Commission of the European Communities

Evaluation of the Biomolecular Engineering Programme-BEP (1982-1986) and the Biotechnology Action Programme-BAP (1985-1989)

(Volume 1)

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Commission of the European Communities

Evaluation of the Biomolecular Engineering Programme-BEP (1982-1986) and the Biotechnology Action Programme-BAP (1985-1989)

(Volume 1)

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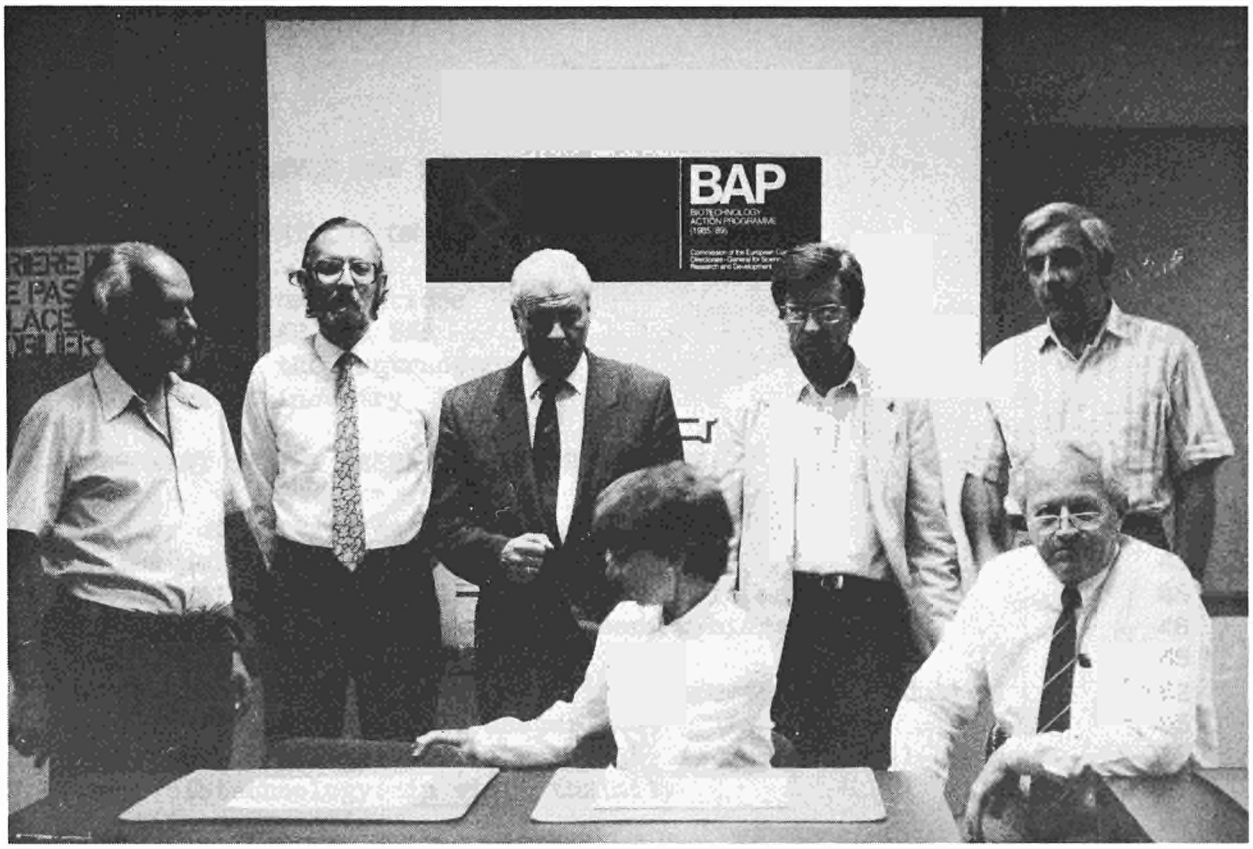
The biotechnology evaluation panel in Brussels.

From left : Fotis KAFATOS, Geoff WALKER, Günther SCHMIDT-KASTNER, Charlotte af MALMBORG (Chairman), Paolo SAVIOTTI, Jan KOEMAN (seated), Pierre FEILLET.



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List of abbreviations

AIM	: Advanced Information for Medecine
BAP	: Biotechnology Action Programme
BEP	: Biomolecular Engineering Programme
BIBRA	: British Industrial Biological Research Association
BIC	: Business and Innovation Centre
BRIC	: Biotechnology Regulations Interservice Committee
BRIDGE	: Biotechnology Research for Industrial Development and Growth in Europe
CEFIC	: Confédération Européenne des Fédérations de l'Industrie Chimique
CGC	: Comité de Gestion et de Coordination
COMETT	: Community programme to stimulate co-operation between university and Enterprises regarding Training in the field of Technology.
COST	: Cooperation On Science and Technology
CUBE	: Concertation Unit for Biotechnology in Europe
DG	: Directorate-General (of the Commission)
DNA	: DeoxyriboNucleic Acid
EBCG	: European Biotechnology Coordination Group
EBN	: European Business Network
EC	: European Community
ECLAIR	: European Collaborative Linkage of Agriculture and Industry through Research
ecu	: European Currency Unit
EFB	: European Federation of Biotechnology
EFTA	: European Free Trade Area
ELWW	: European Laboratories Without Walls
EMBO	: European Molecular Biology Organisation
FAST	: Forecasting and Assessment in Science and Technology
FEMS	: Federation of European Microbiology Societies
FLAIR	: Food-Linked Agro-Industrial Research
IRDAC	: Industrial Research and Development Advisory Committee
IPR	: Intellectual Property Right
kecu	: Thousand European Currency Units

Mecu	: Million European Currency Units
MINE	: Microbial Information Network Europe
MS	: Member State
NIH	: National Institutes of Health (US)
OECD	: Organisation for Economic Co-operation and Development
OJ	: Official Journal
OTA	: Office of Technology Assessment (US)
PREST	: Policy Research in Engineering, Science and Technology
SCIENCE	: Stimulation des Coopérations Internationales et des Echanges Nécessaires aux Chercheurs Européens
SD	: Standard Deviation
SE	: Standard Error
SME	: Small and Medium-sized Enterprises
SPRINT	: Strategic PRogramme for INnovation and Technology transfer
STD	: Science and Technology for Development

List of Countries

B	Belgium
D	Deutschland (Federal Republic of Germany)
DK	Denmark
E	Espana (Spain)
F	France
GR	Greece
I	Italy
IRL	Ireland
L	Luxembourg
NL	Netherlands
P	Portugal
UK	United Kingdom
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S	Sweden
US	United States of America

EVALUATION OF THE BIOMOLECULAR ENGINEERING PROGRAMME, BEP (1982-6) AND THE BIOTECHNOLOGY ACTION PROGRAMME, BAP (1985-9)

0. Executive summary : description, conclusions, recommendations, methodology.

0.1. Programme description

0.1.1. The first Community programme in biotechnology, BEP, was proposed by the Commission in 1979. It was approved by the Council on 7 December 1981 with a budget of 8 Mecu[1]. The programme was revised by the Council on 26 October 1983 and an additional 7 Mecu was provided[2].

0.1.2. The programme ran from April 1982 to March 1986. It contained two activities, research, which involved 50% support through contracts for some 103 projects, conducted largely in universities and public laboratories, and training, through fellowships awarded to some 77 Community scientists to spend 1-2 years in a laboratory in another Member State.

0.1.3. The research was sub-divided in five sectors :
- second generation bio-reactors
- animal husbandry and agro-food
- upgrading of plant products, particularly ligno-cellulose
- plants and organisms important for agriculture
- contamination detection and risk assessment.

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[1] OJ n° L375, 30.12.81, pp. 1-4

[2] OJ n° L305, 8.11.83, pp. 11-13.

0.1.4. The second Community programme, BAP, was proposed by the Commission in 1984. It was approved by the Council on 12 March 1985 with a budget of 55 Mecu*. The programme provided for a continuation of the research and training activities and aimed at:

- the establishment of a supportive infrastructure for biotechnology research in Europe;
- the elimination of bottlenecks which prevent the exploitation by industry and agriculture of the methodologies originating from modern biology.

Work was divided into a number of sectors under each subprogramme, as follows :

Subprogramme I : Contextual Measures

Bio-informatics

Culture collections

Subprogramme II : Basic Biotechnology

Enzyme engineering

Genetic engineering of agricultural species

Cellular and genetic engineering of microbial species important to industry

Risk Assessment

Genetic engineering for animal husbandry / novel methodologies of animal cell cultures

In vitro evaluation of the toxicity and of the pharmacological activity of molecules.

BAP also introduced a new element, concertation, with the objectives of "improving standards and capabilities in the life sciences, and enhancing the strategic effectiveness with which these are applied to the social and economic objectives of the Community and its Member States". Nine specific tasks were allocated to a special unit (the Concertation Unit for Biotechnology in Europe, CUBE).

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* O.J. N° L83, 25.3.85, pp. 1-7

0.1.5. The research work has continued to be mainly of a fundamental character conducted in public laboratories with open publication of the results. However applicants for contracts were required to form partnerships with laboratories in other Member States, and were also encouraged to seek written "expressions of interest" from industrial firms.

0.1.6. Under BAP, some 262 research contracts have been awarded to laboratories grouped in 95 projects. There were 169 "expressions of interest" from industry, but only 16 of the contractors were actually industrial firms. Some 189 fellowships have been awarded, the majority to relatively junior scientists (pre-doctoral or just post-doctoral).

0.1.7. Currently, the Commission are seeking a "revision" of BAP, which would provide an additional 20 Mecu to be committed up to the end of 1989. This would be used particularly for :

- research on risk assessment
- research on the application of information technology to biotechnology, including culture collections, genome sequences and protein modelling
- research contracts for Portugese and Spanish laboratories (who were not strictly eligible for most of BAP)
- a doubling of the training programme
- an increase in the staff of CUBE.

0.1.8. The third Community biotechnology programme, BRIDGE (Biotechnology Research for Industrial Development and Growth in Europe) is now in preparation. The Council have earmarked 100 Mecu for this in the second Framework Programme that was adopted last September[4]. In parallel with BRIDGE, there are or will be a number of other cost-shared research programmes relevant to

[4] O.J. L302, 24.10.87, pp. 1-23

biotechnology, listed below together with their budgets :

agro-industrial, ECLAIR[5]	80 Mecu
food-linked agro-industrial, FLAIR[6]	25 Mecu
tropical agriculture and medicine, STD2[7]	80 Mecu
agricultural competitiveness and resource use	55 Mecu

Some other programmes (medicine, non-nuclear energy/biomass, environment, SCIENCE) also include sectors relevant to biotechnology.

0.1.9. The biotechnology programmes (including CUBE) are administered by some 11 professional staff of the directorate for biological resources within DG XII in Brussels.

0.2. Conclusions

0.2.1. We consider that the research programmes have been well administered by a competent and enthusiastic Commission staff. They appear to have supported work of a good scientific standard, which has led to genuine trans-national scientific cooperation in Europe. The system for selection of contractors struck us as fair, if rather cumbersome, and it was based primarily on scientific merit. The process of contract negotiation seems to us often to have been slow, particularly in view of the rather small sums involved. But many witnesses told us that the monitoring of the work by the Commission staff had been very good, although they had not had enough time to visit all the contractors at an early stage. The contractors' and sectoral meetings appear to have been exceptionally well-run and useful.

0.2.2. The programmes have certainly contributed in a significant way to

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[5] European Collaborative Linkage of Agriculture and Industry through Research

[6] Food-Linked Agro-Industrial Research

[7] Science and Technology for Development, second programme.

the establishment of a supporting infra-structure for biotechnology research in Europe. Furthermore they have led to a number of substantial scientific achievements, as shown by the high level of citations and degree of transnationality. However we consider that the programmes' objectives were over-ambitious for the resources available, which were reduced by the Council. Moreover in some sectors goals to be attained and bottlenecks to be removed were insufficiently defined, and consequently significant breakthroughs were not made, perhaps because a critical mass of researchers was not assembled. In other sectors, such as the genetics of plants and of industrial micro-organisms, where goals were specified, some highly significant technical breakthroughs were indeed achieved, see Annex 3.

0.2.3. We have concluded that a major achievement of the research programmes, and one that is important for the future, has been to break down national frontiers between laboratories. We commend the Commission's initiative in linking groups into European Laboratories Without Walls (ELWWs), a useful concept that could be applied in other domains. We were impressed by the way some contractors, who had initially been sceptical about trans-national cooperation, were now enthusiastic. Indeed, transnational cooperation, once begun, may prove easier than national cooperation because the researchers are usually not direct competitors. There is evidence from our bibliometric study (see Annex 6) that BEP has brought about a significant increase in transnational cooperation among its contractors, and this trend must have been strongly reinforced under BAP.

0.2.4. Nevertheless, there have remained too many small unrelated projects. The size of most contracts (averaging 50,000 ecu/year), despite their undoubted value to certain research groups, was often too small to attract either significant industrial participation or (in some cases) leading academic groups in Europe. Because of the small size of the contracts it was very

difficult for us to identify how much has been achieved by a group that would not have occurred anyway, albeit perhaps slightly later.

0.2.5. Although there have been many "expressions of industrial interest", few firms have actually participated in BAP as contractors, and of these, even fewer are large. According to our survey (see Annex 2, 2.4.4-2.4.10) even now, almost two-thirds of European biotechnology firms claim to have insufficient or no information about the EC programmes. Another reason why firms may not participate is that in biotechnology even quite basic research may lead to patentable, and therefore commercially valuable, inventions. Industry fears that patent protection may not in fact be secured because of academic interest in publication. The consequence has been that industry has been shy of participating in the scientific meetings for fear of revealing too much, and on some occasions may not have been welcomed by the contractors from academe. Conversely, some of the work has been conducted by contractors without enough knowledge of what would be useful for industry, or indeed of whether industry has not already covered the same areas with its generally greater resources. However, many of the research groups told us that they had well-established contractual links with individual firms on a proprietary basis : there are therefore routes whereby commercial exploitation could occur.

0.2.6. From our many interviews with the fellows, their supervisors, and former fellows under BEP (see Annex 4), we have concluded that the training programmes have been successful. We have noted the good standard of the fellows, and of the training they have received, the utility of the fellowships in helping them obtain employment, and the continuing transnational links between fellows and their host laboratories. We found that virtually all the fellows were glad to have stayed in Europe, rather than going to the USA, and this augurs well for future European linkages.

0.2.7. However we think that the training programme is currently poorly marketed and therefore undersubscribed, and we discovered that contact between the fellows and the Commission is minimal. The fellows are not well informed about the European Community and its work in biotechnology, and some of them see little of their host country except the lab in which they work.

0.2.8. The concertation activity has been characterised by an enormous volume of work, but although there have been some successes (the new sugar and starch regimes, and the ECLAIR proposal, for example) there have also been some failures (lack of agreement on the approach to a European regulatory regime, little use of the elaborate data base, poor public understanding of the advantages of biotechnology and the nature of the attendant risks, no coordination of inputs from other DGs to the research carried out in BAP). The problem seems to have been that the concertation tasks were too numerous, and more difficult than was originally realised. The lack of permanent secretarial assistance for CUBE has also been a handicap. The consequence has been that CUBE's efforts have been dissipated too widely, and it has not had enough time to look at some important longer-term issues.

0.2.9. Biotechnology research is a highly competitive activity world wide. The European position is currently quite strong in some sectors, e.g. plant science, but is weak in others, such as microbiology. It is clear that a continuing investment in fundamental scientific understanding is needed for commercial success. It is also clear that, although some commercial developments will occur fairly soon, others will require a decade or more to come to fruition, notably in plant science where much work remains to be done on plant physiology. Industrially, a major European weakness, with limited exceptions, is the lack of vitality of the small science-based firm sector. Most of the industrial research takes place in large companies, but they are,

as noted earlier, little involved in the EC research programmes.

0.2.10. Two European handicaps relative to the US were repeatedly mentioned to us, namely the lack of a soundly-based common regulatory regime, and uncertainties on intellectual property rights (IPRs). These are serious "bottlenecks" preventing the exploitation of the European scientific strengths.

0.3. Recommendations

0.3.1. We recommend that the research programme of BRIDGE should be divided into three parts. The main part, which should absorb 45% of the total budget, should be clearly focussed and directed towards the solution of major trans-European problems through large-scale projects. The second part, with 25% of the budget, should consist of science-led projects in response to an open call for proposals. We have given some specific suggestions in Annex 3. The third part, with 5% of the budget, should be coordinated action, building on the existing COST 48 and COST 87 Projects, in which the Commission would pay only for scientific meetings and short-term exchanges. We recommend that the Commission should also seek to use the fellowships from the training programme to provide additional support for these cooperative projects and for those ELWWs that show promise.

0.3.2. The large-scale part of the research programme should involve a limited number of major multi-disciplinary projects. The Commission should appoint an external or internal project manager for each project. Each project should have a budget sufficient to support a critical mass of researchers. Individual contracts should be large enough to attract high quality European research laboratories, including industrial firms where appropriate. Nevertheless, in most areas it would not be appropriate to insist on industrial contributions, although active participation through secondment of industrial staff to research centres should

be encouraged. Where industrial contributions are required, we recommend that the Commission should take account of the size of the participating firms and set stiffer targets for large companies.

0.3.3. Among the large-scale projects that we consider should be the subject of particular initiatives are the following :

1. To sequence the yeast genome completely.
2. To develop detailed molecular genetic maps for one plant and one animal species of economic importance to Europe.
3. To undertake a focussed programme in protein engineering so as to understand and modify in a multi-disciplinary manner the structure and biological and/or physical properties of a few proteins.
4. To elucidate the control of gene stability, transcription, post-transcriptional and post-translational processing, protein over-production, and secretion in one major industrial micro-organism through genetic manipulation, biochemistry and cell physiology.
5. To apply recent progress in molecular biology to the physiology and improvement of major European crops, including gene transfer to, and cell regeneration of, cereals.
6. To establish a complete interconnexion and cataloguing system for the major culture collections in all Member States with on-line access, for a fee, by all research workers. A pilot scheme, involving the current BAP contractors, should achieve these objectives by 1991.
7. To continue to develop appropriate methodology for an assessment of the safety and ecological consequences of the release of genetically-modified organisms, especially bacteria and viruses, in order to develop guidelines for best practice in the production and use of such organisms.

Except where noted otherwise, the above goals should be attained by the end of the BRIDGE programme, and most of them by 1994.

0.3.4. We recommend that these large-scale research projects should be organized through a framework developed by the appointed project manager in close cooperation with the Commission' services. This framework should be used to invite applications from potential contractors, or consortia of appropriate laboratories, from throughout the Community. The strategy for each project, and the individual proposals, should be appraised by ad hoc committees invited by the Commission that include industrial experts and members of other Commission services as appropriate. The selection criteria should be based on scientific merit and relevance to the project goals.

0.3.5. The training programme should be expanded to absorb 15% of the total budget of BRIDGE and provide about 50 grants per year. It should be more vigorously promoted, with a target of at least four candidates per fellowship. The normal tenure should be two years, extendable exceptionally to three. The objective of the fellowships should be to provide training in disciplines currently in critical supply, either locally or throughout the Community.

0.3.6. The training programme should be managed by at least one full-time professional staff member. Short-listed candidates should be asked to attend an interview and briefing in Brussels before appointment. The fellowship manager should maintain contact with all fellows during their tenure and hold occasional informal meetings of fellows in a Member State or region. He or she should also maintain and publish a directory of all EC biotechnology fellows, past and present, and their supervisors.

0.3.7. The level of monthly payments to the fellows should be reduced by 10%. However the money saved should be used for an approved programme of travel primarily within the host country, occupying about two weeks per year of tenure. Bench fees should be paid in

respect of junior fellows, as well as for senior ones, and negotiated with host laboratories.

0.3.8. The concertation activity should also be expanded in line with the general growth of the biotechnology research programme, to about 10% of the total budget of BRIDGE. We propose that Task Forces for major initiatives which involve the work of several DGs should be created as necessary. The need for such task forces could be identified by CUBE, but they would be distinct from CUBE as at present constituted. They would be temporary and report to the Commissioner for Science Research and Industrial Affairs. They would need a leader of sufficient status to ensure effective decision-making. The operating cost of these Task Forces would be paid from the 10% earmarked for concertation.

0.3.9. CUBE should concentrate on four major tasks, of which the last is new :

1. The coordination of the Commission's approach to biotechnology, including the dissemination of information internally (currently task 3), and the formulation of proposals for future initiatives.
2. The concertation of biotechnology activities of Member States.
3. The provision of information on the advantages, limitations and safety of biotechnology to politicians, scientists and the general public in the Community and in Associated States under the Lomé Convention (currently tasks 6 and 8).
4. Activities designed to promote the formation and growth of small and medium-sized biotechnology firms.

0.3.10. In order to undertake the third task, CUBE should recruit one or more experts in communications and should devote funds to the production of suitable educational and other material, including translations.

0.3.11. We recommend additionally that the research programme in biotechnology should be opened to the EFTA countries, on a programme or project basis, so that leading research teams in these countries may be integrated in the European scientific networks, as they have been under the two COST Projects.

0.3.12. We have advocated a focussed programme emphasizing carefully selected goals. We must note, however, that important sectors of biotechnology, such as separation technology, downstream processing and health biotechnology, are not at present covered in the BAP programme. Furthermore, the overall level of funding is inadequate to support the expanded coverage and intensified effort which are necessary for Europe to be competitive in the important and rapidly evolving field of biotechnology. Therefore, given the long-term strategic importance of the subject, we strongly recommend that the funds for biotechnology should be increased in the revision of the Framework Programme expected during 1989.

0.4. Methodology

0.4.1. We were appointed to serve on the evaluation panel as individuals and not as representatives of countries or institutions. Nevertheless our varied nationalities (D, F, GR, I, NL, S, UK) and backgrounds (four of us have academic posts, three are or have been in Government, and two in industry) have helped us to understand the programmes. Our terms of reference are set out in Annex 1. We have tried to keep them constantly in mind but have not attempted to answer every question mechanically.

0.4.2. We have, in particular, concentrated on the impact of the programmes and certain organisational issues, rather than the scientific merit of the individual projects. Our principal source of evidence has been personal interviews, but we have also been given access to many reports published by the Commission's

programme managers and other literature (see Annex 8). During the evaluation, we have met five times in Brussels as a panel, and we have undertaken missions in groups of three, totalling 17 days, to eight Member States. These missions afforded us time to get to know each other well, and helped us to work together effectively as a group. We commend the method to other evaluation panels.

0.4.3. In Brussels, we have received presentations from, and had individual discussions with, all the programme managers. We have had meetings with the current and two past CGC chairmen, and with CGC delegates from ten of the twelve Member States. We have also met Commission officials from DGs III, VI, VIII, XI and XVII.

0.4.4. During our missions we arranged interviews, typically of 3/4 hour, with some 84 contractors or their representatives. Most of these were in central locations but we were also able to visit a few laboratories to see work in progress (mostly in the plant sector). We interviewed some 23 current fellows and 21 supervisors, and also 9 former fellows under BEP; these interviews typically only lasted 20-25 minutes but they gave us a valuable insight into the training programme (see sections 4.4, 4.5, 4.6). We were rather less successful in securing interviews with industrialists and have commented elsewhere on this paucity; nevertheless we managed to see 24 of them, including several members of the IRDAC Working Party on biotechnology.

