UNIVERSITY-INDUSTRY RELATIONS - THEIR ROLE IN TECHNOLOGICAL INNOVATION: THE CASE OF BIOTECHNOLOGY IN THE UK

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SUMMARY

Biotechnology is one of a series of new 'generic technologies' that have been identified by western governments as possessing strategic economic opportunities. In this thesis I examine the characteristics of the technology and the government policies that have been developed to both promote and exploit the underpinning scientific research for biotechnology. The approach I have taken involves an in-depth analysis of the role of university-industry research relations in the development of biotechnology. To this end I carried out a detailed survey of biotechnology companies in the UK on the nature of their interactions and objectives. Through individual case studies of the SERC and DTI club mechanisms in biotechnology, I provide a contemporary appraisal of the development of new mechanisms involving co-ordination and cooperation between industry, government and academia, established to couple state funded science and national economic development. The public policy implications of the club funding systems for science in the UK are examined.

KEY WORDS

Biotechnology; Science policy; Innovation; University-industry collaboration.

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LIST OF ABBREVIATIONS

ABRC	Advisory Board to the Research Councils
ACARD	Advisory Council on Applied Research and Development
ACOST	Advisory Council on Science and Technology
AFRC	Agricultural and Food Research Council
BJAB	Biotechnology Joint Advisory Body
BRIDGE	Biotechnology Research for Innovation, Development and Growth in Europe.
BRITE	Basic Research in Industrial Technologies
BTG	British Technology Group
CBI	Confederation of British Industry
CEST	Centre for the Exploitation of Science and Technology
CRGS	Co-operative Research Grant Scheme
CVCP	Committee of Vice Chancellors and Principals
DES	Department of Education and Science
DNA	Deoxyribonucleic acid
DOI	Department of Industry
DTI	Department of Trade and Industry
EC	European Community
EEC	European Economic Community
ESPRIT	European Strategic Programme for Research and Development in

GNP	Gross National Product
HEI	Higher Education Institution
HORC	Heads of the Research Councils
IRCCCOB	Inter Research Council Coordinating Committee on Biotechnology
IUCR	Industry/University Cooperative Research
MAb	Monoclonal antibody
MRC	Medical Research Council
NBF	New Biotechnology Firm
NERC	Natural EnvironmentaI Research Council
NGBT	New Generation Basic Technologies
NRDC	National Research and Development Corporation
NSF	National Science Foundation
OECD	Organisation of Economic Cooperation and Development
OTA	Office of Technology Assessment
PGTK	Plant Gene Tool Kit
rDNA	recombinant DNA
R & D	Research and Development
RACE	Research and Development in Advanced Communications Technologies in Europe
RS	Royal Society
SERC	Science and Engineering Research Council
SRC	Science Research Council

SRA	Society of Research Administrators
UK	United Kingdom
US	United States
VLSI	Very large scale integration

CHAPTER ONE: A discussion of the research problem and research methodology

1.1 Introduction

In the 1980s, science and technology policy have become increasingly linked with policies concerned with the promotion of industrial innovation and technological change. Technological innovation has become the central priority of research and development (R & D), and science (at least in certain fields) has become 'strategic', in that it is seen as being directly exploitable for national economic gains. The 'white heat of technological revolution' would seem to have returned; science and technology policies now have as their emphasis the rapid development of new technologies and their application to the economy (1).

There is a consensus amongst the governments of the advanced industrial nations on the areas of technology that are going to be economically significant to at least the end of the century:

Table 1.1. New technologies and national interests

Japan	**USA**	**EC**
Electronics	Electronics	Information technology
Software Eng.	Automation	New materials
New materials	Computing	Biotechnology
Biotechnology	New materials	Energy
Biomaterials	Medical technology	
	Thin layer technology	
	Biotechnology	(Sources, 2)

These new technologies appear to share a number of similar characteristics:

> they are heavily 'science-based' or 'science-related', with their products embodying to a significant degree the results of advanced research and development. Secondly, they reflect the emergence of new 'generic' technologies with pervasive applications. Thirdly, they are calling on the expertise of an increasing range of scientific disciplines. Fourthly, some of the new fast growing sectors demand a much closer and more interactive relationship between fundamental research and commercial production than has hitherto been the norm. Biotechnological products and technologies have been described for example, as "growing directly out of the laboratories", (EEC, 1988).

A new and central concept to the 'new' science policy is the notion of an exploitable area of science (3). This can be seen as an expression of a more sophisticated conception of the innovation process than that informing previous attempts to exploit or commercialise science performed in publicly supported institutions (4). Within the context of science policy the old divisions of categorising research; whether science is applied or basic, long term or short term (distinctions crucial to the Rothschild customer - contractor system of managing and 'exploiting' science), seem to be diminishing in importance. Throughout the more recent policy literature it is possible to trace the development of a new discourse, a new vocabulary articulating the new policy concerns; research is now 'strategic', or where companies are actively collaborating at the research level of the

product cycle, it is 'pre-competitive' or 'generic' research.

One central theme to this (and referred to in the above quotation), is the blurring of the distinction between science and technology. Basic or academic research is deemed important in establishing this new technical field, but the exact nature and mechanism of the science-technology linkage is still a somewhat problematic area and many studies addressed to the subject yield contradictory results. One emerging characteristic of these new technologies is their increased 'scientification'. Some observers have concluded that the 'scientification of technology' has changed the nature of the innovative process and made it possible for academics to play a much more direct role in innovation. In his book The New Politics of Science, David Dickson (Dickson, 1985), quotes a calculation by the National Science Foundation that between the 1950s and 1962-74 the percentage of references to university research in basic United States patents rose from 28 to 48 per cent. In a paper provocatively titled "Is Science becoming Technology ?", Francis Narin argues that the similarity in the timing and content of recent papers in the bio-sciences and patents in biotechnology, indicates that in the high technology areas, at least, science and technology have come much closer together, (Narin and Noma, 1985). Many accounts of the role of science in technological innovation in the areas of micro-electronics and electronics exist (see for example Braun and Macdonald 1982, Branscombe, 1983). Many of these studies are reviewed in Chapter two as part of the literature review of this thesis.

1.2 University-Industry Collaboration and public policy

The need to stimulate innovation in these new science based technologies has focused the attention of the public policy makers and industry, on the innovative process and in particular the contribution of fundamental science and new knowledge. As universities are, in almost all countries, the main performers of this type of research, there is pressure at this interface, between industry and the university system, for increased collaboration. This thesis sets out to examine one aspect of this linkage problem and describes how the United Kingdom's (UK) science research policy is changing to facilitate the increased relevance of science for industry.

In the UK there has been pressure on the higher education institutions to better exploit their research, since the early 1970s. A series of studies, reviewed in Chapter two of this thesis, found that industrial exploitation of university research was not very effective, consequently university - industry relations in the UK became summed up in the phrase "good at invention, bad at innovation". Several factors have been identified as contributing to this, firstly there has been an underlying weakness in university - industry relationships, where industry has been apparently uninterested in what universities have to offer (the 'not invented here' syndrome), while universities have been accused of being aloof from industry's needs, ('ivory towerism'). The institutional environment in the UK, in terms of

funding, has also been identified as inhibiting the exploitation of university inventions.

In the light of these criticisms many universities have developed, encouraged by the various governments of the day, a variety of 'interface' structures to try and assist industry. These range from consultancy services and liaison offices, to science parks. However, these changes at the (micro) level of the individual institution have also been accompanied by gradual changes taking place in the funding priorities of the Research Councils, where specific areas began to be picked out for special support. This was a policy particularly emphasised by the Science and Engineering Research Council (SERC). One reason for the developing policy of selectivity and concentration (see Farina and Gibbons, 1979) was the rising cost of performing research (the so called sophistication factor). The growing cost of research had brought the science budget under much closer political scrutiny, at a time when public spending was being limited generally, and this had led to calls for the need for selectivity and concentration in spending on research. A report produced by the Advisory Board for the Research Councils (ABRC) in 1987, pointed out that:

> 2.1 The UK performs some, 5% of the world's research. It would in theory be possible to spread this effort evenly across all fields of scientific activity. But while this might just sustain enough research in many fields to permit us to keep in touch with developments elsewhere, it would not support any world class research. Just as the total effort in a particular field can be spread across too many institutions, so the nation's effort can be spread too thinly across fields, (ABRC, 1987).

