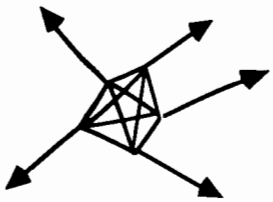
The intermediate results gradually consolidate the networks (economists talk about "irreversibility" of networks) and indicate time flow : they mark changes in phases. So an intermediate result encompasses two complementary dimensions :

- it is an embodiment of the agreement which has been established among the teams; this agreement in turn points to two simultaneous types of effect : the links which the teams have built up to obtain the result (structuring effect) and the

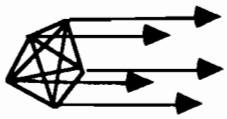
common references they have had to adopt to be able to work together (alignment effect : languages, experimental practices, etc.);

- it helps to broaden the network's base. The result has substance only if it is taken over and used. It thus triggers the transformation of the network, to a greater or lesser extent depending on the subsequent increase in the activities of those already involved and the number of new actors brought in. These two scenarios trace different courses for the action; in the first case the scientific and technical work is amplified; in the second the base is progressively broadened, until it reaches universality. The gradual mobilization of new actors is indicative of the actual course of the concerted action. It gives substance to the series of translations identified during the definition of the finalities and the objectives, which are no longer abstract terms but are fleshed out in the form of actors interested in the products (present and future) offered by the action.

FIG: THE NETWORK BEFORE AND AFTER THE PROTOCOL



preparation of a joint protocol



implementation of the joint protocol

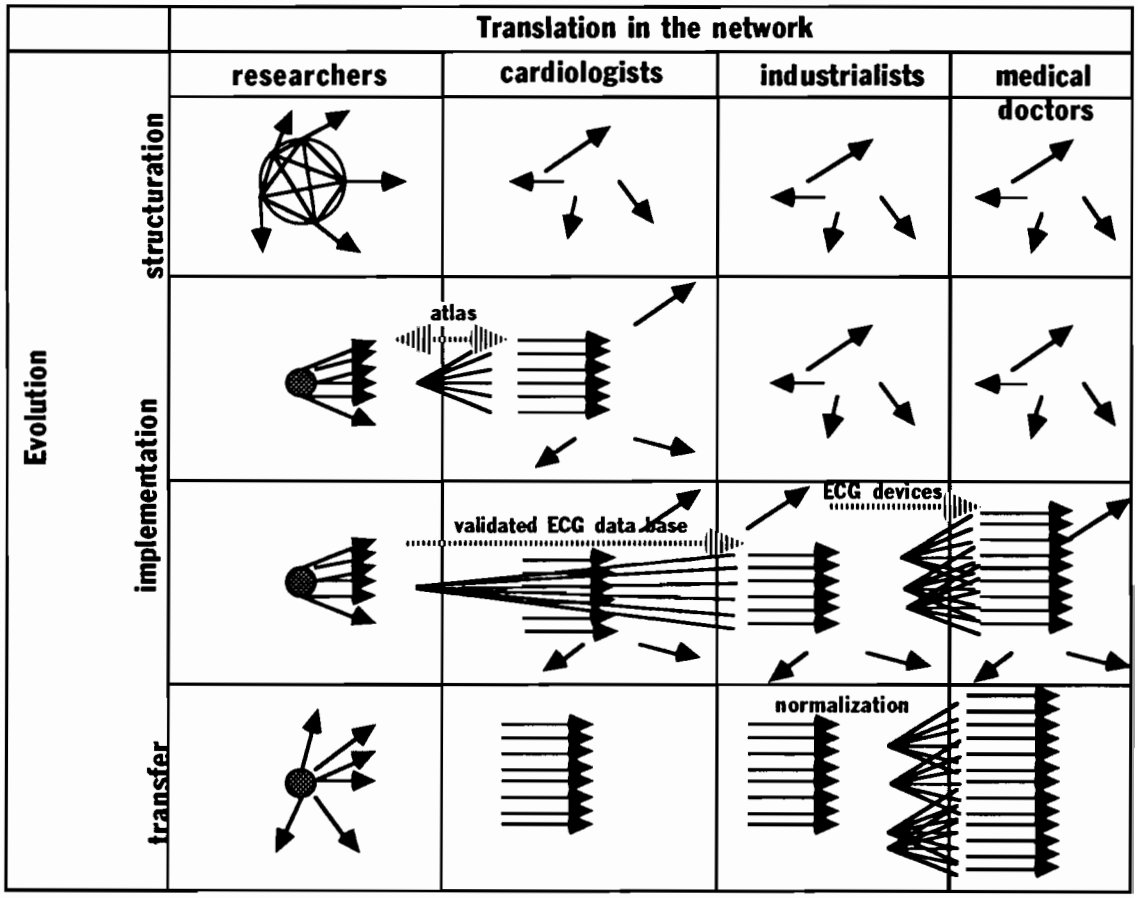
We can therefore follow the progress of a concerted action by relating the involvement of new actors (thanks to the intermediate results, which signpost such advances) to the phases undergone.

In the concerted action on the standardization of the recording and computer analysis of electrocardiograms, for instance, the development of the network can be described as follows (see figure below). The columns correspond to the various categories of actor which the network will gradually reach and mobilize. The lines correspond to the various phases of the action. The boxes correspond to the intermediate results and their effects on the teams which produce them and on those which take them over. The diagram shows the structuring of a nucleus of teams and the gradual alignment of an ever-growing number of actors. The end result corresponds to a standardization of equipment for the recording and automatic interpreting of ECG tracings.

If we look down the "researchers" column we see that a group of research teams regularly exchange messages, algorithms for measuring and interpreting ECGs, working papers, data files and recordings. The exchanges are such that this interlinked network can soon be treated as a single entity : the network has become one. At the same time, the research orientations of the teams in this network are concentrated around a number of common paths. When the work is completed and the common objectives have been attained, the teams will probably explore new avenues of research while maintaining close, if slightly relaxed, ties with one other.

The other actors, who are mobilized only gradually, do not normally have contact with one another. They are associated with the network via the central interlinked network. Relations between cardiologists consist of exchanges of ECG tracings : original tracings on which the cardiologists have to indicate cutting points, and tracings thus marked which are submitted for a second or even a third opinion. The only time the cardiologists actually interact is during the fourth round, when they come together to reach a consensus on how to cut the 3% of tracings for which the above procedure has failed to produce agreement.

THE TRANSFORMATION OF THE ECG NETWORK



Legend: the arrows represent the actors. The direction of the arrows indicates the alignment or non-alignment of the actors' activities. The lines represent exchanges. The direction and content of the exchanges is shown by the striped arrows (except for the relations between researchers, where they indicate numerous and diverse types of interaction). The dark circles indicate that researchers are interacting to such an extent that the other mobilized actors can consider them to be a single entity.

The industrialists are aligned via the data bases of validated ECG tracings they purchase from the network. They compare, test and "spontaneously" conform their electrocardiographs with reference to this base. The fact that the new instruments which they then manufacture and sell are aligned on the reference base means that the production and analysis of tracings by doctors using those instruments will also be aligned. However, conformity with the reference base is

not compulsory (it is more a de facto standardization), and some doctors may continue to cut and interpret tracings differently. Across-the-board alignment of all industrialists and doctors can come about only through such binding measures as would emanate from standardization bodies, for instance. Similarly, alignment of industrialists and their apparatus on the reference base means that the data generated by the various teams' ECG tracings and their digital recording can be compared. Moreover, new exchanges may get under way between cardiologists, for example, leading to new research networks. A new step forward may be achieved; a problem may be solved and others may arise.

The action's success is here being measured in terms of the gradual involvement of more actors. However, this is not linear. The cardiologists needed to set up the base are not needed to operate it. As far as the action's objectives are concerned, what is important at this stage is that industry should adopt the base and make the relevant adaptations to its products, which will in turn influence the practitioners. An initial loop is then complete whose success can easily be gauged by the number of instruments sold and the resultant impact on medical practice. Thus as the action progresses towards its end result it carries with it a growing number of ever more like-minded actors, whether they be direct members, direct users of the end results (industry) or secondary users (practitioners using the industrial products). Only at the third remove is the ultimate beneficiary, the properly diagnosed patient, reached. This analysis is not unique : the survey on potential users of MHR4 (see file 4) shows a similar overall pattern.

V - END RESULTS AND TRANSFER PROBLEMS

One might pursue this example and underline the problems facing this concerted action today. How to shift from mere influence to generalization by standards? How to work quality requirements into standards concerned primarily with safety? Who should undertake the task, by what right and in what framework? This faces MHR4 with the nature and extent of the "transfer" problems.

The table on the probable scenario at the end of MHR4 shows the following situations. Of the 104 concerted actions in the sample, 18 will at best have reached the end of the structuring phase. Should they prove successful (and there are still no adequate means of determining what constitutes success in terms of structuring), they will be destined to continue. The same applies to the 21 concerted actions which will be in the thick of the operational phase when the funding comes to an end. It is hard to imagine them simply stopping. What remains to be assessed is the nature of the "extension"; is it, as in so many research operations, a delay which merely entails spreading expenditure over a longer period (File 3 shows that, in spite of everything, there is an administrative problem which is hard to understand and, apparently, only half solved), or does the continuation of operations call for additional funding?

Aside from these CAs, which, subject to the "stocktaking", will be continuing, the others (60% of the sample) should have met their assigned objectives. Does that mean that they are no longer of concern to the programme? Far from it. The same table shows the following patterns. 15 CAs are forum actions. Should they be continued, as has so far been the case for "technologies for the hearing-impaired", for instance? 22 CAs will be in a "service" situation. What approach should the programme take towards these tools which it helped create?

And, among the 28 concerted actions which have genuinely reached the final stage, are examples such as that referred to above, along with the questions it raises for the programme.

Thus the classic problems of what to do with results seem to differ somewhat from those facing the ESPRIT or BRITE technology programmes. In building up networks, MHR does not only produce scientific and technical results for subsequent application by socio-economic actors; it also produces networks. It is with this twofold output in mind that we should look at the products of MHR.

Transfer problems

Concerted actions produce various forms of results. File 1 underlined the dual content of the results obtained:

- On the one hand, scientific knowledge, which, like any other new knowledge, has to win the approval of peers before being validated. This is where publications come in, playing a very important role in the process. It is part of the researcher's job to see that his findings are recognized; there is no need for the programme to intervene specifically.
- On the other hand, this same data highlights the applied dimension (i.e. in the long term) of a number of concerted actions. It shows the importance which the participants attach to products, methods and instruments intended for medical practice and the application of health policies.

What are the dissemination problems facing this second group of results? We are dealing here with the familiar innovation triad of development, standardization and dissemination. Does this call for specific intervention under the programme? Can it be left to the teams? Should it involve the relevant departments in the Commission? Should specific means be provided, e.g. for everything relating to dissemination? A few brief examples will illustrate these different situations.

A number of concerted actions are aiming to develop new designs for apparatus and instruments. For instance, one of them is trying to develop a new type of artificial heart to provide temporary assistance for patients. At the end of the action the stake will still be far distant, yet the action will have fixed design criteria and even if it remains a group effort (encompassing three or four laboratories with complementary expertise) its chief problem will be to develop a prototype with or without help from industry. Logically those in charge will favour a renewed approach similar to that of AIM, which is often quoted in reference. Should the programme be concerned about this or should it consider that it has done its share and that it is now for the teams themselves (a subgroup of the concerted action) to find their own funding?

The example of electrocardiograms and the corresponding interpretative software illustrates a problem which is likely to loom larger as more and more actions of this type reach completion : how to have standards incorporate recommendations which, strictly speaking, do not deal with the immediate safety of users, but with the quality of the diagnosis, which constitutes a special form of "consumer protection"? Can a project leader alone deal with the alterations this requires to the approach to health standardization? Should the programme not be organized to operate relays and ensure liaison, within the Community, with those who steer the European standardization process?

The two concerted actions on objective medical decision-making pose a typical problem of dissemination. By the time they are completed, one of them should have come up with diagnostic aid software for use by clinicians and practitioners. The publications will no doubt be useful, but they will be no substitute for the aid to the general practitioner which the quasi-"expert system" developed could provide. What should the approach be here? Should the team be allowed to sell it to a distributor, who will treat it like any other instrument in his catalogue? This would cast doubt on its dissemination ruthm and pattern. Or should we envisage distribution policies geared towards rapid availability (e.g. by means of an agreement with a journal, which would distribute an initial disk with one of its issues)? We might also cite the distribution of material on oral problems to schools and dentists. In this respect the concerted action on self-assessment practices in hospitals provides a typical example of these problems, having been designed specifically to help disseminate a practice which has already been developed and to encourage awareness in hospitals. Without going to such extremes (planning dissemination actions), MHR will in the years ahead be faced with the considerable problem of how to exploit results. Our work on potential users of the programme (File 4) has shown that one of the strengths of the networks is precisely their heterogeneous composition, which often leads future users to take part in the work. Economists have shown the importance of "lead users" in demonstrating the feasibility of innovations. This is clearly recognized in Community programmes (the demonstration programme on non-nuclear energies has three times the funding of the research programme). Should this be a matter for the programme?

> *These few examples underline the problems posed by the "end" results of the concerted actions. These problems are very familiar and are not specific to this programme. Yet they are not "conventional", since their "customers", the potential "users", do not express their interest through purchases, through recourse to a market. This is particularly true of the dissemination of practices to an essentially public target group (practitioners and clinicians) in systems which are administratively very fragmented and very different. The question which then arises is that of relays between public bodies, if we do not want Community research efforts to go to waste.*

How big are the problems facing the programme? Once a concerted action reaches the service phase it may be assumed that it will deal directly with problems of dissemination, as should therefore be the case with the five CAs relating to surveillance networks and with the dissemination of results on objective medical decision-making. Of the 22 other CAs held to be at the transfer stage, only one (Eulima) deals with treatment. This extreme case, the development of costly equipment, points forward to the problems which the development of new treatments will bring to the programme, e.g. if the CA on diabetes or the BNCT action achieve a breakthrough.

Five actions concern techniques, though only one of them - ECG - raises the problem of standardization. However, the way in which it is tackled, and solved, will have a major impact on the many concerted actions still in the operational phase, many of which have been built up along the same lines.

15 concern medical practice. As has been seen, most of them do no more than take stock of the situation, the results of which can be satisfactorily disseminated through articles and books. However, several of them pose specific problems. Four of them are confined to preliminary studies to validate a protocol (CA on "organic solvents neurotoxicity") or carry out initial contextualizing (CAs on "head injuries" and "use of DRGs in hospitals"); should plans be made to pass on to the next stage, and in what form? Similarly, one of the actions is organizing a network of reference laboratories on heritable connective tissue disorders; what steps can be taken to ensure that the network can sustain itself? And again for the laboratories testing for the presence of the HIV virus, what steps can be taken to ensure that "good practices" are adopted?

> *The same question arises for all these concerted actions : what is the point of encouraging the construction of networks only to ignore the problems of dissemination? And when dissemination does not take place through traditional market mechanisms (where interested users turn into customers and producers into industrial vendors) the state operator must realign its responsibilities to prevent investments going to waste. In one sense, the work is completed only once the relay has been ensured, i.e. when results are taken up by other state operators, those directly responsible for the targeted users. What should the procedure be? The variety of targeted customers effectively precludes recourse to a standardized procedure for each finality or subprogramme. And the very slow rate at which CAs are reaching completion (only 20 or so by the end of MHR4, of which scarcely half present problems) allows scope for an individualized final assessment procedure, which appears as the only proper way of assessing any operational problems.*

Results embodied in networks

Economic theories on technical change claim that it is the cost of marriages and the numerous preliminary error trials which prevent the networking of individual actors, since no individual is willing to bear those costs. This justifies state funding, but at the same time sets a limit to it : once the network has been set up and tested, the actors will have been able to ascertain the value of such collaboration and of maintaining it themselves. In this respect, there should be no question of supporting a network which has proved its worth and is producing results. These results, obtained from the study of cost-shared Community programmes, have only a slight bearing on the networks we have observed under MHR.

It may be assumed that in the majority of cases (e.g. the forward study on children born of seropositive mothers) the network really holds together only thanks to the common scientific interest which motivates the teams, who will go their separate ways once the result has been attained (possibly to come together on another action). However, this is not the case in four standard situations.

PRODUCTION CENTRES FOR NEW TYPES OF TREATMENT

The first involves an unusual case, confined to CAs on the development of new types of treatment, but one which our first example highlighted : with the success of the concerted action, the centralized facility becomes a production unit (e.g. extraction and purification of B cells). The facility is an integral part of the

result and the logistics it has developed largely foreshadow those which will apply for the standardized processing. One might agree with the project leader that "it ought to be self-financing". Yet the process for making this possible has still to be developed. Should this fall within the ambit of the programme? Should the programme at least act as intermediary between the various European and national authorities concerned? The same will apply with regard to the organization of treatment at Petten if the concerted action shows that BNCT works.

SURVEILLANCE SERVICES

In several cases the network is an integral part of the result. The research has built it up, often at the cost of long years of effort, and has proved its validity. Besides, the scientific result is no more than a demonstration of this validity and a proof of utility. This is clearly the case of the concerted actions on the construction of surveillance networks, three of which (Eurocat on congenital anomalies, the CA on avoidable deaths and the CA on the epidemiological monitoring of AIDS) will be fully operational by the end of MHR4. A question mark hangs over their future, too, as is shown by the experiment set up around Eurocat, with costs to be split down the middle by DG XII (research) and DG V (health). This example suggests a strategy for MHR : ensuring transition. How can the ground be laid and preparations made sufficiently in advance for the transition not to last too long or place too great a strain on the programme's budget? The choices made will weigh on the future of six other networks which should soon (1993-94) have proved their worth.

SERVICES FOR EVALUATING TREATMENTS/TECHNIQUES/PRACTICES

A similar situation deals with the networks set up, at the cost of much time and effort, to evaluate treatments, techniques or practices. Once they have proven their effectiveness through an initial "example", what approach should be adopted? Five concerted actions will be in this situation at the end of MHR4 : ENTA on AIDS-related treatments, EMIP on the evaluation of expensive pre-hospital treatments, OMDM on tools to assist objective medical decision-making, the CA on tests and analyses relating to perinatal surveillance and the "tissue characterization" project (diagnostic tools). The last case would appear to indicate the chosen approach since, having shown its value on an initial technique under MHR3, the CA has been renewed for the analysis of a second technique. Other concerted actions (such as those on treatments of viral hepatitis Eurohep - or the targeting of drugs) clearly fall into the same category.

In this case, initial intervention(s) by MHR enabled the network to be set up, a methodology developed and the CA's performance demonstrated. The next step is to turn to other fields of activity so as gradually to cover the thematic field concerned. It may be assumed that if the programme gave its initial support to these projects it was because it felt the field to be important enough to justify that kind of approach. Should it see the action through to its conclusion or should it provide for a handing over of responsibilities for actions unlikely to be fully catered for by the "market"?

JOINT RESEARCH FACILITIES

Not all the "services" built up this way will be of use in health policies. Far from it. For instance, six "central facilities", handed over lock, stock and barrel to the scientific community, will all be in the same situation : the chimpanzee and macaque facilities, the AIDS virus sequencing or antiviral molecule screening facilities, those producing transgenic rats and aged mice. The concerted action has

above all paid for them to be set up and has won recognition for their value to the research community. Who should be responsible for maintaining such facilities? Can they be made a long-term feature of concerted actions? Can we assume that, once recognized, they will attract their own funding (through national institutions or through researchers who are willing to pay and will themselves seek out the necessary funds)?

In addition to these "central facilities", the programme builds several "collection structures". The examples already shown (ECAT on angina pectoris and Euronut on nutrition) have indicated the nature of these networks, which consist of an intellectual service of alignment and the logistics for mobilizing a group of clinical teams focusing on the assessment of methods of care, research into risk factors, prevalence studies, etc. It has often taken more than five years, or even a decade, for these infrastructures to become fully operational. Do they justify the cost involved solely by serving the operation for which they were created? The question needs to be put, since five of the projects will be in this situation at the end of MHR4, and the programme needs to provide a reply, especially since it is hard to imagine the actions being taken over by Member States without the "reference centres" which sustain them being taken over at the same time at European level.

This analysis points to a major conclusion : the fact that a concerted action achieves its assigned objectives does not release the programme from all future responsibility. Programme funding should enable some 50 concerted actions (half the total number) to achieve their objectives by the end of MHR4. Three types of end result require a response from the programme.

- The first type raises the question of dissemination to clinicians and practitioners in the various countries. Are publications and conferences sufficient? Clearly not, since some CAs have focused on preparing material for dissemination, while one even had the goal of initiating a dissemination process. Differences in health services and the fact that they are state-run makes it difficult to rely on the "market" (where potential users of a piece of knowledge turn into customers of a manufacturing business). The programme must therefore try to make the results attractive to the public bodies responsible for the relevant users in the various Member States (no doubt a dozen cases by the end of MHR4 out of the 28 CAs at the transfer phase).

- The second type of result leads to the same conclusion, but for the takeover (total or partial) of durable structures, whether these be "surveillance services" or "services for the evaluation of treatment, techniques, practices". This usually means takeover by other European structures and, for the programme, organization of relays. While this question has already been tackled with regard to surveillance services (see the Eurocat experiments carried out in collaboration with DG V, three CAs by the end of MHR4), the same is not true for "evaluation services" (five CAs at the end of MHR4). Should MHR4 take them over on a long-term basis?