0.4.5. In order to study on a more quantitative basis the main output of BEP, namely scientific publications, we asked for a small bibliometric study to be carried out for us by the University of Manchester. A synopsis of the results is given in Annex 6. The purpose of the study was essentially two-fold :

- to see if BEP papers were more transnational than other biotechnology papers with EC authors;
- to see, through their citation record, if BEP papers had had a

significant impact on other scientists.

0.4.6. We received written representations from 13 external correspondents, following the circulation to the technical press and to biotechnology associations of an open invitation to interested parties to submit evidence. We circulated a written questionnaire to former BEP fellows whom we were unable to meet, and received 21 replies. We also sent out a written questionnaire to some 210 industrial firms, most of whom had not been involved with the programmes, to ask why not : we have so far received replies from 60 (see section 2.4.).

0.4.7. A full list of all the witnesses who kindly made themselves available to see us, and those who took the trouble to write to us or return our questionnaires, is given in Annex 7. We should like to express our appreciation of their help, and to record in particular our thanks to all the programme managers who were unfailingly courteous in their responses to our enquiries and in the provision of help. We would also like to add to this our thanks to Mr. Luigi Massimo, Head of the Evaluation Unit, and to our Secretary, Dr. Grant Lewison, who has applied a continuing enthusiasm and professionalism to the vital job of organizing the work of this panel. The task of evaluation has been positively agreeable, largely because of the warm and friendly reception that we have been accorded both in Brussels and during our travels, notably in several of the Commission's press and information offices in Member States.

Charlotte AF MALMBORG (Chairman)

Pierre FEILLET

Fotis KAFATOS

Jan KOEMAN

Pier Paolo SAVIOTTI

Günther SCHMIDT-KASTNER

Geoff WALKER

Brussels, 30 June 1988

ANNEX 1

TERMS OF REFERENCE AND MEMBERSHIP

1.1. The panel is composed of persons who are appointed by the Director General for Science, Research and Development (DG XII), as individuals and not as representatives of particular organizations or countries. Their views in no way commit their employing organizations. They are required to keep confidential any evidence, written or oral, submitted to them that witnesses indicate should be so treated.

1.2. The panel is to evaluate the Biomolecular Engineering Programme, April 1982-March 1986 (BEP), and the Biotechnology Action Programme, January 1985-December 1989 (BAP), although the latter is still in progress.

1.3. The panel is to assess :

1.3.1. the scientific and technical achievements of the programmes taking into account their original objectives and milestones, and whenever relevant of changed circumstances;

1.3.2. the quality and practical relevance of the results including (whenever relevant) commercial development and exploitation, and possible spin-offs;

1.3.3. the effectiveness of management and of the use of ressources;

1.3.4. the programmes' contribution to the development of Community policies and to the social and economic development of the Community;

1.3.5. the benefits resulting from the implementation of the programmes at the Community level (Community added value).

Quantitative indicators will be used whenever appropriate.

The panel's assessment of achievements and benefits should take into account the expenditures applied.

1.4. The evaluation should lead to recommendations on the following :

1.4.1. the future continuation, alteration, or termination of biotechnology research by the Community;

1.4.2. the management of the programme;

1.4.3. the use of research results by organizations carrying out the work;

1.4.4. the transfer of technology to other organizations, by movements of personnel, by licensing, and by other means.

1.5. The panel, in making its assessment of the programmes' achievements, should give particular attention to the following questions :

1.5.1. whether the programmes have brought or are likely to bring about several highly significant breakthroughs;

1.5.2. whether the programmes have already attracted the interest of European industrial firms, as shown by their participation in projects and recruitment of scientists who have worked on them, and whether at least half the projects are likely to lead to additional development expenditure by European industrial firms of sums greater than the total expenditure on projects supported by the programmes;

1.5.3. whether the work supported by the programmes has removed or is likely to remove previously identified "scientific bottlenecks" and in particular has led or will lead to :

- significant improvements in fermentation technology;
- new or improved germ plasm which could be introduced in breeding programmes for the development of crops needed for a market-related agriculture in Europe;
- new or accelerated methods to produce plants and seeds for commercial sale;
- the detection, prevention, or treatment of diseases of farm animals or agricultural crops;
- improvements in the safety and quality of animals and crops for consumption or processing;
- solutions to environmental problems;
- improvements in the time, cost, and level of assurance for the demonstration of the safety of new biotechnological products and processes;
- improvements in the testing of new products on cell cultures rather than animals;
- the scientific basis for new or improved regulations governing biotechnology in the European Community or in individual Member States.

1.5.4. whether the training provided to the trans-national fellows has been given by laboratories of high scientific quality and whether the fellows are subsequently employed in Europe where they can make good use of their training;

1.5.5. whether the programmes have led to effective trans-national collaboration on a continuing basis between scientists and laboratories in different Member States, whether there has been an increase between 1981 and 1986 in the proportion of scientific papers in leading journals in biotechnology published by

laboratories participating in the BEP that have authors from more than one Member State, and if so, what proportion of this increase can be attributed to the programmes;

1.5.6. whether there is clear evidence of trans-national marketing of biotechnology research facilities, resources and support services in the Community as a result of sub-programme 1 of the BAP, and whether this is leading to increased trans-national demand for such services;

1.5.7. whether the concertation activity has effectively executed the nine specific tasks listed (as Action II of the Council Decision of 12 March 1985) and whether through these activities or otherwise this action has enhanced the application of biotechnology to the social and economic activities of the Community and its Member States.

1.6. Subject to the prior approval of the Commission, the panel members may travel within the Community to interview persons about the programmes and to see work in progress. Subject to the same approval, the panel may also retain consultants or experts in order to examine particular questions in detail.

1.7. The panel is required to produce a report by 30 June 1988. This report will be published by the Commission. The panel may also prepare a confidential annex for the Director General of DG XII if it feels that this is desirable and necessary.

1.8. List of panel members

Chairman :

Dr Charlotte AF MALMBORG (S)
Department for biotechnology and life sciences
Swedish National Board for Technological Development
Stockolm

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ANNEX 2

GENERAL OBSERVATIONS ON THE PROGRAMMES

2.1. Evaluation considerations

2.1.1. Any programme has strategic goals, an internal organisation or structure, and produces impacts. All three can be evaluated ex-post, and the first two can, in principle, be appraised ex-ante. Different evaluation criteria will be appropriate for the three aspects of the programme. Thus for the goals, one can consider whether they are correct, appropriate and consistent; for the structure, one can describe and parametrise the mechanisms; for the impacts, one can list the types of benefit-social, economic, etc.

2.1.2. For BEP, the stated goal was the removal of bottlenecks preventing application of molecular and cellular biology to agriculture and the agro-food industry. The structure consisted of shared cost research contracts, contractors' meetings, and training contracts. The expected benefits were the removal of these bottlenecks, a general improvement in European scientific capability in biotechnology, and transnational cooperation. For BAP, the research goals were extended to include the improvement of the infrastructure and better means of risk assessment, and certain other goals involving concertation were added. An additional structure, namely CUBE, was provided. The benefits should also have included the construction of a European infrastructure in bio-informatics and for cell cultures, and better knowledge and control of bio-hazards deriving from biotechnology.

2.1.3. The criteria for the evaluation of the goals of a research programme are not absolute, but they have to fit with the general economic and political goals of the programme sponsor, here, the Commission. Under the second Framework Programme for R&D adopted

by the Council in September 1987, there are five conditions under which Community action can be justified :

- When the work contributes to the cohesion of the Community and to its harmonious development.

- Where the work is on a large scale so that individual member states could not otherwise afford it.

- When the work would save money through avoidance of duplication.

- When the work addresses trans-national problems and requires coordinated efforts (e.g. on pollution).

- When the work contributes to the achievement of the Common Market e.g. through standards.

Goals should also be coherent and verifiable. For scientific programmes, the consideration of the goals should take into account the development of the relevant science, and of the associated technology, as discussed below.

2.1.4. The criteria for the assessment of programme structure involve the detailed description of the procedures used to implement the programme, with numerical data. Thus for the research contracts information is needed on :

- total number of contracts
- distribution by technical sector
- distribution by type of contractor (university, industry, etc)
- distribution by country

and for each contract :

- duration
- value
- number of participants

- contact with industry
- subsequent trans-national activity of participants.

For the contractors' meetings one needs to know :

- number of meetings and topics
- participants at each, including contractors, industrialists and others.

For the training programme, the examination should cover :

- distribution by duration, and senior/junior level
- total number of fellowships
- matrix of fellow's country/host country
- criteria used for selection

and for each fellowship :

- the scientific reputation of the institutions involved
- previous experience of fellow
- experience of fellow during training (problems, publications, etc.).

2.1.5. The impacts and benefits should be fairly straightforward to evaluate if the goals have been stated in a verifiable form. Several types might be considered :

- scientific, through the effect of the research on other scientists, e.g. through their citation of publications and other measures of esteem;
- economic, through the development by industry of new products and processes, although this may not occur for some years and even then the link may be indirect;
- social, through the formation of intra-community links for research and other purposes. The improved cohesion of the Community's less-developed regions with the rest should also be considered.

However it is important that there should be a plausible link between the means used to implement the programme and the expected benefits.

2.1.6. We next consider some general points on technological change that pertain to the evaluation of BEP and BAP. Biotechnology is not a single technology but a series of technologies all of which use biological materials as inputs. The span stretches from traditional fermentation processes (cheese, wine) to protein engineering whose products are barely emerging. Now several theories of technological innovation postulate a series of qualitatively-different stages :

- emergent : heavy dependence on basic science, variety of organisations involved, slow growth of sales;
- new : many product designs, incomplete technology, sales expand rapidly;
- mature : dominant design, well-established processes and organisations, sales growth reduced, but possibility of technology rejuvenation exists
- obsolete.

The above model can help us to assess the prospects for development of different technologies. We should also be aware that, although technology is visibly embodied in machinery and goods, which constitute the revealed technological performance of the industry, it depends equally on the "knowledge base" of industry, i.e. individual skills, design and operational procedures, and communication patterns. The competitiveness of industry depends at least as much on the latter, especially in the early stages of the innovation process.

2.1.7. Individual firms can choose between a number of innovation strategies[1] :

- offensive
- defensive
- imitative

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[1] Freeman, C "The economics of industrial innovation", Francis Pinter, London, 1982.

- dependent
- traditional
- opportunist

The higher up the list a firm chooses to go, the more it will depend on a high level of research and development in order to be first to bring a new product to market. It is valid to consider what is the most appropriate innovation strategy, not only for an individual firm, but for European industry as a whole.

2.1.8. Ergas[2] has classified rational technology strategies as mission-oriented or diffusion-oriented. The former implies the support of large projects, such as for defence procurement. The latter implies the aim of spreading awareness of new technology to many firms in the sector so as to enable them to use best technological practice. Finally, new technologies may be limited in their application, or of value in many industrial sectors, when they are sometimes called "generic". An example is microelectronics.

2.1.9. We are thus led to ask the following questions :

- Is biotechnology sufficiently homogeneous that a common policy can be defined at the national or European level ? If so, can a life cycle be defined and its present position identified ? If not, can we do this for different sectors such as brewing and the production of monoclonal antibodies and identify the the likely influence of research and consequent benefits?
- Do we need to choose a pattern of specialisation at either the national or European level ?

We note that in biotechnology the USA appears strong in the application of recombinant DNA techniques in pharmaceuticals and diagnostics, and Japan in industrial fermentation for fine

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[2] Ergas, H. "Does technology policy matter?" OECD, Paris, July 1986.

chemicals and the food industry, whereas Europe has strengths in antibiotics and plant science.

- Should Europe aim to remain a leader in selected areas and concentrate its research efforts there ? If so, how much work is needed to keep abreast of developments elsewhere in other sectors ?
- How strong is the "knowledge base" of European research institutes and industrial firms, both individually and transnationally, in comparison with their competitors elsewhere ? (This implies a careful monitoring of research capabilities.)
- Is it important or necessary to adopt different innovation strategies (see Freeman, op. cit.) for different sectors of biotechnology either at the national or European level, bearing in mind that the Member States vary in their degree of development ?

2.1.10. In summary, it seems appropriate that the strategy for biotechnology in emergent and new sectors should be flexible, and be based on an analysis of existing developments. On the other hand, a strategy for more mature sectors, where the development patterns are clearer, could involve the concentration of resources on a few large projects. Similarly, it would be wise to restrict decisions about patterns of specialisation to these more mature sectors.

2.2. Overview of BEP and BAP

2.2.1. From written and oral evidence to the panel we agree by and large with the analysis of the programmes made by the staff of the Commission. The scientific quality of the work is very good, shown inter alia by the number of publications in renowned scientific journals. The degree of transnationality achieved is impressive. Many contractors express a clear opinion about the importance of going European. Hence, two of the main goals from

the onset have been reached.

2.2.2. In BEP the main topic of interest was genetic engineering for agriculture. The topic with least attraction was risk assessment. The same tendency is prevalent in BAP where the majority of contracts are on the biotechnology of microorganisms, plants and animals and there are still few on risk assessment. This reflects the worldwide interest in molecular biology instilled by the economic prospects attributed to this area. However the road is long, costly and full of pitfalls before a commercial product can be brought to market.

2.2.3. To what extent scientific bottlenecks preventing the exploitation of modern biology have been eliminated through BEP and BAP is hard to say. Our impression is that the scientific merits are more dominant than the industrial ones. Few industrial firms have in fact been active in the contracts. The reasons for this include the small size of the contracts, the lack of information to industry, the emphasis of the programmes on basic long term research, fears about loss of IPR, and the reluctance of some firms to do research with their competitors. There was also a lack of commercially-oriented and verifiable goals. As the work under the BEP and BAP was intended to be precompetitive, verifiable goals would have been difficult to define. The aim of BEP and BAP was to introduce new knowledge, and so the goals had to be science-driven. For BRIDGE, however, conditions are more favourable for a major part of the work to be objective-led.

2.2.4. When goals cannot act as steering signals coordination activities become more important. Here the programme managers have played a key role. We are impressed by their drive, enthusiasm and skill in running the programmes. This is confirmed by the witnesses we met. The programme managers' efforts are highly appreciated. They have effectively contributed to the establishment of the European network in biotechnology which is now in existence.

This has been achieved by the collaboration itself as well as by the different initiatives taken by the programme managers :

- establishment of the ELWWs (European Laboratories Without Walls)
- arrangement of sectorial meetings
- programme managers' visits to contractors
- programme managers' attendance at sectorial and other scientific meetings
- invitations to leading experts in the world to meet and discuss with the contractors
- efforts to convey the message that there is more behind the Commission than just money.

2.2.5. Scientists have and should have one thing in mind - to pursue their science, so they look for resources. Quite naturally BEP and BAP meant to them from the beginning chiefly a new source of money. Indeed, although the Community Biotechnology programme is relatively small, it is impressive how important it has become for even some of the best research groups in Europe, because of its flexibility and its awarding on the basis of merit. An additional widely recognised value of the programme is its transnationality. Without the coordination activities by the Commission's services this would not have been possible. On the national side CGC delegates and national programme managers have contributed by their involvement in the selection procedure for, and the marketing of, the programmes.

2.2.6. We regard the selection procedure as fair but too cumbersome. Under BEP 103 contracts were negotiated from 293 applications. Under BAP the figures were 262 and 1357 respectively. Fears were sometimes expressed to us about the work load in coming programmes. This is one reason why we believe that a major part of BRIDGE should comprise a limited number of major multi-disciplinary projects.

2.2.7. The relationship to national or to other Community programmes is not clearly specified. On the national level it is important that the support is complementary to the Community's. There should not be a reduction of funding on the national level for contractors who have been successful on the EC level - a fear which was expressed in several countries. On the Community level it is important not to divide the resources among too many small projects so the contracts become subcritical in size. Also good applications may have to be turned down if they do not fulfil the requirements set out.

2.2.8. The marketing both of the scientific and the training programmes could probably be more systematic and thus more efficient. Opinions expressed by some witnesses were that
- not all good scientific groups are involved
- the topics are not all of true European interest
- the number of applications for training grants is too small to permit a rigorous selection among candidates (see Annex 4, section 4.1.4).

2.2.9. It has been difficult for us to get a clear view of to what extent industry has adopted the results from BEP or BAP. We have met only a few industrialists. They were positive about the existence of the programmes but did not express a deep commitment, and some were concerned that the industrial relevance was weak. Therefore we consider that it is important to involve industrialists in the future selection procedure, as is planned for BRIDGE.

2.2.10. Under BEP, twelve patent applications were filed and under BAP, contractors are encouraged to protect their results through patenting. Here a note of warning may be appropritate. It should be borne in mind that the role of a patent is to protect an invention and not new knowledge. To file an application and to hold a patent costs money. Patent expertise and the necessary

financial resources should be sought as soon as it becomes apparent that an invention has been made. In biotechnology it has often been claimed that commercialization follows closely on the scientific result but this is in fact rare.

2.2.11. An even more important obstacle for commercialisation of biotechnology in Europe is the lack of appropriate and uniform regulations, which take into account safety as well as expected benefits. An important task for the future is therefore to achieve harmonisation of the regulatory framework for biotechnology in the EC Member States. We endorse the principle recommended by OECD that the safety of products should be assessed through their inherent properties and not through the nature of the process by which they were made.

2.2.12. Dissemination of results from the programmes has been through reports, articles, papers and meetings. The meetings have been highly appreciated for being well organised and very informative. But opinions regarding the printed material vary from "too bulky" to "too scarce". It therefore seems advisable for the Commission to analyse further who are the recipients of the information and what measures they are expected to take after having been informed. It is very important that people are well informed and that the information is at the right level.

2.2.13. Before the advent of BEP and BAP, biotechnology in Europe was fragmented and dealt with solely on a national basis. Now an infrastructure has been established with nodes of excellence in many areas. We have seen clear evidence that in plant molecular genetics, Europe is considered to be competitive and even ahead of the United States. There is a growing supply of trained people with skills appropriate for the further development of biotechnology. Many of them have been trained in Europe. The US is no longer regarded as the ultimate training site.

2.2.14 However, much remains to be done before biotechnology can have its full impact on European society. For the future it seems necessary to concentrate on issues of importance to Europe and to set out verifiable goals. Harmonisation of legislation, information network systems and culture collections, safety assessment, and information to the public based on scientific facts are all areas where increased activity and coordinated action on a European level is desirable.

2.3. The views of the contractors

2.3.1. During our missions, we met some 84 contractors or their representatives, who were responsible for a total of 27 out of 105 BEP contracts (26%) and 78 out of 274 BAP contracts (28%). They were taken from those who responded positively to the panel's original invitation to some 176 contractors : these were chosen purely on a geographical basis as being located near to the cities that panel members could conveniently visit in the time available.

2.3.2. The interviews lasted, on average, about 45 minutes and normally began with a short presentation by the contractor of the research work and the results obtained. Our conclusions on the work carried out in the different sectors are given in Annex 3. In the paragraphs below we give a summary of the contractors' views on a number of organizational issues.

2.3.3. One question sought to determine whether the EC contract had affected the directions in which the contractor's group's research had gone. For four (5%) a new area had been started, for 18 (21%) it introduced a major change, and for 17 (20%) it made a modest but significant change. It thus appears that the EC programmes have caused some noticeable changes of direction for about half the contractors.

2.3.4. There was usually a lot of discussion about trans-national cooperation. Although some contractors expressed scepticism about the genuineness of other trans-national links, none doubted the value of their own. In fact, the greatly increased volume and intensity of such collaborations was one of the most striking features to emerge. Thirty one respondents (37%) had much more positive attitudes and a further 35 (42%) were a bit better disposed to them. One contractor commented that because of competition between researchers within Member States, trans-national cooperation was in some ways easier.

2.3.5. Attitudes to trans-national links between industrial firms and research centres/universities were less easy to determine. Links seemed to remain largely with firms in the same Member State, but 9 contractors (11%) now had much more positive attitudes to trans-national associations, and 21 (25%) were a bit more positive.

2.3.6. Community support for research is normally limited to 50% of the costs, and one question asked who provided the remainder of the money. The overwhelming answer was government; 64 or 76% mentioned support by national or regional organisations. Some 27 (32%) referred to the receipt of industrial support, quite often through the secondment of an industrial scientist to work in a university or through contract research placed with the group, (In France and Italy, because of employment legislation, EC money was used only for equipment, consumables, and travel, not for personnel; elsewhere each contract typically supported one post-doc and a student or technician.)

2.3.7. A later question concerned the means whereby the research work supported by the EC might be exploited commercially. The principal route (where one was specifically identified) was through contract research (18, or 21% mentioned this); patenting and/or licensing would be undertaken by 11, or 13%. Six

contractors referred to movements of personnel, such as industry hiring a scientist from the project or paying for a fellow. One of the contractors had set up his own firm to exploit his discoveries.

2.3.8. Finally, contractors were asked to comment on the way the Commission had administered the programme. Some of them gave ratings on five aspects, and the table shows the percentages of responses in different categories:

	Excellent	Good	Fair	Poor	Abysmal	No rating
Call for proposals	2	11	4	17	1	65
Selection process	4	8	6	2	0	80
Contract negotiation	0	12	4	14	1	69
Progress monitoring	11	32	2	5	0	50
Dissemination of results	12	13	2	2	1	70

2.3.9. As the table shows, the main areas to be criticised were the call for proposals and the contract negotiations. Major complaints were the short notice provided and that the application procedure was cumbersome, especially in view of the small size of the contracts. Several contractors felt that there should have been clearly-defined goals but one took the opposite view and suggested that there should be encouragement for work that might lead to unexpected results. The problems with contract negotiation almost all involved the long time required, although in some countries there were problems about the ownership of equipment only part of whose cost had been met by the Commission. On the other hand, the EC money was flexible and could be used for different purposes if needs changed during the course of the work.

2.3.10. The programme managers were clearly highly regarded, alike for their very helpful individual visits to laboratories as for their organization of sectoral meetings. Time and again contractors said how useful these had been, how they had led to good trans-national contacts, and how they had thereby helped the research.

The enthusiasm and professional abilities of the Commission officials were repeatedly mentioned.

2.4. The views of industry

2.4.1. During our missions we were able to talk to representatives of 16 industrial firms, 5 of whom were BAP contractors. This represented a disappointingly small sample of the 54 firms to whom we wrote originally. Almost half the firms did not even reply. We are forced to conclude that the Community's biotechnology research programmes are of marginal industrial interest, despite the number of firms who originally wrote "expressions of interest" in particular projects (some 112).

2.4.2. Subsequently we sent a written questionnaire to some 210 firms, most of whom had not been involved in the "expressions of interest" exercise. Responses were received from 77 (by 3 August)*, and they are reported in paragraphs 2.4.4. - 2.4.10. below.

2.4.3. Among the 16 industrial firms seen personally, the sectors covered were plant breeding (6), pharmaceuticals (4), agricultural inputs and food and drink (3 each), and animal health and fine chemicals (2 each). The prevailing view (expressed by 8) was firmly that EC research programmes should be driven by science, not by industry, although the latter could usefully participate through the secondment of staff to research institutes. The existing contracts were seen as much too small and too scattered to have an impact or solve problems, but at least they brought scientists from different countries together and allowed an outside view on the state of European science.

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* This Annex was completed later than the Summary Report and consequently includes more responses.

Safety assessment was seen as an important future topic and was mentioned spontaneously by 6 firms. The Commission's training programme's value was endorsed (also mentioned by 6 firms); there was, however, a particular need for more people to be trained in plant physiology and cell biology.