The public policy question of science policy has become one of how and by what criteria are particular fields selected for funding (see Irvine and Martin, 1984). This decision appears to have been facilitated by the scientification factor described above. Those fields where basic research 'contains a substantial element of strategic significance' (ABRC, 1987), will be prioritised in any funding decision. This explicit inclusion of economic factors in decision making about research expenditure is reflected in the ABRCs changed criteria for evaluating the funding of research which was announced in 1987 (see Table 1.2).

1.3 Organising science: The special case of biotechnology

What is perhaps more significant as far as the funding and organisation of scientific research in the UK is concerned, was the growing perception that a clear cut customer-contractor relationship or demand pull theory of bringing forth innovations from the research carried out in the universities is perhaps not applicable to these new 'generic' types of technologies, which have a pervasive range of applications and call on a multidisciplinary array of sciences. The new technologies seem to indicate that new methods for organizing knowledge may be required, (Baker, 1983, Blume, 1986). The UK has, since the Rothschild reorganisation of 1970,

Table 1.2 ABRC criteria for scientific priorities

Ref: Turney, T.H.E.S 31.7.87

decentralised system for making science more responsive to market demands (see Blume, 1982). The "Spinks" report on biotechnology points out (see below) that this mechanism with its crude division of applied and basic research does not provide a suitable mechanism for exploiting the new technologies;

> a subject like biotechnology which, at this state, straddles the divisions of responsibility both among Government Departments and among Research Councils and the arbitrarily fields of fundamental and applied research, is handicapped by the present structure of public and private support of Research and Development in the United Kingdom. Strategic applied research is, in general, ill-served by our research funding mechanisms and the way they are being applied, especially in those areas where there are neither established university departments to promote it, nor well-developed industries to provide market pull. There is difficulty in identifying a source of funds to carry a project forward from the point where the primary research has been done but the commercial development has not yet begun - the 'pre-development gap', (ACARD/ABRC/RS, 1980).

The subject of organising science in the field of biotechnology to enable its exploitation by industry would seem to provide fertile ground for investigating developments in science policy that seek to assist with the growth and development of new science based industries. The research subject provides a locus of a convergence for (at least) two trends, the scientific community largely dependent on public subsidy is engaged in an activity that requires an expansion of resources at a (political) time of controlled and static public expenditure, and a suspicion of its

ivory-tower attitudes (Robbins and Webster, 1987), paralleling this is a renewed interest in science based technology as a source of economic growth. Under the twin influence of these factors it is possible to see how science policy and industrial policy, which have been in existence for many years with close to no interaction have merged into a new policy; strategic innovation policy.

I have outlined the UK policy for biotechnology in some detail in my M.Sc dissertation, (Williams, 1983). However to put the present research in the context of post-Spinks policy actions, it is necessary for me to provide a brief sketch of the policy background within which this research is situated.

Biotechnology is expected to become one of the major new industries of the twentieth century, (5). A calculation based on UK accounts shows that more than 40% of manufacturing output is biological in nature or origin: add in agriculture and health and one has over 20% of GNP, (Cantley, 1981). Concern, at a high political level, over the ability of UK industry to develop to use this new technology, prompted the setting up of a joint working party drawn up from members of the Advisory Council for Applied Research (ACARD), the Royal Society, and the ABRC 'to study the industrial opportunities of biological knowledge', (6). The terms of reference for the group were to review existing and prospective science and technology relevant to industrial opportunities in biotechnology and to recommend action by government and other bodies to facilitate British industrial development. The Spinks report, as it became known (after its chairman,

the late Sir Alfred Spinks), marked a watershed in the development of a UK policy for biotechnology.

In the analysis of the report, the working group spelt out the initiatives that they considered necessary for stimulating the field in the UK. Lacking any established industry, the field was seen as requiring 'technology push' for its development, 'reflected in a firm commitment to strategic applied research'. The analysis and recommendations of the report, attached a clear importance to the role of academic research in both the generation of commercial ideas, and in the production of skilled manpower necessary for the widescale development of industrial biotechnology. The working group were particularly concerned by the poor relations that existed in Britain between universities and industry:

> Co-operation between British universities and industry seems particularly poor in the biological science and traditional attitudes of indifference and mistrust are prevalent on both sides. Even where the commercial potential of a new discovery is recognised and there is a desire to establish contacts, there is much uncertainty about how to improve the situation...The ignorance of most academic scientists about the complexities of patenting, industrial markets, profitability and cash flow problems limits their immediate usefulness to industry. Many would, however, be happy to devote part of their time to applied problems, but they seldom know what these are. British industry lags behind that of most other countries in the extent to which it uses academic consultants, (ABRC/ACARD/RS, 1980).

Their analysis brought to the foreground many of the

problems associated with academic-industrial collaborations, as the two institutions differ greatly in norms, organisation, incentives and objectives. All of these factors were highlighted by the advent of commercial potential of biotechnology. Biotechnology set out in paradigmatic form, the major elements of science policy in the 1980s; science as a source of technology; linkage of universities and industry; and the development of a more entrepreneurial breed of academic, ("3.10 If British industry is to be regenerated through high technology, it will need to be much easier for academic researchers to become involved in business"). The report suggested that an emulation of the US success with New Biotechnology Firms (NBFs), small start up companies funded with venture capital and usually incorporating academics (see Kenney, 1986), offered another route to exploit research.

> 3.19 We would like to see the National Enterprise board regard biotechnology as a 'high technology area' within the terms of its remit, and in conjunction with the NRDC to establish within the United Kingdom, and with some public funds, a research-oriented company of the kind established with such apparent success elsewhere, (ABRC/ACARD/RS, 1980).

The report also found a role for established companies by getting them involved in the science policy process:

> We believe that in the interests of improving industrial competitiveness and paving the way for industrial innovation, a concerted approach is now needed from Government and industry to provide a coherent framework and mechanisms necessary for the successful development of biotechnology and of industries based on it, (ABRC/ACARD/RS, 1980).

1.4 Previous Studies

1.4.1 Introduction

The literature review part of my research presented preliminary conclusions about the present state of university-industry relations and their significance, which could then be used as a set of hypothesis to test regarding the role of universities in the process of technological innovation. It also brought to light studies that were able to assist my own research regarding questions of methodology.

1.4.2 University-industry studies

Industry, science and the Universities: The Docksey report. The broad terms of reference for the report were "to study the existing relationships between the universities and industry in the field of research, and to make recommendations". This study made use of a questionnaire of expert opinion. It was a large study covering all areas of industry and universities in general. Although my own study was focused on one (smaller) aspect of university-industry relations, the basic approach used in the Docksey report (i.e a structured questionnaire) seemed suitable for my own research.

A study was carried out by Elmima Johnson and Louis Tornatzky of the Productivity Improvement Research Section at the US National Science Foundation. They carried out a study of 118 industry/university cooperative research projects (IUCR) supported by the National Science Foundation. The purpose of the study

was to describe how IUCR projects develop, how they are implemented and discover what project features contributed to a successful technical and organisational outcome. In designing the study the authors became aware of the minimal empirical information that was available on university-industry research interactions. In order to select variables for the questionnaire they developed a useful analytical approach using integrating concepts from organisational sociology. They suggested three major factors which shape the degree of interaction: 1. goal congruity and compatibility; 2. boundary spanning structures; and 3. organisational incentives, (7).