- This question ties in with that raised by the "joint research facilities" whose emergence, or at least the recognition of whose use, has been made possible by MHR. By the end of the fourth programme there should be six

"central facilities" and five "collection structures" in this situation. Their purpose being the production of a service for the scientific community, their existence will make sense only over a longer period than the duration of MHR4. Should the programme concern itself with this, and if so, how? It is clearly this process of building lasting research instruments, set up directly at European level, which led a number of the project leaders interviewed to speak of the beginnings of a Community NIH.

GENERAL CONCLUSIONS

With seven finalities, five forms of organization, five main categories of exchange and five probable scenarios by the end of MHR4 (not to mention three main types of composition), a set of indicators are now available for characterizing the concerted actions and their dynamics.

Simple calculation of the possibilities shows that there are very many combinations, however rarely some of them occur. It has been shown elsewhere that networks are flexible arrangements which bring together actors from different backgrounds but look different depending on where the observer stands. Potential industrial users will not see the network with the same eyes as the researchers who change their practices. Government departments will take yet another view, since they are not directly interested in the results but, above all, in comparing performance in order to ensure better allocation of the incentives which they distribute. There is, therefore, no single perspective allowing a hard-and-fast, definitive classification of the networks.

Here the programme operator's point of view has been taken. What does this approach teach him? What expectations does it permit? What changes in practice does it suggest? This choice of perspective is all the more warranted by the recent adoption of the fifth round of the programme to follow up the fourth, which is nearing completion. Consequently, the programme operator faces a series of conventional but nevertheless difficult questions concerning the progress made so far, the quality of the output, the strategies to pursue, etc.

The starting point is, indisputably, the progress made with the actions. Which will be completed? What transfer problems do they raise? Which will have reached the end of the structuring stage and how successfully? And what are the requirements of the projects which will be in the operational phase?

However, another side to consider is that of implicit commitments. Which networks has the programme built? Which can be counted as new research infrastructure? What can be done to ensure that they continue to operate and provide the services which prompted the programme to support or encourage their establishment? Whatever the declared purposes, the decisive factor nevertheless remains the achievements, i.e. the type of construction defined by the analysis of the exchanges and intermediaries.

The analysis set out below therefore focuses on the dual aspects "progress" and "category of exchange". It takes stock of the situations and of the questions which they raise before the final section analyses the strategic and organizational implications for the operator of the MHR programme.

FORUMS : ONE STAKE OF THE PROGRAMME?

Out of the 100 or so actions analysed, 15 are "exchange forums". Forums are a finality, a form of organization, a category of exchange ("meetings") and a specific output intended to help initiate joint projects all at the same time. The only output which they produce are summary records of the meetings (if any are kept) and the interest aroused amongst the teams. In this connection, the very high response rate to the questionnaires posted to the teams participating is striking.

Most of these projects come under the two subprogrammes with the largest number of concerted actions: BME (6 actions) and AIDS (5 actions).

Some project leaders argue the merits of such an approach in two specific circumstances - for a small specialized community or for a new problem on the frontier of the existing disciplines. They feel that the managers of the MHR programme no longer give forums their rightful place but instead try to transform them into "pseudo-projects" on a specific topic or else put an end to them as soon as a project emerges. Consequently, this dual definition mixes projects of unlimited duration (sustain a community) with others with a fixed timescale (the time needed to deal with a problem). The programme therefore faces two strategic questions (which communities must be sustained in this way? Why these rather than others?) and two questions of assessment (has progress been made on the problem which generated all this activity? Is the form adopted still suitable?).

STRUCTURING - OFTEN A HEAVY BURDEN

If all goes according to plan, 18 actions will have completed the structuring phase by the end of MHR4. In most cases, the effort required was grossly underestimated at the action definition stage. In one case it took two years to define a protocol, in another harmonization of practice entailed the adoption of reference materials, in yet another exchanges of equipment were limited by the competitive position of the suppliers, etc. All these situations cause delays and, frequently, force project leaders to conclude that by the time they will be ready to start the real work, their grant will have come to an end.

These actions centre mainly around two finalities. The first, as only to be expected, is the establishment of specialized research communities (9 of the 13 actions with this finality). The inclusion of five actions on the development or evaluation of new techniques is a clear sign of the difficulties which the programme faces in this area.

These actions have two important points in common.

- They are almost all organized around the project leader and his team, who run this difficult phase on their own (only four cases of shared management). This is matched by the choice of form of organization : either small, superimposed groups working in parallel (thematically partitioned) or a star network in which the teams gravitate directly around the project leader's team. The number of teams involved is often large and, in many cases, still unstable (many project leaders draw a sharp distinction between simple participants and "active members").

- Three out of four of these actions are still at the structuring stage, since they require harmonization of practice, including exchanges of materials or samples, circulation of phantoms, etc. In other words, they are in the midst of a complex process of aligning the teams to ensure that their output is truly intercomparable.

These two traits are evidence that these actions are very recent. Nothing has yet been stabilized, neither the participants and methods of working together nor the project which the teams will be capable of conducting together. The stake linked to the action serves simply as a rough statement of the project leader's objective rather than reflecting the actual situation in the field. By contrast, the nature of the consensus reached, i.e. the practical result of the action by the end of MHR4, will give an idea of the potential dynamics of the action in question and, consequently, of any follow-up needed.

FINISHING ACTIONS (1) : A LIMITED NUMBER OF DISSEMINATION PROBLEMS

As seen earlier, MHR's responsibility does not end with attainment of the set objectives. To avoid wastage of Community funding, it must also ensure dissemination of the results. In view of the organization of health care systems, this can raise specific problems. What exactly is the situation? By the end of MHR4, 22 actions, or less than one in four, will have reached the dissemination stage. The majority of these cluster around two finalities : evaluation of techniques (5 cases) and harmonization of practice (15 cases). One in two of the actions comes under the HSR subprogramme. These actions have three features in common.

- Only limited investment is entailed, either because the actions are limited to meetings (6 cases) or because protocols were already available when work on the action started and called for no specific skills on the part of the teams collecting the data (10 cases). This is reflected in the method of initiation, with half the actions activating "latent" networks developed by various European associations and the other half initiated by COMAC ("to gain a clearer picture"?).
- This is paralleled by a limited number of participants (on average 20) organized in a star network orchestrated by a project leader.
- The result usually takes the form of updating of information (example : Euromac), a situation report (example : mental health problems of deaf people) or information packs or publications to increase public awareness (examples : "HIV and oral problems" and "ICPC classification"). A few of these actions could open the way for future large-scale actions (examples : "use of DRGs in hospitals" or "head injuries"). A few rare examples raise the problem of formulation of recommendations which will have to be disseminated (example : "HIV serological methods").

The six actions which fail to fit into this pattern are all one-off cases presenting the programme with specific problems foreshadowing the others which lie ahead :

- the problem of generalization of the best practices, as in the case of "care delivery systems" or "self-assessment in hospitals". How can the results be passed on from the 100 or so hospitals "enlisted" to all hospitals in Europe?;
- the problem of maintaining ad hoc surveillance services tested in the course of specific operations (examples : the Eurosentinel networks of general practitioners tested in two separate concerted actions);
- the problem of the future of predevelopment actions, such as EULIMA (where the CA will have allowed completion of the "final conceptual design");
- finally, the problem of the incorporation of a quality standard in legislation (on diagnostics) in systems hitherto concerned solely with operator and user safety, as in the case of the ECG action.

FINISHING ACTIONS (2) : QUESTION MARKS OVER THE FUTURE OF THE SERVICES CREATED

By the end of MHR4, 20 more actions will have attained their objective but will present the MHR programme with another problem of their own : the future of the investments made. At the end of an often lengthy process (most of the actions in question started under MHR3), these actions have built up fully-fledged services :

(i) surveillance services (three cases) as in EUROCAT on congenital anomalies and the 20 or so regional networks set up from scratch or the "epidemiology of AIDS" action's reference centre for monitoring the spread of the disease in Europe;

(ii) services for the evaluation of treatment (two cases) based on the establishment of complex collection infrastructure for opportunistic diseases associated with AIDS (ENTA) and costly pre-hospital treatment (EMIP);

(iii) services for the evaluation of medical techniques (two cases), such as the CA on "tissue characterization" and the EUROSPIN test specimen packs which it developed;

(iv) service for the evaluation of practices (one case) for "objective medical decision-making" to follow up the achievements of the first two operations (methodology, material support and national networks);

(v) finally, research services, whether in the form of production centres (three cases), for example for artificially aged mice or transgenic rats, or of analysis centres (four cases) as for "HIV genetic screening" or collection infrastructure (five cases) as for ECAT (for lung diseases) or EURONUT (for nutrition).

Twelve of the actions which will be at the service stage by the end of MHR4 share the same finality : joint research facilities. By definition, this raises the question of their continuity. Can the programme rely solely on the teams' own capacity to raise the funding needed for them to continue? Possibly yes for most of the "centralized" facilities (seven cases). But it will be far more difficult for the collection infrastructure and the associated reference centres and logistics, as in the case of the five structures set up to evaluate treatments, techniques or practice. In these cases, the programme is approaching a turning point : how can it move on from encouragement for setting up such facilities to long-term support for the infrastructure developed as a result? LEBM-style "case-by-case" solutions no longer seem commensurate with the type of problems encountered.

ACTIONS STILL IN PROGRESS AND THE ESTABLISHMENT OF COMPLEX RESEARCH INFRASTRUCTURE

By the end of MHR4, 21 actions will be in the midst of the operational phase. There are three main reasons why these actions were unable to complete the processing phase during MHR4:

(i) Either the actions build up "large number of cases" data bases, usually backed up by banks of samples of blood, tissues, cells, etc. This applies particularly to six of the 11 surveillance services (examples : "asthma prevalence" or "Eurodiab" on diabetes prevalence and complications) and to three of the actions on the evaluation of practice or techniques ("use of blood" and two actions modelled on the CA on ECGs with a view to standardization of techniques, namely "antenatal ultrasound screening" and "quantitative assessment of osteoporosis").

(ii) Or the actions correspond to integrated projects linked to the development of new treatments. We have already described most of the 5 actions falling under this heading which are all based on production centers ("B cells and diabetes treatment", "BNCT"), on joint research facilities ("European vaccine against AIDS" and "interaction between HIV protein and cell membrane") or complex collection infrastructure ("human stem cell action").

(iii) Or, finally, harmonization has taken a long time, as in the case of four actions on the establishment of specialized research communities. Three of these

four actions are expected, if seen through to the end, to culminate in services (two on the development of treatments - for chronic arthritis and for multiple sclerosis - and one on monitoring of dementia).

Consequently, the common feature of all these actions is that they rely on heavy investment (to harmonize collection conditions, to provide the logistics required for the large number of cases involved or to build up and use the often complex data bases and data banks). These investments are all the greater since often a large number of teams are involved (average around 40) and, in 15 of the 21 cases, shared strategic management was needed to implement the action.

In essence, nearly all actions link back to the previous situation : services which will have to be dealt with (6 surveillance services, 5 services for the development and evaluation of treatment and 5 production services which may be transferred once the treatment has proved its worth.

TOWARDS A COMMUNITY FORM OF NATIONAL INSTITUTE OF HEALTH (NIH)?

Eventually nearly one action out of three will face the programme with a quite unexpected question : what is to become of the heavy capital and intangible investment generated in the course of the programme? Will the marginal financing which made it possible to make these investments still be needed to maintain them?

The future of the Community intervention in medical research will depend heavily on the political answer to these questions since, in the final analysis, it is obvious that this programme produces three main types of result : (1) forums; (2) comparative studies taking stock of the situation; and (3) complex networks which cannot pay for themselves from the initial scientific results that they were set up to produce, thus raising the question of how to keep them in operation on a lasting basis. These, and not the question of financing research on a cost-sharing basis, are the reasons warranting the opening of discussions on a Community form of NIH.

FILE 3
THE MANAGERIAL DIMENSIONS OF CONCERTED ACTIONS

PROBLEMS WITH REGARD TO MHR ORGANIZATION AND PRACTICES

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JUNE 1991

CONTENT

THE MANAGEMENT OF CONCERTED ACTIONS AND ITS IMPLICATION ON MHR ORGANIZATION, PRACTICES AND STRUCTURES

INTRODUCTION

MHR has evolved from a small experiment started in 1978 with 3 Concerted Actions (MHR1) to a programme that brings together over 3000 teams within 120 Concerted Actions (MHR4 officially started in 1987). Each Concerted Action is thus the core of a large network which also combines teams from various institutional backgrounds (see file1).

MHR organization has remained quite stable for over the last eight years (during which the abovementioned rapid increase has taken place). Heading the programme, as is usual with all EC research programmes, is the CGC (previously called the CRM - Comité de la recherche médicale) comprising two representatives of each member country. As COST countries have progressively entered the programme (which is another specific dimension), they also participate in the CGC. The programme is divided in six subprogrammes (two were added with the fourth MHR), each being overseen by a specific sub-committee : the first four committees created as far back as 1980 have been called COMACs (Comités d'actions concertées) since 1983 and the last two, which follow the recently created areas, are known as Working Parties (WPs). Membership of COMACs seem to parallel that of CGCs : they are mostly composed of representatives of national authorities. There seems to be more confusion in WPs (at least in AIDS) with quite a few PLs also acting as WP members. Each subprogramme is managed by a single EC programme manager (some of them are lucky enough to get an assistant). This programme manager is in charge of links with the Project Leaders and he also acts as the secretary of the corresponding subcommittee.

In all four editions of MHR, COMACs/WPs have been entrusted the role of selecting and monitoring the Concerted Actions (CAs). Until MHR4, they did it by themselves taking direct initiatives for selecting themes, finding suitable Project Leaders, organizing meetings of interested teams... MHR4 has introduced a general call for tender which has produced a very large number of answers between which the different COMACs/WPs have divided up nearly all available funds, and they have therefore relinquished in practice their initiating role while, thanks to the open call for proposals, broadening the scope of their action.

When speaking about MHR management, we are thus describing a very limited structure which, faced with the rapid increase in size of the programme, had no other possibility but to delegate widely to people designated to take charge : the "Project Leaders". Such a limited structure makes it difficult for the MHR management, however competent and active, to collect and gather suitable information for external monitoring. Annual reports, proposals and committees' minutes were made available to us. We used them to prepare a first database on

CAs and to organize a mailed survey. Our mailed survey has shown that the teams which responded are on average far more involved in the programme than their corresponding average EC funding. They consider that a quarter of their activity is directly linked with the Concerted Action in which they participate. These figures, quite unexpected from most observers, required an in-depth analysis to understand this apparent discrepancy better.

We had no other choice than to devise a new approach and to organize direct interviews of Project Leaders. More than 100 were interviewed (an interview lasted on average between 3 to 4 hours) and information was gathered on the following aspects :

. origin of the Concerted Action (CA),
. teams mobilized,
. organization of CA and role of Project Management Group (PMG),
. CA trajectory and main steps,
. type of activities performed,
. present and expected results,
. visits and meetings,
. exchanges performed and their organization,
. development or/and use of a central facility or a collective tool,
. role of EC funds and relations with EC,
. visibility and external links of CAs,
. future of CAs.

These interviews represent the major source on which this report relies for its analysis while at the same time constituting, to our knowledge, the only in-depth discussions which have taken place with PLs about their action. File 2 has been devoted to what we consider to be the six major dimensions which make it possible to describe the nature, activities and socio-economic dynamics of the Concerted Actions. This file focuses on the managerial dimensions of CAs : how are they initiated, developed and managed? Of course, in such a process, problems have been encountered that question MHR organization and practices. We will examine them in the second part of this file, pointing out from the analyses and suggestions made by PLs, possible directions of change.

PART I : THE MANAGEMENT OF CONCERTED ACTIONS

Developing a Concerted Action implies that participants not only do research but also take charge of the complete definition and management of the work to be performed in their project. The MHR programme delegates this task to the PL, leaving him with considerable autonomy to lay out the design of the Concerted Action, to organize its work and define what are the collective means to achieve "concertation". Through the successive analysis of the start of a Concerted Action (point 1), of its management (point 2) and of its daily life (point 3), we shall see how MHR philosophy can be defined in practice around a "management delegation process" and an experimental definition of "concertation".

I- STARTING A CONCERTED ACTION : THE PL VERSUS THE UNKNOWN

How are CAs initiated? The question is crucial to the future of the programme since it helps to understand the effects of the present practices and the ways the various sectors of the public were informed of the programme and got interested in its approach and aims. We shall see how fortuitous the encounter generally is, leaving considerable room for more voluntary approaches; we shall also look at the problems associated with the definition of the project and the bringing together of the teams and the choices made by MHR: delegation on a major level to the potential Project Leader provided he fits the canvas of constraints imposed de facto by the MHR.

The PL meets the MHR : often a chance encounter

Three situations can be clearly differentiated. First, the potential PL has already identified a major problem he wants to address on an international level. He is actively seeking funds to do so and will come in contact with MHR while doing so. In the second situation, the PL has in mind a research project but he is not actively looking for money at EC level because he did not think of going in at the international level or it was feasible; a call for tender will prompt him to do so. Finally, there are numerous subjects the PL would like to work on and other teams in Europe have shown interest in some of them. An encounter with MHR will promote one of these topics to the forefront of the PL's mind.

In the first case, the PL's experience has led him to believe that, to achieve his goals, he needs to go beyond his national borders. He is seeking financial support that will allow him to take part in multilateral collaboration. Through our interviews, we have encountered many different reasons, the major ones being the following :

(i) to reach a critical size (access to large enough a number of data or cases, optimize the use of a "central facility"),

(ii) to break out of isolation : the field is so technical or so advanced that there is only a limited number of teams per country; gaining recognition or achieving cooperation requires the breaking down of national barriers (institutional, psychosocial),

(iii) to boost a research field : "United we stand, divided we fall, so let us speak the same language"; harmonization of language (common classifications...) and practices are then at the core of the concerted action,

(iv) to disseminate a technique or knowledge : extend results recognized at the national level to the European level (cases mainly centered on the build-up of adequate health information or on the evaluation of practices and techniques.

These situations imply reaching a level beyond traditional academic collaboration whether to make it really multilateral or/and make it more intense. Faced with this situation, the PL is seeking a way to develop cooperation. He will approach the EC directly but most of the time with difficulty or indirectly through his institution or through someone who is known to be in touch with the EC. Alternatively, he will happen to put his hands on the "call for proposals"; there, the proximity effect comes into play, with people living in Belgium or who already work for the EC appearing to have an easier access to the information on the existence of the MHR.

In the second situation, the potential PL has a priority project in mind but never thought of going to the international level to address it. He happens to hear of MHR funding and wishes to use this possibility as a mean to foster his own research work. To do so, he has to consider the collective dimension of his project while he makes a few phone calls, sends fax messages or organises a small informal workshop to have a handful of teams to put on the proposal. Information on MHR could have come to him informally through someone aware of it or directly by seeing the "call for proposals". It was frequently mentioned that the "call for proposals" came to the research institution when the deadline was near or passed. It was also repeatedly stressed that delayed and imprecise replies after inquiries to the EC about MHR are frequent. These problems complicate the first steps for the PL in putting together a proposal. In fact, the efficiency of this "call for proposals" procedure seems to vary widely from one country to the other. Many times during interviews, Netherlands has been acclaimed for the dissemination of adequate information to relevant teams.

The last situation is a hybrid between the two previous ones. A project with a collective dimension already existed in the mind of the potential PL and sometimes of other teams around Europe. Nevertheless, none of them would feel it so precise or urgent that they would have already been driven to chase after funds for it before. Coming across the MHR will provide this project with a bonus because of its collective dimension. Thus, the project will attract attention and achieve top priority because it fits the requirements of MHR.

In all these three situations, we have been struck by the way this encounter happened. Very seldom did the encounter derive from an organized process. In programmes like ESPRIT or BRITE, there is a continuous flow of information about them, about their main themes, about each "call for tender". At the national level, there are meetings organized so that people know about it, there even are specific national "newletters" to bring potential participants all the information needed to get involved. Here, apart from the Netherlands, no such a situation was described to us by PIs : even when they were consciously looking for EC funds, they came across the programme most of the time through indirect channels. This problem of both information and visibility will be dealt with at length below.

The PL and the formation of his network of teams

THE INITIATION PHASE : TWO OPPOSING SITUATIONS

After his encounter with the MHR programme, the first task of a potential PL is to incorporate teams in his Concerted Action. Two extreme situations can arise with the possibility of numerous intermediate combinations.

At one end, the PL is already in contact with an existing network of teams that know each other well and work together or would like to. They could be in contact through informal links evolving from scientific meetings. However, these contacts often derive from participation in international institutions whether general (WHO plays a significant role) or specific : medical or scientific societies, patients' organizations. PLs will often describe this situation as a network waiting for an umbrella to give it life. MHR would then play this role. When this is the case, a very precise and detailed proposal will usually be submitted by a core of teams to which, at that time or later on, will be added other teams to provide the competences or the geographical coverage lacking in the Concerted Action.

At the other end, the PL is virtually alone and will have to build his network from scratch. In this task he can benefit from three channels of information. First, he has informal contacts with teams he has met previously at international congresses or which worked with him in the past. Second, he can search out the names and location of teams through the scientific literature. Third, he can organize a small informal meeting or benefit from a preliminary workshop organised through MHR that provides a forum for interested teams sometimes with the addition of outside experts who will possible join the Concerted Action later. These allow the potential PL to be recognized as such, to measure interest in the project, to compile a list of other interested teams to be contacted and to define the major lines of the project.