2.4.4. The written questionnaire was sent to firms active in biotechnology research in the six Member States with panel members, who furnished the lists. The numbers sent out and returned (by 3 August) were as follows:

	Sent out	Returned	
D	28	15	54%
F	38	16	42%
GR	2	1	50%
I	40	4	10%
NL	45	24	53%
UK	57	17	30%
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	210	77	37%

Some 55% of the respondents were independent; most of the rest were subsidiaries of larger concerns.

2.4.5. The initial questions sought to establish the size of the respondent firms, in terms of their overall numbers of staff, and numbers of professional research staff. The results were as follows:

Size of firm: payroll	N	
1 - 200 "small"	35	45%
201 - 500 "medium-sized"	3	4%
501 - 5,000	21	27%
5,001 - 50,000 "large"	13	17%
> 50,000 "very large"	5	6%

Size of firm: research staff	N	
0	1	1%
1 - 10	35	45%
11 - 100	29	38%
101 - 1,000	9	12%
> 1,000	0	-
No answer	3	4%

The following sectors of biotechnology business were represented with some firms being active in several:

- Fine or specialty chemicals	31	40%
- Human pharmaceuticals	26	34%
- Diagnostic kits	17	22%
- Agricultural inputs	16	21%
- Seeds & plants	15	19%
- Bulk chemicals	14	18%
- Food and drink	12	16%
- Waste treatment	11	14%
- Equipment and instruments	10	13%
- Animal husbandry	8	10%
- Other	16	21%

2.4.6. The first substantive group of questions asked about the firms' awareness of EC biotechnology programmes and whether they received regular literature from the Commission. 30, or 39%, were adequately informed, but 44% would have liked more information and 13% had not heard of the programmes. Only 25, or 32%, were on a mailing list. However 28, or 36%, had read scientific papers deriving from BEP and BAP, and 16, or 21%, had found them useful.

2.4.7. The next questions asked about "expressions of interest". 34, or 44%, had been invited to make one, and of these most (74%) had accepted. The reasons for declining inclued difficulties in finding another industrial partner, reasons of confidentiality, and concern that the application process was too slow and cumbersome. Rather fewer had been asked to attend a seminar or workshop by the Commission, only 17, or 22%, admitted to this, though all but two went and found the proceedings very or fairly useful.

2.4.8. Questioning then turned to the preparation for BRIDGE. A definite pattern was clear, with only 11, or 14%, having played

any part, whereas 46 (60%) would have wished to have been consulted and 40 (52%) wished to play a role in the selection of research contractors.

2.4.9. As for the content of BRIDGE, there were mixed feelings about whether industry should be required to participate financially. 42, or 55%, said they should, but 9 said no. Over half the respondents (58%) felt that the initiative for proposals could come equally well from research institutions or industry, but 10 (13%) felt that industry should be in the lead.

2.4.10. Despite the desire of industry to see a more industrial face to BRIDGE than BAP, there was no great willingness to contribute themselves. Only 13 (17%) said they would be willing to contribute in cash or in kind, but 40 (52%) were quite happy to continue with the present system of "expressions of interest", to be followed by receipt of new publications and invitations to meetings. Only 7, or 9%, did not wish to play any part in BRIDGE.

ANNEX 3

ASSESSMENT OF THE RESEARCH SUB-PROGRAMMES

3.1. Summary of activities

3.1.1. Under the first programme, BEP, there were five sectors for research, and a total of 103[1] contracts were let, as follows :

1. Second generation bioreactors for detoxification and for industrial applications including agro-food : 18
2. Improved production of substances for animal husbandry and agro-food industries : 29
3. Upgrading of plant products, particularly ligno-cellulose: 11
4. Improvement .. of plants and microorganisms .. important .. in agriculture : 54
5. Development of methods for detecting contamination and for the assessment of possible risks : 2

The total commitment for research contracts was some 10.4 Mecu out of the total programme budget (including the revision) of 15 Mecu. Thus the average contract was about 101 kecu.

3.1.2. Under the second programme, BAP, there were two sub-programmes, of which the first comprised 'contextual measures' and the second, six sectors of 'basic biotechnology'. There was a deliberate attempt to group different contractors into projects, with an average of 2.8 laboratories per project, virtually always with at least two Member States involved. The numbers of contracts and projects per sector were as follows :

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[1] The numbers in each sector are taken from the BEP catalogue of contracts, and involve some double-counting (they total 114).

	Projects	Contracts
Subprogramme I :	Contextual measures	
Bio-informatics	12	42
Biotic materials	5	13
Subprogramme II :	Basic biotechnology	
Enzyme engineering	17	45
Plant cells	23	64
Micro-organisms	13	35
Risk assessment	3	7
Animal cells	16	40
In vitro toxicity	6	16
	95	262

The total commitment for research contracts was some 37.7 Mecu out of the total programme budget of 55 Mecu (less 5.5 Mecu for the concertation activities), so the average contract value was about 144 kecu. In practice, the contracts were typically for three years, so contractors each received about 50 kecu per year.

3.1.3. It has been difficult for us to assess the effectiveness and impact of each sector as it consists of so many small contracts. As section 2.3. showed, we talked to many contractors, but they still represented a fairly small sample of the whole. The reports and papers are similarly too numerous to allow other than a rather cursory examination. We have set out below our comments on each of the sectors in turn, and have tried to assess :

1. the quality of the scientific work and of the groups involved;
2. whether there have been major scientific breakthroughs and bottlenecks removed;
3. what the major constraints on research in the sector are (if any);
4. the extent of transnationality of the projects or "European added value" (this really only applies to BAP);

5. the extent and durability of links between industry and academic or government laboratories;
6. how well the Commission staff monitored the work;
7. the arrangements made by the Commission for dissemination and exploitation of the research;
8. what the future goals for the sector should be.

3.1.4. The sections below follow the order of the BAP sectors, and include comments on work carried out under BEP as well, where appropriate. A number of contractors received support under both programmes, and their work under BAP was often a continuation of work begun under BEP. Despite the fact that the BEP programme nominally ended in March 1986, money is still being spent on the support of BEP research contracts, some research is still taking place, and scientific papers can be expected to be produced over the next year or two. On the other hand, results from BAP are already beginning to occur, and BAP papers are being published. In practice, therefore, the two programmes overlap to a great extent, and it is not possible to draw a clear distinction between them for purposes of evaluation.

3.2. Contextual measures : bio-informatics

3.2.1. Several distinct activities can be recognised in this section of the sub-programme on contextual measures. In its management, the Commission has quite properly separated those projects relating to software for problem engineering and for bioreactor control, and has managed them as part of the relevant areas within the basic biotechnology sub-programme.

3.2.2. The contextual projects themselves consist of three in data capture, two in databank creation, and one for software to provide access to protein sequence databases. The small number and size of most of the projects makes it most unlikely that the

sub-programme will reshape the European market for laboratory instrumentation for the life sciences, though at least one of these projects is highly novel and has an industrial contractor within it.

3.2.3. The most ambitious project has been to develop a European network of microbial culture collections (MINE). In contrast with the USA, the European life scientist is faced with a considerable number of well-established, well-funded, highly competent microbial culture collections, distributed across the countries of the Community. Amongst these collections, on-line computerised searching is still the exception rather than the rule.

3.2.4. The objective of the MINE project was to harmonise the organisational methodologies of one or more large microbial culture collections in each of five Community countries, to use that as the basis for computerisation of each collection, and then integrate these national "nodes" into a European network.

3.2.5. The project has achieved the establishment of common hardware and common (or at least compatible) software and the first exchange of data between some of the national collections. However, it is evident that the project has progressed much more slowly than it should have, partly because only now, some two years after the initial contracts were let, has an effective project management structure begun to emerge. It has also become evident to the Commission and the contractors that a distributed network will be impractical, especially when additional European collections are added in the future. The contractors have proposed an extension to the project, to allow the establishment of a centralised database, into which the data in all the participating European culture collections would be entered. One example of such a centralised database is that developed in the UK for its various national culture collections.

3.2.6. We believe that the Commission should use the extension of the BAP programme in part to fund this extension of the MINE project, so as to achieve the initial objective by 1991. It should ensure that a project manager is appointed and that, in parallel with the development of a centralised database to provide an on-line search capability, its long term financing is agreed with the contractors, to the same deadline. In subsequent projects, including those under BRIDGE, further European culture collections should be invited to join the centralised database, according to the needs established by consultation with European industrial and academic researchers.

3.2.7. The preparations for an integrated, searchable database already made by the MINE project offer the opportunity for a system which would be in advance of any other system in the world in its size and accessibility. It should therefore be able to offer a significant advantage to European researchers, and greater demand on the contributory collections. In principle, this ought to provide the basis for a self-financing operation.

3.2.8. The establishment of a European node protein sequence databank has progressed well. However, as noted later in our consideration of protein engineering, the overall resource so far committed to creating novel databanks and making them readily accessible has been sub-viable, and needs to be co-ordinated with the relevant part of the AIM programme (Advanced Informatics for Medicine).

3.3. Contextual measures : collections of biotic materials

3.3.1. Five projects were set up under BAP, one to improve the methodology of fungal preservation and the others to create collections of novel materials.

3.3.2. Life science research has depended on and will always require physical preservation of life forms, from those which protect plant species from extinction to those which catalogue the genetic determinants (some as yet to be identified) of man's illnesses. In most of the projects supported by the Commission, it is encouraging that the more recent techniques for identification of and discrimination between species (restriction fragment length polymorphism, 2-dimensional gel electrophoresis, etc) are being systematically applied.

3.3.3. The Commission programme appears to be achieving an added value by creating viable biotic collections from those which had previously been fragmented. However, the programme as a whole needs more vigorous action in making such collections available to on-line searching and in advertising their availability.

3.3.4. The breadth of biotic materials available to industrial and academic researchers in Europe is not yet matched by its accessibility, nor by the apparent willingness of researchers to pay for access. CEFIC[2] has set out its objective for European industry in "Bio-informatics in Europe" (May 1987), and "The Approach of the Biotechnology Industry to BRIDGE" (November 1987). The Commission should develop a strategy based on these objectives, through further discussion with industrial and academic researchers, and should explore means of speeding up further developments through industrial funding.

3.4. Basic biotechnology : enzyme engineering / bioreactors

3.4.1. Several of the projects are of considerable quality and industrial interest, notably those on computer modelling, microbial transformations of fatty acids, and the continuous

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[2] Confédération Européenne des Fédérations de l'Industrie Chimique.

synthesis of fine chemicals. Also of high quality, but of more academic interest, is the work on co-factor regeneration and retention. The transnational project of the groups of Compiègne, of Napoli, of the National Hellenic Research Foundation and of Hannover is potentially of interest to the oil industry. On the other hand, the bio-electric catalysis project is unlikely to be realistic on an industrial scale. The project on enzyme-loaded erythrocytes is somewhat futuristic with its combination of rDNA and cell technology.

3.4.2. There have been no major breakthroughs reported so far, although all the projects have some potential to remove bottlenecks hampering industrial applications.

3.4.3. Although the sector is of potential industrial interest, the very small size of contracts has deterred industry from making applications. Moreover many of the academic groups we saw seemed primarily concerned with open publication rather than with securing patent protection or working with industry on a proprietary basis.

3.4.4. There was effective trans-national cooperation, involving seven Member States, but surprisingly Denmark was not among them despite its strength in biotransformations.

3.4.5. There was only one industrial firm (Henkel) involved as a contractor under BAP. Despite the multitude of expressions of industrial interest, few firms participated actively in the work. However industrialists will probably take a more direct interest in the synthesis of fine chemicals project involving GBF, Braunschweig, the Fraunhofer Gesellschaft, Stuttgart, and the CNR in Milan.

3.4.6. The research activities in this sector are well monitored and managed by the Commission officials. The Commission staff have

been active in disseminating the results (e.g. through the BAP Progress Report 1987), and through sectoral meetings (Compiègne 1986, Capri 1987).

3.4.7. For the future, a prime goal is to transfer the academic research results to industry. There are potential applications of biocatalysts for biotransformations in bioreactors in the chemical and agricultural industries, and for waste water treatment. Genetically-modified biocatalysts should be explored, as should the use of biotransformations under extreme conditions of pH, temperature etc, and with inorganic solvents. There is also scope to develop optimised bioreactors, preferably integrated with downstream processes and involving the participation of equipment manufacturers.

3.5. Basic biotechnology - plant cells

3.5.1. As in the other sectors, there was intense competition for contracts and only about one in five proposals could be funded. The contractors included most of the best European groups working in the sector, who were also able to assist and encourage ones with less experience. Both BEP and BAP produced some notable scientific results, although it is not always possible to identify the specific role of Community support.

3.5.2. The main achievements of the research in this sector have been a greater knowledge (the mechanism of regulation) and new tools (vectors), rather than products in the form of new plants. This was indeed the original intention, which was correctly specified some years back. Some particular results are worthy of note :

- the identification and the cloning of the regulatory gene for the production of zein (a storage protein poor in lysine) in maize
- the transfer and the expression of genes implicated in the

regulation of nitrogen fixation from soybean to Lotus corniculatus.

3.5.3. The original scope for the sector, set out by the Council, covered five fields :

1. Extension of developments in molecular biology to plants and microorganisms of importance to agriculture.
2. Physiology and genetics of plants and micro-organisms.
3. Technology of cell culture
4. Breakdown of lignocellulose materials
5. Risk assessment.

Since the programmes' budgets were very much smaller than those originally requested by the Commission (15 Mecu instead of 26 for BEP, 55 Mecu instead of 88.52 for BAP), with the agreement of the CGC, the full scope of the plans set out in the Council Decisions could not be covered. A major effort was made in molecular biology, but there have been few projects on cell culture or risk assessment. The physiological work was abandoned, and the ligno cellulose sub-sector was re-oriented.

3.5.4. One of the most positive achievements of the work in this sector has been to develop, or even to establish, intensive collaboration between groups working in the same area. Wider links have been created in the context of the 11 European Laboratories Without Walls, ELWWs[3]. This new development is an interesting initiative and it deserves further support. Some of

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[3] - Fundamental aspects of plant cell regeneration.
- Regulation of expression of nodulin genes.
- Cell biotechnology for crop improvement.
- Molecular biology of cereal seed proteins.
- Mitochondrial molecular genetics in relation to crop improvement
- Host pathogen interactions with fungi.
- Molecular biology of phytopathogenic Erwiniae.
- Plant hormone receptors.
- Late symbiotic genes : construction of improved strains.
- Pollen biotechnology.
- Hairy root and auxin sensitivity.

the ELWWs should receive stronger support through work on clearly-defined research projects which would be specifically supported by the Commission.

3.5.5. Industry has not been ignoring the work and has shown (and continues to show) a lively interest. However the benefits are still too distant in time for firms to be prepared to participate financially in the research, and indeed only 4 of the contractors are industrial firms. Nevertheless the fact that a score of university groups working on BAP contracts have established links with industry shows that their partners are really interested in their work.

3.5.6. The Commission staff have run the sector with exemplary efficacy and dynamism. The majority of the research groups have thereby been inspired to work yet more closely together. Because of the close attention they have paid to the work being carried out, the officials have managed to reorient the sub-programme on transformation of ligno cellulose products towards the study of cellulotic activities and pathogenic pectolytic agents such as Erwinia spp.

3.5.7. In future, more thought should be given to the relationships between research workers and industrial firms. We consider that two ideas should inform such consideration. First, the pay-back time from research in this sector is very long. Second, the very survival of the European seed industry (and perhaps the independence of agriculture) depends on a commitment to long-term strategic research. This will lead eventually to the mastery and dissemination (as both seeds and plants) of a modified genome coding for improved agronomic traits or better grain properties. But most European seed firms are small and cannot afford to support such research work. It therefore falls to public authorities to provide the funds and to ensure that the results are well-disseminated. We think that in such an important sector

it would be wrong to require industrial contributions to projects in BRIDGE. Industry can however help to define the objectives of the work and to select the contractors, and we think it should be encouraged to do both.

3.5.8. We were disappointed that there was no call for proposals in cell physiology. It is of no use to master how to transfer genes to different plants and to know how to switch them on if one doesn't know where the new tools should be applied. Moreover it is very clear that the tools and the insights provided by molecular biology can make a big contribution to plant physiology. Thus BRIDGE projects should not merely be transnational but also multi-disciplinary.

3.5.9. We believe that the following should be the main priorities for future research objectives :

1. The molecular foundations of cell physiology in plants, with the work being steered towards the mechanisms of cell regeneration (especially in monocots) and of gene regulation, (e.g. for the determination of plant responses to environmental stresses and pathogens, or for changes in the composition of the storage components which govern the plant's utility).
2. Studies of interactions between plants and micro-organisms including means for their identification and the reactions of the micro-organisms to the plants.
3. Assessment of the potential benefits and hazards from developments in this sector <u>together with</u> a programme to communicate the results to the public, to be managed by CUBE (see Annex 5, section 5.3.4.).

We recommend that, to the extent that it is scientifically feasible, work should be focussed on six major species, including both monocots and dicots, that are important for European agriculture (especially cereals) rather than on model species, although the latter should be used as necessary. The priority

must be for the use of the tools that molecular biology has fashioned.

3.5.10. Bearing in mind the praiseworthy work that Commission officials have done to identify the research groups in this sector in Europe, and to persuade them to work together, we do not consider that a formal "call for proposals" is the only way to proceed. It should be possible to specify several projects of strategic importance, to bring together the research groups who express interest in working on them, and to identify a project manager. His or her responsibility would be to coordinate the work and ensure that the various teams helped each other. For such strategic projects there should be composite progress reports.

3.6. Basic biotechnology : micro-organisms important to industry

3.6.1. The projects in the area of microbial species important to industry cover a very wide range. Some 35 different laboratories are involved in 13 groups, concerned overall with 9 major industrial species of bacteria, yeasts and fungi. In most of the 13 groups the project has been concerned with a fairly well-defined model for genetic manipulation of the particular organism. In practice, both the contractors and the administrators have found it difficult to develop much synergy between the 13 groups, although there is evidence that efforts towards this end will prove significant in the formulation of the industrial micro-organism component of the proposed BRIDGE programme.

3.6.2. All the contractors interviewed were enthusiastic about the quality of the science produced by their fellow contractors, and compared it favourably with parallel work performed outside the community programmes. They were also enthusiastic about the benefits of collaboration, expressed in terms of complementary

skills and materials and of exchange of personnel.

3.6.3. The impact of the groups on the totality of European research on the genetic manipulation of industrial micro-organisms has however been constrained by the wide spread of the projects within a limited budget. Many of the leading research laboratories have not participated in BEP or BAP, though steps to begin to correct this imbalance have been taken by the Commission through meetings it has arranged in the "brain-storming" sessions that are leading up to the formulation of BRIDGE.

3.6.4. The lactic acid bacteria project has made clear progress, and the work under BAP undoubtedly benefited from the precursor projects in BEP as well as from the transnational collaboration effected by the BAP programme itself. Industrially, the output can be seen both in the elucidation of phage susceptibility and resistance and in the development of vectors to effect expression and secretion of model proteins.

3.6.5. While reasonable scientific progress has been made in many of the other projects, the small numbers working on any one organism has prevented any dramatic impact. Some of the organisms for which work has been supported reflect a level of industrial interest which was perhaps true of the late 70s/early 80s but has now been much reduced.

3.6.6. Therefore, while it is evident that some European added value has been gained by the complementarities in project skills and materials, the programme as a whole has not drawn as effectively as it might have done on the full strength of European research.

3.6.7. Possibly for this reason, the number of industrial companies that have participated either in the contracts or in the sectoral meetings has been relatively low, compared with those interested in the sectoral meetings on plant genetic manipulation. The

results of some specific projects are being closely monitored by industry and very probably will be taken up and exploited by them. However, we consider it likely that much less than half the projects will lead to additional development expenditure by these companies and that that expenditure will therefore be less than that committed under this programme.

3.6.8. All the contractors complimented the Commission on the care taken to implement each contract, and on its organization of meetings which were especially valued for being gatherings of specialists. Many noted that the programme manager had not visited individual laboratories very much after the initial period, but made this only a minor criticism in view of the other benefits they had obtained. Some noted that the meetings involving all the 13 groups were less useful, as there was less of communal interest to discuss.

3.6.9. The Commission has been active since the second half of 1987 in promoting discussion within the programme and also with non-contractors to formulate the equivalent programme under BRIDGE. Academic and industrial groups have identified a much narrower range of organisms on which to concentrate, and have recommended an emphasis on multi-disciplinary teams to tackle the control of gene stability, overproduction, and secretion through genetic manipulation, biochemistry and physiology.

3.6.10 In the same way that the Commission has used its initial academic contractors to widen the discussion to include non-contractors, so also it needs to widen its range of industrial participants and collaborators. Through such initial collaborations we believe it should seek to advertise the value of its present and future programmes taking special account of small and medium-sized enterprises which cannot devote much manpower to discovering such values for themselves. The number of model micro-organisms for multi-disciplinary projects needs to be

reduced still further, to perhaps one major project.

3.7. Basic biotechnology : risk assessment

3.7.1. We consider that the quality of research in this sector is good. The most ambitious project seems to be that on the field release of genetically-manipulated baculoviruses. However no scientific breakthroughs have so far been reported.

3.7.2. The number of contracts is very small (7) and does not reflect the degree of concern which, rightly or wrongly, exists in our society today with regard to the possible negative aspects of biotechnology.

3.7.3. Nevertheless, the work appears to us to be suitably transnational in character. There was a successful meeting in Bayreuth in October 1987 with 41 participants, including two from industry and several representatives of Member State governments.

3.7.4. The work is closely monitored by the programme managers, who have visited almost all the contractors. There are well-established means for the dissemination of the results, and we note with satisfaction that the Commission will be sponsoring a major seminar later this year, probably in Berlin.

3.7.5. A major goal must be to expand the activity in this sector. We strongly endorse the plans, under the revision of BAP, to devote over 4.6 Mecu out of the 20 Mecu to additional work. The main emphasis will be on the environmental release aspect, for example, the fate and possible ecological and human health problems caused by transgenic organisms, as well as the possible transfer of genetic material between organisms.

3.7.6. Although we regard such work as vital in order to demonstrate that new biotechnological products and processes are safe, we are concerned that the current title of the sector may give a misleading impression. We would prefer it to be called "safety assessment", see para 2.2.11.

3.8. Basic biotechnology : animal husbandry and animal cell culture

3.8.1. This sector comprises two sub-sectors, of which the former is much the larger with 13 projects as compared with only three in animal cell culture. We are impressed with the work in animal husbandry : the scientific quality is very good and there are a number of very promising developments although no major breakthroughs have been reported. One criticism is that most of the work is concerned with viruses and consequently there is a rather small community (only 4 groups) working on bacteria, not enough to form a critical mass. Similarly, in the animal cell culture sub-sector, the small number of contracts (only 10) has restricted the amount of mutual benefit arising from sectoral meetings like the one held at Seillac in May 1987.

3.8.2. The transnationality of the work is one of the most successful aspects, and some half dozen ELWWs are under way (cf. para 3.5.4). Two meetings were supported in 1987, both in Salamanca : one was a sectoral one on genetic engineering and the other was an independent one on African swine fever and pig immunology. Both were very successful, although the latter would have benefited from the active participation of DG VI, whose own research programme includes African swine fever.

3.8.3. Both sub-sectors are developing good links with industry, and there are three industrial contractors (Solvay and Wellcome; Bertin). We noticed, however, that the more successful the research in animal husbandry, the less industry seemed interested

to collaborate. In animal cell culture the work is largely pre-competitive.