The study design consisted of a structured mailed survey and a set of case studies of representative projects. The latter assessment presented a qualitative description of the same phenomena as the survey.

In 1982 the New York University Centre for Science and Technology Policy carried out a study on the Current US University-Industry Research Connections. This study formed the basis of the National Science Boards fourteenth Annual Report; University/Industry Research Relationships - Myths, Realities and Potentials. Information was collected on over 465 cases of university/industrial research interactions, the methodology was based on site visits and interviews. As a result interviews were carried out with 150 scientific administrators and over 400 scientists. The

study provides a useful description and categorisation of the interactions and the underlying motives of

industry for cooperation. The study did not focus solely on biotechnological issues, but frequently covered the subject.

In the introduction to the study they outline their broad view of university-industry research interaction:

> Our field of investigation of university-industry research interactions documents their variety and multi-faceted character... interactions can be formal or informal. They involve not only monetary support of research, but also include donations, transfers, exchanges and sharing of people, equipment and information. The duration of successful interactions can be far less than an hour or for more than twenty years. An important interaction can be as simple as a telephone call, or as intricate as a ten year contract Some require collaborative efforts either among scientists of different disciplines or between university and industry scientists, others the work of only one scientist, (Fusfeld and Peters, 1982).

A number of studies have attempted to provide a classification of interactions amongst the ones I found most useful were: University-Industry Co-operation: A Preliminary Analysis of Existing Mechanisms and their Relationship to the Innovation process (Brodsky, Kaufman and Tooker, 1980), and the OECD study on Industry and University: New Forms of Co-operation and Communication (OECD, 1984).

1.4.3 Biotechnology studies

The study that had the most impact on the research direction of this thesis was the Sprinks Report on biotechnology outlined above. There were also a number of "academic" studies also concerned with

biotechnology.

The largest ongoing research is the Harvard Project on University-Industry Relationships in Biotechnology. This was set up in 1984 to investigate the extent and consequences of university-industry relationships that involve the new biotechnologies, (8). The project consists of a series of surveys and case studies. In the first reports of their results they point out:

> despite much speculation and anecdotal reporting of large-scale support by a few companies such as Hoechst and Monsanto, relatively little systematic information exists concerning the prevalence of university-industry research relationships in biotechnology, the characteristics of such relationships, or their consequences for industries, universities, or society at large. Such information is vital to informing emerging policy debates, (Blumenthal, 1986).

A study by Lois Peters and Herbert Fusfeld at the New York University Centre for Science and Technology Policy, was carried out to determine the feasibility of stimulating commercialisation of biotechnology in the New York - New Jersey Metropolitan Region. The study was aimed at identifying 1. the extent of current activity, 2. what resources are available, 3. how the region's activity compares with the technical and commercial growth in biotechnology nationwide, 4. what areas of opportunity might be suitable for the region, and 5. what type of actions should be considered by both the public and private sectors to help the region optimize its economic position in this field in the shortest possible time. The research consisted of interviews, mailed surveys, and a literature search.

Two US doctoral dissertations have also been of assistance to my research, by illustrating contrasting methodological approaches to questions of university-industry interactions. Derek Fowler's thesis, entitled: Study of the Need for and the Impediments to Improved and Novel University-Industry research Relationships. The main part of the research constituted a mailed questionnaire carried out in 1982 to determine barriers to enhanced university-industry relationships. The factors representing barriers were derived from a literature review.

Patrick Ruscio carried out doctoral research in the specific area of biotechnology in his thesis entitled: University-Industry Relations in Biotechnology: A Study of the Public Policy Issues. The research uses a case study approach to examine whether universities are changing their policies and organisation structures to adapt to the changing conditions brought about by the commercialisation of biotechnology.

1.5 Aims of the thesis

This thesis, by studying a part of the science policy process in the UK, describes and analyses specific developing themes of science and technology policy that have occurred throughout the 1980s. In order that the research can be carried out within the context of a single doctoral thesis I restricted my analysis to examining only a narrow sector of the UK science policy, that sector is developments in the UK policy for biotechnology.

The research seeks to study the actual amount of industrial interest there has been in the transfer,

from the academic sector to industry, of scientific knowledge, products and processes in the area of biotechnology, since the publication of the Spinks report. In this thesis I aim to provide such an overview detailing the extent, variety and the significance of current academic industrial interactions with industry. The study aims to provide a clear analysis for science policy makers of the present and future role that the academic sector is likely to play in the development of the biotechnology industry.

Having established the general area of study for this thesis I would now like to refine the research question further. The research aims to establish:

What role academic - industrial collaboration play in the structure and growth of the biotechnology industry. Of qualitative interest is the recent development of research agreements linking a number of (potentially) competing firms with universities. The case of initiatives like the Protein Engineering club serve to highlight the interplay of these factors and the growing sophistication of the systems used to exploit fields of science and technology;
How strategic are external linkages to the achievement of a companies technical goals, and what are the implications for science and technology policy;

Which of these activities may evolve into a pattern of interdependence, what is the likely future of university-industry relationships in biotechnology;

To what degree do national programmes funded by

governments complement, compete or conflict with private linkages formed by companies.

1.6 Structure of the thesis

The thesis is essentially in two parts. In the first part I review the general literature on academic - industrial interaction. University - industry relations has been the subject of much attention by scholars and these have come from various perspectives. A study carried out by the Society of Research Administrators (SRA) found over one hundred books, articles and papers concerning university - industry relations. The publications were found to fall into the following major categories:

1 Review Articles (3%)
2 Policy Studies and Recommendations (5%)
3 Initiating/Improving University - Industry Relationships (45%)
4 Case Studies (42%)
5 Historical Items (3%)
6 Statistical Data (2%)

(SRA, 1984)

A review of the literature reveals several themes and common issues which, taken as a whole, suggest the current state of knowledge and opinion on the topic. I review this work in Chapter two and make use of various findings to assist with my analysis of science policy in the UK and placing the science policy issues in an international context.

The literature review also involves a study of academic-industrial relations in terms of the linkage between science and technological innovation. The biotechnical innovation process is not well understood and there is much speculation about its significance and about what linking mechanisms will most effectively stimulate its rapid growth and application. In the life sciences basic research activity may be particularly important to development efforts, so there will be a significant role for higher education institutions. The literature review looks at current knowledge and opinions on innovation and on organisational factors connected with successful innovation.

The final part of the literature review considers current strategic management literature to see whether the university -industry cooperative function has been integrated into the corporate strategy literature. The structure of science based industry itself has changed and this may have effects on science policy. I have already indicated how the Spinks report responded to the successful use in the US of small venture capital financed firms (NBFs) to act as vehicles for commercialising academic research. The more recent phenomenon of private sector research consortia (US) and public private consortia (Japan) could also have effects on science policy and the organising of academic science for commercial exploitation.

Following the literature review I carried out a structured survey. During the course of this initial survey phase it became clear the results from that would not provide me with all of the data I required in

order to take into account new policy developments occurring primarily within the Science and Engineering Research Council (SERC), to promote biotechnology. New organisational developments were occurring to encourage the performance of strategic research. As a major research question of the thesis concerned the performance of strategic research it was felt an ideal opportunity to study the emergence of these new forms, I therefore decided to add a third part to the thesis by undertaking a series of case studies of these new organisational sites of strategic research, and to contrast them with previous attempts the SERC had implemented to improve university-industry collaboration. The importance of this research was underscored by the absence of any significant research in the area.

The concluding chapter summarises the results of the empirical research and presents an analysis of UK science policy with regard to biotechnology, with particular reference to how effective the club mechanism as a means of bridging the interests of the Research Council funded work carried out in higher education institutions and industry; how the science funding mechanism of the Research Council came more to embody and prioritise the concept of 'economic' relevance, and to facilitate the exploitation of science and technology, in its decision making.