Creating a network is a demanding and time-consuming task. Part (and sometimes all) of the energy and time of the Concerted Action are devoted to this task. The recent evolution of MHR has tended to favour projects in which team networks already existed or could virtually be fully established during this initiation phase. In some cases however, the area addressed is either too new, too complex or too vague for the preparatory meetings to establish the network. Although precise objectives for Concerted Actions seem to be the tendency in the new MHR programme, several PLs emphasized the valuable and specific role that MHR has to play in promoting the alternative approach as it did in the past. They argue that MHR should pick out those concerted actions where networks are difficult to construct and give them special treatment (i.e a probationary phase).

COMPLETING THE NETWORK : THREE MAJOR CHOICES

Once their initial network has been built and the proposal accepted, the PL and his new Concerted Action are faced with three major choices to complete the network of teams.

Optimum size

As one PL puts it, the alternatives are quite simple : on one hand, a limited number of very active homogeneous participants as a highly trained task force with the risk of appearing or becoming a club; on the other hand, a diluted Concerted Action which favours dissemination of knowledge, techniques and

results to the detriment of effective research because of the level of scientific heterogeneity of the participants. Many Concerted Actions (in particular when field data or samples are mandatory for their success) have by-passed this problem through the existence of two levels of participation, although they will not emphasize this distinction. A core of teams (most of them participating in expert or steering committees) will perform the crucial or elaborate tasks when the average participant will only collect data and/or samples and/or be present on a mailing list or at meetings. In some cases (but not all), such teams are classified as "observers".

Commitment

Although not general, there is a tendency to ask potential participating teams, before they enter the project, what expertise they have and how they would like to contribute to the Concerted Action. This allows the PL to make an inventory and better organize the workload. Then, a minimal commitment is defined and required from teams to be considered full participants. Sometimes even a written agreement specifying rights and duties has to be signed by participants. This may help the PLs to deal with teams which do not fulfill their commitments. Exclusion is a problem many PLs face and which they are often reluctant to address, choosing rather to keep these teams at the periphery of the Concerted Action.

Number of teams

Some projects start as and remain a scientific club you need to belong to from the start if you wish to participate. This could be due to the existence of a protocol which does not allow other teams to enter once the study has started or it could simply result from a wish to maintain a stable configuration during the life of the Concerted Action. For those projects that have chosen an open configuration, budget size seems to be the limitation and in most cases, a loose concept of participation goes along with an organisation in which a large share of teams have only marginal acivities in the project. Some PLs argue that their budget should contain a given spare amount of money allocated to this.

FACING MHR CONSTRAINTS

Although a PL has broad autonomy and liberty in his recruitment of teams, he nevertheless faces recommendations or restrictions from MHR on four points : European coverage, role of COMAC in team recruitment, rules on CA funding, industry participation.

European coverage

European coverage appears to be strongly recommended by the EC staff to PLs if they wish to have their project accepted. Although the presence of all countries is not mandatory and is not always observed, each Concerted Action will do its best to get in touch with teams from countries that do not yet participate. Making contact with some countries seems to imply specific problems.

Germany was often mentioned as a country where identifying teams is a difficult task. Division in Länder is held responsible for this, since it seems to create an administrative and organizational barrier that is difficult to overcome. Never was it said that the EC or the Federal Government administration was of any help in solving this problem when it was encountered. Most of the time, connections rely on informal contacts that frequently end up in irrelevant teams.

Thus several attempts are sometimes necessary. This seems to be particularly true when recruiting clinical teams (to collect data on patients) or when participation of Länder administrations (to get access to registers) are needed. This problem relates mainly to the difficulty of establishing the first contact with the right team.

Participation of what PLs recognize as "southern countries" (Spain, Portugal, Greece and sometimes Ireland or Italy) is generally considered as a way to raise the scientific level in these teams and is taken as an investment for the future. For epidemiological studies, collecting data in these countries is frequently seen as of particular and instructive value for comparison. Further, even if technical capabilities may be limited, contributions to brain storming and diversity of thinking are also recognised as worthwhile. To summarize on this point, PLs usually tell us that they would not have incorporated teams from these countries if they did not feel obliged to do so to meet the wishes of the MHR. At the same time, they do not criticise this aspect and appear in the end to be satisfied with this situation. Some PLs would like to see part of the budget devoted to training scientists in these countries and eventually provide them with extra funding during the CA.

Participation of Eastern countries seems to be seen in the same way. PLs favour it and many times regret that this cannot already be done on an official basis. Some already have limited links. Most of the time, incorporation of such teams poses a problem of adequate funding and/or technical expertise. Nevertheless, some PLs feel it necessary to incorporate teams from these countries, if only to get an insight of what the situation is as a preliminary step for future cooperation. Contact with the TEMPUS programme seems difficult to establish.

Role of COMAC in team identification and recruitment.

In previous MHR programmes, PLs had to submit potential teams to the COMAC which produced the final agreement. The PLs who experienced such a situation, remember it as complicated, cumbersome and slow. This no longer exists in the fourth programme. Nonetheless, some COMACs suggest teams they would like, for whatever reason, to be included in the project. They can also aid PLs who ask for help in finding specific teams (specific expertise or geographical location, especially in "southern countries"). The feelings on this are generally mixed. On the one hand, PLs recognize the interest of such a process but, on the other hand, they generally think that COMACs perform poorly, either not answering quickly enough or even often providing irrelevant teams. This is a matter of concern since quite some time can be lost when first contacts are established with irrelevant teams. In addition, in some cases, suggestions by COMAC are perceived as mandatory by PLs who will incorporate suggested teams even if they feel there is no need to do so.

Rules on CA funding

The most stringent restriction of MHR concerns rules for sources of funds from European and local sources. How to coordinate the search for national funds (in different countries) with the allocation of European funds which do not cover the research costs per se? Getting national funding coordinated with what is planned for the Concerted Action is sometimes very difficult. Actions where this has been done before the start have a significant advantage. When this is not the case, some teams may drop out, disturbing the project which has to find alternate candidates and reallocate funds during the course of the Concerted Action. This

matching of sources is complicated by the fact that teams will often use their participation in a Concerted Action as a way to secure funding from their national authorities. Some PLs advocate priority consideration of their project by national funding institutions once it has been accepted by the MHR.

Industrial participation

MHR does not seem to have a clear policy on industrial participation. We have encountered all situations from full participant (whether contributing funds or not) to non-member status (again whether contributing funds or not). Rules seem to differ from one level of the EC to another, from one COMAC to another, from one CA to another, from one team to another. PLs repeatedly stress the need for guidelines on this subject, especially on matters such as level and type of participation and funding allowed or distribution of the benefits of research. They emphasize the impossibility of getting clear answers from the EC on these problems. They think that solving this problem could boost the participation of private companies if the EC wished. Although it is rarely the case, some Concerted Actions have developed written agreements between them and private companies. However, most of the time, the situation is one of individual contacts and links between teams and companies rather than overall links at the Concerted Action level.

> *How does one go about starting a Concerted Action? We have seen how much a Concerted Action depends on chance contacts between the potential Project Leader (PL) and the MHR programme. We have also shown that the core of the European role - the construction of a network of collaborating teams - lies entirely in the hands of the PLs who are the only link between the EC structures and the teams. "Un pour tous, tous pour un" and "Je ne veux voir qu'une tête" are common French sayings which apply very well to the Concerted Actions : for Brussels, the only scientist they deal with is the PL; for participating teams, the PL is not only a project director but also the representative of the unknown world of EC wishes and constraints. The Project Leader thus appears as the major connecting point between two apparently separate universes which are often labelled by PLs "EC administration" and "Scientific Community".*

II- MANAGING A CONCERTED ACTION : A DEMANDING TASK

As link-man, the PL is at the centre of the project from the outset. We shall now see that getting a concerted action under way requires firm commitment from the PL who will often delegate at least part of this responsibility to other members.

Acquiring PL status within the CA

PL status is not just handed out. It has to be earned. How do PLs operate? They perform a number of different functions which we will examine in turn : recruitment of teams, project formalization, information management, budget management, internal rules, key operational activity.

Recruitment of teams

We have seen previously how the PL deals with team recruitment. This represents the first opportunity for him to inform people about MHR and present himself as the depository of EC opportunities for research. Teams can either ignore him or bypass him and build up their own project or get behind him. If the latter choice is made, it represents an initial recognition of his status.

Project formalization

Writing the proposal and the draft project is a second way to secure PL's position. The conceiving of a proposal can be achieved through two different processes. In the first, the potential PL alone is responsible and simply informs or asks for comments from people he knows well and trusts. Later, he will often incorporate them in the concerted action, frequently as key members. Alternatively and most often, the potential PL chooses certain teams through his informal contacts or international literature and calls a small informal or formal meeting to write a draft proposal or discuss one he has already prepared. Once the proposal is written or sometimes even before, the MHR programme will make it possible to set-up a preliminary workshop of potential participants. On the basis of the proposal, this meeting can produce a draft project (which has sometimes already been prepared by the potential PL alone or with a small group of teams). This preliminary workshop is the first explicit recognition of the PL's position because his name has to go on the project. Nomination by a small group of key members, tacit approval of his position by participants or sometimes a plain election process are most frequent ways to settle this problem. In all the concerted actions we have seen, any change of PL was always done before this stage was completed. Even if the PL was changed, his substitute was always associated from the start with the initiation and development of the proposal and draft project. Thus, these first steps seem essential for the PL to obtain recognition of his status by other teams.

Information management

Once the project is started, PLs use three complementary ways to manage information. One is to work out a system of "exchange" "counter-exchange". In this scheme, each exchange and/or action requiring CA funding has its counterpart in a letter or a report sent to the PL. The second solution is to issue a regular newsletter to inform participants of the CA's progress. This places the PL at the nodal information point within the concerted action, since he will need to collect information from each participant. Thus, the PL obtains recognition not only as the depository of knowledge on the MHR programme but also as the person participants have to go to if they want information on the concerted action. Further, providing information through a newsletter also shows participants that they belong to a collective project and gets them involved in its destiny. Visiting teams is a third way for the PL to gather additional information on concerted actions' work and problems. At the same time it increases the PL's visibility and accessibility. Teams get used to referring to him when they need to and thus personalize the project they are participating in.

Budget management

Whatever method has been chosen within the concerted action to allocate and control funds, the PL is the only person in charge of spending EC funds and bears ultimate responsibility for its use. Any financial problems encountered by participants (even for their own research funding) will be referred to him. Given

the importance of this dimension and the large number of problems, we have chosen to devote a specific chapter to funding and budgetary aspects.

Internal rules

Many problems need to be solved during the life of a CA which require "internal rules" whether formal or not. We have already mentioned rules on commitment and exclusion or on information returns associated with the allocation of funds, but such questions as publications, access to data, access to a central facility... need a common attitude. File 2 provides a full account of their role and importance. What should be mentioned here is the central role the PL plays most of the time both in their drafting and even more their application : whatever the level of general agreement on the rules, it is normally the duty of the PL to ensure that all teams comply with them.

Key operational activity

All the areas referred to so far are dimensions of management. Nonetheless, it clearly appears from our interviews that the basis of the recognition of the PL's status lies in the scientific and technical activities he performs for the concerted action. In more than one case in two, the PL carries out a vital task within it. Should the PL withdraw, the concerted action would be severely damaged because it would be very difficult for another team to take charge of this task. There are many different ways to achieve such a position. One is to organize the logistics of the exchanges : provide participants with reagents or small instruments (tubes, syringes, etc.), organize shipments from one team to the other, store them in the interim, check that they reach their destination in time. The management of a collective tool has a similar effect, i.e. the PL operates a central databank or controls a technique which is unique and thus all participants have to send him data or samples and rely on his work if they want the project to proceed and achieve its goals. Performing the final analysis of the results allows the same kind of recognition : because he has a specific knowledge (statistical analysis for example) or because he gathers together all the information (analyses made in different countries or on different aspects of the problem), the PL is the only one able to sort out the results. Whatever the means, personalization occurs and teams relate this crucial step to the PL's name.

Delegating responsibilities within CAs

Getting recognition requires many complementary actions from the PL. It has one major consequence. A lot of work and energy have to be devoted to acquire this central position. PLs emphasize that this requires a strong personal commitment and that, in order to keep time for other scientific activities and avoid being the only one to shoulder the burden of managing a concerted action, they need to find ways to delegate within the concerted action.

How do they do this? And what are the main configurations observed? Normally, management inside a concerted action will involve the PL and a limited number of very active teams. This structure very often develops through what sociologists call a "negotiation process" and through mutual compromises in order to accommodate potentially conflicting objectives. These teams are generally the most interested in the expected results and their participation in all major decisions reinforces their interest, creating a type of "virtuous circle" which builds up lasting relationships. This results in more complex organizational

structures. We have found three major approaches which can be either exclusive or complement each other.

Delegation within the PL's team

For a senior scientist, activity as a PL may be contradictory with other scientific and administrative activities, a position which may be difficult to sustain with his institution. This explains why many of them ask for official recognition of their status by the EC. The need for quality secretarial assistance is particularly emphasized and sometimes implemented on the EC budget. As an alternative solution, some PLs have chosen to delegate their responsibility to a qualified assistant who will use this opportunity to get rapid recognition at a very high level inside the scientific community. The official PL gives up the daily operational work and sometimes will only stay as an official figurehead, giving advice when needed and helping through the politico-administrative process.

Using the PMG structure

The "Project Management Group" (PMG) is one of the official constraints imposed on the creation of a concerted action. We shall see later that the same denomination can apply to other coordination structures (what MHR calls "Working Parties"). Here we focus on the internal organization of concerted actions and the constraints imposed on them by the four COMACs to create a PMG. This constraint is often used by PLs to organize a collective management structure with the most active teams.

The composition of a PMG reflects both the initiation phase of the project and strategic choices about its future. In some cases - where the proposal has been collectively written - PMGs formalize what already exists : a core of teams collectively taking over the management of the CA. In any case, PMG members are rarely elected, being normally nominated by the PL or a consensus obtained at the first general meeting. It is generally composed of five to eight people, although, in some cases PLs told us of COMAC requirements (four people only in one case, complete geographical cover in some others).

Where do members come from? Keeping a geographical equilibrium is a constant preoccupation. However, within this context, two attitudes can be observed. The first relates to adequate representation of the various kinds of expertise represented within the project; this is frequently the case when the proposal has been drafted collectively whether by a small group or through a preliminary workshop. The second focuses on national representation : in such cases, frequently observed in epidemiological studies where efficient collection of data is of crucial importance, PMGs are generally larger.

PMGs do not play the same role in all CAs. Again, three main situations can be observed : the "*decision-making*" structure, the "*advisory*" structure where all important points concerning the project are discussed, the "*endorsement*" structure in which the only reason for existence is to agree on the PL's propositions or decisions.

Creating further "ad-hoc" committes

The creation of ad-hoc committees is another way of delegating responsibility in the concerted action. The most common form is through committees in charge of setting rules and giving access to a common facility (whether large equipment, a laboratory technique, a database or a tissue bank). Other possibilities deal with specialized problems (ethical, statistical, etc.) or delegation at the national level. Such aspects are accompanied by very elaborate

and complex organization. The PMG is, then, the gathering where the heads of each ad hoc committee meet to plan, monitor and evaluate the progress of the concerted action.

The special case of collectively initiated projects

In some concerted actions, which are built up on a collective basis from the start, it is not just a matter of delegation, but true collective management, since every step described above has been performed jointly. The PL, in a way, is simply the elected representative of a management board and represents it at EC level. There are not many CAs of this kind and generally they represent only a limited number of teams. They often appear during the initial phases of an action which then develops on other lines, bringing in other teams in its second phase and thus having, like most CAs, at least two circles of teams : a core circle dealing with strategic and operational management, surrounded by "ordinary" participants.

Three models for CA management

The result of all these choices for delegation (or non-delegation) can be summarized under three major organizational frames which are encountered in most concerted actions even though each CA has its own specific nature, which makes it unlike any other.

In the first model of "*centralized management*", the PMG or "ad-hoc" committees discuss problems and matters relating to the CAs, but decisions and their implementation are the sole responsibility and task of the PL. The PL, possibly assisted by members of his own team, is the only one to be in contact with all participating teams.

By contrast, in the second model of "*collective management*", all decisions are taken and implemented collectively by the PMG with the PL at its head. Each PMG member is in contact with all the participants in the concerted action, sometimes for different parts of the work to be performed.

The third model of "hierarchical management" corresponds to an intermediate situation where each PMG member assumes a share of the management and has certain responsibilities for implementing decisions. Each PMG member has contacts with some participating teams but not with all of them. Two complementary situations can be observed in this third model depending on the delegation process : either on a subject basis (generally three to five sub-projects within the CA), or on a geographical basis (with up to 12 national contacts : this last form is often encountered in epidemiological or clinical projects).

> *Thus the MHR programme can be seen as a two-level management delegation scheme. The PL is, as we have already seen, the nodal point between two separate universes : the scientific community and the EC. However, he is also at the centre of two processes : one, outside the concerted action per se, from COMACs to PLs, the second, within the concerted action, from PLs to PMGs and/or ad hoc committees. This double delegation process makes the project leader the central figure of the concerted action he is in charge of : to follow the path he takes and understand his problems is to follow the path and understand the problems of his concerted action.*

III- THE DAILY LIFE OF CONCERTED ACTIONS : POSSIBILITIES AND LIMITATIONS OF THE MHR FRAMEWORK

Once participants have been recruited, schedules established and management structures settled, PLs (and PMGs where delegation operates) have to deal with the MHR framework for the daily life of concerted actions. The aim of this section is not to reproduce what has been developed in other files but to underline four major dimensions : (i) what does "concertation" mean in practice for PLs? (ii) which major benefits do PLs think CAs produce in addition to scientific results? (iii) what relations does the concerted action have with the MHR structure? (iv) what links are needed outside the concerted action for its proper development?

What measures can a *CA* take? "Concertation in pratice"

The recent evaluation report states: "interpreting the Council decision of 1987 which laid down the objectives of the programme's work, it can be assumed that collaboration is a method to, rather than the ultimate goal of, MHR4. CAs make it possible for the scientists involved to meet periodically and exchange staff for short periods. CAs do not finance scientific research, they permit but do not require the sharing of data, they permit but do not require collaboration in the design of experimental protocols. CA meetings may lead to the agreement of common objectives but if their implementation requires research financing, this is contingent on the funding decisions of Member States".

Such a definition allows a large degree of liberty and flexibility for PLs : they are permitted to do many things provided they get the adequate funding. And indeed, even though funding problems do exist, they have extensively used this leeway. Other files in this report give an extensive description of the diversity of exchanges. Data, biological samples, reference materials, protocols, softwares, prototype equipment and instruments are all interchanged between teams and represent a back-up to the numerous collective tools used or designed. There is a similar diversity observed in organizing relationships between teams within concerted actions.

From what we have seen during our interviews, PLs seem eager to exploit any possibility that can help in their quest for results. PLs often told us that, in doing so they felt they were infringing MHR "rules" and had gone beyond what they thought was allowed. When we told them about other concerted actions' practices, they were relieved but, at the same time, stressed that it was impossible to get clear answers from the EC on such matters. We also encountered the opposite situation : some PLs were amazed when we described the solutions adopted by other concerted actions facing similar situations to their own.

> *In a way, one could say that MHR has adopted an experimental approach, leaving to the PLs the responsibility to imagine and develop suitable solutions to problems encountered. From this emerge both a "catalogue" of what can be done under the MHR scheme and a philosophy which is slowly establishing a revised definition of "concertation".*

Major effects

Scientific results and academic recognition are what most often push PLs and teams to enter the tiresome process of building up a concerted action. One must always remember these dimensions before analysing other effects. Nevertheless, the collective "extra-scientific" results must be underlined. Most of these appear as burdens at the beginning of a concerted action but come to be recognized as a comparative advantage in the end.

Such is the case whenever the need to develop a *common language* is experienced. Most of the time, this is more difficult and tedious than thought at the beginning since words used in a medical context can be understood differently in other contexts. A similar difficulty can be encountered when concepts or institutions differ from one country to another and requires a *common conceptual framework* before any other task can be envisaged. Another dimension often mentioned is the sharing on a larger geographic scale of a *common interest* in a problem which was considered to be neglected at the outset. For instance, some sicknesses identified as important in one part of Europe may have been completely neglected elsewhere. "*Mutual understanding*" is not just a slogan and has real consequences when considered at the concerted action level. In particular with "clinical research" where general practitioners and clinicians are faced both with the difficulty of their very different national settings and with their different levels of participation (they are professionals involved in their practice and international communication is not part of their normal working life).

Much closer relations is another benefit, at least for the most active teams. Many PLs stress that, instead of only knowing teams through publications or conference exchanges, they are now used to working with them. They emphasize the lasting effects of this collaboration which very often should result in other collaborative work on the same or other subjects, within or outside the MHR.

Creating a European centre of excellence on a subject is also directly identified as one of the most important results of some concerted actions. In many cases, PLs link it to US predominance and the feeling that the only way to get recognition from their American partners is through proper organization at the European level. All these dimensions need to be taken into account when in appreciating the results achieved by CAs and, in a way, constitute as many criteria for monitoring or evaluation.

Relating to the structure of the MHR

Three dimensions have to be taken into account : information, advice and monitoring. In all three dimensions PLs are faced with a difficult problem : whom to turn to?