3.8.4. The programme managers have been active in monitoring the work, and have visited most of the contractors. Apart from the reservation in para 3.8.2. above, the means provided for the dissemination of the research results seem to us to be appropriate. We note with approval that links are being formed between groups involved in animal cell culture and those concerned with bioreactors and with in vitro toxicology, and that a joint meeting is being planned in Nancy towards the end of 1988.

3.8.5. Future research in animal husbandry should continue to concentrate on the two themes established for BAP, namely production of vaccines and interspecific gene transfer. In addition, it is important to support at a precompetitive level the development of modern diagnostic procedures in animal husbandry (e.g. for hormones, viruses, other micro-organisms and parasites).

3.8.6. We consider that animal cell cultures will be used increasingly to generate novel products for human and animal health. Animal cells (both vertebrate and insect) have a number of advantages over bacteria and yeasts, notably the capacity to bring about certain post-transcriptional enzymatic reactions such as glycosylation. We consider it desirable for this sub-sector to be continued and expanded, and to be linked to the sector on industrial micro-organisms.

3.9. Basic biotechnology : in vitro toxicity

3.9.1. There are six projects in this sector and their quality is good. Two of them are especially noteworthy, namely the one on altered

immune gene expression, and that on in vitro screening for anticonvulsant teratogenesis in neural primary cultures and cell lines. The work on a new method of immunotoxicological screening strikes us as being a real breakthrough.

3.9.2. Once again, the major constraint is the small number of contracts (16) in relation to the diversity of the subject. Given the limited budget, it would have been better to have concentrated on work that was likely to lead to improvements in basic knowledge, and to have excluded the more medically-oriented work on specific organs (skin, kidney, pituitary).

3.9.3. The work has led to good transnational cooperation, although it is strange that none of the 16 contractors is in the Netherlands whereas five are in the UK. One ELWW has been established, based on the Centre Paul Broca in Paris and BIBRA[4] in Carshalton, UK.

3.9.4. For exploitation of the work, it is necessary to involve both industry and national governments, and this is occurring. Skin models are now commercially available for medical use. Although there are no commercial firms among the contractors, BIBRA is a private-sector research association serving both industry and government, and so the new immuno-toxicological screening method is likely to find rapid application.

3.9.5. The Commission's programme manager monitors the work closely. The results are well disseminated, both within the sector and to the scientific world outside. Meetings, like the one held in Bad Irsee, near Munich, are of major importance for the purpose.

3.9.6. We should stress that this sector not only exploits the new developments in biotechnology, but also can contribute new insights that will be of value both within the sector and to

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[4] The British Industrial Biological Research Association.

others. Thus we believe that future research should concentrate on two main lines. First, basic biomolecular research that is aimed primarily at the modulation of genome expression and cell differentiation by potentially toxic chemicals and drugs should be pursued. Second, novel test methods should be developed to identify possible undesirable effects on human health of new biotechnological products such as peptides and proteins. But as we noted above (section 3.9.2.), we consider that any organ-specific work should be undertaken within the medical and health programme.

3.10 Protein engineering

3.10.1 This is a relatively recent sector with five projects activated in the second half of 1986 and four activated in the first half of 1987. However, some evaluation is already possible. The scientific quality of the teams involved, and of the projects themselves, is high. The programme includes most of the best European groups with heavy representation of the countries with a strong tradition in the field (D, F, UK), and some representation from high quality groups from Mediterranean countries (GR, I, P). The transnationality and multilaboratory aspects are very good.

3.10.2 This sector is markedly multidisciplinary, requiring inputs from X-ray and other protein structure determination procedures, modelling and structure prediction methods, classical enzymology and genetic engineering. The Commission staff has recognized and properly insisted on the multidisciplinary nature of the sector which, together with the high quality and multinationality of the groups engaged, augurs well for the projects. It should be noted that in this sector a multidisciplinary team focussed on the same project cannot easily be assembled even in the most advanced European countries. This points to the real necessity of transnational collaboration.

3.10.3 The sector has important industrial applications. Two industrial laboratories are involved in the programme, but the value to industry really lies elsewhere : in the training of high quality specialists in the academic laboratories supported by the programme, and in the interactions possible though BAP-associated workshops such as the one held at Capri last year. Major industrial firms in Europe are building in-house groups in protein engineering, with resources far exceeding those provided by BAP and with guaranteed confidentiality. Thus, industrial interaction with the academic groups participating in this programme is a reasonable goal, e.g. through secondment of staff and active participation in meetings, rather than direct involvement of industry as contractors or as suppliers of funds.

3.10.4 Europe has substantial strengths in this sector, although the number of specialists in some key fields (such as X-ray crystallography) is not large world-wide, and Europe is faced with increasingly strong competition from the US (in part because of major financial support by the Howard Hughes Medical Institute). It is important for Europe to maintain and consolidate its position, and support of research and training in protein engineering should therefore remain of high priority in BRIDGE. Finally, the sector overlaps with and is dependent on bio-informatics and other contextual measures. A number of projects in the latter sectors are of very high quality and represent a valuable input to the protein engineering sector.

3.11 Genome studies (mapping and sequencing)

3.11.1 This is a sector that has not been identified in past programmes. However, we consider that it merits separate discussion, since it encompasses projects planned for the BAP extension and for BRIDGE, and since it exemplifies some of the potential but also the limitations of the European response to the biotechnology

challenge.

3.11.2 Recent advances in molecular biology and genetics (including developments in DNA sequencing and mapping procedures) have now made it feasible to envisage a complete knowledge of the complex genomes of higher organisms at the chemical level. This is symbolized by (but by no means limited to) the proposal for obtaining the complete sequence of the human genome ($3x10^9$ base pairs of DNA). That proposal was acrimoniously debated in the scientific community during late 1986 and early 1987, the acrimony largely generated by the fear that such a "big science" project would drain scarce resources from ongoing "small science" programmes. Remarkably, over the last year consensus has crystallized on the desirability of genome studies, not only on the human genome but also on selected model systems (such as bacteria, yeast, nematodes, Drosophila and the mouse). This development was partly stimulated by the deliberations and favorable conclusions of a National Academy of Science/National Research Council Committee in the US, and by the focus on genome studies in the Human Frontier Programme proposed by Japan. It is important to remember that key approaches to genomic studies were pioneered in part in Europe (e.g. DNA sequencing by Sanger; construction of complete physical maps by Sulston).

3.11.3 The underlying justification for a major initiative in this new sector is its importance both for basic biological knowledge and for applications in the fields of human health, agriculture and industry. For example, the detailed characterization of the human genome, with the resulting identification of a wealth of medically important genes and the generation of probes for detecting abnormalities in these genes, can be justifiably considered an investment in preventive medicine. Similarly, genomic mapping of plant and animal species of economic importance will be valuable for agriculture and pest control.

3.11.4 A measure of the rapid international growth in this sector is the US response. Less than a year ago, the National Institutes of Health (NIH) committed $ 17.2 million for a year, which are being assigned to peer-reviewed grants and will be fully disbursed by the end of September 1988; increased funding is expected for the next and subsequent years, and the Nobel laureate J. Watson is being recruited to oversee this sector as an Associate Director of NIH. Furthermore, the Department of Energy is initiating major activities though its National laboratories (e.g. Los Alamos, Livermore), and additional major funding is expected from the Howard Hughes Institute and other non-governmental sources.

3.11.5 An important European initiative in this field is the plan to sequence part of the yeast (Saccharomyces cerevisiae) genome, in coordination with American, Japanese and other teams that will be pursuing parallel studies. In the BAP second phase, 2.4 Mecu for 2 years are earmarked for this purpose, and a total of 10 Mecu are envisaged for scaling up the effort within BRIDGE. In addition, 2 Mecu are earmarked for sequencing the Bacillus subtilis genome, and smaller amounts will fund the development of instruments and other contextual measures.

3.11.6 In other EC programmes a start has been made in genome studies under the Stimulation Programme (Drosophila, 0.7 Mecu over 5 years) and it is expected that 15 Mecu over 3 years will be made available for the human genome sequencing project through the medical research programme. While these developments are encouraging, we note that the projected level of support is significantly lower than in the US, and that actual funding is mostly lagging behind the US by nearly one year. At the moment no plans have been made for similar work on species of agricultural importance (plants, insect pests).

3.11.7 Finally, an important gap seems to us to be developing in bio-informatics; a proposed 10 Mecu allotment for DNA-related work under the AIM programme (Advanced Informatics for Medicine; DG XIII) has been unfortunately eliminated by the planning group of that programme, which did not include experts in genetics. We must stress that for many uses of information technology in biotechnology, Europe risks becoming totally dependent on the USA. The limitations of the European initiative in genome studies may reflect the generally low level of funding for research in the life sciences, and slow and diffuse administrative procedures, which we discuss elsewhere in this report.

3.12. Concluding remarks

3.12.1. We have noted in several sectors the need for large scale projects, which would use the advantage of the European scale to make the maximum impact on major bottlenecks. Such projects would comprise multi-disciplinary teams of the necessary critical mass. We have also noted that the current system, of an open call for proposals, is not the only way to proceed (3.5.10)

3.12.2. We therefore recommend that for each such large scale project the Commission should appoint a project manager who, in close cooperation with them, should organise a framework for the project for use in inviting applications, which would then be judged both on scientific merit and on relevance to the pre-set goals.

3.12.3. We also noted earlier (2.2.6) that the small size of contracts offered under BEP and BAP (approximately 50,000 ecu/yr) was one of the factors that inhibited the participation of industry, and of some major academic laboratories. We therefore recommend that a flexibility should be introduced to allow some contracts to

support up to 6 researchers in one laboratory (principal scientists, postdocs, technicians,etc). This would imply some contracts of up to 200,000 ecu/year, assuming a continuing requirement by the Commission that contractors undertake 50% of project costs. Such contracts would often be within the context of the above large-scale projects which are envisaged as having an overall cost to the Commission of 1/2 million ecu/year or more.

3.12.4. We believe it would be advisable in the future to plan for a degree of continuity for ELWWs and also to introduce some flexibility into Commission programmes, by instituting some kind of rolling mechanism into the calls for proposals. This could be done, for example, by staggering the periods of awards, and by repeating periodically the call for proposals, especially in the science-driven part of the research programmes.

3.12.5. Such a flexibility would permit the pursuit of new ideas or new developments in the various sectors, and would also allow recruitment of further laboratories either as they are established or as they become more attuned to the needs of the programmes.

3.12.6. It is also desirable to continue the process evolved during the BEP and BAP programmes to increase the scientific cohesion of the Community. In particular, special efforts should be made to seek the full participation of competent laboratories and scientists from less-developed regions of the Community. Such a special effort should certainly not involve quotas or the lowering of scientific standards. Instead it should focus on increasing the awareness and relevance of the programmes through means such as :

- Assisting national authorities in searching out and fully informing laboratories in these regions about the available possibilities, including those arising from potentially complementary proposals being put together by laboratories in

more developed regions.

- Making more frequent calls for proposals, as suggested in 3.12.4., thus reducing the significance of disparities in access to information.
- To the extent that this is scientifically tenable, encouraging application of research to targets relevant to the less-developed regions (e.g. Mediterranean crops).
- Encouraging the holding of sectoral and other workshops in less-developed regions and otherwise enhancing the contacts of young scientists from these regions with scientists from more-developed parts of the Community.

ANNEX 4

ASSESSMENT OF THE TRAINING ACTIVITIES

4.1. Summary of activities

4.1.1. Fellowships have been awarded to 'young' scientists since 1983 under both BEP and BAP to provide advanced training in a number of disciplines within biotechnology in good-class laboratories in another Member State. Under BEP, the fellowships were mostly 'senior' ones for scientists with several publications already to their name. The fellows were paid a monthly stipend (the current rate is about 1711 ecu/month) and their host lab received a bench fee of 10,000 ecu/year. Under BAP, the emphasis has been shifted towards younger scientists, both new PhDs and doctoral students; they receive about 1369 ecu/month but no bench fee is paid.

4.1.2. The total numbers of fellows and the financial allocations to date (May 1988) have been as follows :

	Senior	Junior	Total	Commitment, Mecu
BEP	72	5	77	3.2
BAP	59	130	189[1]	2.5

A total commitment of 5 Mecu under BAP is planned for the training programme.

4.1.3. Applications can be submitted at any time; they are selected for funding following quarterly meetings of the CGC on the basis of written evidence from the fellow, his/her previous supervisor and potential host. Most fellowships are for one year initially but a fair number of extensions for a second year are granted.

4.1.4. During BEP, there were 222 applications so the chance of success was about 35%. So far under BAP there have been 369 applications and the success rate has risen to 51 %. The most common ground for rejection appears to be that the training programme proposed

[1] A further 43 fellows have been selected but are not yet in post.

is not relevant to the aims of the BAP.

4.2. Conclusions

4.2.1. We regard the training element of the biotechnology research programmes as having been a success. The reports (see 4.4, 4.5, 4.6) are very favourable : the fellows seem to be well-qualified, work hard, and bring a fresh approach to their host laboratory. Moreover, the fellowships are mostly instrumental in fostering continuing trans-national collaboration, and have played a significant role in enhancing subsequent job opportunities for the fellows.

4.2.2. We have seen the results of a survey of some 42 fellows and 57 supervisors conducted by postal questionnaire in December 1987 by the programme managers. These largely confirm our own findings, based on personal interviews. The quality of the training and the standard of the host laboratories were regarded as very good in both surveys, although we doubt that the predominantly young fellows are really able to judge the latter because of their lack of standards for comparison.

4.2.3. Despite these laudatory comments, there are some criticisms. On the administrative side, the procedure, although reasonably efficient, is very impersonal. There have been some difficulties with initial payments - one-sixth of the fellows complained about this. For most junior fellows, one year is insufficient to generate significant research results which they need in order to obtain a job afterwards.

4.2.4. The level of stipend seems to us to be on the generous side : in some countries junior fellows are paid more than established scientists of the host laboratory. On the other hand, the lack of bench fees for these junior fellows is clearly a major source

of complaint in many laboratories, especially university ones, and may cause some resentment, and a lack of feeling of independence for the fellow.

4.2.5. A further problem is the lack of money for travel by the fellows to symposia and workshops, and to visit other laboratories in their host country. We feel that as a consequence many fellows do not obtain sufficient professional contacts in, or personal knowledge of, their host country.

4.2.6. The points in the above three paragraphs were also made by the respondents to the Commission's postal survey, but they came across quite vividly in some of our interviews. Our conclusion is that a more positive approach to management of the fellowship programme must be made, including better marketing of the programme, and the promotion of closer contacts for the fellows with the Commission, and with other fellows in the same host country.

4.3. Recommendations

4.3.1. The training programme should be continued under BRIDGE and should be expanded to absorb about 15% of the budget (cf. 9% under BAP, 21% under BEP). This would provide for some 50 fellowships per year under the revised conditions we recommend below. The objective of the fellowships should be to provide training in disciplines currently in critical supply, either locally or throughout the Community.

4.3.2. The programme should be much more vigorously promoted, and should be managed by at least one full-time professional staff member- plus administrative support. An appropriate target would be to attract at least four candidates for each fellowship.

4.3.3. The selection procedure should include personal interviews in Brussels for short-listed applicants, and the opportunity should be taken to provide candidates with briefing about the Community, and the biotechnology and other related research programmes.

4.3.4. The Commission should provide detailed briefing material for both the fellow and his/her supervisor explaining what is expected of each, and giving up-to-date information on administrative matters for each Member State (e.g. liability to income tax, payments for health insurance, arrangements for annual leave and sick leave).

4.3.5. The total payments to the fellow should be at the current levels, but 10% of the monthly stipend should be withheld and used to pay travel costs and a daily allowance for an approved programme of travel and visits to other laboratories in the host country totalling about two weeks per year of the fellowship duration. The stipend should be paid monthly in advance, and travel expenses should be paid promptly.

4.3.6. Without precluding appropriate training activities of shorter duration, fellowships should normally be for two years, with the possibility of a third year in exceptional cases. The Commission should have the right to terminate a fellowship after one year if reports are unsatisfactory.

4.3.7. Bench fees should be paid for junior fellows as well as for senior ones and should be at similar levels. The fees should be negotiated for each case individually and some account should be taken of the relative expense of the laboratory work in different topics.

4.3.8. The responsible Commission official should visit or maintain contact in other ways with fellows during their tenure, and should encourage contacts between fellows in the same Member State or region through occasional meetings.

4.3.9. The Commission should maintain a list of the names and addresses of all former fellows and their supervisors and keep in regular contact with them in order to provide news of biotechnology research initiatives and encourage former fellows to participate. This list should be published from time to time.

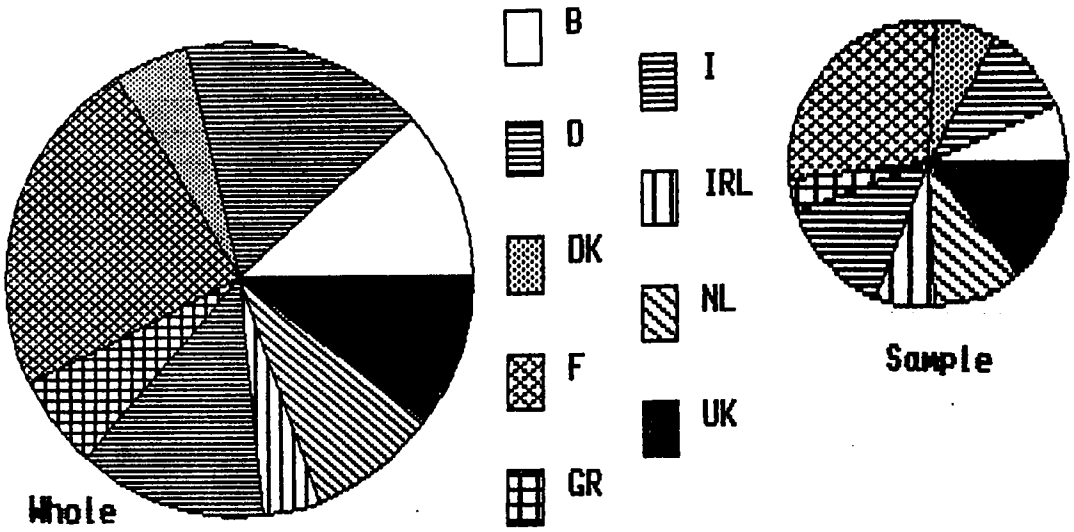
4.3.10. We note with interest the support being given to the provision of intensive workshop and training courses in biotechnology in Greece, Portugal, and Spain. We should like to see this activity continue and expand.

4.4. Analysis of questionnaires : BEP fellows (29)

4.4.1. There were originally 77 BEP fellows, and it was necessary first to obtain their current address from their former supervisors. Eventually 56 such addresses were obtained. During the missions, personal interviews lasting 20-30 minutes were held with 9 fellows, and 20 others filled in a written questionnaire. Responses were therefore obtained from 29 or 38%. They were distributed by Member State as follows (numbers in parentheses correspond to the whole cohort):

B - 2 (9)	GR - 1 (5)	L - 0 (0)
D - 3 (13)	I - 4 (10)	NL - 3 (7)
DK - 2 (4)	IRL - 2 (3)	UK - 4 (8)
F - 8 (18)		

The sample was therefore fairly good except that Belgium, Germany and Greece were under-represented. Spain and Portugal were not Member States at the time and so did not participate.



BEP fellow distribution by Member State

4.4.2. The distribution of the host-laboratories of the 29 BEP fellows compared with the total population was as follows :

B	- 6	(11)	GR	- 0	(2)	L	- 0	(0)
D	- 5	(15)	I	- 0	(2)	NL	- 2	(3)
DK	- 2	(5)	IRL	- 0	(1)	UK	- 13	(27)
F	- 1	(11)						

The UK was therefore somewhat over-represented and France under-represented.

4.4.3. Of the 29 fellows, 21 were now living in their country of origin, and 2 had gone to the U.S. Six had stayed on in their host country after their fellowship. Of the total of 56 fellows who were traced, 18 no longer resided in their country of origin (32%, cf. 28% in the sample of respondents) including 7 out of 8 from the UK.

4.4.4. The fellows were on fellowship on average about 1 1/2 years, and had finished their tenure a mean of 2.4 years ago. They were thus able to reflect fairly well on the time they spent in another country. The principal advantages mentioned were

contacts with other scientists (18), better scientific knowledge (13) and new techniques (13). There were personal advantages, too : 10 mentioned an improvement of their language, mostly English, and 7 enjoyed social and cultural contacts.

4.4.5. Twelve found their fellowship better than they expected, but 5 were disappointed. Problems included late payment of stipend or bench fee (5 mentions), a new language (3) and the lack of opportunity to go to scientific meetings (3). But these problems were generally out-weighed by the professional advantages of having trained in new techniques in a good laboratory, with possibilities for publications (25 out of 29) and continuing links with their supervisor (24 maintained these).

4.4.6. The fellowship seems to have had a beneficial effect on future employment : 14 thought it had a major influence and a further 6 that it was of some help. (Most of the rest had a job to which they returned.) It was also thought to have a significant long-term career advantage by 18 out of the 29.

4.4.7. Fellows mostly returned with better impressions of their host country and the Commission. On their host country, 10 considered it much better and 7 a bit better afterwards; only two thought it worse. The Commission was much better appreciated by 14 and somewhat better by a further 11, but 3 were disappointed - mainly because of slow or cumbersome administration.

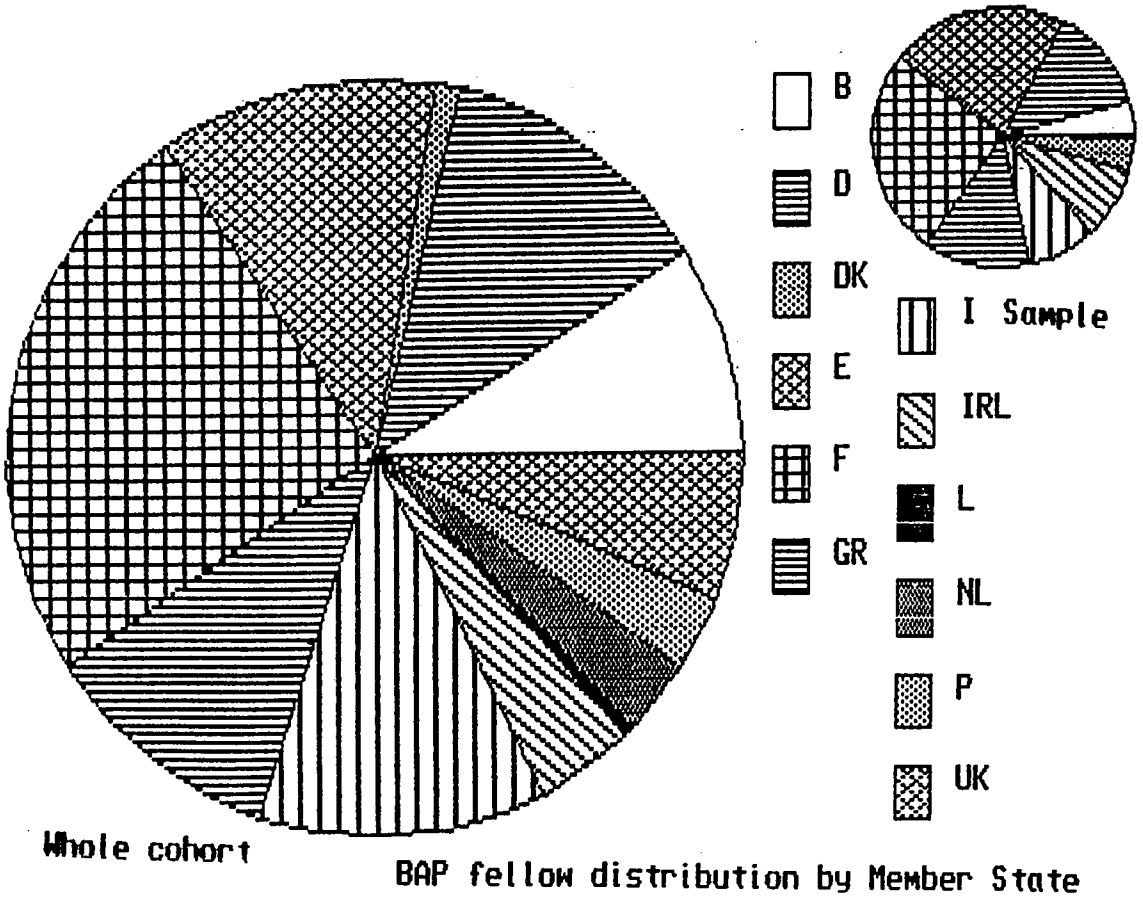
4.5. Analysis of questionnaires : BAP fellows (23)

4.5.1. Twenty-three fellows were interviewed by groups of three panel members during their missions. Of these 18 were female and only 5 male, a disproportion which is at variance with the overall ratio for BAP fellows of 2 females to 3 males. For 14 of the fellows, panel members also saw their supervisors.