1.7 Research methodology

In this section I will outline the design of the research and the methodologies used. These included the use of a mailed structured questionnaire and a series of case studies.

1.7.1 Questionnaire survey

The first part of my empirical study approach was to prepare and, after testing it with a small group of knowledgeable respondents in a pilot study, to revise and send out a survey on this subject to 90 industrial research managers in the biotechnology sector. These names were obtained from the Department of Trade and Industry's Directory Of British Biotechnology (1986) and because of the dynamic nature of the emerging industry, new entrants were found through monitoring the scientific and technical press.

The survey consisted of a structured questionnaire designed to determine the nature of the relationships and activities involved in university - industry collaboration. It consisted of five sections listed below;

1. Determination of corporate involvement in basic and strategic research;

2. Details of corporate involvement in academic research;

3. The major mechanisms used for interacting with academia;

4. The nature and purpose of academic - industrial research cooperation in biotechnology;

5. Respondents additional comments on the issues raised, (optional).

In sections 1 to 4, the respondents were asked to use a four-category Likert-type scale from extremely important through very important, fairly important and not at all important. An attempt was made to carefully and crisply define each of these categories for the respondents.

Section five was indicated as being optional for response by the participants and it asked for more detailed information as to their opinions on the general area of university-industry relations. Section five was left as optional as it was felt from the pilot testing that the preceding four sections cover the principle points of concern, and was therefore not essential to the primary goals of this study. Section five would allow the respondents a chance to express opinions if they wish to devote more time to answering the questionnaire.

1.7.2 Transmittal of the questionnaire

The questionnaire was sent out with a covering letter.

The letter was addressed from myself in the role of researcher. It explained who I was and what the study was about and asked that the respondents take the necessary time (calculated at approximately 15 minutes) to reply personally to the survey. The confidentiality of the individual response was emphasised and we provided the respondent with pre-addressed, pre-stamped

envelopes with which to return their responses.
A copy of the letter and the survey is enclosed in Appendices 1 and 2 respectively.

1.7.3 Initial analysis

The initial analysis of the results of the responses to the questionnaire consists of a simple aggregated tabulation of the various responses, and a determination by visual inspection of the opinions and perceptions of each group. At this point the first comparison could be made between the results of the survey and the conclusions which one would normally deduce from the literature search.

The results have been divided into two parts;
Part One: Academic- Industrial Collaboration In Biotechnology; - focusing on the mechanisms and the type of research performed.

Part Two: Technology Linkage in Biotechnology.
An analysis of the biotechnologies involved in university-industry research relations.

1.7.4 Results

From the combined results of the literature reviews and the empirical study using the responses from the questionnaire, it was hoped to derive a clear cut profile of the major factors involved in university-industry research relations in biotechnology. This would give policy makers a better idea as to what

points in the interaction attention should be focused on if we wish to follow current public policy objectives that seek to improve the productivity of such interactions.

1.7.5 Follow up interviews or Reviews.

It was recognised in the original research plan for this thesis that follow-up interviews or detailed reviews of specific research arrangements might be necessary or desirable to complete the study. The actual targeting, format and extent of such interviews or reviews would have to await the results of both the literature review and the responses to the questionnaire. However, due to the course of events this approach was modified slightly. The impetus for detailed study of specific research arrangements came more from the review of the literature (particularly in Chapter two) and certain developments in the policies of the SERC, notably the creation of the Biotechnology Directorate and the establishment of the club mechanism for performing strategic research. These developments encapsulated many of the themes under investigation in the survey and it was felt appropriate to carry out a series of case studies on these new developments.

1.7.6 The Case study approach.

Context plays an extremely important role in explaining changes that might be occurring in university-industry research interactions. Consequently the research design must explicitly include treatment of the context. Yin (1981) has suggested that a case study is

a research strategy to be likened to an experiment, a history or simulation which may be considered alternative research strategies. Each strategy can be used for exploratory, descriptive or explanatory purposes. He suggests that the distinguishing characteristic of the case study is
that it attempts to examine (a) a contemporary phenomenon in its real context, especially when (b) the boundaries between phenomenon and context are not clearly evident (1981:59). It is suggested here that this research strategy is appropriate to the issue of university-industry 'club' interactions as the subject is a current phenomena indicating that university research is possibly playing a critical role in the development of an industry, along with the potential to play a central role in the future.

The research is exploratory and tends to be qualitative, the objective being to put the phenomenon in perspective by answering the research questions and to generate suggestions and hypothesis for future research. Nachimias and Nachimias (1976) have suggested that the case study research design is actually

> pre-experimental, useful in exploratory research...it is particularly useful in unformulated areas of further research (1976:42).

Such an 'insight-stimulating' research design would be worthwhile for a study of the role of the university-industry interactions in the commercialisation of biotechnology. As Seltiz, Wrightman and Cook (1976)

note, " scientists working in relatively unfamiliar areas, where there is little experience to serve as a guide, have found the intensive study of selected examples to be a particularly fruitful method for stimulating insight and suggest hypothesis for research". Given that the case study method is useful in exploratory research and in generating insight for further research, we may suggest this as a further reason for its use in the thesis. The case study method implies a good deal of description; in a new field of research this itself has some merit. Another reason for selecting intensive studies is that only a few clubs or consortia were involved.

A common critique of case studies is that their findings cannot be generalised across the population. However, general findings are not necessarily the intent of this research. The history of science policy suggests that institutional modifications have become widespread only after a few 'prototypes' had been developed and withstand the test of time. An intensive study of the current prototypes will indicate the advantages and its advantages for later efforts. It is recognised that the explanation is offered from a certain perspective and other approaches may suggest other explanations. The other limitations of the method are also recognised, namely that there can be no control or manipulation of the independent variables, there are no checks on validity, and the method is of little use in testing causal relations.

1.7.7 Case study research design

Yin has pointed out that successful use of case studies

requires that individual cases, whether part of a multiple case design or not, all follow an explicit design. At a minimum the design should specify the main topics to covered by the study, the type of individuals (or their roles) from whom information might be obtained and the unit of analysis at the case level. The unit of analysis in the case studies of this thesis is the research 'club'. The sequence of issues to guide data collection are given below:

1. The organisational dimension: organisation structure; formal research policies covering issues such as the licensing and patenting of inventions; the preference for a directed programme of collaborative research; and research management;
2. Product cycle dimension. The focus of the clubs on pre-competitive or strategic research;
3. Technical spectrum. The choice of the research area;
4. Programme integration. The attempt to achieve some degree of programme integration between 1, 2 and 3. The mechanisms used to push and/or pull basic research through to markets.

Yin (1981) indicates that the case study method has often been confused with a. a data collection method and b. a particular type of data. With respect to a. the case study does not imply a certain data collection method (i.e participant observation), data may be collected by several methods (survey unobtrusive/secondary data/ or direct observation). In this research, data was collected by means of personal

interviews and through archival sources. With regard to point b, although case studies frequently rely upon qualitative data, they may be done using quantitative data or combination. In this research, qualitative evidence comprises the majority of the data, but quantitative data is included whenever it was available to enhance the form.

The use of several data collection methods and types of evidence has proved to be vital to the performance of this research. Because of the nature of the subject matter, in the discussion of strategy and new products and processes in biotechnology, there were problems of confidentiality, which were a constant source of difficulty for data collection. In these case the data collection was more akin to Mintzbergs 'inductive detective work':

> The tracking down of patterns, consistencies. One searches through a phenomenon looking for order, following one lead to another. But the process itself is not neat, (Mintzberg, 1979).

A similar approach was used by Miles in a study of the strategic behaviour of tobacco companies, "systemic, longitudinal, comparative investigation, reporting..not seeking to test a specific hypothesis, but to describe events, their causes and their consequences: and from that process to raise issues and implications about the process of organisational adoption", Miles (1980).