PLs perception of MHR management is confused

The first point deals with the role of the CGC : when looked upon from the Brussels point of view, the CGC appears central to the management of the programme. However, to most PLs it is not a familiar interlocutor (apart from those who in fact participate or have participated in COMACs/WPs) : whenever PLs had complaints to express, it was always addressed to the EC bureaucracy or to the COMAC (or the Working Party for AIDS and Cancer) but never to the CGC as such. This clearly points up the central role these six committees play in the life of

the programme and in its visibility : most CAs, when creating their letter headings mention the name of the COMAC and not MHR. For a PL, each COMAC manages a programme per se with its own rules and practices. Whenever a project was shifted from one COMAC to the other, it was always seen by PLs as a completely new procedure with major recast of the project, new criteria for judgment and even contradictory recommendations about objectives. Furthermore COMACs have doubled the normal link PLs have with EC programme managers for daily management by providing CAs with "liaison officers". A liaison officer is a member of the relevant COMAC appointed to provide a personal link between the COMAC and the CA. They are informed about all meetings and can, if they wish, participate in them. Nevertheless, they are rarely cited as actual contacts in case of problems and their role is seen by most PLs as ambivalent : in some cases, the liaison officer appears as an advisor (to provide information about MHR and its priorities, to help to find solutions ...), more often than not he is seen as a kind of "spy" (as some PLs nickname them).

This scheme is very different from those we have observed in most EC cost-shared programmes where permanently employed EC programme managers are the nodal point for contractors. And, if there are "experts", they act under the supervision of the EC programme managers. Here there does not seem to be any connection in practice between the "liaison officers" and the MHR programme managers. This, in fact, is the source of problems for PLs who have often mentioned to us the contradictory answers they get. This has often driven PLs to use their own personal contacts to make their way through the EC machinery and find a solution (we have come across contradictory "solutions" for similar problems). One easy way, at least in some countries, has been for PLs to link up with their national representative to the COMAC, illustrating once more the central role COMACs (or WPs) play in the life of the programme.

Information problems : the mirror effect

Many times, once the interviews with PLs were finished, PL would ask us for further information on the organization of the other CAs. This reveals both a deep interest in the programme and a considerable desire which remains unfulfilled. Why? We have already seen the difficulty of finding adequate contacts. This is further complicated by a series of unresolved problems.

First, delays in answering or even a complete lack of answers to written questions have often been quoted. Personal contacts or indirect channels (often through a related team in the CA) are a clear expression of a communication problem at the level of the MHR management structure. Even when answers cannot be instantly given, PLs would like programme managers and COMACs to send an acknowledgement and make sure that their questions are dealt with.

The second point mentioned, the absence of feedback on reports and other documents sent by PLs, is badly felt. As one PL told us, "how can you make a concerted action or report better when you do not know what is wrong with it?". This leads to a more general question that we have already mentioned: the lack of knowledge about what the others do, the way they are organized, the managerial tools they have devised or the collective tasks they fund.

Give to others, get from them in return : in this way "a mirror effect" can evolve by means of which PLs can more effectively situate and adapt their own project and action. The MHR has already started to provide answers to these questions : the first MHR newsletter has been well received and many PLs would like to see a special section included with "actual examples" of CA management

and organization. The two-day meeting of the COMAC for BME has been mentioned by most PLs as a good way to learn about others' projects and to start up useful connections, since, as one PL told us, what larger reservoir of expertise can we have than a programme which links over 3 000 teams?

Monitoring problems

We have mentioned the mixed feelings about the "liaison officers" who, furthermore, are seldom specialists in the field in which the CA is active. Annual reports are another example of this : even when some guidance has been issued (see recent efforts for BME), such reports show a remarkable degree of diversity, which does not help the outside reader to get any clear idea of the actions and makes it impossible to compare them. The only other way suggested for COMACs to form an opinion of a CA remains the annual presentations made by PLs to the COMACs. The attitude of PLs to these presentations is almost unanimously negative : some consider it humiliating and dislike the idea of senior scientists being treated like junior students; and most PLs found them useless : how can you explain such complex projects, their achievements and their present status in ten minutes to such a disparate audience. Discussions are necessarily limited and most of the time judged "poor".

Connecting with the outside "world"

Relations with other Concerted Actions

Relations between concerted actions seem to be very rare, even when they are working on similar subjects. The only exception are those CAs which are the offspring of on-going concerted actions and which often involve teams with common participants (a situation which is often encountered in AIDS). Otherwise, when relations exist, they remain at individual level through teams participating in several concerted actions at the same time or having informal contacts between them. We have seen from the quantitative survey that such cases do not occur very often. Formal exchanges can happen as in the case where HLA typing is concerned, but this is exceptional. Nowhere has there been systematic access for the teams to reports or newsletters of a concerted action they do not belong to. Many PLs regret this situation. All those we saw after the first European newsletter was issued pointed to the usefulness of this publication (even though they thought it came too late). They insisted that it was not sufficient just to have the title and address of projects and that there should be short summaries on objectives and the methods chosen to achieve them. Those aware of it also had very positive views on the recent two-day meeting organized by the COMAC-BME where each PL was given time to explain to the others what was carried out in his CA and how.

Relations outside MHR

There cannot be any clear-cut frontiers between the relations that the teams have within the concerted actions and relations they have through their other activities. This continuum plays a very important role in the life of a concerted action which very often relies for its success to an extent on the previous connections of individual members. However, all of them cannot be dealt with informally and the concerted action as such is often confronted with problems in its relations with outside teams or institutions at the European level but also, and sometimes more often, with non-European institutions.

Relations with national funding institutions will be dealt with later on, but these constitute one of the major dimensions underlined by PLs for the internal coherence of their project.

Another dimension which must not be underestimated in relations with national institutions is that of ethical regulations : what data can be collected? What methods of data collection are accepted? What steps must be taken by the CA in order to get access to relevant data/cases/patients? Such questions have in some cases led to a complete redefinition of the direction of the CA and even resulted to new objectives.

Second come relations with multinational institutions such as patient societies or clinicians associations which are very often established at the European level and constitute a logical counterpart to the discussion of problems and dissemination of information and/or results. They can also be of crucial importance when cases/patients need to be obtained. International institutions, in particular WHO, seem to play quite an important role in a few concerted actions when the European operation appears as part of a larger programme.

As mentioned above, bringing Europe up to the same level as the USA may indeed be a recognized objective of some CAs. This, in turn, opens up a more difficult question : how to deal with extra-European collaboration. Some PLs openly ask about clear rules for negotiating with NIH or Japanese teams with a view to establishing their CA at world level.

Third come relations with industry. We have already mentioned the problems encountered with direct participation in CAs by industry. For quite a few CAs relations with industry are compulsory if they wish to have adequate equipment or reagents or access to sophisticated analysis. As indeed can be significant financial dimensions : major cost reductions, even free operations, access to equipment not yet on the market or even specially built equipment. This generally assumes specific returns for the company and agreements to write. Again PLs faced with such situations do not receive adequate support from the EC; they ask for more help or at least clearer knowledge of potential limitations or rules.

Even if these dimensions have been recognized, all PLs faced with them emphasize the difficulties they have encountered. They all think that EC action such as having various types of "framework agreements" with larger institutions such as WHO or NIH, and establishing clearer rules about sharing of profits with industry would have helped greatly in such situations. Also, even though no PL openly declared this wish, by giving to the PLs a type of "institutional" recognition that helps them in their individual contacts.

> *Looking at the daily life of CAs, we have underlined the "experimental" approach of MHR which, through a great deal of delegation, autonomy and responsibility allow the PLs to define "in practice" what concertation means : which tasks can be termed as collective and thus funded by MHR. The list is long, even if there still exists some unresolved problems which we shall be examining below. However, at the same time, we have also seen there are a number of unresolved problems which may delay and, in some cases, even endanger the aims of the CAs. The organization and choices made by the MHR programme in dimensions as different as information practices, visibility of the programme, monitoring practices or even the global setting of the programme and the relations between*

COMACs (and/or WPs) are called into question. The second part of this report will now deal with these issues.

PART II : IMPLICATIONS FOR MHR MANAGEMENT

The purpose of the first part of this report was to give a picture of the conditions under which concerted actions are created and managed, and the managerial problems faced in their daily life. In a word it concentrated on what could be termed, as a complement to our other file, the managerial dynamics of a concerted action. It led us to underline what we consider the major specific feature of this programme : its management delegation philosophy. A feature which emphasizes three major dimensions of this programme. First, the central position of the "Project Leader" who is granted full responsibility in the conception and management of the concerted action. In a way, selection of a CA is selecting a PL and a finality (more often a theme). The PL then has full responsibility for transforming it into action, choosing the proper direction and defining all the intermediate results, which will normally pave the way towards the achievement of the final objective for a period which, in 50% of cases, is nearer a decade than the two years for which funds are granted. This "job description" relates very much to what we have observed for programme managers in cost-shared programmes (see our evaluation of the NNE3 programme). The consequences of this is an "experimental" definition of "concertation" whereby PLs, through the choices they make, through the tasks and operations they fund, create "in practice" a framework of this uncodified form of action known in EC terminology as a "concerted action". This definition is very far from what has been recently observed during the evaluation of the COST actions (see evaluation report by GMV).

Accompanying the process of delegation are all the principles, rules and practices which (1) create limits to the autonomy granted to PLs (such as those dealing with PMGs or geographical coverage), and (2) enable the MHR structure to monitor ongoing action (such as those dealing with annual reports or presentations to COMACs). The second part of this file concentrates on this last dimension : the organizational framework of the MHR programme. It focuses on four major points which emerge strongly from the analysis of the problems encountered by PLs in initiating, creating and managing their concerted actions : fund allocation and use, information flows, monitoring practices and, deriving from all this, MHR organization (for strategic and daily management).

I- THE FUNDING OF CONCERTED ACTIONS

Officially[1], "the Programme's funding covers mainly the coordination of research in the Member States and in other European participant countries (mainly the COST countries) via the establishment of research networks. The research itself is to be funded by individual Member States. The networks are supported by means of meetings, workshops, short term staff exchanges and

[1] Presentation by the MHR pprogramme of the list of CAs, first MHR Newsletter, 1990.

visits, information dissemination and other activities. Funding is also provided for centralized facilities (databanks, preparation and distribution of reference materials)". What does this actually mean for projects and teams? We shall first examine the different roles played by MHR funds before, in the second part of this chapter, entering the changes desired by the PLs and the recommendations formulated by them.

MHR money for PLs

"Seed" money...

For some PLs, not funding research per se puts considerable limits on the possibility of MHR. CAs are seen simply as a preliminary step toward true collective research which helps in the establishment of a new research project. This "seed" money is useful for achieving what has been previously described as "collective extra scientific results" : a common language is needed for collaboration! But it does not make it possible to really tackle the abovementioned objectives which, most of the time, require actual research work : these PLs thus favour the creation of a European equivalent of the NIH, although they sometimes question the relations between such an agency and present national bodies. This view does not appear to be commonly shared and most PLs adhere quite strongly to the MHR scheme, underlining the positive aspects of such an approach and offering solutions to the limitations they face under the present methods.

...which implies an outward-looking attitude and a two-stage selection process...

Participating teams have to find their own funds. Most of the time, this involves going outside their own institution : national administrative authorities are most often quoted, but voluntary organizations, industry and even international organizations (other than the EC) must not be underestimated. In some cases, PLs while stressing the limited amount of EC participation in the total budget for their concerted action, explained to us how they had (or will have had for the coming phase) to raise amounts several times greater than those provided by the EC. They emphasized how EC status helped them in this task. Thus, they highlighted "lever" provided by MHR in their search for funds.

This mechanism can operate at concerted action level, and also for individual teams requesting support from their national research authorities or industries. At this second level, wide variations are observed from one country to the other depending on the level of national recognition for the team, but also on the attitude of national authorities : there seem to be major differences between EC countries and this, in turn, has an effect on the attitude of teams to MHR. Not a few PLs mentioned that their direct intervention, especially in smaller countries, helped the teams to get adequate recognition and funding. Others mentioned the difficulties encountered by British teams in obtaining adequate funding for their share of the research effort in actions in which they actively participate.

The Funding of MHR projects can be assimilated to a two-stage selection process : after EC selection, national authorities (and other funding bodies) have the chance to appreciate their participation in relation to their own criteria. MHR acts as a catalyst, but, as always in such a situation, it means that all its actions have to be endorsed by all other funding bodies. It is a well-known process, and the sociology of innovation has shown that aggregating interests requires adaptation

and continuous reworking of the project. There is, thus, a continuity between the funds allocated (and their consequence : the need to interest other funding bodies) and the management choice made by the programme (a high degree of autonomy to define the actual project).

...demonstrated by a change in spending attitude

This is clearly demonstrated by the change of attitude in the budget control philosophy of concerted actions. In some of the older CAs, PLs told us they had to provide the EC with a priori detailed indications of expenses and then justify them systematically. This period is remembered as tedious and a bureaucratic harassment. Today, PLs say they only provide the EC with a broad estimate of the overall budget breakdown and can, if necessary, during the life of the project reallocate money between teams and headings; they have only to notify the EC subsequently, which enables them to focus on scientific and technical management. Thus, on-line budget control is in the hands of the PLs (in some cases, this responsibility is delegated to a PMG member because of his management abilities). PLs told us many times how they appreciated being able to release MHR money when they need to without bureaucratic hassle and red tape.

What do CA funds cover ?

"Seed" money that can be allocated as required by the progress of the CA is an important aspect. But what does "seed" mean in this case? Do actual outgoings only cover the costs of meetings and travel? Other files have emphasized how many different activities and exchanges are carried out as part of the CA. What role do MHR funds play in these activities. The interviews provide a very long list of items that are, at least in one CA, financially covered by MHR money and illustrate the possibilities offered by this so-called "seed" money.

They can be classified under two main headings. Tools or tasks of collective value, in the philosophy of the CA, relate to small-scale central facilities : software or equipment purchases, central sample storage, centralized biological analysis, central technical apparatus or database maintenance, central statistical analysis, central secretarial help, etc. When PLs express their feelings, they argue that the European scale is necessary to justify these tools and that some of the analyses performed would not be worthwhile at the national or individual level because the cost would be too high, because they would come up to the critical size or lack specific comparative data.

Exchanges come under the organization and financing of logistical matters. It is not only persons that circulate but also materials and samples, which may require specific containers (standardized tubes to collect samples ...) or special transport conditions (for instance when a sample must be maintained at -30°C throughout a journey or when delivery must be made within a limited time for the sample to remain valid). Even collecting data often requires special questionnaires, sophisticated practices to ensure adequate translation, printing costs ... (see File 2). The opinion of the PLs is favourable here, since they have usually difficulties in providing for these things from their national funding.

Through this use of funds, the PLs provide a general practical definition of what we have termed the MHR "philosophy" : fund exchanges (persons as well as all material support) and tools or tasks of collective interest.

Limitations of the present scheme

Keeping this "philosophy" in mind, PLs stress present malfunctioning and suggest changes to optimize this scheme. Two points appear as permanent items of annoyance in the life of concerted actions. A few PLs who have been involved in previous MHR programmes told us they have already given notice of these problems in previous evaluations of the programme. In other words, they accepted them in the past but cannot understand why they have not yet been resolved. The six other points require the MHR to devise new procedures if the programme is to tackle them.

Repeated delays endanger the credibility of MHR

The first and major matter of concern is the virtually systematic delays observed between handing in the proposal, approval of the project and actual release of funds. Delays are often several months to a year at each step of this process. Although it has been said that the brainstorming which took place at the EC level during the switch from MHR3 to MHR4 was partially responsible, but this does not seem to be the only reason. Even now, delays are still frequent in the allocation of funding in the later stages. EC funding normally being allocated for a limited period (two to three years) and being only a small part of the total, problems have frequently been encountered in organizing adequate connections with other sources of funds. To fit in with their schedule, some PLs had even to ask their university or bank to provide them loans to allow them to start the project in due time.

The problem of yearly allocations

According to the PLs, funds are allocated on a yearly basis and cannot be reallocated from one year to the next. Thus, some PLs had either to disguise the utilization of some funds under different headings or to modify their schedule from one year to the next even when this was detrimental to project efficiency. These problems remain within the present MHR funding framework and only require improvement of its administration. But the lack of feed-back and follow-up, when these situations were reported by PLs to the EC administration, have had a very negative effect that was repeatedly stressed during interviews.

Matching EC and national funds

With this question, we enter the sphere of suggestions made by PLs with a view to the MHR scheme providing better answers to the problems they meet. Of course, we have only selected those which are common to a number of actions and have thus been mentioned many times. If the "two-stage selection process" is maintained (as long as MHR does not turn into a cost-shared programme), the MHR should do something to organize it better. Many teams experience difficulty in matching the EC timetable with the deadlines for funding at local level. Thus, it sometimes happens that teams which show interest in a project have to give up. In some cases, this has led to a considerable lack of organization or unbalancing of the project when it really had to start working. Many PLs ask for better coordination between MHR and national authorities and some suggest negotiation with national authorities (which participate in the EC selection process) in relation to specific mechanisms which would favour national teams participating in a given CA.

Can the budget be adapted to the actual number of teams participating?

Funds are allocated at the beginning of a concerted action for a certain number of teams. Some projects keep within these limits, but others need time to reach any level of stability with regard to the number of teams and their involvement. Thus a PL has to face the following choice. On the one hand, if he keeps participation to the declared number the CA may appear to be a club, but this will allow the concerted action not to overrun its budget. On the other hand, if he accepts extra teams for the benefit of the project, this brings budgetary problems. This choice, which is not just financial, is a difficult one. Some PLs suggest the creation of a special mechanism (within the budget of each CA or at EC level) which could cope with this problem and make it possible to adapt the yearly allocations (in one direction or the other - there are quite a few CAs which have far fewer active participants than hoped).

Integrating teams from "Southern countries"

Many PLs told us of specific problems when they have to incorporate teams from "southern countries" which lack basic research or communications facilities, a situation which impairs their participation in the project. They think that the problems will even be bigger if the MHR wishes to favour associations with teams from Eastern countries. For some PLs, discrepancies in technical abilities require specific funds to insure minimal requirements if the EC really want to push in this direction.

Ensuring the participation of "specialists"

Some teams that are vital for the concerted action, because they have specific expertise or cover a local situation which is important for purposes of comparison, are not able to get local funding and thus put the whole project in danger. PLs faced with this situation suggest that it should be taken into consideration in further programmes, either through a specific mechanism developed at programme level or by allowing them to keep part of their budget for this purpose. In the same way, certain specific tasks or instruments of collective interest (not recognized as a central facility) need to be carried out or to exist in a single location. As their local cost exceeds local benefits, their funding is difficult to justify or refused by local administrative authorities. Thus many concerted actions have had to devote a share of their budget to covering these expenses, whether they considered it to be allowed or not. The PLs concerned request clear recognition of this practice as being part of the common framework of the MHR programme.

Funding post-graduate exchanges

For most PLs, one very efficient way to promote joint research work between European teams is to favour a systematic exchange of post-graduates. These aspects are difficult to cover with the limited budgets allocated by MHR and often meet difficulties at the national level in obtaining grants high enough for "high potential" students to be attracted. A special mechanism devoted to long-term post-graduate exchanges is strongly advocated by some PLs.

Transfer problems

We have seen in file 2 that some projects have already reached their "final" research stage and that quite a few others should do so by the end of MHR4. Such is the case for example when a central data bank monitoring a particular disease has proved its feasibility and can act as a continuous public monitoring service. In one

particular case, MHR has already chosen to organize a transition period scheme and to co-finance the development of the "service" with another Commission DG. The situation in which large multilateral clinical trials will have to be organized once their feasibility on a small scale has been evaluated by MHR is another similar case. This is particularly true with subjects that do not interest industry because they do not involve the prescription of drugs... In these situations, PLs often regard the MHR as a "feasibility driven" structure but emphasize their need for another leg of the relay once this phase is completed. Some would like the EC to provide them with an adequate mechanism to go on or at least to help them find other means to fund the continuation of their project. Some even think that it is the duty of the MHR to help them in this task, otherwise EC money will have been spent in vain.

How to deal with these eight points? Two of them only require administrative solutions (delays and yearly allocations) and one an official recognition of present practices without any financial effect (ensuring the participation of specialists). Four others require specific actions and funds to enable teams from southern (or eastern) countries to participate, to favour the exchange of post-graduates, to allow adaptation to the changing number of participating teams, to organize the transition period whenever the final result deals with a service or a standard that has to be continued or permanently established. How should they be organized? Within CAs through the systematic recognition of a "free" percentage in any budget allocation? At MHR level by organizing one or more special funds to which the teams can turn? Or even outside MHR, the programme organizing specific connections and links. These are open questions and the PLs have no definite position (although there seems to be a slight preference for the second solution : keeping a share of MHR funds for "specific" problems). A last point to be mentioned concerns the relations between the EC and national authorities : how can links be established between the selection of a CA and the specific funding of participating teams at national level. For those PLs who know of the existence of the CGC, there is a large question mark concerning its role.

II- INFORMATION FLOWS AND THE PROGRAMME VISIBILITY

In part 1 we addressed this question from various points of view, illustrating clearly what could be considered as a major under achievement of the programme : its ability to circulate information both within the programme and outside, to all concerned.

Towards a programme information "structure"?