4.5.2. The distribution of fellows by nationality was as follows :

B	- 1	(17)	F	- 6	(47)	L	- 0	(1)
D	- 3	(23)	GR	- 3	(20)	NL	- 0	(6)
DK	- 0	(2)	I	- 2	(24)	P	- 1	(6)
E	- 5	(23)	IRL	- 2	(8)	UK	- 0	(12)

(Numbers in parentheses are for all the BAP fellows.) The sample was 12%.



BAP fellow distribution by Member State

4.5.3. Three of the fellows were classified as 'senior', the other 20 were 'junior', (cf. 59 and 130 for BAP as a whole) of whom 7 were working towards a PhD degree. Most (14) had tenure for one year; 7 had received a second year's extension. Nearly all (19) had not previously lived or worked in another Member State.

4.5.4. The main reasons for the fellows having applied were personal (primarily to learn English or to experience living elsewhere in the EC) and professional.

4.5.5. The fellows had heard about the scheme from a variety of sources - their professors (8), notices or advertisements (6), and other fellows (4). Some had sought to work with their supervisor first and had then learned about the scheme from their host-laboratory.

4.5.6. One question asked about the relative attractions of Europe and the USA to potential fellows. Hardly anyone would have preferred to go to the US; the award was considered at least as good as one for the US by 10 and, if anything, superior by 5.

4.5.7. The stipend was regarded as about right by 10 out of the 23 and generous by 8. One said the money was not enough; the other four did not comment. However three fellows complained that their initial grant was late in arriving, and several suggested that the stipend should reflect the high cost of accommodation in certain large cities (notably London and Paris).

4.5.8. As expected, there were problems for some in finding accommodation (mentioned by 6), coping with the language, and settling to living in another country. But most of the fellows settled easily and received quite a bit of help from their host laboratory.

4.5.9. The host labs were well regarded by the fellows, 8 saying they were an improvement on those of their own country, and 7 at least as good. (Only one was less well-equipped.) The main advantages were seen as the high level of training (seen as excellent by 7 and good by 9), the contact with other scientists through seminars, etc. (6 mentions) and good equipment (8 mentions).

4.5.10. The fellowships have been reasonably successful in changing people's attitudes about Europe. Nine fellows now had much better views of their host country, and four a bit better; only two were less well disposed (because of the lack of sunshine in northern Europe and the cost of living). There were many

positive remarks about the friendliness of the people of the host countries. But several fellows lacked for personal contacts and would have liked to meet other Community fellows in their host country for mutual support.

4.5.11. The Commission, though regarded as a courteous and efficient source of support, was viewed as a rather remote and impersonal body. Only 3 now regarded it in a much better light, 10 a bit better, and 7 were unchanged - they had no feelings about it.

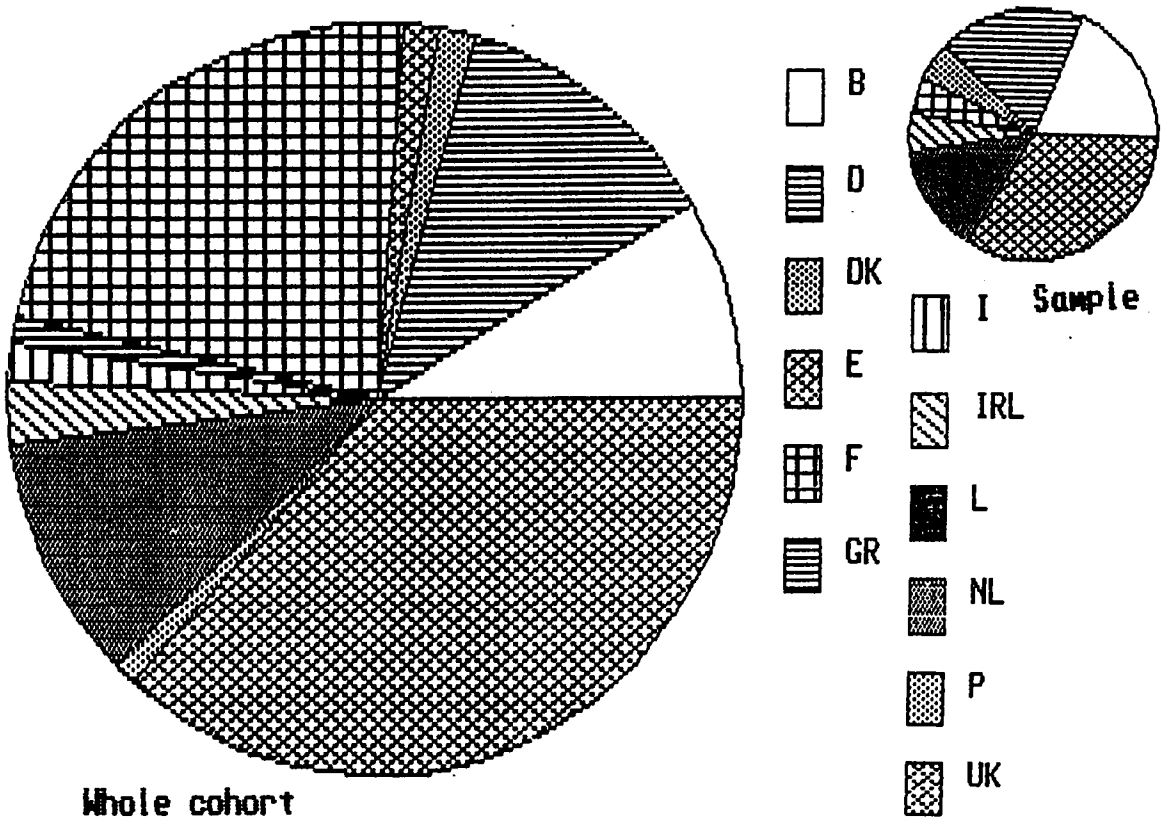
4.5.12. As regards their future career, 13 fellows felt the fellowship would have a very positive effect and 2 a small effect; none felt it would be negative. Eight fellows expected to return to their country of origin and a futher eight might do so, but five thought it unlikely - mainly because of the lack of available jobs.

4.6. Analysis of questionnaires : supervisors (21)

4.6.1. The responses were again obtained through face-to-face interviews, averaging 20-25 minutes, with panel members during missions. A total of 21 supervisors were interviewed, who were responsible for some 25 fellows, one of whom had not yet taken up his post. They were distributed by Member State as follows :

B - 4 (16)	F - 1 (43)	L - 0 (0)
D - 4 (23)	GR - 0 (2)	NL - 3 (20)
DK - 1 (3)	I - 0 (3)	P - 0 (2)
E - 0 (3)	IRL - 1 (5)	UK - 7 (69)

Numbers in parentheses show the total numbers of supervisors who have taken part in the BAP training programme. The sample was 11 %. France was under-represented but Belgium was over-represented.



BAP Supervisor distribution by Member State

4.6.2. The distribution of their BAP fellows (21 out of 25) by nationality was as follows :

B	- 2	(17)	F	- 8	(47)	L	- 0	(1)
D	- 2	(23)	GR	- 3	(20)	NL	- 1	(6)
DK	- 0	(2)	I	- 2	(24)	P	- 1	(6)
E	- 0	(23)	IRL	- 2	(8)	UK	- 0	(12)

4.6.3. The majority (15) of the supervisors were initially approached by their prospective fellows directly; most of the other contacts arose from a pre-existing link with the fellow's professor or supervisor in his/her country of origin.

4.6.4. Two thirds of the supervisors said that the fellow had made or was making a very positive contribution to the laboratory, often more than would be expected from a host-country national because of different scientific approaches or contacts, and because many

of the fellows worked extremely long hours. There were no adverse reports on fellows.

4.6.5. The presence of the fellow involved extra costs for the host laboratory; one-third indicated a sum between 3,000 and 10,000 ecu/year, and one-third said it cost them over 10,000 ecu/year. This money had to be found (in the absence of a bench fee paid by the Commission) by the laboratory, and was a considerable impediment for 8 supervisors, although 7 seemed able to manage without a bench fee (notably at the well-funded EMBL at Heidelberg.)

4.6.6. Most of the supervisors expected publications to result from the fellowship (16); none said it was unlikely although the short tenure, normally only one year and in one case, six months, clearly made it difficult for a fellow to make a significant contribution in a new area.

4.6.7. The supervisors were divided on whether the fellowship was likely to generate useful contacts in the fellow's country of origin. Four said yes, the fellowship was very helpful in this regard, and a further 7 thought it was quite helpful (some of these would have already had close contacts); 9 said it would not be useful.

4.6.8. On relations with the Commission, 2 claimed a much better relationship and 4 that it was a bit better, but for 6 it was unchanged and for 3 a bit worse. The negative aspects were the lack of contact, poorly-designed literature, the absence of a bench fee, and the denial of a possibility of renewal of the fellowship. The limitation of fellowships to 12 months, at least initially, was criticised by eight supervisors : there was a clear consensus that two years was needed for young scientists (although one year might be enough for a senior scientist on a sabbatical).

4.6.9. Six supervisors said that the fellowship had helped them to work more closely with industry; nine said it made no difference. None said there was any problem.

4.6.10. On future prospects, 11 supervisors were happy to continue to receive EC fellows, but 9 said that the conditions would have to change, mainly through the provision of a bench fee or a longer period of tenure.

ANNEX 5

ASSESSMENT OF THE CONCERTATION ACTIVITIES

5.1. The need for concertation in biotechnology

5.1.1. CUBE, the Concertation Unit for Biotechnology in Europe, is in general responsible for concertation in the area of biotechnology and more specifically it is responsible for the concertation activity within BAP (Council Decision of 12 March 1985). We therefore consider first the need and rationale for the concertation activity per se and then the particular institutional implementation that this activity has been given in CUBE.

5.1.2. Concertation is required when a given R&D activity, such as biotechnology, is located in many different centres of both decision making and implementation, separated by institutional boundaries. Different types of concertation can be identified within this general area :

- Intercountry concertation.
- Interinstitutional concertation.
- Intrainstitutional concertation.
- Interdisciplinary concertation.

5.1.3. In order to effect the previous types of concertation the following activities are required :

1.Information gathering and dissemination/communication. This activity implies locating and storing the right type of information, identifying relevant audiences who might be interested in it, and adapting and communicating the information to those audiences.

2.Act as an operational linkage helping in setting up and implementing decision making processes involving institutional

centres which are for most other purposes separate and independent. This could happen for example by means of the establishment of committees or working parties with a joint membership from the different interacting institutions. Even this activity involves gathering and communicating information but in addition it contains a 'catalytic' role in starting and contributing to the implementation of some actions.

5.1.4. These requirements for concertation are not unique to biotechnology or to BAP but they are common to many if not to all other research programmes. What may be different for biotechnology could be both the degree of interdisciplinary interaction required to advance the research frontier in this area and the number and type of centres involved in decision making and implementation. Evidence that the diversity of sources of information that could be generally classified as belonging to biotechnology is particularly great is provided in the ASFRA Report[1] which stresses the extremely large number of publications and of professional fields to which they belong. This makes the task of keeping up with new developments even more difficult than for most other fields of study. Again, although this situation is not unique to biotechnology the extent to which it is true here may be higher than in most other fields. Furthermore one could argue that for a field of knowledge (involving many disciplines) as broad and as <u>new</u> as biotechnology (see section 2.1) institutional boundaries may be particularly fluid and it is at this stage that the greatest extent of concertation is required.

5.1.5. In summary it is quite possible that the optimum extent of concertation is higher for biotechnology than for other R&D areas and programmes. This would justify the differential importance

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[1] Franklin, J. "The role of information technology and services in the future competitiveness of Europe's bio-industries", ASFRA, Edam (NL), Jan 1988.

given to it within BAP. Furthermore some aspects of concertation activity have been given renewed importance by the recent Single European Act (see for example Article 130-I, which provides for a framework programme of R&D activities, and 130-N, which provides for cooperation with third countries and international organisations.)

5.2. The tasks given to CUBE

5.2.1. If we accept that concertation is a particularly important activity in biotechnology then the problem becomes that of identifying the specific concertation actions required in biotechnology and BAP and the institutional responses which these requirements should be given. Now the Council decision setting up BAP[2] identified for the concertation activity two goals and nine tasks. These goals and tasks are related to the previous types of concertation activity, as the following examples show :

1. Intercountry concertation: between different member states of the EC (task 4), between the EC and less developed countries (task 6).

2. Interinstitutional concertation: between industry and universities (task 4), with the European Federation of Biotechnology (EFB) and with the European Biotechnology Coordination Group (EBCG) (task 9).

3. Intrainstitutional concertation: between different Commission services (tasks 3, 5 and 7).

4. Interdisciplinary concertation: this was not prominent amongst the tasks set for CUBE, at least in the sense of concertation

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[2] O.J. N° L83, 25.3.85, pp 1-7.

between different scientific disciplines. On the other hand tasks 1,3,7 and 8, requiring the monitoring and gathering of information about the social, economic and legal aspects of biotechnology require concertation between scientific disciplines and the social sciences.

5.2.2. With respect to the two activities in para 5.1.3. above, CUBE has carried out an information-gathering activity (CUBEDOC), has acted as secretariat for BRIC*, has contributed to the design of programmes like ECLAIR and FLAIR, has contributed to the setting of agricultural price regimes in 1985 etc. A complete list of all CUBE's activities and actions would be pointless here, and interested readers are referred to CUBE's 1984-8 report. What is immediately clear from the list of tasks and activities of CUBE is the extremely wide scope of both of them. This very wide scope could give rise to different modes of institutional implementation which can be analysed in terms of three dimensions:

Size/resources : Large----------Small

Organisational style :
Formal/bureaucratic----------flexible/entrepreneurial

Role : Implementation----------Catalytic

In terms of these three dimensions CUBE has so far been small, flexible/entrepreneurial and catalytic.

5.2.3. We have been very impressed by the energy and dedication of the members of CUBE that we have met and by the very large number of initiatives in which they have been involved. Most of these activities are so important that a reasonable share of the

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* Biotechnology Regulations Interservice Committee.

responsibility for their success would be enough to justify CUBE's existence. We can give as examples the setting of the agricultural price regimes in 1985 and the BRIC committee. However, we have to admit that the evaluation of CUBE presents particular difficulties. We would like to offer some observations about these difficulties not with a negative aim but in order to point out some ways in which CUBE's activities could be improved.

5.2.4. For example a catalytic role is very difficult to evaluate due to the impossibility of running a control experiment without the catalyst. In other words it is extremely difficult to determine CUBE's share of responsibility for the success (or failure) of the activities in which it has been involved. The only way to do this would be to obtain the opinion of the members of the institutions with which CUBE has interacted in the process of concertation. We talked to a number of Commission officials from outwith DG XII (see Annex 7), but the CGC delegates, industrialists, contractors and fellows whom we saw hardly mentioned CUBE. While it must be recognised that to be evaluated is not the aim of any institution the previous observations point to a problem of institutional identity and image for CUBE. It is particularly difficult to answer questions such as : What is CUBE ? What has it done ? However the individual staff of CUBE seem to be better known than CUBE itself.

5.2.5. In what follows we have tried both to make some comments and to pose questions generally applicable to all CUBE's activities, and to offer some observations specific to particular activities and actions. However, we have not attempted to examine systematically all of CUBE's activities.

5.3. CUBE's performance of its tasks

5.3.1. Diversity/scope of tasks : at present CUBE's limited resources are spread over a very wide variety of tasks. Are they spread too thinly? Would it be better to concentrate on a smaller number of better-defined tasks?

5.3.2. Status : some of the concertation activities in which CUBE is involved (e.g. BRIC) require the simultaneous presence of different Directors-General of the Commission. When such concertation activities have to lead to some form of implementation (e.g. regulations) delays resulting from ineffective concertation can be very serious. What would be required in these situations is a decision maker (person or institutional subset) having the status required to obtain a relatively rapid outcome. The problem arises of either giving CUBE this status or of creating different institutional mechanisms to improve this type of concertation activity.

5.3.3. CUBEDOC. This is a database consisting of periodicals, articles, reports by other organisations (e.g. OTA, OECD) about biotechnology, mission reports etc. It now contains more than 21,000 items. However we have the impression that the database is not well organised or easy to access, and that therefore that it does not reach many potential users. Consequently we recommend that CUBEDOC should be re-examined with a view to its improvement or discontinuance.

5.3.4. Public opinion. The importance of public opinion has been stressed by CUBE members as well as by other biotechnology commentators. Given the importance of the issue, it might be necessary to include in CUBE communication specialists having professional skills in the use of the media required to reach the general public. Some of CUBE's existing literature seems to us to be too complicated and even we found it difficult to digest.

5.3.5. University-industry collaboration. This activity has so far had very low prominence. To the extent that it is considered an important CUBE task it should be strengthened.

5.3.6. Future orientation/scope. At present CUBE's tasks seem to be more oriented towards concertation of existing activities. We wonder whether in order to perform more effectively its role as a 'catalyst' it would not be better for CUBE for incorporate some longer-term forecasting activities in biotechnology.

5.4. Small biotechnology firms

5.4.1. We believe that there is clear evidence of a need to stimulate greater activity in the biotechnology small firm sector and that there is a role for the Commission to play in such stimulation on the European scale.

5.4.2. The Commission already has a number of programmes aimed at the needs of small and medium-sized firms "SMEs" (i.e. fewer than 500 employees).

- the Commission's Task Force on SMEs
- support for Business and Innovation Centres (BIC) in Member States and the European Business Network (EBN) through DG XVI
- the COMETT programme for cooperation between universities and enterprises for training in technology, run by DG V
- the investments made by the European Investment Bank, which works closely with DG II and XVIII
- the initial support for the European Venture Capital Association (from DG XIII)
- the SPRINT programme to aid transnational technology transfer to SMEs, run by DG XIII

Any fresh initiative should therefore take the form of a concertation of the existing programmes (including also national schemes), in order to focus on biotechnology SMEs. Such a

focussed initiative may well identify gaps in the programmes and it should be an early objective to identify any such gaps and to formulate means to fill them. The operational costs for the concertation activity and for the formulation of subsequemnt programmes would be borne by the budget for concertation, which we have recommended should be expanded under BRIDGE.

5.4.3. The overall objective, through focussing on the biotechnology industries, would be to maximise the European (ie transnational) impact in the stimulation of SME activity, so assisting them to operate in a continental dimension.

5.5. Summary

5.5.1. We consider that concertation activity is particularly important in biotechnology and therefore that there should be a unit like CUBE.

5.5.2. CUBE has been given a large number of tasks. We have been very impressed with the great energy and resourcefulness of CUBE's members and with the large number of initiatives in which they have been involved. However we find that CUBE's performance could be improved by a clearer definition and reduction in the number of its tasks.

5.5.3. An improvement in the Commission's decision-making mechanism is needed for major problems that affect more than one DG. CUBE can identify them, but they need a Task Force, distinct from CUBE, for their resolution. CUBE should retain the small, flexible and entrepreneurial structure it has had so far.

ANNEX 6

BIBLIOMETRIC STUDY OF BEP PUBLICATIONS

6.1. Summary

6.1.1. The bibliometric study was set up to examine the transnationality of BEP papers as compared with other European biotechnology papers, and their scientific influence as determined by their citation record compared with other papers in the same scientific journals.

6.1.2. The study identified some 420 BEP papers published in or accepted by refereed journals by mid -1988. Of these 420, 260 were identified through a questionnaire and 31% had a trans-national authorship. Many of the BEP papers (probably 190, of which 177 were identified) were published in 10 leading journals named in the BEP Final Report. The papers by EC authors in these journals with a trans-national authorship averaged 7% over the years 1981-87 and this figure was sensibly constant during the period. Thus it appears that BEP papers were several times more trans-national than other EC biotechnology papers published in leading journals.

6.1.3. The BEP provided only a small amount of the overall support for biotechnology in the EC while it was in operation. During the four main years for BEP publications (1983-6), they only represented about 4% of the total output of EC biotechnology research, as represented by papers in the 10 journals. However for several countries, notably Belgium and Ireland, BEP papers represented a much larger fraction than 4% of biotechnology research output.

6.1.4. Biotechnology papers in the 10 journals have a distinctive citation pattern, which peaks 2-3 years after publication and thereafter declines with a 4-5 year half-life. BEP papers in the same journals have a similar pattern, but the average numbers of

citations are almost uniformly higher, by some 40%.

6.1.5. Comparisons were made of the relative impacts (through the cumulative numbers of citations in the five years after publication) of particular groups of papers published in 1983. Multi-nationally authored EC papers were more highly cited than single-nation papers by 75%, and EC papers as a whole were more highly cited than those from the rest of the world by 29%. These factors largely account for the better citation record of BEP papers noted in the previous paragraph.

6.2. Background and terms of reference

6.2.1. The use of bibliometric studies in the assessment of research is still not universally accepted, partly because publications in refereed journals, which are the subject of the studies, are only one of the outputs of a research programme. In particular, commercial exploitation is not covered. In some research domains, the principal results may be communicated through conferences, whose literature is usually less accessible and is sometimes described as 'grey'. However biotechnology research seemed to us to be worth examination by means of a study of its output publications. The work in BEP (and also in BAP) was very largely of a 'public' nature with open publication being sought, and the final report on it published by the Commission indicated that a significant percentage of all the publications occurred in just 10 journals. These were listed by Dr Magnien, the editor, as being both prestigious and frequently used by BEP authors : they are given in para 6.3.3. below.

6.2.2. We therefore arranged for a study to be undertaken for us by Dr Paul Cunningham of the Programme of Policy Research in Engineering, Science and Technology (PREST), University of Manchester. The study was interactive, and the terms of

reference changed somewhat in the light of the results he obtained, but it was mainly designed to answer two questions :

- are BEP papers more trans-national in their authorship than other biotechnology papers with EC authors?
- have BEP papers been cited by other publications at least as often as comparable biotechnology papers in the same journals?

For the purposes of this study, a BEP paper was defined as one where the author acknowledged, either publicly or privately, some support from the programme. These papers were produced both by contractors, and by the fellows and their supervisors.