1.7.8 Case study summary

The analysis looks at the differences and similarities of the various case studies and looks at their future role as an implementation system for science policy increasingly geared to organising science for commercial exploitation.

Chapter One: Notes

1. An interesting interpretation of this new economic context of science and technology is given in the term reindustrialisation, which is defined as 'the structural transformation of industry into higher added value, more knowledge-intensive sectors and product groups, and the creation of major new technology-based industries and products serving new markets'. A good example of the former can be found in the structural shifts in Japanese industry during the past thirty years; an example of the latter is the emergence in the United States in the 1950s and 1960s of a group of new, high technology industries (Rothwell and Zegveld, 1985).

2. The Status of Emerging technologies: An Economic/Technological Assessment to the year 2000. US Department of Commerce, 1987.
Trends and Themes in industrial technologies, MITI, 1988.
Panorama of EC industry, 1989.

3. A good example of this new commercial interest in areas of basic research is given by the Japanese initiative entitled The Next Generation Base Technologies (NGBT) development programme - which is promoting long term research, technological excellence and the sparing use of government funds to stimulate research among private firms. It demonstrated to the rest of the world that Japan (at both government and industry level) saw economic benefits in pushing further into basic research. The areas covered by this programme illustrate the wide scope of technological opportunities opening up: 1. Fine ceramics, 2 polymer filtration membranes, 3./Conductive polymers, 4. Highly crystalline polymers, 5. High grade alloys under crystal growth, 6. composite materials, 7. Bioreactors, 8. Mass cell culture, 9 rDNA techniques, 10. Super-lattice elements, 11. Three dimensional elements, and 12. Integrated circuits fortified against extreme conditions (Dore, 1983).

4. In general terms it is possible to see different models of technological innovation influencing science and technology policy at different times. In the immediate post-war period up until the 1960s, the 'science-push' model seemed to predominate (Blackett,

1968). By the 1970s the emphasis lay more on the market and demand factors, this culminated in the 'customer-contractor' system of research management introduced in the UK (Rothschild, 1971). Today, innovation is interpreted as being a much more complex theoretical idea, incorporating elements of both previous extremes (Rothwell and Zegveld, 1986). These ideas are discussed further in chapters 2 and 3.

5. The significance of the recognition of biotechnology is illustrated by the list of nationally (and internationally) sponsored reports and surveys reproduced in table 1.3.

6. The Advisory Council for Applied Research and Development (ACARD) has the following terms of reference - To advise Government and publish reports as necessary on -

i. applied research, design and development in the United Kingdom;
ii. the application of research and technology, developed in the UK and elsewhere, for the benefit of both the public and private sectors in accordance with national economic needs;
iii. the co-ordination, in collaboration with the advisory Board for the Research Councils, of these activities, with research supported through the Department of education and science;
iv. the role of the UK in international collaboration in the fields of applied research, design and development related to technology.

The Advisory Board for the Research Councils (ABRC) was established by the Secretary for State for Education and science in 1972 with the following terms of reference-
i. to advise the Secretary of State on his responsibilities for civil science with particular reference to the Research Council system, its articulation with the universities and departments, the support of postgraduate students and the proper balance between international and national scientific activity
ii. To advise the secretary of state on the allocation of the Science budget amongst the Research Councils and other bodies, taking into account funds paid to them by customer departments and the purpose for which such funds are devoted.

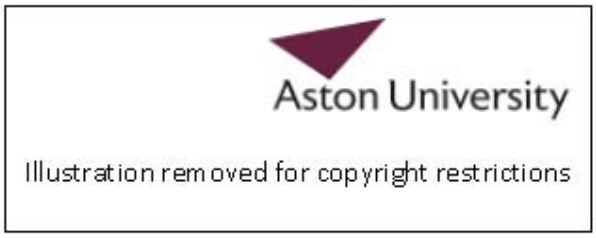
7. These concepts were outlined in another paper (Johnson and Tornatzky, 1981), where they were utilised in examining several cases of university-industry interaction described in the literature: MIT Polymer Processing Program, Harvard-Monsanto Research Project, Rockwell International - Black Colleges, NSF Innovation Centers, Harvard University-Genetic Engineering Company.

The analysis suggested a number of areas for future research, including studies of the perceived incompatibilities between the university and industrial goals, the relative success of different kind of linking mechanism, the role of public funding as a determinant of university-industry links, and the impact of interorganisational structural characteristics on interorganisational relations.

8. Michael Gluck and David Blumenthal of the Harvard project group were kind enough to send me prepublication copies of their findings and their questionnaires, to assist me with my own research.

Table 1.3 National reports on biotechnology

(Ref: Cantley, 1985)



CHAPTER TWO: University - industry interactions: Literature survey

2.1 Introduction

Chapter one outlined the new economic context of science and technology. The interest in generic technologies has focused public policy on the strategic issues of developing and enhancing national capabilities in these technologies. One of the major areas concentrated upon has been the university - industry research cooperation interface as a major enabling factor in increasing technological innovation. As a result of the initiatives by advisory bodies and through the actions of private groups (most notably in the US), there has been a dramatic proliferation of the literature in recent years which has dealt with the subject of the research linkages between universities and industry (1).

The ascension of the issue of university - industry research relations to the top of the science policy agenda can be traced, in the UK, through a series of publications emanating largely from the advisory bodies for science and technology policy. Bodies such as the Advisory Council for Applied Research and Development (ACARD) and the Advisory Board for the Research Councils (ABRC). The emergence of the perception of science and technology as being of major national importance and as a source of strategic opportunity can be largely attributed to these advisory groups, outside government. The main reports focusing on the questions of university - industry research relations are reviewed below and their central role in the new science policy discourse of 'strategic research', 'pre-competitive research' and

exploitable areas of science is also explored.

2.2 University - industry relations : The debate in the UK

2.2.1 Introduction

There has been a long standing debate in the UK on how best to make use of the university system in terms of generating technological innovation. While the actual policies taken in support of science and technology have altered over time, reflecting certain trends in the thinking about how the innovation process functions (and changes in political ideology), there has remained a fairly strong belief that the UK was good at science, good at winning Nobel prizes, but not very good at exploiting the science commercially. Consequently a large proportion of the debate in the UK has been concerned with 'bridging the gap' between the science being carried out in higher education institutions and its exploitation by industry. The problem area was largely seen to be at this interface, rather than in the research areas themselves.

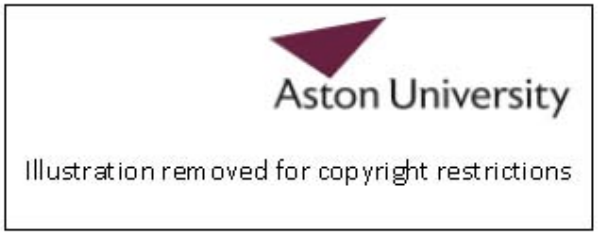
While one part of the policy debate focused on how the science in the universities, generated via its own, largely autonomous funding system (established by Lord Haldane, see note 2) can be better 'transferred' to industry, another debate has emerged in the 1980s to largely supersede it. This second debate views the process of innovation in a rather different way and aims to develop science that is inherently of interest to industry, so that there is less of a gap to be bridged. As Roberts and Frohman point out:

> It is striking that all of the government programs that start to encourage the utilisation of research only after the research and development results have been generated. Yet the most effective industrial approaches to increased research utilisation begin much earlier in the innovation process - as far back as when ideas are generated and selected for development, (Roberts and Frohman, 1978).

This approach calls for more planning in the research carried out in the universities, the identification of sectors worthy of support. The US experience of industry involvement in basic research at universities is a manifestation of this, but at the time of the first wave of US initiatives in the late 1970s, the UK had little to compare.