We have seen that the availability or amount of information about the initial MHR4 call for proposals has been "limited". This is still the case with the PLs' knowledge of the other CAs : such simple questions as their total number and the actual topics dealt with were not known by most PLs before the first issue of MHR newsletter quite late in the life of a programme which is now in its fourth version. Exchange meetings between PLs (apart from the special setting of CANCER and AIDS WPs) are still not a common feature (to our knowledge, the first one was issued by the BME subprogramme for reasons which are not directly connected with the specific purpose of knowing another project). All these recent initiatives

have been very well received by most PLs who see them as initial steps towards a real information and exchange system : with more information about the various CAs, with the possibility of annual reports being circulated, with more precise descriptions of the managerial solutions arrived at by CAs, with regular forums and exchanges between PLs... All this adds up to a typical description for a full-time information officer, provided it includes all the necessary tools and material support. The programme must think about how to organize this general flow of information more efficiently.

Specific recognition of PL status?

We have also seen the difficulties encountered by PLs when trying to connect the "outside" world on behalf of their CA. The problem is twofold. On the one hand, the programme as such should organize institutional links with important international partners (notwithstanding those with EC national authorities as pointed out above), such as the WHO or the NIH, so that PLs can have better relations with these institutions when trying to establish their CA at world level. On the other hand, this is not sufficient : contacts with specific entities connected with bodies such as patient associations or professional organizations of practitioners or clinicians ...), can best be established by the PLs provided these associations know about the EC programme, its organization and the specific role PLs have in it. Such bodies or institutions should be aware that the PL is entrusted by the EC to organize a particular project and entitled to make contacts and arrangements and even organize official collaboration. In a word, this means giving PLs a specific status. How it can be catered for within the EC framework may not be an easy problem to resolve. However, it will have to be addressed if MHR wants its CAs to play an active and long-lasting role. The S&T community at European level cannot be developed without linking it to the other major world partners.

Guidelines versus an information system?

All the problems posed by PLs are linked one way or another to the establishment of the "rules of the game" : how to proceed within the MHR framework? There are two ways to answer the question. One is traditional to many administrative practices and results in the establishment of guidelines indicating what is authorized (everything not being authorized being de facto forbidden). The other is based on present MHR practice : delegate and leave to individual initiatives the responsibility to progressively build a common framework. This, in turn, requires, something which is currently lacking : real visibility. It is thus linked to the building up of the information system we have described. The richness of this approach so far clearly shows, in our opinion, that this is the path to follow.

MHR visibility at stake

All this should help to solve what appears to us to be a paradoxical situation. File 4, the users survey, is astonishing in the poor level of knowledge that national administrations and institutions have about the programme, a situation which contrasts greatly with the situation within clinical circles (at least those who answered our second questionnaire) where the programme is well known. We have more than once encountered this situation when presenting our results on the effects of EC programmes. However, as far as the number of teams is

concerned, MHR is without a doubt one of the largest EC research programmes. Informing the medical and health community at large about CA programmes, operations and achievements should be an effective way of interesting the "outside" world and thus boost potential spin-off. Furthermore, it can be stated that, through MHR, PLs have gained a new experience in creating and managing transnational research. This is valuable and means a great deal at a time where research in biology and medicine seems to be reaching a point where collective research more and more appears to be mandatory (protein engineering, Human genome project, etc..). To recognize PL status is not only a way of aiding the PL but also a way of giving credit to the EC for this achievement.

> *MHR has recently started to take information problems into account by issuing an MHR newsletter and by organizing specific PL meetings. These initiatives have been well received but are felt to be only a first step toward the creation of an effective information system which seems to require a particular structure (and possibly a full-time and properly equipped information officer). The MHR has to choose between a "regulatory" approach, issuing guidelines about what is permitted or not, and an "experimental" approach, allowing PLs the initiative with respect to devising suitable "concertation" machinery. Our analysis of present concerted actions and their achievements in the establishment of a European Health research community, leads us to plead in favour of the second approach. This requires official recognition of the specific role of PLs. Granting PLs official status is one of the major issues for the future enlargement of the Concerted Action approach.*

III- MONITORING AND ASSESSMENT PRACTICES

The delegation of management puts most of the prerogatives and responsibilities in the hands of the PL and the teams he selects for the concerted action. In any delegation process, this autonomy is always related to reporting practices and regular monitoring systems, with, quite often, on top of this, periodic external analysis whether they be called "reviews", "audits", "assessments" or "evaluations". Such a system is not only valuable to the EC administrative structure in the performance of its strategic task, but could also be perceived as a way to help concerted actions and provide them with better feed-back and information. The present situation is far from capable of evolving such a system which many PLs think would be useful for two main reasons : (i) they are often too deeply involved in their action to get a "strategic look" at it; well-informed outside expertise is thus considered as a managerial aid; (ii) they are not satisfied with the present situation and wish to see a clearly-established evaluation process which could prepare for renewals when necessary (without having to undergo the whole process of selection all over again). MHR management is provided with information on concerted actions through three major channels : annual reports, publications and ten-minute presentations by PLs to the COMAC/WP (this probably supplemented by information from the liaison officer). All these have major limitations which we shall examine below.

A standard for annual reports?

An oblique look at annual reports shows that there is no standard presentation either for chapter headings or, when this has been done (BME for instance), for their content. We have had considerable problems in dealing with this work and we had no other choice than to interview the PLs (at a cost that any research team would wish to avoid). This is a typical example of the present limits of annual reports and of the uses that can be made of them. The PLs are full of questions on this point : how often should they be issued (every year does not seem the correct rhythm for some PLs)? How should they be presented (some complain about the changes required all too frequently by EC staff at too short notice)? On top of this, quite a few PLs complain about the use made of their reports :they never receive comments or questions on them, they never seem to be circulated. How can the PLs be expected to produce a well-thought out and informative report if they do not get a clear impression of how it is to be used and disseminated, again a information management problem!

From the problems we encountered and our interviews, we think that the question relates less to an annual report than to a "reporting mechanism" with three clearly separate dimensions or sections.

The first relates to the "strategic" dimension of the CA : what problem is it tackling, what "translation" has been done between the socio-politico- economic problems posed (the aim of the action) and the scientific problem at stake (the goal of the action); what directions have then been chosen to address this problem (the objective of the action); and what is the current direction of the action and what are the intermediate results (see file 2 for further explanations of these four dimensions). This kind of formalization has one advantage : it enables "capitalization" from one year to another. As long as objectives do not have to be redefined (which is often the case for any research action), only the fourth item (direction taken, results achieved, future steps) have to be addressed each year.

The second deals with "managerial" dimensions : teams, meetings, exchanges, expenditure, specific output. All purely factual information that can be compared between concerted actions and be the object of a simple "micro-computer" formalization, so that it can be fed in at the local level in real time without having a time-consuming exercise to undertake at the end of each year.

The third relates to scientific dimensions : where does the CA stand with regard to the rest of the world in its domain, what are its scientific achievements, and what are its scientific choices for future action (what is their basis)? Clear targets are needed which do not have to be met at a fixed date but only when a significant result is obtained and a new step taken. File 2 shows many examples of such dynamics; it also shows that the time scale is far longer than usually expected and that very often a scientific report does not need to be produced every year.

Use of publications as assessment tools?

Publications are traditional means for assessing the activity of individual teams in the research community. Thus, annual reports require PLs to list what has been published by the concerted action. The recent evaluation report has put much emphasis on this dimension by trying to assess whether the "best" scientists were part of MHR CAs and by trying to "measure" the proportion of MHR publications in co-authored papers. Most PLs, when asked about their

practices here, told us of the problems thet met. How do you select what to label as CA output? Practices vary strongly from one CA to the other : some include all refereed publications of participating teams dealing with the theme of the CA, while some others limit themselves to publications presenting CA activities or the joint collective results obtained. In this latter case, it is not surprising that the number of publications is limited and that there are long delays before having anything to write about. Some have decided to publish the proceedings of meetings as supplements in Journals (this is then a major item in the CA budget), while others limit themselves to internal reports. How can these different situations be dealt with? Some PLs even asked us how to deal with products like databases or cell banks, software or other collective facilities which the CA builds up to enable new scientific work to be undertaken (even by teams outside the CA). By mentioning all results obtained through the use of these collective tools, by obliging teams using them to co-author their findings? Publications are the major tool for measuring the solidity and strength of scientific output, but at the same time, using them to assess the quality of CAs requires a deep insight into CA activities and a suitable method for taking their limitations into account (at least to assess on-going activity).

Direct reporting to MHR committees

The third major instrument COMACs use to obtain an idea of concerted actions is the annual presentation of PLs. The present practice is considered far from satisfactory, as we have seen in Part 1. How can a presentation be made in ten minutes and deal with a complete action? How can a COMAC get a clear view of CA achievements in such short periods? Most PLs think that it is impossible by this means and, as the situation with liaison officers is not a satisfying one (in most cases), relations with COMACs get a "bad mark" overall and can only be counter-balanced by relations with national representatives. Such a situation does not help to build up committees able of strategic analysis. We have not examined COMAC practices but rather a number of programme committees (at the EC or the French national level[2]); they clearly show the need for national or institution representatives to have a common approach by being able, through "objective assessment mechanisms", not to limit themselves to being the lobbyists of their "nationally originated" projects.

Even if such problems could be solved, through longer presentations for instance, the composition of the COMACs as assessing panels would still be questionable. They are not seen as "peer committees" by PLs, who underline their growing administrative composition. Not that there should simply be more scientists in COMACs, but to point out the need, if a traditional "peer review" is required, of another way of bringing together "senior scientists" familiar with the field in question, a solution which many PLs would favour, as they would see it as a help in the strategic design of their CA. This kind of classical peer review will not answer the second dimension of all CAs : they do not simply produce scientific results, they build up networks which are to be appreciated as such. How the quality of this is to be assessed remains an open question.

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[2] see D. Vinck article on the subject in "Le management de la recherche; volume 1 : les programmes technologiques", Economica, Paris, Autumn 1992.

This demonstrates the need to have a clear concept of the internal "monitoring" system the MHR wants to organize and what it is aimed at. In connection with the "reporting mechanism" we described above, we think that there are three complementary types of follow-up action.

- *Periodic scientific evaluations* requiring "ad-hoc" solutions, if not for each CA, at least for groups of related CAs (probably over 40 groups for the present programme). As this is not the object of the external evaluations undertaken at DG XII level, this needs to be internally organized and, as usual for any research laboratory, an interval of 2-3 years would be reasonable.

- *"Opportunity" assessments* is a second type of assessment which, from what we have seen when reading CGC and COMAC minutes, corresponds to what they aim at. The question may be summarised as follows : provided the work done is of good quality and that a real network is being built up, is it relevant to invest more money in this present CA, and how does it compare with other priorities the programme has formulated? It is then interesting for COMACs to call in the PLs once they are aware of the dynamics of the CA, not so much to discuss its scientific direction but rather the links between "aims", "goals" and "objectives". A discussion of this kind does not not need to take place every year. Once every two years should be enough (and in some cases where information gathering takes a long time, even once every three years). Discussions of this nature require a certain amount of time "one hour will be far too short in most cases). Reasonably long discussions every two years should be possible to fit into COMAC timetables.

- However, a "strategic assessment" requires a *regular reporting mechanism* such as the one described above. A reporting system makes it possible to have two complementary systems : one provides transparency and fits in well with the information requirements analysed above. Anyone interested can find out about CA directions and achievements from reports circulated, from the information provided in the Newsletter, from information on interesting managerial initiatives. The second produces a "signalling system" : it is only when CAs face problems and that a "correcting" action needs to be undertaken that COMACs and/or CGCs have to intervene and discuss them with PLs. The daily management of such a reporting system, always a heavy burden which tends to be underestimated, is usually (at least in the cost-shared programmes we have examined) the responsibility of EC programme managers.

> *In general, monitoring and assessment appear to be another weak point in MHR management. Most PLs strongly advocate a change in the current tools. On the basis of their proposals, we have suggested the creation of a "reporting system" built on three complementary sets of information : strategic, managerial and scientific. Each dimension should be dealt with at different intervals of time. On this reporting system, on which, by and large, the daily management of the programme is built up, two complementary monitoring systems seem to be necessary. Periodic scientific evaluations are requested by most PLs and these, to be accepted and credible, require a specific solution which the COMACs do not provide. "Opportunity assessments", on the other hand, are what COMACs and CGCs seem to aim at when analysing CAs; these assessments also require a solution other than the current method (short presentations by PIs every year), which could be easily put into action, provided the other systems are developed and make a clear*

differentiation possible, thus clearly establishing the specific role of each MHR managing committee.

IV- AN EVOLUTION IN MHR MANAGEMENT STRUCTURES ?

Adaptations to the budgetary systems and fund allocation, the creation of an information system and structure, the specific recognition of PL status, the development of a reporting mechanism and of an ad-hoc procedure for scientific evaluation, and the adaptation of the present COMAC practice on "opportunity assessment" : all represent quite significant changes to present MHR management practices which are needed if the best is to be obtained from what seems to be the core of MHR programme : the "concerted action" philosophy. This report would not be complete if it did not mention a final point : the confused perception that most PLs and nearly all participants we interviewed have about the organization of the MHR programme.

MHR : a holding of 6 different programmes?

What is MHR for the participants? In simple terms, one could say : a holding of six independent programmes which are, de facto, the only ones to be known by the participants. A joint call for proposals (once every four years) and two issues of a MHR newsletter are not enough to give consistency to the programme as such. Furthermore, selection and monitoring are in the hands of the COMACs which actually delegate a liaison officer to provide a direct link. Even at this level, changing names of committees (COMACs and Working Parties) and a different use of the acronym PMG (at the Concerted action level for CAs which come under to COMACs, as subcommittees for the two WPs) do not make it any easier to understand the organization of the programme. On top of this, the composition of these two sets of committees does not seem to be homogeneous, which, for a programme largely dedicated to European harmonization, seems rather puzzling! We have also been struck by the very different attitudes taken by COMACs/WPs to common problems (industrial participation is a typical example) or to the examination of projects transferred from one COMAC to the other. Finally, there is one very clear symbol of this confusion : CA logos. Most of them mention their relation to the EC via the name of the COMAC "they belong to"... and no PL has ever cited the CGC as a resource or the cause to any problem. One is thus led to question the existence of the programme as such : are not we dealing with six different programmes, MHR appearing only as a grouping created for "administrative" reasons?

The need to reinforce the day-to-day management structure

Most of our recommendations - at least those dealing with administrative problems, with reporting mechanisms and information structures - can be dealt with by the day-to-day operational management provided by EC programme managers. These new activities will introduce important changes to current practices which require a significant reinforcement to manage and follow up such a large programme. As outside observers, we cannot but be surprised by the very limited core of managers that has to deal with the follow-up of CAs in addition to the presentations to COMACs (knowing all the other administrative actions

managers have to undertake in preparing for future programmes). There are many ways to help towards a solution : national authorities could be more active in seconding personnel, examples could be taken from cost-shared programmes which do not hesitate to hire "experts" on a part-time basis for the duration of a programme (a solution which enables adequate expertise to be obtained for the programme and which maintains flexibility for future variation).

Two major strategic functions to be addressed

If we stick to EC R&D philosophy, this management structure should be assisted by committees for all strategic choices. Such committees usually cover a set of activities two of which have been shown to be important in previous evaluations[3] : on the one hand, the preparation of new programmes (including the call for tenders and the distribution of their budgets between topics) and, on the other hand, the selection of teams. For this specific MHR situation, our analysis has pointed up two complementary activities emphasized by PLs : the strategic choices associated with the selection of new CAs and with the opportunity assessments

When a concerted action is proposed, activation of an existing team network has to be compared with the creation of a network from scratch. MHR4 has shown an inclination to favour the first solution but some PLs regret this and see it as a tendency to go for the easiest topics. Some PLs also argue that MHR should not only make a selection of the answers received, they should keep part of the money to directly initiate CAs on important subjects which have received no proposals. These are generally the most innovative ... and the most risky, but, if MHR loses the capacity to take risks, it will lose part of what makes it original in the European Health research landscape.

If "ad hoc" panels can be regularly created for "scientific evaluation", this does not correspond to what we have termed "opportunity assessment" which covers both the continuing support of existing CAs (avoiding their having to undergo the whole process again) and the way to build up "transition" phases to ensure the adequate transfer of the results and not lose the value of the EC money invested in this research effort. File 2 has shown the growing importance of this second dimension and the questions it raises both in term of results dissemination and of the future of results embodied in networks. Opportunity assessments have here a major role to play for the programme to monitor these situations and prepare adequate answers.

What kind of strategic organization?

At present there is a division between the CGC (selection of areas for action, definition of major principles and methods) and the COMACs/WPs (selection and monitoring of CAs). This does not answer all the managerial issues our survey has raised. Many changes are required to tackel them : changes in the denomination, the composition and activities of its sub-committees, changes in its evaluation and assessment practices, changes in some of its spending rules, changes in the efforts made in and organization of communications, changes in its monitoring activities. A study like ours is able to point out problems, it can propose ways of making changes but, being not familiar with the organization, its power games and the

[3] see for instance the NNE3 evaluation.

network of political and administrative constraints it has to live with, it would be presumptuous of us to make proposals.

TO CONCLUDE

The MHR "philosophy" has made it possible to develop what appears a really original solution - the MHR concerted action. It has done so by choosing to delegate responsibilities and grant a large measure of autonomy to some PLs in the conception of their action, in selecting the teams and in finding suitable solutions for the problems encountered. Their initiatives have progressively defined what tasks can be termed collective and so be funded within the MHR framework. The success of the scheme is such that the management structure has had difficulties in adapting to this rapidly changing situation and coping with all the new problems that accompanied this rather unexpected development. Thus, this achievement calls for quite important changes in the management practices and structures of MHR4. Three major areas for change have been pointed out : funding practices (adaptations within the concertation framework), information systems and structures, monitoring and assessment mechanisms. However, it also requires a two-stage development in the organization of the MHR : a clearer recognition of the specific role of Project Leaders, and a clarification of the articulation and roles of the different "management committees".

FILE 4
THE DISSEMINATION OF CONCERTED ACTIONS RESULTS

AN EXPERIMENTAL APPROACH

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CONTENTS

THE DISSEMINATION OF CONCERTED ACTIONS RESULTS AN EXPERIMENTAL APPROACH

INTRODUCTION

Nowadays public research programmes are very much bound up with socio-economic factors. Consequently, an assessment of their results and dissemination is more crucial than ever. This is a general and banal observation, but it has specific and singular implications. The growing importance of societal factors in research gives it an increasingly strategic role. In fact, it is through strategic choices that the links between science and society, between research and its applications, are expressed. It is therefore through them that the results of a research programme can be perceived. The public authorities are the masterminds behind these strategies in which numerous actors are involved[1]. The MHR4 programme is far from being an exception to this rule, but it has two main specific features.

1. The public authority concerned, which oversees implementation of the programme and its use, is the European Commission, a multinational body. The stakes are high : European integration and the completion of a unified market. The programme is therefore specifically intended to encourage, by means of research, the creation of an unprecedented entity : a European health care area.

2. Public-authority intervention does not consist in financing the research work directly, but in promoting relations between the numerous teams working together on joint projects (concerted actions). In other words, the Commission's objective is to form a network to bring together in a collective European project actors who are normally dispersed. It is therefore on the basis of the specific features of MHR4 that the impact of the programme can be assessed. Adopted as a strategy, is the concerted action procedure suited to the task of establishing a European health care area? Do the results of the research carried out in this connection form the basis for a European health care market? How does public-authority intervention encourage the dissemination of these results to users liable to make the best use of them?

The purpose of this analysis is to arrive at a better understanding of the interactions between public authorities, research area and the market place. The health care market referred to here is a general entity made up of actors who use the finished products of medical science. Health research is traditionally carried out by a variety of actors who are often involved in other activities as well. The intervention of the public authorities via the MHR4 programme is part of a pre-existing dynamic process on which it has an effect but which also determines it to some extent. The starting point for this analysis is simple : a description of the web of relationships between the actors explains the link between these three entities. In the first part, then, we will demonstrate how this network of actors works within, but also downstream of, the concerted actions. In the second part, we will describe how these networks constitute a new health care area, which is

[1] M. Callon, R. Chabbal, Ph. Laredo, L'évaluation des programmes technologiques, enjeux et organisation, miméo CSI 1989

lent structure by the relations forged within the framework of the programme or arising from it.

Methodology

Two major sources

The information set out in this report is drawn from two sources :

- the replies to one page of the questionnaire sent out to the 3 500 teams participating in the MHR4 programme. 1421 respondents (40%) provided information concerning the potential users of their work. 426 also gave the names and addresses of persons likely to make direct use of their activities under the European programme. A new questionnaire was sent to these users identified by MHR4 participants.

- 542 users received this second questionnaire, 306, or 56%, returned it duly completed. This high response rate should not conceal the fact that the sample is limited compared with the number of participants in the European programme. These users of the results produced by the participants in the MHR4 programme in their turn pinpointed the categories of persons who make use of their work.

We thus have information relating to actors involved with the programme at three levels : those participating in the MHR4 programme; the primary users of the results obtained by the participants; those who use the results of the work carried out by the primary users, whom we will refer to here as the secondary users. Despite these three levels, the actors are not necessarily divided into three distinct groups. Some of them who are involved at one level may be involved also at another level. The three levels referred to are not therefore mutually exclusive.

Explanations about the terminology used

The network is the set of actors and relations between actors concerned by an innovation. Relations between actors are established on the basis of actual interchange; they are depicted here solely on the basis of what the actors say in the questionnaires. The actors are all the entities active in the innovation process : individuals, institutions, technical facilities, etc.