6.2.3. Each of the above questions is in the form of a comparison, and therefore the study needed to examine what would be an appropriate reference group of papers for the purpose. This proved to be quite a difficult task. The problem of selection of a fair comparison sample is one reason why the results of bibliometric studies are not accepted universally. Neverthless we consider that the results to be presented are sufficient to enable us to answer the two questions with a high degree of confidence.

6.3. Sources of information

6.3.1. It was necessary to compile as complete a list as possible of the BEP papers. This was made up from four sources :

- responses to a questionnaire sent by Dr Cunningham to all the BEP contractors and supervisors of BEP fellows.
- examination of all EC-authored papers in the 10 journals for an acknowledgement to BEP as a source of funding.
- the lists of publications given in the BEP final report.
- lists of publications given by BEP fellows who answered our own questionnaire (see para 4.4)

6.3.2. Dr Cunningham's questionnaire was returned by about 48% of addressees (by 28 June), 57 contractors (52%) and 17 supervisors (42%). It elicited specific information on the nationality of the authors of some 260 papers in refereed journals, and this information was used to answer the first question in para 6.2.2. Of these papers, some 95 were published in the 10 journals; the other 165 were published in a wide variety of journals[1] but none had more than nine papers, whereas six of the 10 exceeded this figure.

6.3.3. The 10 journals are as follows :

EMBO Journal	(EMBO J.)
Enzyme Microbial Technology	(Enz. Micr. Tech.)
Gene	(Gene)
Journal of Bacteriology	(J. Bacter.)
Molecular and General Genetics	(Mol. Gen. Genet.)
Nature (biotechnology papers only)	(Nature)
Nucleic Acids Research	(Nuc. Acid. Res.)
Plant Molecular Biology	(Plant Mol. Biol.)
Plasmid	(Plasmid)
Theoretical and Applied Genetics	(Theor. App. Gen.)

6.3.4. During the five years 1983-7, these 10 journals contained a total of 136 papers where specific acknowledgement was made to BEP. However there were an additional 41 papers identified from the questionnaire and the BEP final report in the 10 journals, so evidently between a quarter and a third of BEP authors did not

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[1] The other main journals used were :

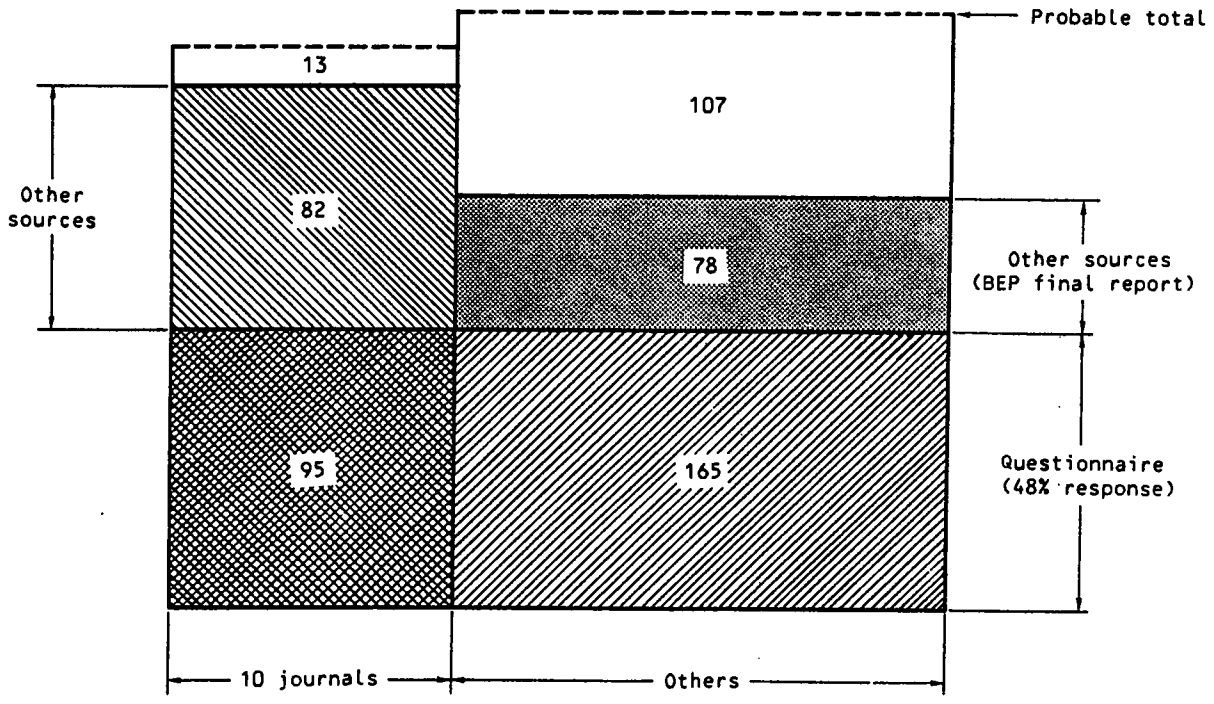
Carlsberg Research Communications	9 papers
Journal of General Microbiology	9 papers
Applied Environmental Microbiology	7 papers
Biochimie, Current Genetics, FEMS Microbiology letters	5 papers
Plant Science, Proc. NY Academy of Science	5 papers
Biotechnology Letters, Plant Cell Reports, Planta	4 papers

acknowledge the programme. For the citation analysis, the combined list of 177 papers was used. Numbers were as follows :

Journal	83	84	85	86	87	Total
EMBO J.	4	5	9	5	1	24
Enz.Micro.Tech.	0	2	1	2	1	6
Gene	2	4	7	6	2	21
J. Bacter.	4	6	8	4	2	24
Mol.Gen.Genet	6	5	14	8	2	35
Nature	1	3	4	1	0	9
Nucl.Acid.Res.	2	1	10	5	0	18
Plant Mol.Biol.	4	5	7	1	1	18
Plasmid	1	2	2	2	0	7
Theor.Appl.Gen.	5	1	4	4	1	15
Total	29	34	66	38	10	177

6.3.5. A final total of 420 BEP publications was identified: this is a large majority of those that have been accepted for publication so far. The totals can be broken down as follows :

	From questionnaire		Other sources		Number listed	Probable total		% coverage
All journals	260	+	160	=	420	/ 540	=	78%
10 journals	95	+	82	=	177	/ 190	=	93%



6.4. Results : transnationality

6.4.1. The authorship of BEP papers by the number of Member States[2] represented, based on the 260 papers in refereed journals itemized in the questionnaire responses, was as follows :

	Number of M. S.			
Year	1	2	3	% multi-state
1983	13	5	0	28
84	27	5	1	18
85	47	16	2	28
86	33	18	3	39
87	34	15	5	37
88	26	10	0	28
Total	180	69	11	31

Thus almost one-third of the papers (in the 48% sample) have a trans-national authorship. There is however no obvious trend for this proportion to increase over time. Of these 260 papers, 231 were from contractors and 56, or 24%, had multi-state authorship. Among the 95 papers in the 10 journals, however, the multi-state authorship was 40 (42%), or 29 (36%) from the contractors.

6.4.2. The questionnaire also asked whether there had been assistance through the provision of biological material or equipment by a laboratory or from scientists in another EC Member State. 82 answered 'yes', or 32%; this figure included 45 papers where the authorship was from a single country. A total of 134 papers had been assisted by discussions with, or other similar forms of contribution from, scientists in another Member State (52%). The total figure for trans-national cooperation in BEP amounted to 68%, made up as follows :

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[2] Excluding Spain and Portugal, which did not take part in BEP.

Total papers		260
Multi-EC authorship	80	
Single MS authors with :		
material /equipment	45	
discussions	87	
less both	(35)	
		177 = 68%

Again, papers in the 10 listed journals scored more highly : among the 55 single M.S. papers, 9 had received material/equipment, 24 discussions, and 8 both so a further 25/55 = 45% should be added to the 42% with multi-state authorship to give a total of 87%.

6.4.3. For a comparison with the above, the 10 journals were examined for the five years 1983-7 and also for 1981 (before BEP began) to determine :

- the total numbers of papers
- the number where the address of the first-named author was in the EC
- the number where there were authors' addresses from more than one EC Member State
- the numbers where acknowledgement was made to loans from or discussions with scientists in another Member State.

The results were as follows :

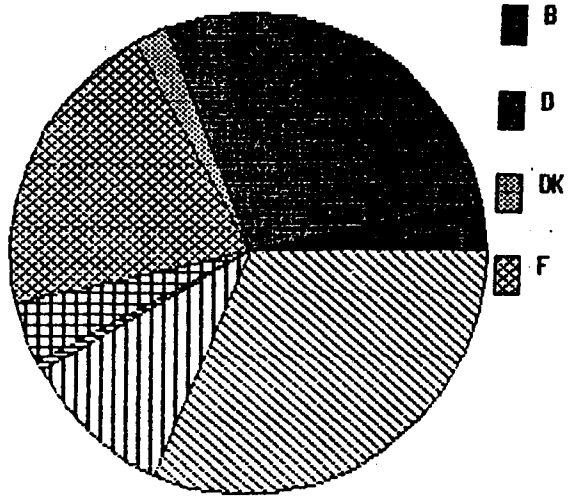
Year	Total papers	EC first author	Multi EC	EC loans	EC talks	% multiEC
1981	2252	660	46	16	11	7.0
1983	2975	1001	68	20	11	6.8
1984	3161	1076	74	27	14	6.9
1985	3412	1157	87	31	20	7.5
1986	3378	1095	73	21	12	6.7
1987	3720	1281	88	32	17	6.9
Total	18898	6270	436	147	82	6.9

6.4.4. It is clear to us from the above table that, although there has been an increase in numbers of multi-EC authored papers over the period (almost a doubling), the proportion of the total EC output has been remarkably constant at 7%. The EC total contribution to the journals is close to one-third and is also sensibly constant over the seven years. However the BEP papers are very much more transnational, whether one considers the total sample of 260, or the 95 published in the same 10 journals.

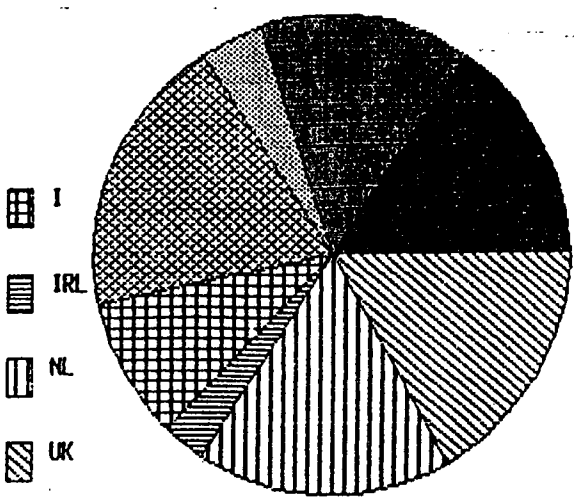
6.4.5. As mentioned above, there are many BEP papers that do not acknowledge their funding source, but we estimate the numbers in the 10 journals during the four years 1983-6 to have been about 178, so BEP has probably contributed to the support of about 4% of the 4329 EC papers in the 10 journals in the four principal years of its output. This is one measure of the influence of the programme on European biotechnology research. Nevertheless, the strong transnationality exhibited by BEP papers does not seem to have caused a noticeable change in the overall percentage. In 1985, the peak year for BEP, with a probable total of about 71 papers in the 10 journals, possibly an extra 23 were trans-national, which is 2% of the EC total. Yet the percentage for that year was only 0.5% higher than in 1981. This suggests that BEP may have captured existing trans-national cooperations without increasing them significantly.

6.4.6. The figure of 4% given above represents several times the ratio of BEP funding to other sources in the same years. This is because the research contracts were only funded at 50%, and our interviews with contractors revealed that EC funding generally represented a much lower proportion than this of the research groups' resources. Nevertheless, EC funding may be significant for some Member States. The breakdown by Member State of the EC first-author papers for the 10 journals in 1983-6 gives the following result :

	Total papers	BEP papers[a]	
B	147	26	18%
D	1193	24	2%
DK	100	7	7%
F	890	32	4%
GR	3	0	-
I	179	16	9%
IRL	33	5	15%
L	0	0	-
NL	444	29	7%
UK	1372	28	2%



EC papers in 10 journals 1983-6



BEP papers in same journals and years

Thus we see that BEP has been particularly important for Belgium and Ireland, a conclusion that agrees strongly with the evidence given to us during our missions.

6.5. Results : citations

6.5.1. The counts of citations given below are all taken from the "Science Citation Index" published annually by the Institute for Scientific Information in Philadelphia, which covers some 3500 journals and is regarded as the most comprehensive existing

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[a] There are some significant biasses here, notably the under-representation of Denmark because many Danish papers appeared in Carlsberg Research Communications

tabulation. It contains some slight linguistic biasses, but these will be insignificant here as all 10 of the journals studied are in English and indeed our study showed that hardly any BEP papers were written in other languages.

6.5.2. One immediate difficulty that we faced because the time and budget available for our study were restricted was that the numbers of citations of any comparison cohort to the BEP papers could vary greatly, depending on whether it contained one very highly-cited paper, whose citation counts could exceed those of the rest of the cohort put together. The result would be that the average citation pattern might be unduly high (or low). There are several statistical techniques to tackle this problem : they involve a mechanical transformation of the actual values before they are averaged. The technique used by Dr Cunningham was to transform the number of citations per paper per year, X1, to a new variable X2 where :

$$X2 = \sqrt{(X1 + 0.5)}$$

The mean value of X2 across a sample cohort of papers from the same year and same journal was then calculated ($\bar{X}2$) with its standard error SE2[4]. The mean value was then retransformed to X3 where

$$X3 = \bar{X}2^{2} - 0.5$$

and the standard error of X3 calculated (approximately) as

$$SE3 = 0.5\ ((\bar{X}2 + SE2)^{2} - (\bar{X}2 - SE2)^{2})$$
$$= 2.\bar{X}2.SE2.$$

The value X3 is an unbiassed estimate of the mean of X1, but with a smaller standard error.

6.5.3. The citation numbers of BEP papers were not transformed and then re-transformed because the papers represented the entire cohort, or at least all the papers from the journals known to derive from BEP. In practice, as mentioned earlier, it was probably about a 93% sample.

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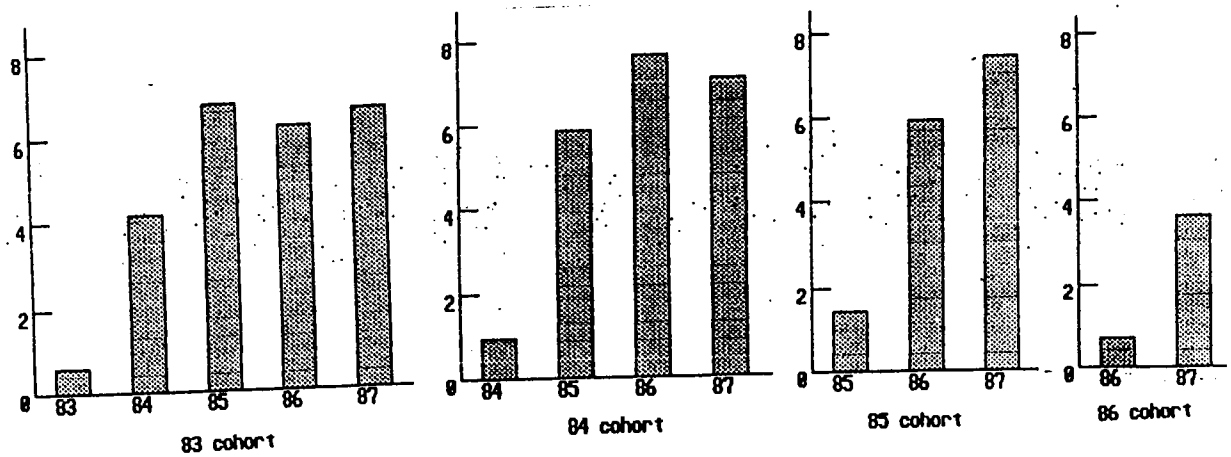
[4] This is related to the standard deviation of X2 by the formula $SE2 = SD2/\sqrt{N}$. There is a 68% chance that the true value of X2 is within one standard error of X2.

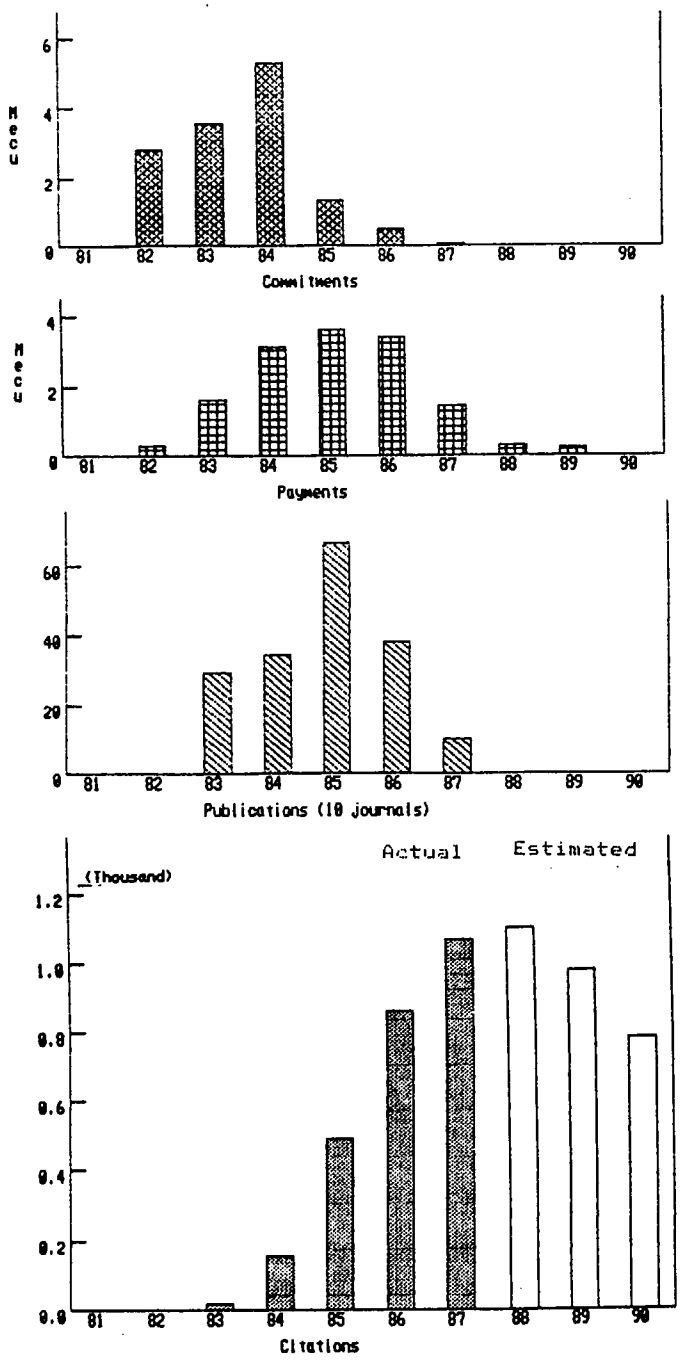
The actual numbers of citations received by all the papers in the five year cohorts were as follows :

	83 cohort						84 cohort				
Journal	N	83	84	85	86	87	N	84	85	86	87
EMBO J	4	2	9	10	4	7	5	9	47	57	56
Enz.Micr.Tech	0	-	-	-	-	-	2	0	2	5	6
Gene	2	0	5	18	27	33	4	0	15	20	37
J.Bacter.	4	4	12	25	14	23	6	7	28	46	41
Mol.Gen.Genet.	6	2	34	37	44	42	5	0	18	27	20
Nature	1	5	16	23	34	36	3	9	59	73	44
Nuc.Acid.Res.	2	2	16	17	10	9	1	1	15	23	21
Plant Mol.Biol.	4	0	10	21	13	18	5	0	6	21	14
Plasmid	1	0	2	11	10	10	2	4	9	12	20
Theor.Appl.Gen	5	2	18	35	24	13	1	1	2	3	3
Total	29	17	122	197	180	191	34	31	201	261	242

	85 cohort				86 cohort			87 cohort	
Journal	N	85	86	87	N	86	87	N	87
EMBO J	9	20	88	99	5	10	42	1	0
Enz.Micr.Tech.	1	0	2	0	2	0	2	1	1
Gene	7	8	23	36	6	5	25	2	2
J.Bacter.	8	8	31	34	4	5	9	2	1
Mol.Gen.Genet.	14	14	65	74	8	6	26	2	2
Nature	4	26	96	90	1	1	14	0	-
Nuc.Acid.Res.	10	9	46	60	5	0	8	0	-
Plant.Mol.Biol.	7	4	17	40	1	0	3	1	0
Plasmid	2	2	5	20	2	1	5	0	-
Theor.Appl.Gen.	4	2	20	37	4	0	4	1	2
Total	66	93	393	490	38	28	138	10	8



6.5.4. The pattern of citations, which, as we shall see, is also typical of the reference sample cohorts, is for the numbers per paper per year to build up to a peak in the second or third year after publication, and then for the numbers slowly to decline. The total number of citations to all the BEP papers in the 10 journals in each year is shown in the diagram below, together with the numbers of papers and the pattern of financial



commitments and payments. This shows that the scientific impact of BEP was still rising in 1987. (Estimates based on the citation patterns of similarly-sized cohorts of reference papers in the same journals for 1977 - see para 6.5.7 - have been made : these indicate a peak for BEP citations in 1988 and thereafter a decline.)

6.5.5. Any comparison of the BEP papers' citation record must be with papers that have been "exposed" for citation for precisely the same length of time. However we can see from the numbers involved that it should be possible to assess the influence of a group of papers quite well after only, say, three years even though they will by then have received fewer than half of their expected total numbers of citations.

6.5.6. We had some difficulty in choosing the reference cohorts, as we were again constrained by time and cost to limit the numbers of papers to be examined. We decided to take cohorts from two years, 1977 and 1983. The 1977 cohort allowed us to determine the citation pattern for biotechnology papers over a span of ten years, and thus to gain an insight into the longevity of papers in what is considered to be a rapidly-devloping field. The 1983 cohort allowed us to compare the changes in average numbers of citations, year by year, over a span of years : we know that many more biotechnology papers were published in 1987 than in 1981 (say), but there was correspondingly a larger "pool" of papers that could have been cited, both cumulatively and within (say) the last three years.