The weakness of university-industry relations in the UK have been recorded in a series of studies. A major study was carried out by the Confederation of British Industry (CBI) and the Committee of Vice Chancellors and Principals (CVCP) in 1970 (it became widely known as the Docksey report). The report identified the failure of both sides to communicate as a major obstacle. This was largely put down to the different cultures of industry on the one hand and the academic culture of the universities on the other. The report published a list of the various methods by which universities do - or could - collaborate. The list reproduced in table 2.1, gives a useful typology of the perspective in the 1970s.

Table 2.1



Source: CBI, Industry, Science and Universities, 1970, Table 64.

2.2.2 The pre-development gap

A later report commissioned from within the Research Council structure itself (the Science Research Council or SRC), entitled Academic, Industrial Collaboration in Engineering Research, was published as a result of the deliberations of a working group chaired by Professor E J Richards in 1975. This report although narrowly focused on one aspect of university-industry collaboration did prove to be an important text in the debate. The report developed the term the 'pre-development gap' to explain the funding and conceptual gap that existed between the discovery in the laboratory and its being taken up commercially. It also recommended the establishment of a pre-development scheme, to fund 'three-way' research, involving SRC, an academic institution and a collaborator (private firm, nationalised corporation, government department, research association, etc). This concept of the 'pre-development gap', has come to dominate much of the following science policy debate.

The House of Commons Select Committee on Science and Technology addressed the issue in 1976 in its report on University - Industry Collaboration. The report was largely concerned with the methods of collaboration aimed at improving the take-up of university research results by industry. The report expressed the view that collaboration in research which achieves a greater level of industrial orientation in the universities, would be regarded as beneficial for "that reason alone, whether or not there are demonstrable returns in terms of direct improvements in industrial performance". It reaffirmed the findings of the Docksey report regarding the obstacle presented by the

inherent differences in objectives between industry and universities, and stressed the importance of overcoming this culture gap.

The Report also put technological innovation at the heart of wider industrial and economic policy when it recommended that;

> the stimulation of wealth-creating innovation should now be the principle activity of the Department of Industry.

The report reviewed the growing number of institutional devices that universities had begun to set up throughout the 1970s designed to transfer technology to industry. Examples of these were liaison bureaux and industrial units to provide general consultancy and research facilities, often of a multi-disciplinary nature. These mechanisms were essentially peripheral to the main research carried out at the universities, and were set up to perform time limited problem solving activities and applied research for industrial clients.

The report also touched upon another way universities had found to assist industry. The Richards report had pointed out that one of the conditions for fruitful collaboration was a sufficient overlap in either motivation or purpose. The Select Committee report looked on the relations between academic chemistry and industry (3). In this case there was a complementarity of interest between a mainstream academic discipline, chemistry, and a science based industry. Chemical companies with their large R & D facilities were interested in basic research as a solution to the points

where industrial advance is held up in areas where technological exploitation has reached the limit of knowledge. The Committee believed that the example of chemistry deserved careful study by other industries and other academic disciplines, (4).

The report drew heavily on the conclusions of the Richards report mentioned above, on the gap between research and development, and called for the special funding to bridge the gap between Research Council funds and the funds of the Department of Industry. The role of the National Research and Development Corporation (NRDC) set up in 1967 to support potential innovations across this gap also came under critical scrutiny. The report recommended that its first rights on any patentable invention derived from Research Council funded research should be removed. This was seen as a way of encouraging universities and academics to exploit results for themselves.

2.2.3 A new strategic science policy discourse

An important report on the issue of the linking between higher education and industry was produced in 1983 by the ACARD and the ABRC, entitled Improving Research Links between Higher Education and Industry. The terms of reference for the working group were: to examine current arrangements for academic-industrial cooperation; to assess their effectiveness; and to examine any institutional, administrative, financial or other barriers and disincentives to the formation, progress and extension of links and the scope for their dismantling.

The report reiterated many of the finding of the preceding Docksey report regarding the lack of mutual understanding and the concern over the balance of basic and applied work carried out at universities. The report shows that little had improved over the thirteen years that separated the two studies.

The important economic role ascribed to science and technology, and therefore university-industry interaction, was clearly articulated in the report:

> The links between industry and higher education institutions (HEIs) in research and its application can contribute significantly to the economic health of the UK. Indeed they must do so, if this country is to benefit from a strong base of science and technology. This is a matter of vital long-term importance.

One of the reports main recommendations was that the Department of Industry (DoI, later became the Department of Trade and Industry, DTI) and the Science and Engineering Council (SERC) should collaborate more closely in supporting both joint activities carried out by industry and Higher Education Institution (HEI) partners, and industrially oriented work in HEIs. The working party were concerned with the gap that still existed between the interests of DTI and SERC. They saw the proposals in the Alvey Report, (Alvey, 1982) for overcoming this gap a 'a further step in the right direction'. The reference in the ACARD report to the Alvey programme, represented a new strand of thinking in terms of academic industrial collaboration in the UK, and its importance in terms of UK science and technology policy has been analysed in Alvey and post Alvey - science policy in the late 1980s; a UK perspective, (Williams, 1988). The

Alvey programme was established in 1983 as a five year, £350 million programme to organise science and technology in the broad area of Information Technology in order to facilitate technological innovation. It received funding from the DTI, Ministry of Defence, SERC and the industrial participants. To perform the work company/company, company/university and/or company/research establishment consortia were established. The growing significance of Alvey as a model for performing academic - industrial research cooperation was given a further boost by two other publications discussed below.

Several reports have emerged that articulate an altered view of how universities can be more relevant to industry, in terms of their research output. The report Exploitable Areas of Science, published by ACARD in 1985, gives a representative picture of the new policy approach. The central concept is that of an 'exploitable area of science'. In this guise, relevance is no longer simple problem solving with lots of fragmented bilateral applied research contracts, but instead is one of building up whole fields of research that underpin certain technologies. The policy question then becomes one of identifying the fields worthy of support, and one of creating new organisational frameworks that can maximise the translation of the research into new products and processes. The ACARD report provides a definition of an exploitable area of science;

> One in which the body of scientific understanding supports a generic (or enabling) area of technological knowledge; a body of knowledge out of which many specific products and processes may emerge in the future ...Thus the exercise is not seen as one of picking the winners but of strategic

> policy aimed at creating a reservoir of knowledge out of which the, as yet unidentified, winning products and processes will emerge. (ACARD, 1985).

Science in this framework is seen as pre-competitive and a resource for companies to tap into. The report draws attention to the major players in this new 'strategic policy': "Government programmes with emphasis on pre-competitive research involving collaborations between university departments and industry are one measure which may find wide application in a policy of strategic support". The aim of the new science policy is:

> to seek to organise science in a way that it leads naturally to exploited technology...Strategic science is a national investment to be justified in terms of the national return it promises to generate. The organisation of strategic science should, therefore, reflect this need for results to be followed by exploitation in the national interest. Effective interaction between industry and the scientific community is vital if strategic research is to succeed, (ACARD, 1985).

The exemplar status of the Alvey programme is confirmed by the joint report of ACARD and ABRC entitled The Science Base and Industry, published in 1986. The report emphasised that the resources put into R & D had to be translated into industrial products. Science today has to demonstrate its relevance; its justification is that it is 'strategic' or 'precompetitive' science. On the Alvey programme, the report states that:

> To some extent a start has already been made in identifying exploitable areas, and setting up collaborative programmes to exploit them. The largest and most well known is the Alvey Programme for research into Information Technology... These schemes were born of the realisation that the UK must increasingly determine its priorities,

> concentrate its resources, and develop a programme which will directly involve all those with a contribution to make to the enterprise, and an interest in its ultimate success. We see considerable scope for developing similar schemes in a range of other areas, (ACARD/ABRC, 1986).

This latter view is reiterated in the ABRC Report of the working party on the private funding of scientific research (ABRC, 1986) which stated:

> The Alvey scheme has pioneered, for information technology, an important means of bringing Research Councils, universities, polytechnics, government departments and industry together. It serves as a model which could be usefully extended and applied in other areas of research, (ABRC, 1986).