An illustrative example

OMDM -"Objective Medical Decision-Making, Acute Abdominal Pain"- is a concerted action bringing together 60 or so teams, mainly clinicians, to build a sophisticated diagnostic tool. The participants supply data, the collection of which is standardized by means of a protocol. A data base is thus established which serves as a reference basis for the most objective possible diagnosis of acute abdominal pain. The users are as follows :

- the participants themselves, who can immediately compare cases which they have supplied with those sent by the participants as a whole,
- gastro-enterologists as a whole, who are potentially interested in the data base,
- clinicians as a whole, for whom this new tool offers the possibility of a more accurate diagnostic method,
- national or international health services (EEC, WHO) interested in the dissemination of OMDM with a view to bringing about a general improvement in diagnostic procedures,
- computer and artificial intelligence companies for which the potential software developments offer prospects of new markets.

PART I - THE CONSTRUCTION OF TECHNO-ECONOMIC NETWORKS BY MHR4

The concept of techno-economic networks takes full account of the configurations which exist within and around the MHR4 programme. These are networks which bring together a variety of different actors to work on scientific or technical innovation which is transmitted through intermediaries. These actors and intermediaries fall into three main categories : research (scientific), techniques (development) and the market. What makes the networks unique is the interaction within and between these categories. Innovation is not therefore confined to any one of them, but is a process of continuous traffic from one to another[2]. The concerted actions operate in the same way. We will see further on how varied the participating actors are, the transfers which they make possible and the way in which resources are mobilized by the programme.

1- WIDE VARIETY OF ACTORS

The concerted actions constitute heterogeneous networks. A variety of actors take part in them and pass on material which varies enormously from one project to another. The participants come from a wide variety of institutional backgrounds, including research institutes, university hospitals, public health departments, private laboratories and foundations.

TABLE 1 : INSTITUTIONS TO WHICH PARTICIPANTS IN MHR4 BELONG

Source : File 1

Hospitals	22%
University hospitals	23%
Universities	29%
Public research bodies	14%
Health services	8%
Industry	1%
Foundations	3%

Even within the various organizations and teams, there are a number of professional roles : researchers, clinicians, administrators, managers, etc., usually in combination:

TABLE 2 :

Source : File 1

Teams with researchers only	45%
Teams with clinicians only	12%
Teams with researchers and clinical staff	43%

[2] M. Callon, Ph. Laredo, V. Rabeharisoa, Instruments for the management and evaluation of techno-economic networks, Research Policy (accepted)

Virtually all concerted actions involve several types of teams (see File 1). The combination of researchers and clinicians is particularly common. MHR4 is divided into six subprogrammes (Biology, Biomedical Engineering, Epidemiology, Health Services, AIDS and Cancer) within which the concerted actions relate to various spheres of competence. The topics covered call for a large number of actors who define the content themselves. Depending on the means of coordination, on the exchanges and the results (intermediate and final) there are several different configurations which correspond to a number of types of networks (see File 2). These networks are to a greater or lesser degree "horizontal" or "vertical" depending on whether they consist of actors chiefly involved in scientific research or in activities further downstream. The MHR4 programme comprises horizontal and vertical networks, as well as diagonal networks situated between the two. Dissemination varies depending on whether the network is one of "peers" (participants roughly on the same level) or is a "star" network (distribution of information and results among widely-dispersed actors) (see File 2). A few examples of concerted actions will help to illustrate the point.

- The action entitled "Biomagnetism, a diagnostic tool for brain and heart diseases" combines a considerable variety of technical, scientific and industrial resources. Various participants are involved in devising this diagnostic tool : neurologists and cardiologists, psychologists for the stimuli, mathematicians for modelling, electronic physicists, computer specialists, etc. These skills are provided by different laboratories or large teams such as those of the project leader (PL) or the members of the project management group (PMG). Researchers from industry take part in the meetings and propose appropriate solutions; even industrialists working simply on components may sometimes participate. There is immediate contact between actors, whose activities are linked to such an extent that it is no longer possible to say whether they are working on research, applications or development.

- Another, very different, action is the "Cell-mediated immune response against HIV/SIV and its significance for vaccine development", which mainly involves laboratories carrying out basic cell biology research. The application of this research to the search for a vaccine is part of a different action entitled EVA (European Vaccine against AIDS). The results are therefore taken over into the latter concerted action from the former. Their use is therefore part of an overall strategy for the AIDS subprogramme. The institutional framework here is the player through which the transfer from knowledge to application, from theory to clinical end-users takes place.

These examples reveal one thing : the subject-matter of the research, its application, the formation of the network and the authorities' strategy are all interdependent. In particular, the network emerges by co-opting a core of actors who work in concert with the bodies responsible for the subprogrammes to establish the field of research and its existing or potential applications. We can therefore take as a starting-point the fact that the MHR4 programme, under the label "health and research", involves cooperation between actors at different levels. The composition of the networks built by concerted actions means that the results are circulated between actors, working their way downstream. An effort was made to establish whether this went beyond the projects or was confined to them. The survey among the users of the results of MHR4 describes how these networks are extended.

2- CONCERTED ACTIONS AS THE BASIS FOR TRANSFER NETWORKS

A continuum is apparent between the programme and its users and between the research and the use made of it. The results arising from cooperation within the concerted actions are also taken up by a variety of users.

A DIVERSITY OF USERS

The categories of institutions to which users belong are set out in table 3. The first point to be noted is that the major categories of institutions participating in the programme (see Table 1) are reflected here, with hospitals, university hospitals, universities and public research bodies being well represented. What is new is the growth in importance of the health services and industry, which are particularly well placed as regards application of the research results in the traditional sense. This leads us to another important observation, namely that there is no dichotomy between those who produce the results and those who make use of them, but rather a gradual transition which reflects a varied and sophisticated institutional set-up.

TABLE 3 : CATEGORIES OF INSTITUTIONS TO WHICH USERS BELONG

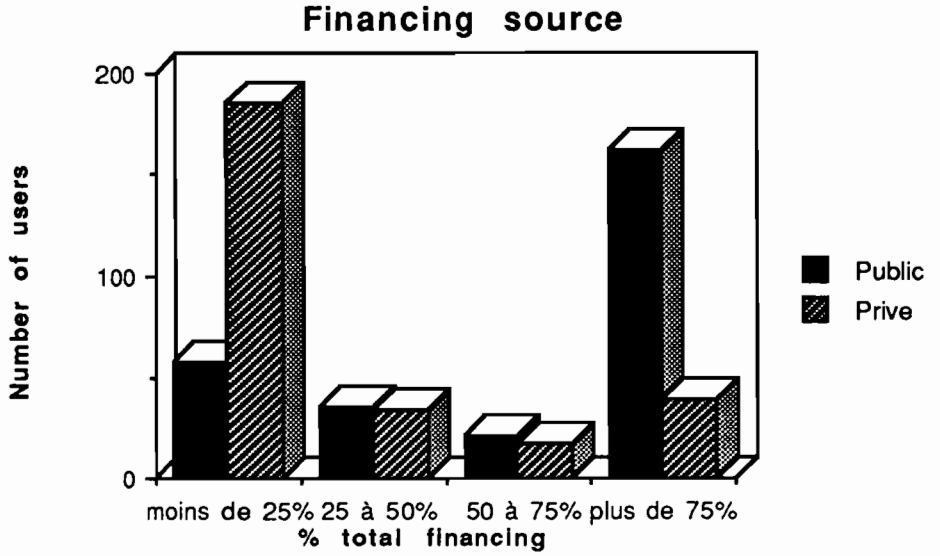
Source: Users' questionnaire

Universities	65	22%
Health services	61	20%
University hospitals	54	18%
Hospitals	39	13%
Industry	37	12%
Public research bodies	26	9%
Others	12	4%
Total	298	100%

The majority of users have little or no access to private funding; some of them receive combined private/public funding (between 25 and 75% of one or the other). A large number (53%) are largely subsidized by public funds (see diagram 1). The users therefore depend very heavily on public sources to finance their activities. This is essentially true of researchers, 61% of whom rely mainly (more than 50%) on public funds, with half relying almost exclusively (for more than 75%) on this source. The figures are even higher for clinicians, at 66% and 63% respectively. By contrast, the small category of users in the industrial and commercial sector relies almost entirely on private funds. However, a significant proportion (12%) of users who describe themselves as researchers rely virtually exclusively on private funding. We can see, then, that the public sector makes a major contribution to the networks at this stage, as well as further upstream in the programme (see File No 1). The health care market would appear to be taking shape with a massive input from the authorities.

DIAGRAM 1: SHARE OF PRIVATE/PUBLIC FUNDING IN USERS' FINANCING

Source : Users' questionnaire, Question 14



Looking beyond their institutional background, we see that users define their areas of activity as follows :

TABLE 4 : PREDOMINANT ACTIVITIES OF USERS

Source : Users' questionnaire, Question 8

Research	153	53%
Clinical practice	62	21%
Administration	37	13%
Service	7	2%
Trade/industry	27	7%
Others	9	3%
Total	290	100%

Research therefore emerges clearly as a predominant activity among those using the results of MHR4. It is broken down into different institutional categories, mainly universities and public research bodies, but also hospitals, health services and industrial and commercial companies to a significant extent. The worlds of clinical practice, health administration and manufacturing and marketing therefore interact directly with research. Actors' answers also reveal that the research they carry out is very often non-exclusive, being frequently combined with clinical practice, but sometimes also with administrative, training or commercial activities (see table 5).

The scientific activity arising out of the concerted actions therefore extends well beyond the confines of the programme. The research is not confined to the programme itself, but is taken up by actors who are active on the fringes, who are likely to translate it into a variety of activities. Diagram 2 represents the dissemination of MHR4 results to 215 users. It shows the proportion of users in each sector of activity, and their degree of involvement in the concerted action

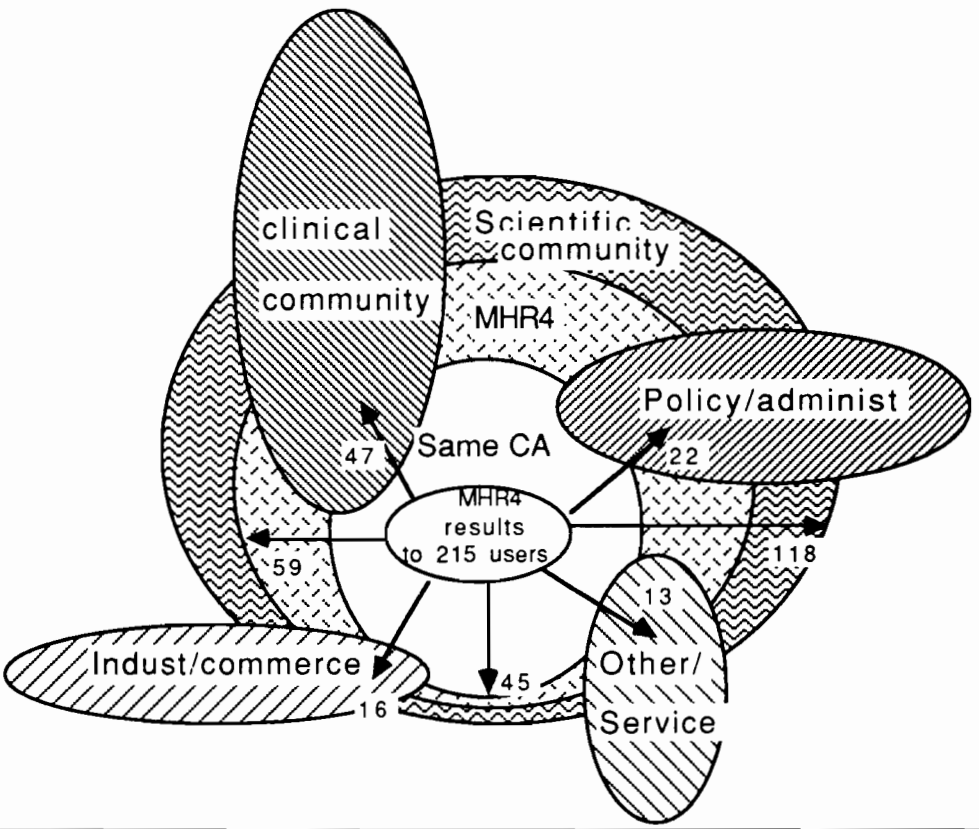
projects. These different sectors revolve, with some overlap, around the dominant "scientific research" community, centred on the core of MHR teams.

TABLE 5 : PREDOMINANT ACTIVITIES BY MAJOR CATEGORIES OF INSTITUTION

Source : Users' questionnaire

	Research	Clinical practice	Adminis tration	Trade & industry
Universities	54	7	1	2
Health services	15	0	37	0
University hospitals	29	23	0	0
Hospitals	13	22	1	1
Industry	14	5	1	16
Public research bodies	22	3	0	0

DIAGRAM 2 : MHR 4 AND USERS GROUPS



Of these 215 users, 59 are participants in the MHR4, with 45 of these belonging to the same concerted action for which they are mentioned as users, and the other 14 participating in different MHR4 projects. Thus, the results circulate both within and beyond the programme or the concerted actions and these visibly establish convergence.

USES OFTEN INCORPORATED IN CONCERTED ACTIONS

While it is true that the research arising out of a concerted action may spread beyond the participants, the use made of it may also be incorporated in the project. The programme results are used first and foremost by the participants in the concerted actions. Two-thirds of these regard themselves as the primary users of the results of the Community programme. In a large number of cases, this means that the results of the concerted actions are not immediately available to and taken up by outside actors. On the contrary, they appear to be incorporated and processed by the participants individually, before in some cases being passed on to others. One-quarter of the users mentioned by the participants are full members of concerted actions.

There is a link, therefore, between participation in a concerted action and use of its results. Teams are involved in the concerted actions at varying levels, with some making a marginal contribution to certain activities and benefiting from the overall results. For example, some of the epidemiology concerted actions employ clinical teams to compile the data, which are then processed by research units and subsequently passed back to the clinical teams. The users mentioned by the participants are sometimes members of the COMAC for the subprogramme to which their concerted action belongs, in which case the public body involved in devising the projects also has an interest on its own account in seeing the results. On other occasions, the project leader is cited as the user, as in the case of some concerted actions which operate in centralized networks (see File 2) and where the participants make partial contributions which are brought together and processed by the project leader, who passes them on in a subsequent phase. In addition to differences in status within the concerted action, the varied nature of the participants encourages internal transfers. The contributions made are therefore many and varied, and there is a diversity of exchanges. A research team specializing in developing diagnostic software, for instance, can make it available to general practitioners who use it on their patients and pass back information to the designers. Another case might involve national government departments forwarding quantitative data on the development of AIDS, which will be processed by groups engaged in another action with a view to drawing up predictive models for the government departments.

We can see, then, that there is no sharp divide between the production of scientific research results and their use, but that on the contrary there is considerable overlap between them. It is this very overlap, indeed, which guarantees the success of the concerted action. There is constant and rapid two-way traffic throughout the process of producing results, making the first partial application and working on them to achieve improved applications. Through making use of the research product and being involved in its development, the participant in a concerted action who is both providing and using ideas, data, samples, etc., has a vested interest in it. The reintegration of the uses into the concerted action is therefore a cohesive factor for the technical/economic network. So, although its focus is on research the MHR4 programme involves actors engaged in activities which, though different, are encouraged to interact. This overlap makes it easier to translate the results into applications. The distinction between participants and users is not sharply defined. In this way the networks form a bridge between the programme and the outside world : on the

one hand, the research generated by the concerted actions may affect teams which have very little direct involvement; on the other hand, the results of the programme benefit willing users who become integrated in the programme.

The programme is thus characterized by the export of the research carried out and the reintegration of its uses. This lends a certain fluidity to the networks, and means that the researchers and users are to a certain extent interchangeable, both within and outside a concerted action project. In this respect, the activities supported by MHR4 can be likened to the kind of basic technological research (RTB) characterized in particular by the versatility of the actors, which invalidates the distinction between basic and applied research[3].

3 - MOBILIZATION OF ACTORS THROUGH CONCERTED ACTIONS

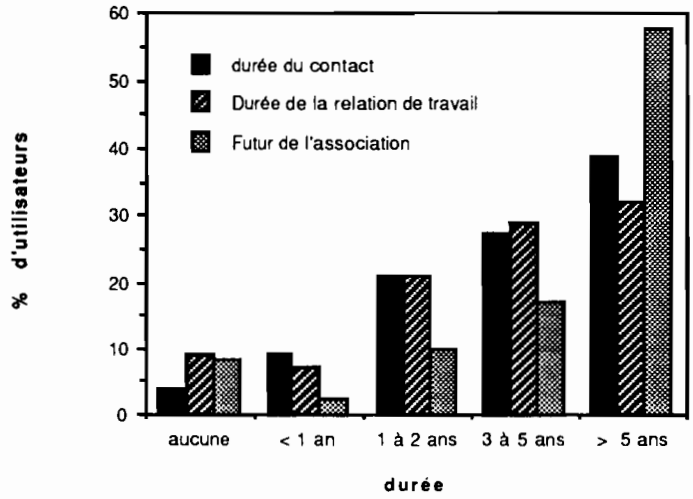
Although it is not rigidly defined, the MHR4 programme nonetheless is of considerable significance to the actors associated with it, even if they are not directly involved. 64% of the users of the programme results are aware of the fact that it is a Community programme (Users' questionnaire, Question 1), which suggests that it has a high profile. Local contacts between participants and users do not occur in isolation from the centre, which is the concerted action : the user is aware that, through the intermediary of the participant, he is linked up to an overall programme in which he has some say. The degree of familiarity with the programme depends on the predominant activity of the user. One surprising finding was that half the public health authorities were not aware of the nature of the programme, whereas the majority of researchers and clinicians (70% and 58% respectively) were familiar with it. National and local administrative bodies are perhaps in some cases relatively far removed from any European connections... The duration of contacts between participants and users suggests that the networks are quite stable, as diagram 3 illustrates.

The majority of users (69%) have known the participant in the programme for more than three years, i.e. even prior to the start of the MHR4 programme (1987). Working relationships appear to have been established more recently, which clearly indicates that there is a certain period during which individuals become acquainted before actually beginning to work together. Finally, these relationships seem set to last, since three-quarters of the users feel that they should extend over more than three years and 60% feel they should last more than five years. Clearly, therefore, we are dealing, not with occasional and opportunistic contacts, but with durable and solid alliances which have in all likelihood been carefully thought out, negotiated and built up. Contacts between participants and users in the public health services are more recent than for the other categories. A clear majority of researchers and clinicians have known the participant personally for more than three years, and even five years in the case of 44% of clinicians. The lasting nature of these links is reflected in their working relationships, with 61% of researchers and 68% of clinicians having worked with a participant for more than three years, or even five years in the case of 39% and 29% respectively.

[3] Ph. Laredo, M. Callon, L'impact des programmes communautaires de recherche sur le tissu scientifique et économique français, Paris, La Documentation française, 1990.

DIAGRAM 3 : PARTICIPANT/USER RELATIONSHIP OVER TIME

Source : Users' questionnaire, Questions 2, 4 and 5



The proportion of public health officials who have long-standing personal and professional contacts with a programme participant is lower by comparison. The fact that contacts between participants and public health officials tend to be recent appears to be part of a trend among Community programmes. The increasing proportion of the public authorities among beneficiaries of research results can be easily explained. The concerted actions are powerful tools for harmonizing medical practices. The HSR (Health Services Research) subprogramme is designed in particular to establish uniform procedures for monitoring and assessing medical services. The Epidemiology subprogramme provides comparative data between regions and countries on the major pathologies. The BME (Biomedical Engineering) subprogramme, meanwhile, encompasses cooperation between European industrialists. In short, the opening-up of Europe, with the attendant strategic changes at the research stage and further downstream, gives rise to increased political and administrative investment. In the face of these issues, which affect them directly, the authorities become actors who are fully involved with the content of the concerted actions, since it is at the heart of these that the strategic choices are made (equipment standards, standards for the assessment of hospital services, prevention campaign methods, etc.). The public services are therefore direct users with a big stake in the research results.

In any case, it would appear that all three categories of users expect the contacts established with the participants to be of long duration, longer than five years in three-quarters of cases. To judge by the comments of the users questioned, MHR4 makes a significant contribution to stabilizing contacts with participants, and thus to the structuring of the networks. Among clinicians and researchers, contacts between participant and user predate the programme in the majority of cases. The way in which contacts between participant and user came

TABLE 6 : OCCASION OF INITIAL CONTACT BETWEEN PARTICIPANT AND USER

Source : Users' questionnaire, Question 3

At a scientific gathering	30%
Through a colleague	27%
Through business contacts	20%
Through a coordinator	8%
Through an advertisement	1%
Other	11%
No reply	3%
Total	100%

Only 8% of initial contacts took place through an institutional coordinator like those attached to the concerted actions. The main channels of contact are more traditional and informal : through scientific gatherings, colleagues or the usual professional contacts. Few contacts arise out of institutional planning, but tend to be forged in an informal manner and within the context of communities linked by their activities and by everyday professional contacts.

Among the users, researchers make contact with participants largely through scientific gatherings, which shows that the internal channels of communication which exist in research circles prevail in this area. Clinicians frequently come into contact with the participant through a colleague. Is this evidence of natural interaction, a sort of osmosis, between clinics and hospitals on the one hand and the research sphere, with which they have daily contact, on the other? None of the categories in particular is characterized by business contacts through the conventional channels linking organized bodies. The networks, then, tend to be formed initially through social channels rather than through cooperation between the national and/or Community authorities. However, to judge by users' statements and the strengthening of working relationships and their durability, the Community programme has a significant impact on the construction of the networks.