6.5.7. Three of the 10 journals were not published in 1977, so for these Dr Cunningham took a sample of 60 papers, or their first year's output if less, from their first year (EMBO J, 1982; Enz Microb Tech, 1979; Plant Mol. Biol, 1981). For the others he took 60 papers spread through 1977, or the year's output if less (Gene,38; Plasmid,45). For the 1983 cohort, a sample of 50 papers from each journal was taken, to give a comparable total number. In addition, all the

remaining multi-EC authored papers from the cohort of 68 (see para 6.3.3) had their citation records determined so that it would be possible to compare the respective performance in terms of citations for papers with authors from :

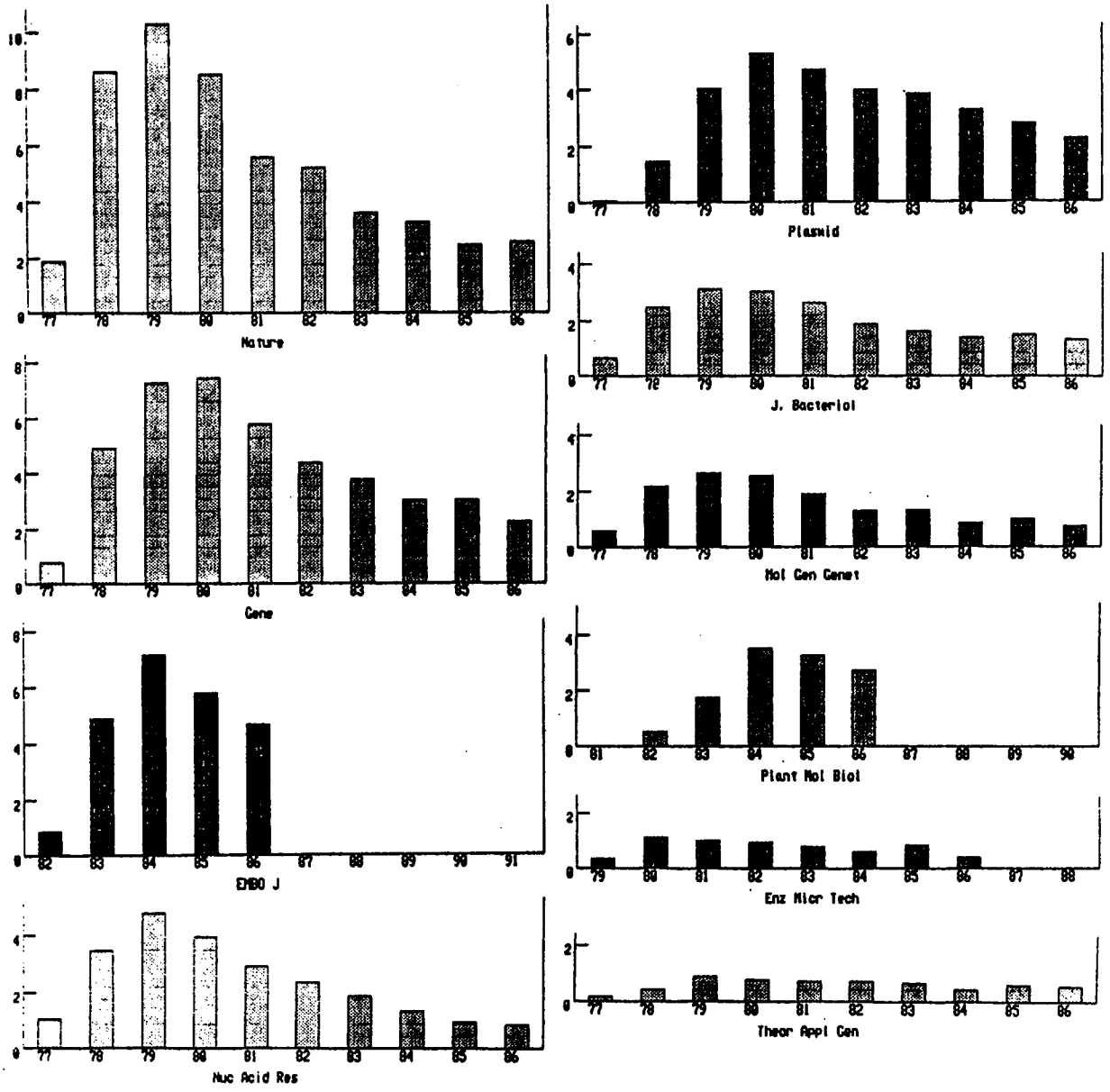
- more than one EC Member State
- just one EC Member State
- elsewhere in the world.

6.5.8. The results were as follows for the 1977 cohort :

Journal	Year:	77	78	79	80	81	82	83	84	85	86
EMBO J	X3	-	-	-	-	-	0.82	4.88	7.12	5.80	4.70
(N=60)	SE3	-	-	-	-	-	0.18	0.60	0.77	0.72	0.69
Enz Micr Tech	X3	-	-	0.35	1.08	0.99	0.96	0.76	0.59	0.84	0.40
(N=23)	SE3	-	-	0.15	0.28	0.24	0.31	0.25	0.21	0.26	0.11
Gene	X3	0.75	4.90	7.28	7.43	5.76	4.38	3.72	2.99	2.99	2.20
(N=38)	SE3	0.16	1.21	2.06	2.64	2.35	2.12	2.05	1.91	1.76	1.48
J.Bacteriol	X3	0.64	2.46	3.16	3.03	2.63	1.90	1.58	1.36	1.49	1.30
(N=60)	SE3	0.13	0.31	0.38	0.38	0.39	0.31	0.26	0.22	0.25	0.21
Mol Gen Genet	X3	0.55	2.13	2.67	2.55	1.87	1.26	1.33	0.83	0.98	0.70
(N=60)	SE3	0.14	0.34	0.46	0.46	0.37	0.29	0.32	0.25	0.32	0.24
Nature	X3	1.88	8.60	10.3	8.48	5.55	5.18	3.56	3.26	2.44	2.51
(N=60)	SE3	0.46	1.57	1.77	1.50	0.93	0.86	0.52	0.50	0.45	0.45
Nuc Acid Res	X3	1.02	3.49	4.79	3.98	2.93	2.39	1.88	1.34	0.93	0.83
(N=60)	SE3	0.22	0.44	0.64	0.59	0.52	0.44	0.37	0.27	0.21	0.18
Plant Mol Biol	X3	-	-	-	-	0	0.47	1.73	3.50	3.26	2.72
(N=20)	SE3	-	-	-	-	0	0.25	0.60	0.88	0.93	0.97
Plasmid	X3	0.03	1.42	4.01	5.31	4.69	3.95	3.80	3.27	2.74	2.19
(N=45)	SE3	0.03	0.25	0.47	0.72	0.67	0.72	0.79	0.78	0.72	0.62
Theor Appl Gen	X3	0.15	0.44	0.87	0.77	0.69	0.71	0.65	0.44	0.63	0.53
(N=60)	SE3	0.05	0.12	0.19	0.13	0.15	0.15	0.15	0.14	0.15	0.12

The pattern of a peak of citations after two-three years that was shown by the BEP papers (para 6.5.4) is very clear, see diagram below. Thereafter the number of citations halves every three-five years, with the highly-cited journals like "Gene" and "Nature" being

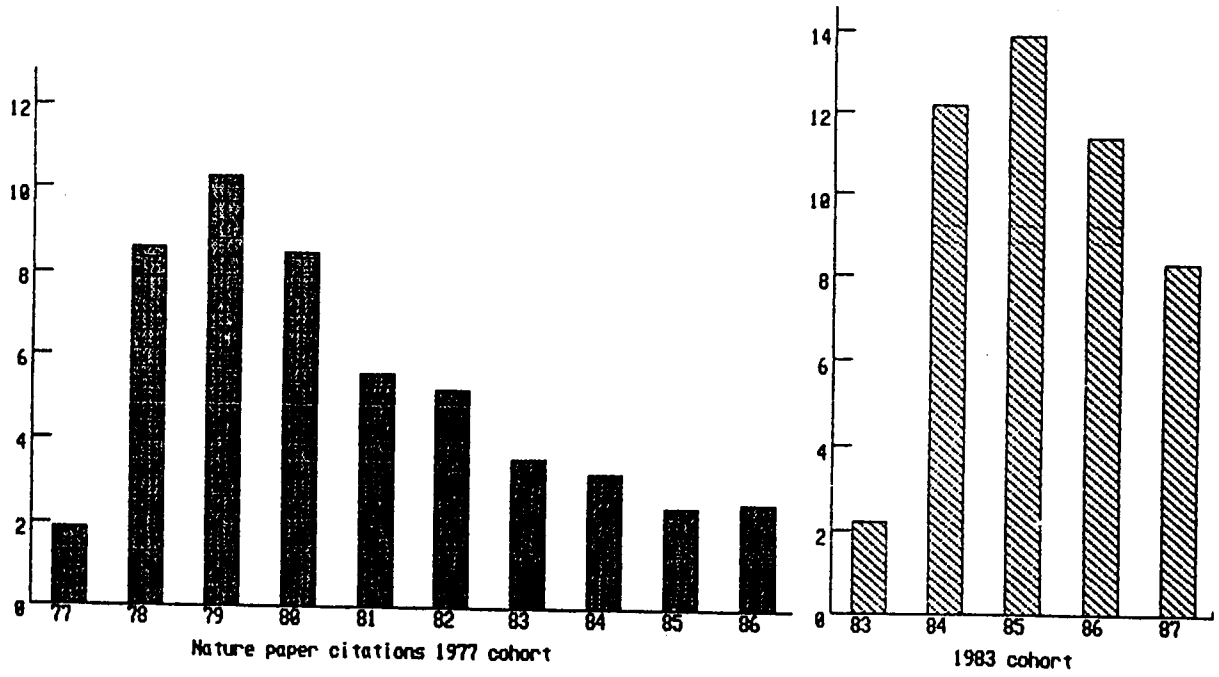
more "short-lived". It is also clear that there is a big variation between journals in average citations, the extremes being represented by "Nature" and "Theor. Appl. Gen." with respectively 10.3 and 0.9 citations per paper on average in the second year after publication.



6.5.9. For the 1983 cohort, the results were as follows (N=50 except for "Plant Mol. Biol.") :

Journal Year :	83	84	85	86	87
EMBO J	1.15	4.81	6.28	5.44	4.26
Enz Micr Tech	0.27	0.78	1.55	1.30	1.09
Gene	0.46	2.61	3.16	3.20	2.24
J Bacter	0.83	2.85	2.88	2.28	2.81
Mol Gen Genet	0.65	3.15	3.12	2.57	2.44
Nature	2.18	12.2	13.9	11.4	8.24
Nucl Acid Res	0.83	4.91	5.23	4.84	4.03
Plant Mol Biol	0.06	1.49	3.63	3.53	2.75
Plasmid	0.57	2.74	2.55	2.46	1.87
Theor Appl Gen	0.35	1.46	2.13	1.96	1.82

6.5.10. The pattern of citations is very similar to that for the 1977 cohort, but the average number per paper in the five years after publication has increased overall by 11.4%, on the basis of means weighted by the numbers of papers in each journal in 1983 although for four journals the numbers of citations have gone down, notably for "Gene" and "Plasmid".



The citation patterns against which BEP papers published in the five

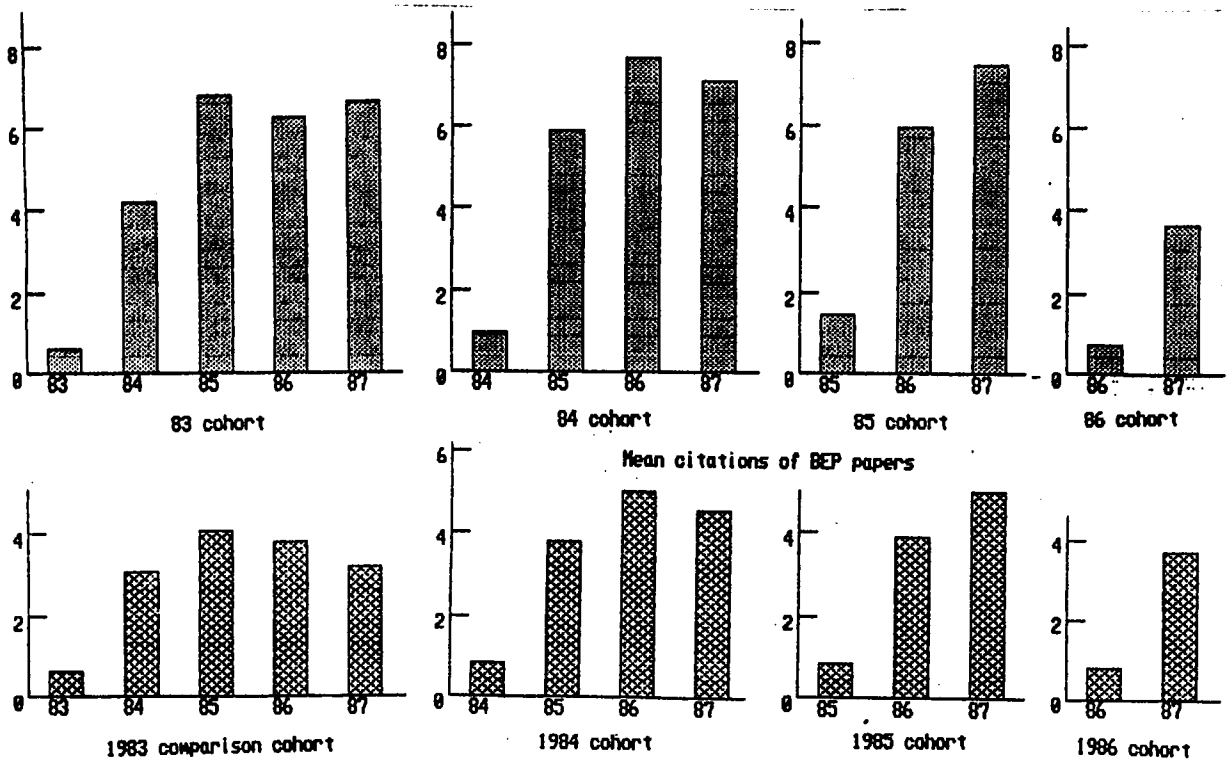
years 1983-7 should be compared have therefore been calculated on the basis of a linear increase of 1.9% per year (i.e., one sixth of the change between the 1977 and 1983 cohorts) applied from 1980, or the appropriate later year for journals first published after 1977, to the means of the numbers given in the two above tables.

For example, the reference citation patterns for "Nature" are as follows :

Publication year	Citation year 83	84	85	86	87
1983	2.26	11.6	13.5	11.1	7.68
1984		2.30	11.8	13.8	11.3
1985			2.35	12.0	14.0
1986				2.39	12.3
1987					2.44

6.5.11. We can now calculate the expected numbers of citations for a reference cohort of papers published in the same year as the BEP cohort, and consisting of the same numbers in each of the 10 journals. These may be compared directly with the figures in the table in para 6.5.3. We give below only the totals and the mean values per paper :

Publication year		Citation year 83 total	83 mean	84 total	84 mean	85 total	85 mean	86 total	86 mean	87 total	87 mean
1983	BEP	17	0.6	122	4.2	197	6.8	180	6.2	191	6.6
	Ref.		0.6		3.1		4.1		3.8		3.2
1984	BEP			31	0.9	201	5.9	261	7.7	242	7.1
	Ref.				0.8		3.8		5.0		4.6
1985	BEP					93	1.4	393	5.9	490	7.4
	Ref.						0.8		3.9		5.0
1986	BEP							28	0.7	138	3.6
	Ref.								0.8		3.7
1987	BEP									8	0.8
	Ref.										0.6

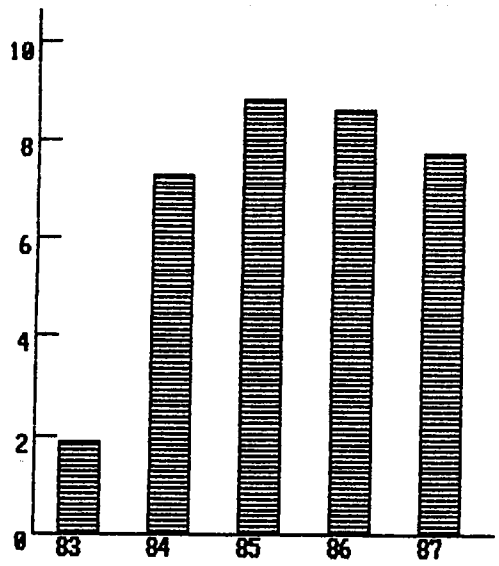


6.5.12. We have also estimated the standard errors of the means given in the above table caused by the comparison cohorts not being fully representative of the whole population, and they are very much smaller than the differences between the means for the BEP papers and the control cohorts. For example, for 1983 BEP papers cited in 1985, the standard error of the mean is 0.7, and the BEP paper citations exceeded the expected value by 2.7, or nearly four times the standard error of the latter. We may thus conclude that, as far as we can determine at present, BEP papers have had a significantly higher influence on biotechnology research than have average papers in the same journals. The ratio appears to be of the order of 1.4 to one, that is, BEP papers received on average 40% more citations than other papers published in the same journals.

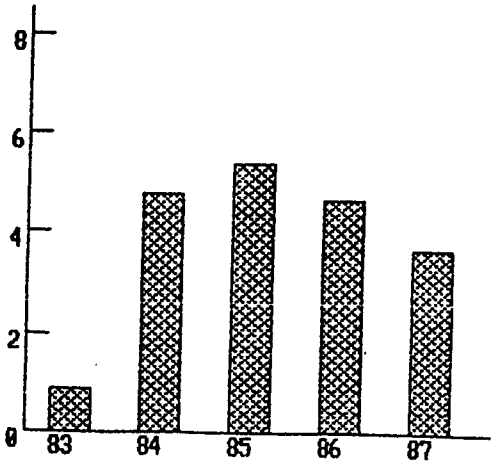
6.5.13. We also obtained data on the relative numbers of citations of multi-EC authored papers, single Member State papers, and non-EC papers

(see the table in para 6.4.3, and para 6.5.6) for 1983 publication. We weighted the mean citation numbers in two ways, First, in order to compare multi-EC papers with one M.S. papers, we used the numbers of EC papers comprised in the table in para 6.4.3. Then in order to compare EC papers with those from the rest of the world we weighted the numbers of citations by the numbers of all papers comprised in the same table. The results were as follows :

Citation in :			83	84	85	86	87
Multi-EC	(N= 68)	X1	1.9	7.3	8.8	8.6	7.7
Single-EC	(N=184)	X3	0.9	4.8	5.4	4.7	3.7

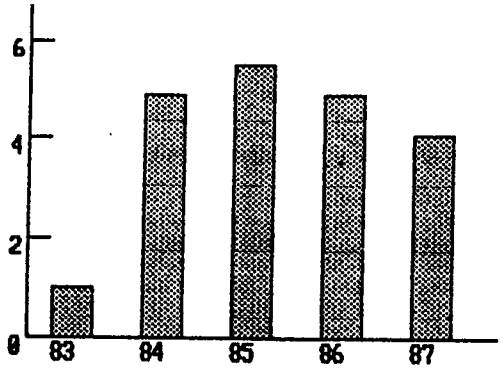


Citations of multi-EC papers

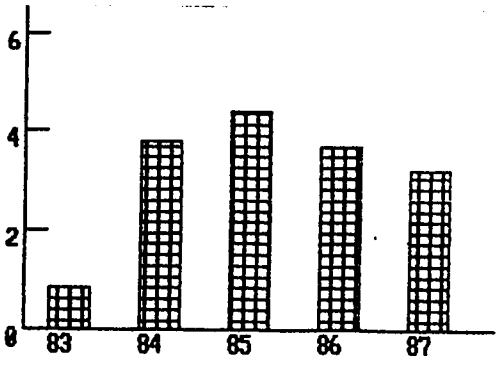


Citations of single-EC papers

Citation in :		83	84	85	86	87
EC authors (N=252)	X3	1.0	4.9	5.5	4.9	4.1
Rest of World (N=290)	X3	0.8	3.8	4.4	3.7	3.2



Citations of papers by EC authors



Citations of papers from rest of world

For the latter table, the values for "EC authors" have been taken as 0.93 x single EC authors + 0.07 x multi-EC authors, to reflect the overall balance of these papers.

6.5.14. The above tables suggest that there are real differences in mean numbers of citations between EC papers with authors from more than one, and just one, Member State, and also between EC papers and those from the rest of the world (predominantly the US). The ratios, based on five years' citations, are 1.75 and 1.29. These differences must account for a large part of the higher citation record of BEP papers found in para 6.5.12. BEP papers are, by definition, of EC origin, and they are also heavily trans-national (especially those in the 10 journals, see para 6.4.1). Application of the two ratios above (1.75, 1.29) to a random sample composed of 58% single-EC papers and 42% multi-EC papers would in fact suggest a citation record 1.5 times better than the journal average. This is surpassed by the 1983-85 BEP cohorts: it is perhaps too soon to draw conclusions about the 1986 and 1987 BEP papers.

6.6. Highly-cited BEP papers

6.6.1. In the course of the analysis, we identified some BEP papers that received large numbers of citations, and may therefore represent scientific work of outstanding merit. We give below the full references of 14 papers, four each for 1983,84 and 85, and two from 1986, which headed the lists of citations for their years.

6.6.2. From the 1983 cohort:

Hoekema, A., Hirsch, P.R., Hooykaas, P.J.J. and Schilperoort, R.A. A binary plant vector strategy based on separation of virand T-region of the Agrobacterium tumefaciens Ti-plasmid. Nature, vol. 303, 179-180.(114 citations)

Petit,A., David,C., Dahl,G.A.., Ellis, J.G., Guyon,P., Casse-Delbart, F., Tempé, J. Further extension of the opine concept: Plasmids in Agrobacterium rhizogenes cooperate for opine degradation. Mol. Gen. Genet., vol. 190, 204-214. (69 citations)

Downie, J.A., Hombrecher, G., Ma, Q-S., Knight, C.D., Wells, B. & Johnston, A.W.B. Cloned nodulation genes of Rhizobium leguminosarum determine host range specificity. Mol. Gen. Genet. vol. 190, 359-365 (63 citations)

Bagdasarian M.M., Amann E., Lurz R., Rückert B., and Bagdasarian M. Activity of the hybrid trp-lac (tac) promoter of Escherischia coli in Pseudomonas putida. Construction of broad host range controlled expression vectors. Gene vol. 26, 273-282. (52 citations)

6.6.3. From the 1984 cohort:

De Block, M., Herrera-Estrella, L., Van Montagu, M., Schell, J., and Zambryski,P. Expression of foreign genes in regenerated plants and in their progeny. EMBO J. vol. 3,1681-1689 (96 citations)

Herrera-Estrella, L., Van Den Broeck, G., Maenhaut, R., Van Montagu, M., Schell, J., Timko, M. and Cashmore, A. Light-inducible and chloroplast-asssociated expression of a chimeric gene introduced into Nicotiana tabacum using a Ti plasmid vector. Nature vol. 310, 115-120 (93 citations)

Hooykaas-Van Slogteren, G.M.S., Hooykaas, P.J.J. and Schilperoort, R.A. Expression of Ti plasmid genes in monocotyledonous plants infected with Agrobacterium tumefaciens. Nature vol. 311, 763-764. (61 citations)

Rossen,L., Johnston, A.W.B. & Downie, J.A. DNA sequence of the Rhizobium leguminosarum nodulation genes nodAB and C required for root hair curling. Nucl. Acids Res. vol. 12, 9497-9508. (60 citations)

6.6.4. From the 1985 cohort:

Stachel, S.E., Messens, E., Van Montagu, M. and Zambryski, P. Identification of the signal molecules produced by wounded plant cells that activate T-DNA transfer in Agrobacterium tumefaciens Nature vol. 318, 624-629 (77 citations)

Van Den Broeck, G., Timko, M.P., Kausch, A.P., Cashmore, A.R., Van Montagu, M., and Herrera-Estrella, L. Targeting of a foreign protein to chloroplasts by fusion to the transit peptide of ribulose-1,5-bisphosphate carboxylase. Nature vol. 313, 358-363 (75 citations)

Koukolikova-Nicola, Z., Shillito, R.D., Hohn, B., Wang, K., Van Montagu, M., and Zambryski, P. Involvement of circular intermediates in the transfer of T-DNA from Agrobacterium tumefaciens to plant cells. Nature vol. 313, 191-196 (58 citations)

Downie, J.A., Knight, C.D., Johnston, A.W.B. & Rossen, L. Identification of genes and gene products involved in the nodulation of peas by Rhizobium leguminosarum. Mol. Gen. Genet. vol. 198, 225-262. (42 citations)

6.6.5. From the 1986 cohort:

Shearman, C.A., Rossen, L., Johnston, A.W.B., & Downie, J.A. The Rhizobium leguminosarium gene nodF encodes a polypeptide similar to acyl-carrier protein and is regulated by nodD plus a factor in pea root exudate. EMBO J. vol. 5, 647-652. (28 citations)

Jensen, J.S., Marcker, K.A., Otten, L., and Schell, J. Nodule-specific expression of a chimaeric soybean leghaemoglobin gene in trangenic Lotus corniculatus. Nature, vol 321, 669 (15 citations)

6.6.6. By way of comparison, the top 4 papers from the 1983 comparison cohorts from "EMBO J.", "Mol. Gen. Genet.", and "Nature" had the following numbers of citations in the 2,3,4, and 5 years after publication :

		2	3	4	5
EMBO J.	1	36	77	126	172
	2	37	75	112	137
	3	26	56	100	128
	4	15	47	89	128
Mol. Gen. Genet.	1	12	26	36	49
	2	11	21	32	46
	3	11	22	33	39
	4	13	24	31	38
Nature	1	85	159	254	330
	2	19	57	95	145
	3	52	86	109	131
	4	34	66	107	127

6.6.7. We conclude from the above comparison that the two 1983 BEP papers in "Mol. Gen. Genet." were outstanding for that journal, although modest in comparison with papers in, say, "EMBO J.". Among the 1984 BEP papers, the first two were among the top four or five for their year and journal (i.e. the top 10%). The 1985 BEP cohort fared better, and all of the four listed would have been among the top 10% for their year (notably the last one, in "Mol Gen. Genet." which had nearly twice the citations in a three-year period of the leading four in that journal).