A detailed assessment of the Alvey programme is provided by E. Arnold and K. Guy in their book Parallel Convergence, (1986).

2.3 Strategic research

2.3.1 Defining strategic research

I would like at this point to consider in more detail the definition of strategic research, as it would appear to be the key site of research convergence between university and industry, and is linked to the process of R & D and innovation. The Organisation for Economic Cooperation and Development (OECD) has produced a 'proposed standard practice for surveys of research and experimental development' in the form of the 'Frascati' manual (OECD, 1981). The OECD manual (1981) defines innovation as 'the transformation of an idea into a new or improved saleable

product or operational process in industry and commerce or into a new approach to a social service' (p15). Research and development make up only one of the steps required in the innovation process. The manual categorises R & D into a three fold distinction:

> Research and experimental development comprise creative work undertaken on a systematic basis in order to increase the stock of knowledge, including knowledge of man, culture and society and the use of this stock of knowledge to devise new applications. ...R & D is a term covering three activities: basic research, applied research and experimental development. (p25)
>
> Basic research is experimental or theoretical work undertaken primarily to acquire new knowledge of the underlying foundations of phenomena and observable facts, without any particular application or use in view. (p25)

The report points out that basic research is usually performed in universities and the results of the research are usually not sold but published in the scientific journals. The scientist when undertaking basic research set their own goals, and largely organise their own work.

> Applied research is also original investigation undertaken in order to acquire new knowledge. It is, however, directed primarily towards a specific practical aim or objective. (p25)
>
> Applied research is undertaken to determine either possible uses for the findings of basic research or new methods or ways of achieving some specific and pre-determined objectives (p54).

> Experimental development is systematic work, drawing on existing knowledge gained from research and /or practical experience that is directed to producing new processes, systems and services, or to improve substantially those already produced or installed. (p25)

Experimental development work is aimed at producing new materials, products and devices as well as the above mentioned process innovations. The institutional locations of these categories of research are thought generally to follow that laid out in figure 2.1.

However, the OECD cautioned the use of these categories, pointing out to the many conceptual and operating problems associated with them. Also it warns against assuming that the categories imply a sequence and separation, which rarely exists in real life. It points out that all three types of activity may be carried out in the same centre by substantially the same staff. And further, that there is movement in both directions.

These categories exclude the concept of strategic research and consequently the operational utility of this system of categorisation has come under question. R. M. Mason (1983) in a the report A Study of Commissioned Research (ABRC, 1984) defined strategic research as "...collateral research required to achieve national strategic objectives that may originate from either of two directions (i) market pull, when a potential user has recognised that more background knowledge in a particular field is needed, and (ii) technology push, when research workers have recognised that a discovery may lead to practical applications".

Figure 2.1

Organization Involvement in the Innovation Process

Ref: National Commission on Research, 1980

An earlier definition was provided by Dainton (1971) and this now seems to be widely used by science policy advisory bodies. The term strategic research appeared in the report The Future of the Research Council System, prepared by the Council for Science Policy Working Group, under the chairmanship of Sir Frederick Dainton. It was published as part of the same document as the (at the time more influential) Rothschild report. It rejected the sharp (Rothschild) distinction between applied and basic research because of the interdependencies of the two types of research for progress in each. The report proposed an alternative threefold classification of scientific work:

> Tactical research - that needed by government and industry to further its immediate concerns, whether research involved was long term or short;
>
> Strategic research - general scientific knowledge underlying tactical science;
>
> Basic research - research and training with no practical objectives other than advancing scientific knowledge and maintaining a corps of trained scientists.

The connections between basic and strategic science were seen as being particularly close, and it was this type of science that the working group considered to constitute the main bulk of the research being carried out at the universities. The operational utility of the Dainton classification in the analysis of the contribution of university science to technological innovation is illustrated by the study of technological innovation carried out by M. Gibbons and R. Johnston:

> The research carried out within universities with the support of public funds, has been shown to be of value in two distinct ways. The first of these refers to the scientific knowledge resulting from research itself. It has been possible to identify a wide range of 'products' of scientific research which can play a role in promoting innovation but from this study we cannot draw any substantial conclusions about the specific characteristics of research which are likely to be more economic to support, beyond the criteria of 'good science'. All the scientific research which was used in the innovations could be classified as either basic or strategic according to the definitions of Sir Frederick Dainton.
>
> They continue, pointing out the policy applications:
>
> As the results of strategic research have the prospect of offering more direct results, and still allow for some of the benefits of basic research, it would appear that, in times of restricted budgets, more general encouragement of strategic research would conserve the quality of the national scientific effort as well as enhance the coupling of the research system with the industrial system, (Gibbons and Johnston, 1974).

These finding appear to have predated the current vogue in science policy thinking. A good example of which is provided in the OECD report The Future of University Research. It suggests that:

> What seems to be needed is a substantial investment in 'strategic' research; that is research addressed neither to the problems of immediate short term relevance, nor to problems which derive their interest solely from scientific theory,' but having as a background a practical orientation. It is via the performance of research of this kind that the university could make a significant contribution to the economy, (OECD, 1981).

Irvine and Martin, have attempted to update the categorisation of research to include strategic research. Their typology differs from the 'Frascati' classification in that basic research has been subdivided into pure/curiosity - oriented research and strategic research. See table 2.2. In this categorisation, strategic research differs most importantly from pure research in the rationale that lies behind its support. With the performance of strategic research there is at least some expectation that it will contribute background knowledge required in the development of new technologies. Furthermore it is by no means confined institutionally, to the university laboratory. Indeed, Irvine and Martin speculate that large science based firms are performers of such research.

The idea of the performance of this type of research as providing a bridge or a "coupling of the research system (of the universities) and the industrial system" is explicitly tested by the questionnaire survey undertaken as part of the research of this thesis, (see chapter six).

Table 2.2

Figure 2.2 Classificatory framework for R & D activities

Ref: Irvine and Martin, 1984

2.3.2 Public support for science; a role for strategic research

There is widespread use of the term strategic research in the science policy discourse: the significance of the concept as defined by Irvine and Martin has substantial implications for public policy for science. They have formed a conceptual link between the support for basic research and economic success in the UK. They argue that:

> it has become clear that many of the important industries of tomorrow will be based on technologies that are highly dependent on basic science. (p28)

They have in essence provided the (basic) scientific community with a plausible argument for mobilising resources: it argues against reducing or even level funding of basic research.

In the 1960s a famous debate raged through the pages of the journal Minerva, these exchanges became known as the 'criteria of choice' debate. One of the major contributors to this debate, Alvin Weinberg, argued that it was necessary to think separately about basic and applied research: that budgets for each were properly to be based upon quite different considerations, (Weinberg, 1964). According to his view, basic research was to be supported for cultural reasons, applied research for utilitarian reasons. This though turned out to be something of an ideal vision:

> In the short term, basic science viewed as an overhead charge on technology is a more practical way of justifying basic science than is basic science viewed as an analogue of art. Until and

> unless our society acquires the sophistication needed to appreciate basic science adequately, we can hardly expect to find in the admittedly lofty view of 'science as culture' a basis of support at the level which we scientists believe to be proper and in the best interest both of society and of the scientist, (Weinberg, 1964).

The necessity of stressing the utilitarian contributions of science, in order to secure public funds was again reinforced by J. Ben-David's influential OECD report Fundamental research and the Universities. In the report he argued that in Europe "science on the whole has been considered as a cultural consumption. Accordingly expenditure on it is limited".

In the report Ben-David went on to illustrate how basic or fundamental research could be considered useful while retaining its basic autonomy:

> investigations of the relationship between scientific research and technological growth are consistent with the view that there is no direct relationship between specific kinds of fundamental research and the eventual application of the findings in practice, and the success in exploiting science for practical purpose does not, therefore , result from the guidance of fundamental research by practical considerations but from constant entrepreneurial activity aimed at bringing to the attention of potential users whatever may be relevant for them in science, and vice versa, (Ben-David, 1968).