Finally, the concerted actions make use of and consolidate previously-established relationships, which are all the stronger because they involve direct contact between the actors and operators rather than between the umbrella organizations. This phenomenon is echoed, moreover, in other Community programmes, which accompany the networking process and reaffirm it. The mobilization of the actors and the strategy of the authorities are interdependent, and are meaningless in isolation from each other. On the one hand, official coordination relies on traditionally strong contacts in the medical world. On the other hand, the strengthening of these relationships through the work carried out, their stabilization and extension owe a lot to official intervention.

The medical world is traditionally diversified and heterogeneous, with the result that it lends itself to the effective structuring of techno-economic networks. MHR4 is an example on a large scale of this kind of networking involving greater interaction between actors. The concerted actions enhance bilateral contacts between those producing and using the results by connecting them to a common base. The networks are formed spontaneously through local contacts which are extended to a multilateral level by the MHR4 programme. In the second part we will examine how this fabric of contacts goes to form a new area.

PART II - FROM MEDICAL RESEARCH TO THE HEALTH CARE MARKET - STRUCTURING BY THE TECHNO-ECONOMIC NETWORKS

For economists, the formation of networks is a an important condition for encouraging innovation and the emergence of products on the market[4]. A basic characteristic of these networks is that they create permanent links between the various actors involved in the innovative process[5]. This permanence ensures the continued development of innovation and makes the search for outlets less uncertain. We have seen that the creation of a Europe-wide health care market is a major issue for MHR4. The promotion of the networks through this programme contributes to the creation, and in particular to the structuring, of a framework of stable relationships.

We will now look at the form and content of the exchanges which make up and reaffirm these relationships, making them increasingly solid. First of all, then, we will take a look at how users acquire the results of the programme and then at the subsequent use made of them, and finally, at which actors take up the new resources created and how these constitute a transformed health care market.

1- APPROPRIATION OF THE PROGRAMME RESULTS BY THE USERS

The networks are characterized by the substance of the exchanges between participants and users and the way in which they take place. The exchanges act as intermediaries which shape and define the networks.

DIFFERENT RESULTS

Table 7 shows the results of MHR4 which users feel to be useful for them. The first category of exchanges between participants and users concerns the intellectual content : 73% of users take on board ideas from the participants with whom they come into contact, and 50% of them use data produced by the concerted actions. The latter therefore act as repositories of know-how and knowledge which generate future developments.

General information is the third product of which use is made, but one which is less finalized and less easy to define than the previous ones. However, general scientific information is of prime strategic importance. Keeping abreast of the latest developments in their field of interest is essential for actors in order to plan the future direction of their work : it is a vital tool for technological surveillance. The actors' desire to maintain a watchful stance is evidence of their awareness of the importance of the programme, as we will see in more detail later on.

The material exchanges arising from the programme are far from negligible, with a quarter of users making use of the technological prototypes developed by the programme and 22% making use of the software produced.

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[4] cf C. Freeman, Networks of innovators: a synthesis of research issues; International Workshop on networks of innovators, Montréal, May 1990.

[5] M. Callon, Réseaux technico-économiques et irréversibilités, in R. Boyer (eds) Les figures de l'irréversibilité en économie, Paris, éditions de l'EHESS, 1991.

So which users make use of which results? The answer to this question gives us a more accurate picture of the position of the actors within the networks.

TABLE 7 : RESULTS OF THE PROGRAMME TAKEN UP BY USERS

Source : Users' questionnaire, Question 10

Output	Numbers	Mentions	Citations
Ideas/New concepts	211	73%	31%
Data	146	51%	22%
General information	144	50%	21%
Technol. prototypes	74	25%	11%
Software	48	22%	7%
New medicines	22	8%	3%
Other/Don't know	27	9%	5%

DIFFERENT USES FOR DIFFERENT ACTORS

First of all, the users who describe themselves as researchers make the most use of the results of the concerted actions and in the greatest variety of ways. However, they have a more specific interest in the production of ideas and new concepts (mentioned by more than three-quarters). The data produced are also a priority for over half of them. While the exchange of ideas appears to carry the most weight in the relationship between participants and researchers, the exchange of physical materials is also very important. 65% of the technological prototypes are taken on board by researchers, probably for the most part in an extended design phase and/or for use as research instruments. The software is used first and foremost by researchers (over 10% of them), often in the form of the intermediate results of concerted actions (see File 2) which are made use of at an early stage. Finally, new medicinal products, which is a minor output of the programme, are used far more by clinicians and researchers than by (pharmaceutical) firms.

We can therefore make one basic observation at this stage, namely that there is no strict divide between intellectual production being passed on to researchers and material applications designed for completely different actors. The researchers make use of a variety of resources, and the physical and material results of earlier work are reincorporated by them to a very large extent. Similarly, the other categories of users take considerable advantage of the intellectual results.

The clinicians make use largely of ideas and new concepts rather than facts and figures. Thus we can see that medical practice gains a great deal from fresh scientific approaches but needs fewer material components to develop its studies. On the other hand, general information, as in the case of the researchers, is important for almost half of clinicians. The MHR4 programme acts as a source of such information, one which all categories avail themselves of at will. This is particularly true of those in charge of administration and engaged in industry and commerce. This reaffirms the strategic significance of this category of results and reflects the concern of these two categories of actors to have access to basic information. Moreover, they also have access to the ideas and new concepts emerging from the programme. This means that as far as industrialists and policy-makers are concerned, the European research programme not only serves to

locate their strategy within a pre-defined framework (by providing general information), but helps to define that strategy (by the introduction of new ideas).

Facts and figures are important, too, for the public authorities : this can be seen in the impact of the health services and epidemiology subprogrammes, which produce large amounts of data subsequently consumed by the public health services.

DIFFERENT VALUES ATTRIBUTED TO OUTPUT

There is some correlation between the quantity of the various products of the programme and the qualitative value attributed to them by the users.

TABLE 8 : COMPARATIVE IMPORTANCE OF RESULTS FOR USERS

Source : Users' questionnaire, Question 11

Output	Very important	Quite important
Ideas/New concepts	99	102
Data	70	70
General information	55	82
Technol. prototypes	37	33
Software	26	21

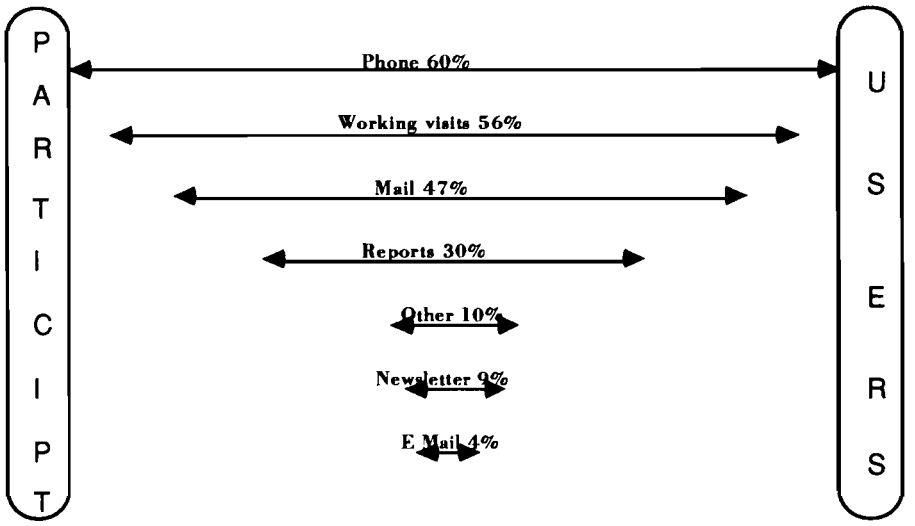
The more substantial the output, the more important it is considered to be by the user (software and prototypes). The non-material products (ideas/new concepts and, in particular, general information) tend to be seen as quite important rather than very important. Opinion is equally divided concerning data, which, although technical, are intangible. The more the product can be put to material use, the more value is attached to it by users. Steady output from the concerted actions, although less frequent, is judged to be more useful.

SUSTAINED AND INTENSIVE WORKING RELATIONSHIPS

In addition to the actual substance of the exchanges between participants and users, the back-up available is a determining factor in their association. Diagram 4 highlights the main media of exchange used. These help us to define the relationship between participant and user. They are very rarely used in isolation, but in combinations of two (three out of four times on average) and sometimes more than two. The mail option, for instance, is very closely linked to the telephone/fax option, and much less closely to the reports. Informal and frequent contacts appear to predominate. The predominance of telephone/fax contacts and working visits shows that the exchanges are study-related rather than formal. Correspondence by post, which can be more formal when used in isolation, is rarely used on its own, but tends to be in addition to other means of communication.

DIAGRAM 4 : MEDIA OF EXCHANGE BETWEEN PARTICIPANTS AND USERS

Source : Users' questionnaire, Question 7b



The following table gives a broad picture of which media are used for the different categories of output of the concerted actions. The indicator used is a weighting calculated on the basis of the frequency of overlap between positive responses per medium and per type of output, in relation to the total for each of these two categories. It therefore takes into account the relative importance of these categories vis-à-vis the others by combining it with the frequency of contact between two of them.

TABLE 9 : MEANS OF COMMUNICATION BY CATEGORY OF EXCHANGES

Source : Users' questionnaire, Questions 7b and 10

	Tel/Fax	Mail	Visits	Reports
Ideas/concepts	0.35	0.29	0.36	0.22
Data	0.29	0.27	0.27	0.20
Tech. proto.	0.21	0.17	0.19	0.16
Gen. info.	0.28	0.26	0.28	0.25
Software	0.15	0.15	0.13	X

The highest figures are for the relationship between ideas and new concepts and working visits and telephone/fax contacts. The latter are also the most used in combination with the transmission of data and information on technological prototypes. However, telephone/fax links and working visits are very rarely used in isolation from other means of communication. All the means of transmission seem to be on a more or less equal footing when it comes to conveying general information. This is the main aim of reports, which are of less importance than the other media and used more often in isolation. This points to fairly loose affiliations in which the report acts as an official medium of communication between participants and users who wish to remain informed of their respective activities. The other means of communication, on the other hand, often combined, point to frequent and intensive contacts between participants and users and to exchanges of a scientific nature. There appears to be a lot of interaction within the network,

with the work often being carried out jointly through direct contacts (telephone/fax, visits). The figures for the weighting would seem to point to a high degree of interaction in the network. The stability and intensity of substantial exchanges, to which actors attribute real importance, are an indication of the largely permanent nature of the relationships set up within the networks. We will now look at how these relationships take tangible shape through the results they produce.

2 - Uses of the programme results

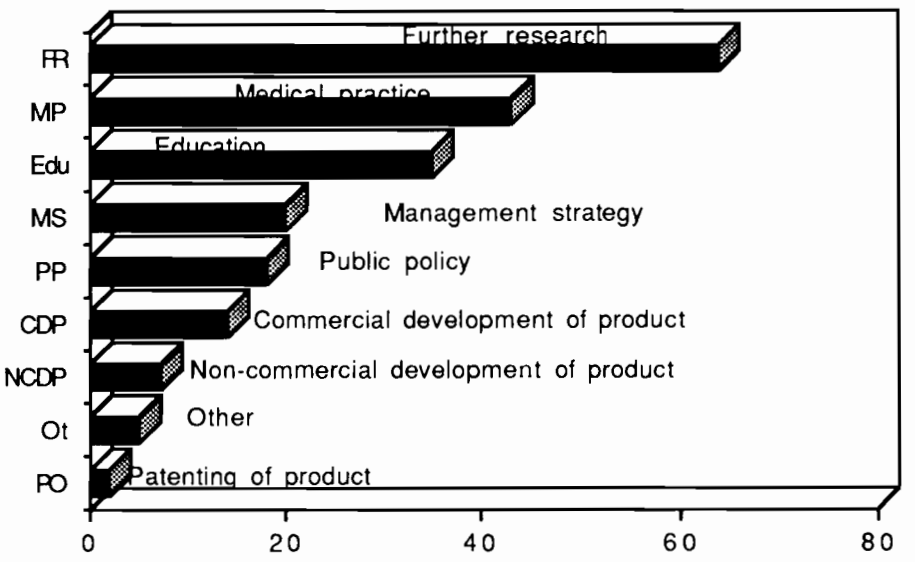
MULTIPLE USES OF THE PROGRAMME

Users are interested in the results of the MHR4 programme for developing their own applications. What use do they make of these results? The answer to this question (see Diagram 5) produces an initial basic finding, namely that the results are not put to a single use but to a variety of uses.

DIAGRAM 5 : USES OF THE RESULTS OF THE MHR4 PROGRAMME

Source : Users' questionnaire, Question 12

On average users mention 2.2 uses at any one time



Research, which involves 64% of users, accounts for only 31% of the overall volume of activity, so that its predominance is entirely relative. Clinical activities and education also concern a large number of users. Thus the European programme has here two very important and virtually immediate areas of application. The end-user (the patient) therefore benefits even at this stage, through medical practitioners, from the value added by the programme to clinical research. The impact on education is also fundamental, bringing about changes in medical practice in the medium and long term through the training of medical and para-medical staff. The new skills acquired by the actors and redistributed within the networks reshape the European health care area. Management, public policy-

making and commercial development of products are all areas in which MHR4 makes a significant contribution.

TABLE 10 : THE VARIOUS USES AND THEIR RELATIVE IMPORTANCE

Source : Users' questionnaire, Question 12

Use	Number of mentions	% citations
Research	187	31
Medical practice	121	20
Education	95	16
Management	66	11
Public policy	58	10
Commercial dev. product	40	7
Non-comm. dev. product	19	2
Other	22	3

The distribution of the various uses among the categories of actors confirms the fact that most put the results to several different uses. Thus, 82% of the researchers use the products of the concerted actions in their research activities. The research arising out of MHR4 therefore makes a major contribution to external research, as pointed out in the first section. Directly, MHR4 concerns only a subsection of researchers within the medical science community as a whole. However, this subsection is not a ghetto, but is in constant contact with other researchers.

A significant number of researchers (42%) also make use of the results of the programme in medical practice, accounting for more than half of those who do so. Clinicians, on the other hand, represent only 36% of those who make use of the programme in medical practice, although 68% of them do so. More than half of these also use the findings for their own research. Researchers and clinicians are virtually interchangeable when it comes to carrying out research or clinical practice. Like the participants in MHR4, the users appear as a general rule to be very versatile.

The versatility of actors varies depending on the category to which they belong, with clinicians apparently more likely to go into research than researchers into clinical practice. Researchers are also very involved in public policy applications of results and in applications in education. Use of the findings in management is more evenly distributed among the categories of actors; those categories which are relatively poorly represented as regards overall use of results have a proportionately large share. Public authorities in particular make significant use of the results for this purpose. Commercial use of the findings of the programme is divided evenly between researchers and businesses. In the case of the former, however, it concerns only an insignificant percentage of the category (less than 10%), while the much smaller second category represents more than one-third of the users who use results commercially. The market, moreover, is a very minor consideration for researchers, who are the main developers of non-commercial uses. The level of activity is roughly the same as for commercial uses, although the latter category is twice as large.

Uses in research, medical practice and education are very often combined. 42 users combined all three; 56 combined medical practice and education, 75 combined research and education and 83 research and medical practice.

The lack of barriers between health-related activities allows the integrated movement of intermediaries throughout the network. As a result of their versatility or their proximity to the other actors, users may transpose the findings for different uses and different end-users. Whatever their status to begin with, actors make use of the programme in a number of ways. The traditional socio-professional demarcations become blurred, and the actors are defined less in terms of their institutional status than by what they do. They no longer follow a single direction within a linear network, but form a link in a series of interconnections.

RESEARCH RECYCLED BY OTHER ACTIVITIES TO WHICH IT CONTRIBUTES

Leaving the actors out of the equation for a moment, we can picture the connections which are formed downstream of the programme by linking its results to the activities which make use of them. Research activity downstream of the programme, for instance, makes use of the different categories of results, principally ideas and new concepts, but also data and general information. Technological prototypes and software produced by concerted actions are also the subject of a certain amount of research activity. Medical practice draws from the same sources and thus makes extensive use of intellectual and physical material. Education, by contrast, makes use above all of ideas and new concepts and of general information, but little use of data, prototypes and software. Management strategies feed on ideas, general information and data, as does public policy, but with greater reliance on data and less on general information and ideas.

As a result, research downstream from the programme mobilizes a whole series of resources generated by the programme : we can see, then, that it is not a closed cycle. Medical practice makes use of a wide variety of tools. Education takes on board knowledge and new approaches which point to a long-term impact on medical practice. Strategic and political applications look to hard facts and figures to lend substance to the guidelines arrived at through more abstract activities. To sum up, then, there are no exclusive or preferential activities; on the contrary, MHR4 is put to a variety of combined applications.

3 - NEW RESOURCES AND DOWNSTREAM ACTORS : FRESH IMPETUS FOR THE HEALTH CARE MARKET

Continuing through the cycle, we sought to establish who makes use of the material produced by the primary users of MHR4.

CLEAR DIVERSIFICATION AMONG THE SECONDARY USERS

Table 11 identifies the categories of actors who make use of the work of the primary users based on the research findings of the participants in MHR4.

The first observation to be made is that virtually all the users know and can identify those who make use of their work. This indicates a close-knit network within which actors identify each other readily and are aware of what information

is being circulated. The second point to note is the diversification of the categories of actors at this stage. Scientists, clinicians and academics continue to be well represented among secondary users, as they were among primary users. But some new groups emerge in significant numbers, namely businesses, international organizations and consumers.

TABLE 11 : GROUPS OF SECONDARY USERS

Source : Users' questionnaire, Question 13

	numbers	percentage
Researchers	205	71%
Medical practitioners	169	58%
Universities	164	57%
Government depts.	103	35%
Business	94	32%
Internat. organizations	65	22%
Consumers	49	17%
Voluntary organizations	26	9%
Others	15	5%
Don't know	8	3%

The predominance of researchers, practitioners and universities has diminished compared with their importance among the primary users. However, the dominant areas among the secondary users coincide with the most important activities among primary users, namely research, medical practice and education. As regards the detailed breakdown, it would appear that the results of users' research are taken up primarily by other researchers (26%), followed by academics (20%) and practitioners (18%). The results of medical practice are taken up by practitioners (27%), researchers (24%) and academics (21%). Education is passed on to researchers (23%), academics (22%) and practitioners (19%).

The profile of the categories making use of users' work corresponds closely to the overall configuration of the work. The research work is not just carried out, but also taken up, by researchers. The passing-on of results does not imply systematic application, transposal from one sphere of activity to another. This pattern is repeated in contacts between primary and secondary users. Out of 155 user/researchers, 130 say that the results of their activities are passed on to researchers, and 49 out of 60 clinicians mention medical practitioners as the beneficiaries of their work. A similar observation can be made as regards public health officials and administrators (33/36). Thus the transfers are largely internal, the results being made use of first and foremost within the player's own sphere. Only a small proportion of results are passed on to other spheres. The transfer of results from primary to secondary users remains very largely within the author's own sphere. Only in a second stage, in some cases after being processed within this sphere, are some of the results likely to be exported. It is therefore clear that the transfer from actors and activities upstream of the programme to those downstream of it takes place very slowly. This reflects the length of the networks through which medical innovation travels.

INCREASING DISTINCTIONS BETWEEN ACTORS

Why is the work of primary users in the scientific, academic and medical spheres not disseminated to a greater extent in different spheres of application?

There are two factors behind this phenomenon. First, research work, clinical practice and teaching are not just reintegrated into the scientific community but are at the same time exported, albeit to a lesser extent, to other groups. This is particularly true of research findings, which find their way into all the other categories : businesses, government departments, international organizations, voluntary organizations and even consumers. Research results are actually better distributed than may appear at first glance. The same is true to a lesser extent, and with some qualification, of education. Second, it must not be overlooked that these categories are permeable and flexible, that actors often belong to several simultaneously and that the results of the work carried out may be taken up by several at the same time. This is illustrated by table 12. A linkage index shows how the categories of secondary users are associated or juxtaposed for the purpose of making use of the primary users' work. This was calculated by relating the number of joint occurrences between two categories to the total number of cases in the smallest category. It indicates the maximum frequency for cooperation between actors from different categories on the same work or on different work from the same user.

TABLE 12 : SECONDARY USERS BROUGHT TOGETHER BY PRIMARY USERS

Source : Users' questionnaire, Question 13

	Govt.	Int.	Cons	Pract.	Res.	Acad.
Business.	0.43	0.40	X	0.47	0.79	0.59
Govt. dept.	X	0.74	0.55	0.60	0.68	0.60
Int. orgs.	X	X	X	0.68	0.78	O.68
Consumers	X	X	X	0.65	0.73	0.55
Practitioners	X	X	X	X	0.75	0.65
Researchers	X	X	X	X	X	0.85

There is a very significant degree of cooperation between academics and practitioners on the one hand and researchers on the other when it comes to processing the work of the primary users. Here again, then, we find a high level of interaction between actors in the composite scientific, clinical and academic community. Researchers have extensive contacts with all the other categories of actors, while the other two categories are more exclusive. This means that the work of primary users is very often taken up by researchers at the same time as by others. Government departments and international organizations have frequent contact among themselves, but very little with the private sector, which in turn has very little contact with consumers or practitioners. Elements of public policy and management strategy appear to be of use to both national and international organizations. The latter can really only hope to pick up elements of management strategy from private companies. The work of primary users passed on to firms, practitioners and consumers rarely involves any cooperation between these three categories of actors. For instance, the commercial development of a product is taken up by firms and to a lesser extent by consumers, but rarely by both at once.