ANNEX 7

PERSONS WHO GAVE EVIDENCE TO THE PANEL

7.1. ORAL EVIDENCE

7.1.1. Commission officials (DG XII unless otherwise noted)

A. Aguilar	
R. Batti	DG VIII
U. Bertazzoni	
M. Cantley	
G. del Bino	DG XI
D. de Nettancourt	
I. Economidis	
G.L. Ferrero	DG XVII
W. Floyd	DG VI
A. Goffeau	
P. Gray	DG III
S. Keegan	DG III
A. Klepsch	
E. Magnien	
R. Petrella	
A. Saint Rémy	
K. Sargeant	
B. Schmitz	
B. Traill	
F. Van Hoeck	
B. von Wüllerstorff	

7.1.2. Members and former members of CGC

A. Albert (E)

R.H. Aram (UK)

F.J.A. Carvalho Guerra (P)

J. de Brabandère (B)

D. Jonas (UK)

M. Lelong (F)

A.F. Lott (UK)

K.A. Marcker (DK)

I. Petersen (DK)

P. Printz (F)

J. Ryan (IRL)

C.E. Sekeris (GR)

D. Thomas (F, ex-Chairman)

A.S. Tsaftaris (GR)

M.C.F. van den Bosch (NL)

R.R. van der Meer (NL, Chairman)

H.C. van der Plas (NL, ex-Chairman)

E. Warmuth (D)

7.1.3. Contractors and their representatives. (GBI = BEP contracts)

BELGIUM

M. Boutry/M. Briquet	(BAP-0019 -B)
J. Davison	(GBI-3-106-B, BAP-0048-B)
P. d'Oultremont	(BAP-0121 -B) subcontract
W. Fiers	(GBI-4-065-B, BAP-0248-D)
G.L. Hennebert	(BAP-0028-UK)
J.P. Hernalsteens/H. De Greve	(BAP-0089- B)
C.M. Lapiere	(BAP-0278- B)
J. Limet	(BAP-0123- B)
N.M. Nolard-Tintigner/C.Vuncks	(BAP-0028-UK)
J. Rommelaere	(BAP-0121- B)
P.G. Rouxhet/Navamoses	(GBI-1-006-B, BAP-0069-B)

DENMARK

B.S. Adamsen/K. Kleiding	(BAP-0023-DK)
A. Brandt	(GBI-4-024-DK, BAP-0025-DK, BAP-0091-DK)
R. Rajagopal/J. Marchison	(BAP-0077-DK)

FRANCE

J.P. Bourgin	(GBI-6-071-F)
J. Cohen	(GBI-2-080-F, BAP-0156-F)
G. Corvier	(BAP-0144 -F)
Y. Dattee	(BAP-0014 -F)
L. Dubertret	(BAP-0277 -F)
F. Dufau/D. Duval	(BAP-127-F)
H. Fukuhara	(GBI-2-093-F, BAP-0026-F)
M. Guerineau	(GBI-2-081-F, BAP-0268-F)
L.M. Houdebine	(BAP-01079-F)
J. Janin/S. Baudet	(BAP-0049 -F)
A. Koutoujansky	(BAP-0212 -F)
J.C. Mercier	(GBI-2-082-F)
V.M. Nigon	(GBI-2-126-F, BAP-0124 -F)
A. Parmeggiani	(BAP-0066 -F)
B. Perret	(BAP-0031 -F)
R.J. Poljak	(BAP-0221 -F)
F. Quetier/B. Lejeune	(GBI-4-104-F, BAP-0022 -F)
M. Weiss	(BAP-0017 -F)
R.G. Whalen/P. Herbomel/S. Cereghini/F. Tronche	(BAP-0145 -F)

GERMANY

C. Bachem/L. Moore	(BAP- 102-UK)
A. Böck/D. Sizman/C. Kalman	(BAP-0040 -D)
G. Cesareni	(BAP-0252 -D)
R. Cortese	(BAP-0115 -D)
K. Esser/F. Meinhardt	(GBI-4-102-D)
F. Götz	(BAP-0196 -D)
K.D. Kulbe	(BAP-0059 -D)
H.P. Lepers/Fluggen	(BAP-0033 -D)
H. Lörz	(BAP-0013 -D)
H.J. Rziha	(GBI-2-056-D, BAP-0233- D)
C. Sander	(BAP-0227 -D)
P. Schreier	(BAP-0096 -D)
W.L. Standenbauer	(BAP-0045 -D)

P. Starlinger (GBI-4-130-D)

R. Thompson (BAP-0213 -D)

R. Wingender-Drissen/F.Kreuzaler (BAP-0087 -D)

IRELAND

D. Higgins (BAP-0137-IRL)

D. Mc Connell (GBI-2-092-IRL, BAP-0263-IRL)

M. O'Connell (BAP-0080-IRL)

ITALY

P. Arosio (BAP-0246 -I)

L. D'Angiuro (GBI-1-075-I)

G. Carrea (GBI-1-051-I, BAP-0065-I)

M. Motto (BAP-0214 -I)

S. Riva (BAP-0122 -I)

F. Sala (BAP-0084 -I)

A. Vecchi (BAP-0273 -I)

THE NETHERLANDS

L. Bosch (BAP-0057 -NL)

W.M. De Vos (GBI-2-084-NL, BAP-0011 -NL)

C.J. Keijzer (BAP-0202 -NL)

W.F. Stevens/H.Nieboer/P. Van Lelyveld (GBI-1-077-NL, GBI-3-063-NL, BAP-0251-NL, BAP-0109 -NL)

H.J.J. Nijkamp (GBI-4-110-NL, GBI-3-061-NL, BAP-0020-NL)

P.H. Pouwels (GBI-2-009-NL, GBI-5-118-NL, BAP-0064 -NL, BAP-0018-NL)

C.H. Theunis (BAP-0202 -NL)

W.Van der Valk/W.Verhuizen (GBI-4-109-NL, BAP-0083-NL)

L. van Vloten-Doting (BAP-0083 -NL)

H.J. Wilms (BAP-0202 -NL)

UNITED KINGDOM

R. Barr (BAP-0280 -UK)

C.J. Bostock (BAP-0237 -UK)

F. Brown (GBI-2-053-UK, BAP- 232 -UK)

R. Casey (GBI-4-113-UK, BAP-0063 -UK)

R.B. Flavell/V. Colot/A. Goldsbrough/M. Thomas
(GBI-4-027-UK, GBI-4-115-UK, BAP-0106-UK)

B. Gillham (BAP-0284 -UK)

B. Hartley (BAP-0265 -UK)

D.L. Hawksworth/D.Allsopp/D. Smith (BAP-0004 -UK, BAP-0028-UK)

L.R. Hill/M. Costas/V. Hughes/L. Sloss (BAP-0138 -UK, (BAP-0002 -UK)

P. Hirsch (BAP-0024 -UK, BAP-0100 -UK)

R. Hull (BAP-0097 -UK)

A.W.B. Johnston (GBI-5-070-UK)

M.G.K. Jones (GBI-4-023-UK, BAP- 101 -UK)

M. Kreis (BAP-0099 -UK)

M.D. Lilly (GBI-1-008-UK)

K. Miller/Gangoly/Hard (BAP-0272 -UK)

E.R. Pike (BAP-0293 -NL)

F. Stewart (GBI-2-088-UK)

7.1.4. Current fellows under BAP

V. Blank (D)

B. Carpentier (F)

M. Crozatier (F)

P. Eraso (E)

P. Fiorentini (I)

G. Godin (F)

H. Hoffman (D)

N. Houba-Herin (B)

M. Kavanagh (IRL)

N. Leduc (F)

A. Luzzago (I)

J.A.S.P. Matos (P)

P. Ottaviani (F)

B. Papadopoulou (GR)

A. Phanopoulos (GR)

F. Pinto (E)

F. Portillo (E)

E. Tinois (F)

G. Soldevilla (E)

V. Sophianopoulos (GR)

U. Schmitz (D)

M. Storrs (IRL)

E. Yagüe (E)

7.1.5. Supervisors of fellows (nationality / host country)

P. Borst (NL)

P. Brown (UK)

G. Cesarini (I/D)

R. Cortese (I/D)

F. Brunel (B)

G. Douglas (IRL)

. Dufour (B)

T. Gaspar (B)

A. Goffeau (B)

T. Graf (D)

L.A. Grevell (UK/NL)

S. Hartley (UK)

M.C. Kielland-Brandt (DK)

D. Lonsdale (UK)

L. Luzzato (UK)

M.E. Selkirk (UK)

A.D. Smith (UK)

M. Stanley (UK)

P. Starlinger (D)

H. ten Cate (NL)

P. Trieu-Cuot (F)

7.1.6. Former fellows under BEP

C. Gebhardt (D)
S. Giovenco (I)
R. Götz (D)
C. Hussey (IRL)
E. Jackson (UK)
K. Larsen (DK)
J. Nicaud (F)
B. Nieuwenhuis (NL)
M. Verhoeyen (B)

7.1.7. Industrial representatives

B.S. Adamsen, Danish Distillers A/S (DK)
J. Britton, Irish Sugar Co (IRL)
F. Brown, Wellcome Biotechnology Ltd (UK)
A. Bruggink, OCE. Andeno NV (NL)
B. Cantwell, Guinness Co Ltd (IRL)
P. d'Oultremont, Solvay S.A. (B)
F. Dufau and D. Duval, Bertin et Cie (F)
A. Formigoni, Sipcam Spa (I)
G. Freyssinet, Rhone-Poulenc S.A. (F)
D. Gunary, Nickerson Seed Co Ltd (UK)
J. Herrman, Glaxo plc (UK)
J. Leemans, Plant Genetic Systems NV (B)
J.H. Mahler, Novoindustri A/S (DK)
P. Niebes, Searle (B)
M. Hilmer Nielsen, Novoindustri A/S (DK)
S. Paleoyannis, Biohellas Hellenic Biotechnology Cie (GR)
S. Petersen, Novoindustri A/S (DK)
K. Powell, ICI plc (UK)
M. Soria, Farmitalia Spa (I)
A. Stavropoulos, Vioryl SA (GR)
P. Van den Elzen, Mogen International BV (NL)

R. van der Meer, HOM NV (NL)

F. Vecchio, ORIS Spa (I)

7.1.8. Other persons

N.H. Axelsen, Statens Seruminstitut, Kobenhavn, (DK)

C. Christiansen, Gensplejsningsgruppen, Lyngby, (DK)

R. Dietz, Laboratory of the Government Chemist, London (UK)

P.O. Larsen, Forskningskirektoratet, Kobenhavn (DK)

L. Philipson, EMBL, Heidelberg (S)

W.F. Stevens, Medical Biological Laboratory, TNO Rijswijk (NL)

M. Tsogas, Ministry of Industry, Athinai (GR)

J.N. Wingfield, Agricultural and Food Research Council, London (UK)

7.2. WRITTEN EVIDENCE

7.2.1. Commission officials

M. Cantley (XII-F-1)

G. del Bino (XI-A-2)

W.B. Traill (XII-H-2)

W. Floyd (VI-01)

7.2.2. Former fellows under BEP (questionnaire)

A. Athanassiadou (GR)

A. Bacolla (I)

G. Bensi (I)

M. Charbonnier (F)

F. Chauvat (F)

T. Cogan (IRL)

C. Crétin (F)

M. Crouzet (F)

M. de Crombrugghe (B)

T. Delaunay (F)
W.M. de Vos (NL)
A. di Pietro (F)
F. Düms (D)
P. Durrens (F)
J.P. Dyson (UK)
S. Junker (DK)
S.S. Manian (UK)
G. Romeo (I)
L. Sibold (F)
J.M. Tempelaar (NL)
P. Woolley (UK)

7.2.3. Industrial representatives (questionnaire)

G. Alexander, Transgene SA (F)
Aline, Doittau Emuldo (F)
K. Ashley, Mast Laboratories Ltd. (UK)
C.P.W. Boeder, Sensys (NL)
W.H. Boldingh, Akzo Pharma BV (NL)
G.A. Brooker, Celltech Ltd (UK)
A. Capelle, Avebe BA (NL)
R. Chabannes, Mero-Rousselot-Satia (F)
H. Chmiel, Fraunhofer Institut (D)
W.B. Christie, Premier Breeders Ltd (UK)
R. Connett, Agricultural Genetics Co plc (UK)
K. Coupland, Croda Universal Ltd (UK)
D. Czeschlik, Springer-Verlag (D)
C.H.M.M. De Bruijn, Euro-Diagnostics BV (NL)
M. Delaage, Immunotech (F)
W.H. De Niet, Sanbio BV (NL)
A.C. De Ruiter, De Ruiter Zonen (NL)
P. Desmettre, Rhone Merieux (F)
R.A. Dicker, Dairy Crest Ltd. (UK)
M. Dubois, Sanofi-Elf-Bio-Recherches (F)

H. Durand, Cayla (F)

L. Flohé, Gruenenthal GmbH (D)

J.E. Fonteyne, Centocor Europe BV (NL)

C.R. Franks, Euro Cetus BV (NL)

A. Frouin, Lab. Soredab (F)

W.W. Gerard, Cambridge Life Sciences plc (UK)

M. Gervais and J.M. Le Moullec, Roussel Uclaf (F)

P. Giordano, Bio Rad Laboratories SRL (I)

G.I. Glikmans, Technip (F)

P.J.F. Hack, Paques BV (NL)

A. Hamilton, Amersham International plc (UK)

G. Hubert, Institut de Selection Animale (F)

E.J. Hudson, Albright & Wilson Ltd (UK)

M.H. James, Shield Diagnostics Ltd (UK)

J.P. Jarry, Lafarge Coppé (F)

M. Kloft, Biotest Pharma GmbH (D)

R. Kron-Morelli, Agrifutur (I)

K. Koerts, Suiker Unie Research (NL)

P. Koning, Holland Biotechnology BV (NL)

H.G. Kooreman, International Bio-Synthetics BV (NL)

H. Kragen, Mero-Rousselot-Satia (F)

R.W.F. Le Page, Biotal Ltd (UK)

W. Leuchtenberger, Degussa AG (D)

H.C.G. Ligtenberg, Sentron VOF (NL)

J.P. Mégnin, Moët-Hennessy-Louis-Vuitton (F)

E.M. Meijer, DSM Research (NL)

J-C. Morell, La Cellulose du Pin SA (F)

A.D. Mulder, Royal Sluis BV (NL)

Nordmann, Bayer AG (D)

S. Paleoyannis, Biohellas SA (GR)

F. Parenti, Lepetit Research Centre (I)

K.H. Pelster, Millipore GmbH (D)

G.S. Plastow, Dalgety plc (UK)

M.H. Pranger, Duphar BV (NL)

R. Reiner, Röhm GmbH (D)

F.M. Roberts, Bioprocessing Ltd (UK)

P.J. Rodgers, ICI plc (UK)

A.J. Savill, Fermentech Ltd. (UK)

H.U. Schenck, BASF AG (D)

Schöls, Siemens AG (D)

J.F. Seitzer, Kleinwanzlebener Saatzucht AG (D)

J.J. Snoijink, Nordic Immunological Laboratories (NL)

Sonneveld, DSM (NL)

B. Spruijtenburg, HWZ Bodemsauering (NL)

J. Tretzel, Akzo Research Laboratories (D)

J. Van Burg, Applikon Dependable Instruments BV (NL)

Van Weperen, Bio-Intermediair BV (NL)

J.E. Veldhuyzen van Zanten, Zaadunie BV (NL)

Vente, Euribrid (B)

J.A.J. Vink, CSM biological division (NL)

G. Volpe, RASA - Realtur Spa (I)

Wandrey, Nuclear Research Centre Jülich (D)

T.J. Warren, L.H. Fermentation Ltd (UK)

A. Weber, Schering AG (D)

J. Winter, COMASSO (D)

Anonymous : - Laboratoire Barreret et Ducloux (F)
- Courtaulds Research (UK)

7.2.4. Other persons

J.M. Bove, Association pour le développement des biotechnologies en Aquitaine (F).

E. Drioli, Societa Chimica Italiana (I).

J. Hamill, Cruachem Ltd (UK).

W.A. Hamilton, University of Aberdeen (UK).

P. Monsan, Association pour le Développement de la Bio-Industrie (F).

C. Ratledge, University of Hull (UK).

K. Schügerl, Universität Hannover (D).

R. Shewry, Rothamsted Experimental Station (UK).

C. Shirlaw, Scottish Development Agency, (UK).

D.A. Stafford, Society for Applied Bacteriology (UK).

G.J. Stegehuis, Centraalbureau voor Schimmelcultures (NL).

C.M. Thomas, University of Birmingham (UK).

K.N. Timmis, Gesellschaft für Biotechnologie Forschung mbH (D).

ANNEX 8

LIST OF DOCUMENTS CONSULTED BY THE PANEL

8.1. Extracts from the Official Journal

1. Council Decision of 7 December 1981 (BEP)
   L 375, 30.12.81, pp 1-4

2. Council Decision of 26 October 1983 (BEP, second stage)
   L 305, 8.11.83, pp 11-13

3. Council Decision of 12 March 1985 (BAP)
   L 83, 25.3.85, pp 1-7

8.2. Commission documents

1. Proposal for a Council Decision (BEP)
   COM (79) 793 final, 11 January 1980

2. Proposal for a Council Decision (BAP)
   COM (84) 230 final, 26 April 1984

3. Review of BAP
   COM (86) 272 final, 21 May 1986

4. A Community framework for the regulation of biotechnology.
   COM (86) 573 final, 4 November 1986

5. Proposal for revision of BAP
   COM (87) 481 final/2, 19 November 1987

6. Proposal for a Council Decision (ECLAIR)
   COM (87) 667 final, 18 December 1987

7. Proposal for a regulatory framework for the use of genetically modified organisms.
   COM (88) 160, 29 March 1988

8. Proposal for a Council Directive on the protection of workers from the risks related to exposure to biological agents at work.
   COM (88) 165 final - SYN 129, 5 April 1988

8.3. Commission publications

1. Research and training programme in biomolecular engineering : catalogue of contracts with classification of activities.
   EUR 9857, 1985.

2. Biomolecular engineering in the European Community, E. Magnien (Ed); Martinus Nijhoff, Dordrecht (NL); EUR 10658, 1986.

3. BEP/BAP/Biotechnology, (brochure)

4. Biotechnology Action Programme (1985-1989) :
   catalogue of contracts with classification of activities,
   B Nieuwenhuis (Ed), EUR 10954, 1988.

5. Biotechnology Action Programme, Progress report 1987, E. Magnien (Ed), volumes 1 and 2, EUR 11138, 1988.

6. Vade-mecum of Community research promotion.
   CD-46-86-266-EN-C, 1987.

7. STD/Science and Technology for Development (brochure).

8.4. Commission mimeographs

1. BEP and BAP : press cuttings on activities and results during the period 1984-1987.

2. Training activities implemented in the framework of the Biomolecular Engineering Programme.

3. Training activities implemented in the framework of the Biotechnology Action Programme : the opinion of trainees and of training supervisors.
   M. Mongini and D. de Nettancourt.

4. Risk assessment for the release of genetically manipulated micro-organisms. Meeting papers, Bayreuth, October 26-28, 1987.

5. IRDAC opinion on future R&D programmes in the field of biotechnology, December 1987.

6. In vitro evaluation of the toxicity and pharmacological activity of molecules, Meeting papers, Bad Irsee, March 30 - April 1, 1988.

7. CUBE report, 1984-1988 : retrospect and prospect. Draft of 9 March 1988.

8. The future of the European food system : implications for science and technology policy. Executive summary of FAST study, February 1988.

9. Science and Technology for Development, 1987-91. Information file.

10. BAP: Autopsy of a call for proposals, Facts and Statistics. June 1988.

8.5. Miscellaneous

1. "What regulatory framework for biotechnology in Europe ?" Proceedings of a seminar held by Centre for European Policy Studies, Brussels, 23 February 1988.

2. "Rhizobium leguminosarum as a model for investigating gene transfer in soil". PR Hirsch and JR Spokes. In : "Risk assessment for deliberate release", ed. : Walter Klingmüller; Springer-Verlag, 1988.

3. "The impact of biotechnology on European agriculture". G. Junne, with J. Bijman. University of Amsterdam, Department of International Relations and International Public Law, 31 August 1987.

4. "Mapping our genes. The genome projects : how big, how fast ?" Office of Technology Assessment, Washington DC, April 1988.

European Communities — Commission

EUR 11833 — Evaluation of the Biomolecular Engineering Programme-BEP (1982-1986) and the Biotechnology Action Programme-BAP (1985-1989)

Ch. af Malmborg, P. Feillet, F. Kafatos, J. Koeman, P. Saviotti, F. Schmidt-Kastner, G. Walker

Luxembourg: Office for Official Publications of the European Communities

1988 — VIII, 128 pp. — 21.0 x 29.7 cm

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In accordance with the Commission's policy of carrying out an independant external evaluation of each research programme (see the Plan of Action, O.J. C14, 20.1.87 pp. 5-8), a panel of seven members was asked to evaluate the Biomolecular Engineering Programme (1982-6) and the Biotechnology Action Programme (1985-9).

Their report gives a brief description of the programmes, the panel's conclusions and recommendations for the future, and details of their evaluation procedure.

There are eight annexes:

1. Terms of reference
2. General observations on the programmes
3. Assessment of the research sub-programmes
4. Assessment of the training activities
5. Assessment of the concertation activities
6. Bibliometric study of BEP publications
7. Persons who gave evidence to the panel.
8. List of documents consulted by the panel.

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