To conclude, then, the transfer of the work produced by primary users appears, with the exception of the research field, to be relatively selective and exclusive to particular categories. The researchers play the pivotal role in

disseminating research, with other actors moving on the periphery with much less contact between them.

This concentration on the research aspect, both among participants in the programme and among primary and secondary users, is quite revealing, and highlights the intensely scientific nature of the health networks. A long chain of interconnections is often required, therefore, in order for medical innovation to get as far as the market. Is this structure inherent in the health care system? Is the process of making use of MHR4 necessariily a slow one, and is the European health care market hopelessly removed from it?

THE VARYING LENGTH OF THE NETWORKS FROM RESEARCH TO THE MARKET

The overall picture presented here needs to be qualified in some respects. First of all, the length of the networks is not unique to the medical sphere, but is characteristic of the pathway followed by scientific and technical innovation in numerous fields. Furthermore, while the non-research applications of scientific activity may sometimes take time, we have also observed that the point of production is very close to the end users, the patients. The laboratory is located within society and interacts, sometimes through intermediaries, with those who represent that society. For example, data on blood samples may be compiled, processed and compared by means of exchanges with European partners, and subsequently used in the treatment of patients, all by the same unit. The local combination of actors and intermediaries within the networks thus makes virtually instantaneous application possible. Interaction in the socio-medical sphere, therefore, is likely to produce speedy results. We have seen this to be the case in the large number of applications in clinical practice and education even at the primary use stage. In addition, the significant proportion of consumers (17%) among the secondary users suggests that certain activities are passed on quite quickly to the end user. The length of the networks arising out of MHR4 and the slowness of the transition from research to the market do not appear to be structural, but depend on the content of the concerted actions and the number of actors involved.

SIMULTANEOUS SHAPING OF RESEARCH AND THE MARKET BY THE NETWORKS

It has already been observed that the networks do not follow a single direction, but that dissemination takes place in both an upstream and a downstream direction. Equipment, software, reagents, samples, phantoms and sometimes even patients travel towards the research end of the spectrum, reaching even the concerted actions (see file 2). Scientific research and the market help to shape each other, with the intermediaries passing between the two via the networks. We can see, then, that there is not a one-way transfer of scientific produce towards the market.

As economists have shown, we are actually dealing with a system of loops with permanent action and counteraction between research and its application[6]. The market is built up and moulds research in accordance with these cycles, and there are no strictly defined pre-existing segments with gaps which can be filled

[6] S. Kline, N. Rosenberg, An overview of innovation, in R. Landau and N. Rosenberg (eds), The positive sum strategy, Chicago, Academy of Engineering Press, 1986.

exactly by research. Demand is expressed through "spokespersons" who guide research and are influenced by it[7]. This is particularly true as regards the creation of the European market, and specifically the creation of the health care market by MHR4. These spokespersons tend to be the public services and industrialists, or in some cases clinicians, all of whom, as we have already seen, were important participants in the concerted actions. This integration of the representatives of the market in the innovation process is essential.

Studies have clearly shown the need for involvement of these actors at a very early stage in order for innovation to be successful, particularly where medical technology is concerned[8]. In the MHR4 programme, the public health services represent 8% of participants and industrialists 1.4%. These relatively low figures (which, incidentally, rise significantly at the next stage, that of primary users) should not mislead us. The authorities have a decisive role to play in guiding the projects (see first section), while industrialists are closely involved in the content of projects, particularly the BME project. Their participation, moreover, is greater than the figures suggest, as they frequently participate as observers at meetings and workshops. Project leaders, project management groups or all the participants are often anxious to maintain a certain autonomy where they are concerned.

Individually the members of the concerted actions are in close contact with the industrialists, who sometimes finance part of their activities. Controlling the access of industrialists to information is not a sign of resistance in research circles to participation by outside bodies, but rather of a shift in the means of exchange, cooperation procedures, and transfers within the network, at the point where the interests of the market come into contact with those of research. This transition from one system to another, from scientific thinking to market-oriented thinking, is put into practice by the actors. This emerges from the descriptions of the individual contacts between participants in MHR4 and primary users in the public health services and industrialists/businesses categories.

FINANCING AND CONTRACTS: MARKING THE TRANSITION

When asked whether they made a financial contribution to any part of the activities of the concerted action, only 28% of users answered in the affirmative. Researchers, clinicians and even industrialists and businesses were below this figure. Only the public health services were above, and by quite a clear margin (40%). We must bear in mind that the European funds do not finance the actual content of the research, but rather the interchange between teams. As a result, the public health departments most likely finance a share of the research carried out under the concerted actions. As we have seen, however, they are not "sleeping partners" in the strict sense, as their various representatives sometimes play an active role within the networks they have helped to construct. Their role in finalizing research is probably quite important : the public authorities finance research work, but they expect a contribution towards achieving precise goals in return. This is perhaps what is behind the formalization of the participant/user

[7] On the notion of "spokesperson" see : M. Callon, Some elements of a sociology of translation...", The sociological review, 1986.

[8] E. von Hippel, The dominant role of users in...instrument innovation process, Research Policy 5, 1976 and : S. Blume, Insight and industry : on the dynamics of technological change in medicine, Amsterdam, 1990.

link, which appears to be well-developed in the "public health departments" category.

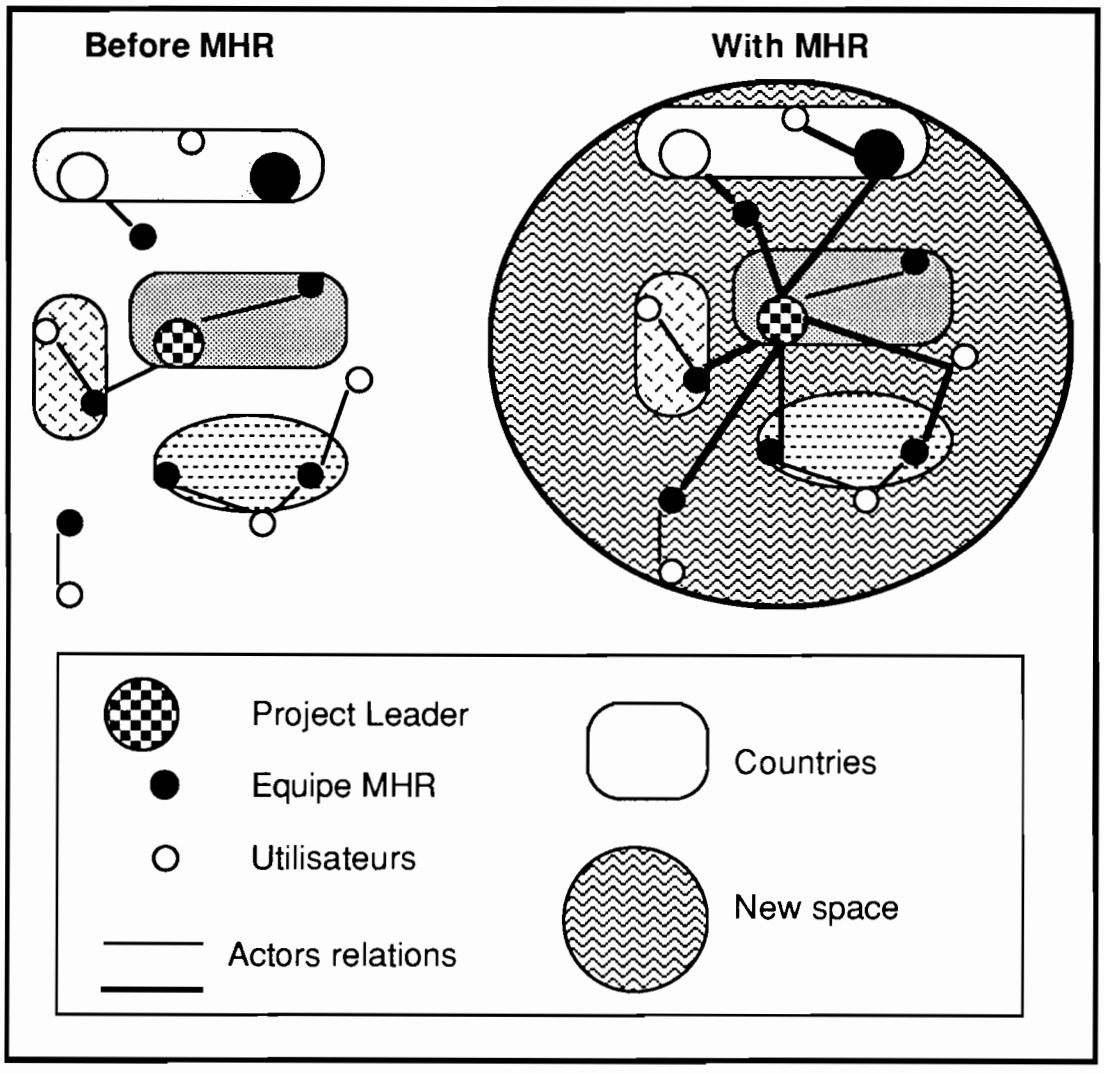
Fewer than one-quarter of users have signed a contract with MHR4 participants, and researchers and particularly clinicians fall short even of that figure. The public authorities, and above all industrialists and businesses are well above it. Some conclusions may be drawn from this information, to be confirmed subsequently. First of all, researchers and clinicians tend not to formalize their contacts, and do not exchange the products of the programme on a commercial basis. In this respect, as in many others, the research and medical community appears to constitute an entity which could be described as the scientific/clinical community. Interchange takes place on the basis of internal procedures such as the transfer of data and research tools or medical practices (see File 2). This community operates on a give-and-take basis and transactions involve professional renown rather than money[9]. The networks are characterized by contacts which receive little attention outside the immediate field.

By contrast, exchanges with actors outside this community require formalization, commitments, sometimes of a financial nature, and the sanction of the law. Industry and business provide little financial backing, but conclude a large number of contracts with participants. The public authorities fund participants, and back up this commitment with a contract. Let us look at one possible theory in this respect, which we will endeavour to substantiate later on. This states that industry and business do not provide direct funding for research with a well-defined direction, but rather anticipate possible developments which might justify their involvement. They monitor events and secure rights of use where appropriate, by means of contracts. The authorities help guide research and anchor the provisions adopted. They play an active role in making the strategic choices which form the backbone of the emerging market. Industry and trade remain geared up to join in once a path has been traced out. The comments of the primary users lend weight to this theory. Those in charge of administrative departments stress the links which exist between the activities of the concerted actions and their own planning, standardization and legislation activities concerning health care and services. Industrialists point to the need to be involved in the preparation of standards and the harmonization of the technical assessment criteria on which they issue and receive opinions. This theory is also backed up by the replies to the question put to users as to whether they already used the results of the programme or were likely to do so in the future. Those responsible for public health, as well as industrialists and businesses, see themselves largely as potential or future users, thus confirming the impresssion that they place themselves in a strategic position to anticipate future developments.

The strategic options outlined above are consistent with the kind of research traditionally labelled "precompetitive". Three out of four users believe that their cooperation with the participant does not result in the creation of a product destined for the market. Out of the 56 users developing a product for the market, 29 were researchers. Thus, 20% of them had this goal in view. The combination of research and commercial exploitation is therefore not particularly rare. By contrast, only one industrialist in two has his sights on the market. Despite the fact

[9] B. Latour, S. Woolgar, La vie de laboratoire : la production des faits scientifiques, Paris, La découverte, 1988.

that they are heads of marketing or R&D departments, they stress above all their interest in the generic development not so much of products but of new approaches to designing them. The concept of basic technological research takes account of this situation which largely takes over from the traditional split between basic and applied research. The number of patents arising out of MHR4 backs this up, with 28 participants (10%) concluding patent licensing agreements. One-third of these are in the biomedical engineering field, for the development of advanced equipment for medical practice. Sixteen of the patents related to marketable innovations. The remaining twelve are therefore tactical patents, designed to enable the participant to take an option on technological developments whose market application is very uncertain. Of the 56 innovations liable to be placed on the market, therefore, 40 are not the subject of a patent application. The transparency and the lack of protection suggest a certain lack of competition, at least at this stage of research.

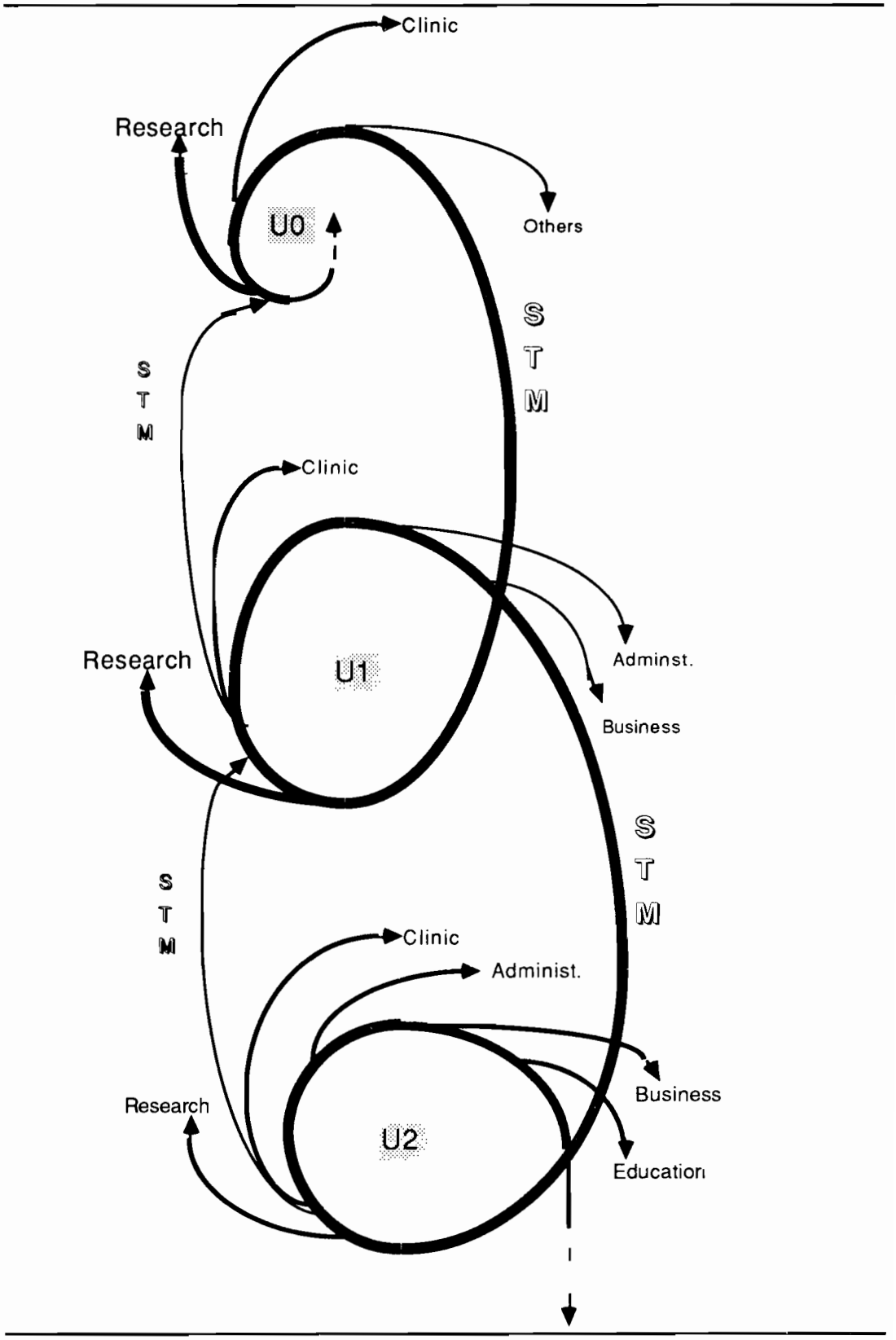


Once links have been established by the networks, market considerations and research merge at the basic research stage, where actors from the two camps join forces to create a European health care area. For this reason, the MHR4 programme has a real impact on the creation of a European health care market. New resources are created through contacts between a wide variety of actors, contacts which are made permanent by the networks. To be sure, the health care market is a very special one. Relations between versatile actors are one of its traditional features which MHR merely reinforces. However, it is a characteristic feature of the European programme that it systematizes and extends these local and disparate relations. In so doing it gives them an international dimension, thus creating a European field of operation for the actors, a sort of expansion chamber for the networks.

The above diagram clearly shows two network segments (A-B and D-E) which the programme connects. Thus two player-users very remote from each other (A and E) become aligned as a result of being associated with the MHR and thanks to the coordination of the project leader. The establishment of a new area is vitally important. The relations established between increasingly numerous actors reshape the context in which they are expressed. By establishing standards which enable remote actors to translate their realities, concerted action makes for harmonization transcending the limits of the network. The different segments of the network, which previously were national and limited, are linked up through concerted actions. MHR4 lends an international dimension to the European health care area by establishing multilateral contacts between actors.

CONCLUSION

We have travelled through the three stages in the build-up of the networks : participation in the programme itself, direct (primary) use of the results and use at a secondary stage via the primary users. We have seen the wide variety of actors involved at each stage, and the growing diversification and differentiation the further away we move from the concerted actions. Research plays a central role at each stage, although it becomes less and less dominant. It is never isolated from the other activities, from which it benefits and to which it makes a contribution. The fact that the networks are centred on research is by no means the sign of an autarkic science which reproduces itself at each stage. On the contrary, the research is fertilized by the other activities, which it in turn fertilizes at each cycle. This ongoing regeneration of research and the other activities is a source of renewal for the health care market, as part of a process of perpetual motion. The diagram next page describes this phenomenon.


Clinic
Research
U0
Others
STM
STM
Clinic
Research
U1
Adminst.
Business
STM
STM
Clinic
Administ.
Business
Research
U2
Education

Categories of actors :
U0: participants in the MHR4 programme
U1: primary users of the programme results
U2: secondary users of the programme results

Innovation pathway :
STM : Science - Technology - Market, long interactions
STM : Science - Technology - Market, short interactions

Dominant activities and actors' output :
Research : scientific research
Clinic.: clinical activity
Other : administration, commerce/industry, education...
Administ.: management, health policy
Business : industry, commerce, consumers
Education : academic teaching

This diagram depicts a rather simplified innovation pathway with inputs from the three corners of the triangle : science, technology, market. A distinction can be made between short and long interactions. The long interactions characterize innovations which aggregate new components at each level (U0, U1, U2) and which possibly return the product after several cumulative stages. Short interactions relate to the rapid recovery of results by those who transmitted their own output at the earlier stage. At each of the three levels the actors export their output : 1) the participants are concentrated under "research", "clinic" and "other" activities, 2) the primary users pay increasing attention to organizational and profitable applications (admin., business), 3) the secondary users reflect a more balanced distribution of activities and results (comparable importance of the different sectors of activity). There is therefore a gradual evolution at each stage which is enriched by the interaction with the preceding one(s).

The diagram reveals two other things: a) innovation is a two-way process, interactions are not one-way and may be reflexive; b) innovation is an infinite process : it is a composite phenomenon which has its origins in a multiplicity of instants and its final expression is only one among many. This cyclical process is far removed from the linear model which sees the market as the culmination of science. We can see here how important is the interaction between the two. The market cannot function properly without the scientific input, and vice-versa.

What is the value of this vortex? Given its great complexity, is it still a workable model for intervention by the public authorities? There can be no doubt about it. First of all, it shows the limits of conventional models, in the case of MHR4 at least. Finalizing research and shaping the market assume a new dimension. There is no such thing as the direct projectory of a natural research object to a target identified on a market. In fact, the actors gradually and simultaneously define all three. By slowly but surely laying the foundations they reduce the uncertainty inherent in the innovation process. This work takes place gradually through the network they build up. The public sector is actively present in the three levels

described where the pathway of innovation is concerned. It is involved in each level in various ways : international organizations, national public health services, local authority officials, etc. The public sector is not, therefore, the external, monolithic agency presupposed by the conventional conception of bureaucracy.

This new, network-based approach is characterized by the numerous actors, the cyclical nature of innovation and the different shapes assumed by the public sector. It is easy to see that it renders obsolete the simplistic ballistic models in which targets and direct projectories mark out the pathway of science. The network concept remains operative without reducing the player and the project to a specific perspective which takes little account of the innovation process. Public intervention is crucial in the perspectives opened by the network-based approach. However, it relates less to the initial fossilized definition of an innovation process than to support for the emergence of networks of actors which are the vectors of this process. MHR4 is an example of this new generation of programmes in which the "public sector" actor promotes transfers between all the others. The concerted action procedure whereby networks of different actors are built up therefore corresponds to a relevant strategic option taking into account the challenges facing Europe : ensuring the mutual adaptation of science and the market.

Commission of the European Communities

EUR 14700 - The Research Networks built by the MHR4 Programme

P. Larédo, B. Kahane, J.B. Meyer, D. Vinck

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The findings of the study were based on a participants' questionnaire (more than 1400 replies), in depth interviews with the project leaders (100 interviews) and in depth analysis of the programme's data.

The study is an effort to characterize contested actions and their dynamics by addressing the following questions:

a) who participates?
b) what does a network seek to achieve and how?
c) what is the involvement of the participating teams?
d) which are the non-academic results?
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