This type of thinking certainly seemed to influence the way governments, such as the UK, thought about the extent to which university research could be mobilised in the post world war years up to the 1960s. This thinking was symbolised in the UK by the creation of the National

Research and Development Corporation (NRDC, now the British Technology Group):

> (NRDC)... was envisaged as a kind of "half-way house" between science policy, and industrial and general economic policy, where the rewards for the patronage of science by government could be translated into industrial uses without any threat to academic autonomy by commercial interests. Thus the Nuffield report, while asserting that the future of industry "will depend in a high degree on its quick and imaginative adaptability to new processes", and recognising the role of science in this ability to innovate stressed the need "to guard against the danger of university departments falling too much under the influence of particular firms or industries to the detriment of their main tasks". The spirit of academic research was characterised as a compound of disinterestedness and neutrality, features which have been explicitly embodied in the administrative procedures built on the Haldane principle. This view was a postulate on which the new institution was based, (Keith, 1981).

The essential utility of fundamental or basic science was then taken for granted as was the academic requirement of autonomy. The Council for Scientific Policy (CSP, see note 5) explicitly used this utilitarian discourse in its first report in 1967:

> The justification for it (basic research) is that this constitutes the fount of all knowledge, without which the opportunities for further technical progress must eventually become exhausted, (CSP, 1967, see also 6).

The unpredictable nature of the arguments for supporting basic research is illustrated by the remarkable about-turn of the CSP, which in its third report (CSP, 1972) declared:" curiosity-oriented research is only rarely the main-spring of substantial innovation". This about-turn coincided with

a wider disenchantment with (and expenditure on) basic research. This led to the Rothschild reorganisation which attempted to make publicly funded research more 'useful' and accountable, (Rothschild 1971 and White Paper, 1972). The reorganisation enacted a 'customer-contractor' principle, which was based upon a simple dichotomy. Either research was 'fundamental', or else it was applied, that is R & D with a practical application as its objective and is therefore of discernable use to a clearly identifiable customer. Under this principle, which came to dominate British science policy, it is much more difficult to make a case for increasing funding for basic science in terms of potential utility, if it was useful it would have a customer, and would therefore be applied:

> Either research is 'fundamental', or else it must be of discernable use to a clearly identifiable customer. The doctrine does not admit of the possibility of utility in the absence of an existing customer, (Blume, 1981).

The symptoms of the failure to obtain funds to support the 'natural' growth of basic science are now being voiced in a number of publications (see for instance Irvine and Martin, 1984, Office of Health Economics, 1986) and the activities of pressure groups such the Save British Science group, which was formed in 1985, by scientists concerned by the threat they perceived to the funding and status of basic research in the UK.

2.3.3 Research classification and culture

There is a wide body of opinion within the sociology of science literature, that links certain types of research with particular cultures and institutional settings. An analysis of these aspects may give some further indication of a 'cultural' need in the academic community for the concept of 'strategic research'.

Beyond the established problems of proving the link between science and technological innovation (outlined in Chapter three), those performing basic research have had the added drawback of being surrounded by a powerful mythology which may have had the effect of prejudicing their ability to raise funds in certain political environments. Basic or pure research is associated with a particular ethos or culture that is mainly located in the universities. As John Ziman has pointed out:

> the epithet pure suggests, this distinction (between pure and applied research) is essentially ideological. It asserts the independence of academic science from all material or social considerations, and proclaims the virtue of doing research 'for its own sake'. It repudiates the instrumental conception of science, and thus preserves the academic ethos, (Ziman, 1984).

Even though this ideal of completely disinterested research rests more upon a notion of how science was performed in the 19th century, it still exerts a hold over those who practice science and governments that fund it. This I believe, can have two important effects. Firstly the existence of this type of academic culture would no doubt inhibit academic-industrial relations:

> The low motivation among academic scientists and engineers to engage in industrially relevant applied work is often attributed to 'ivory towerism' a culturally conditioned set of attitudes, (Stankiewicz, 1982).

But in actual fact the reverse seems to be true in certain countries. Academic culture is not an homogenous set of values as Merton would have us believe, (Merton, 1957). Because of the growing involvement of academics (particularly in the US) in new biotechnology and microelectronic firms, the academic community itself is worried about the erosion of its own 'academic ethos' , (see for instance Wade, 1984).

The second effect concerns the wider public perception of the academic ethos; the apparent inherent academic (ideological) resistance to cooperating with industry. This can lead to a wider external onslaught on the values and culture of universities and the type of research they primarily perform (pure or basic). It seems that over the past few years the idea has re-emerged that the British education system is antipathetic to the economic exploitation of science and technology for national gain. The thesis of Martin Wiener in his book, English Culture and the Decline of the Industrial Spirit, seems to have gained a particularly wide political audience, and this has resulted in a governmental view that the real obstacle to economic 'redevelopment' in Britain may well be that the continuing resistance of cultural values and attitudes represented by the pure research community in universities. The recent Green Paper (The Development of Higher Education into the 1990s, 1985) published by the government, can be interpreted as advocating a policy aimed at dismantling or re-

orientating these values, this is reflected in the use of a new language where liberal ideals are supplanted by "a new functionalist, utilitarian, technocratic and managerial discourse" (Robbins and Webster, 1984). My contention is that this discourse may have to be applied to basic science, because of its close association with the old 'ivory tower' academic culture. This transition in the use of language has however taken place in stages:

> The pure identity has now lost its fund raising value, and it is usefulness not detachment which counts with funding agencies and patrons. Speculative and general research is now called 'basic' or 'fundamental', the clear implication being that it is basic or fundamental to some purpose, undefined but anticipated, (Hales, 1983).

It could be argued that the scientific community as represented by bodies such as the ABRC, has now assimilated this notion of 'managerial discourse' and renamed a proportion of its basic or fundamental research as 'strategic', indicating that it is exploitable. The university system, today, is under pressure to provide trained manpower and exploitable ideas, both for the benefit of industry. This new discourse could be seen as an attempt to meet these requirements. The point is made by Rothman in a report to the ABRC:

> A cynic might say that our scientific community is playing its old game of dressing up its research requirements in the fashionable political garb, it has certainly done so in the past. Today in the words of the ABRC (1985) it is "... to provide the basis for new internationally competitive industries"; thus the concept of 'strategic research' plays the role of translation between government and the ABRCs needs, (Rothman, 1985).

The works of Irvine and Martin, illustrate this process of transformation, where areas of previously 'pure' sciences are being transformed into strategic research, (Irvine and Martin, 1984, and 1986). The authors link this with science budget funding decisions:

> Clearly, if early identification of promising areas of strategic research is possible, then targeted support by governments can increase the likely future economic and technological benefits to industry, (Irvine and Martin, 1986).

The areas of strategic research all tend to focus upon the clusters of technology outlined in Chapter one of this thesis. There is considerable agreement amongst the major industrial nations regarding the technologies worthy of support and linking research areas to these major generic or core technologies, that are so politically 'sweet' can only enhance the prospects for further funding. As Stuart Macdonald comments, high technology has proved irresistible:

> Because high technology is regarded as the antidote to recession, and because its requirements are so indeterminate, it has become irresistible to politicians and bureaucrats. Despite the association of high technology industry with private enterprise and minimal governmental intervention, even governments reluctant to interfere with market forces have been ready to regard high technology policies. So great and so necessary are the benefits from high technology thought to be, and so immediate the results, that a government with no care for promoting its development would nowadays be quite exceptional, (Macdonald, 1986).

The climate for funding of such 'strategic' research would appear to be very good. However, this somewhat cynical view of mobilising resources assumes that nothing has changed in

the relationship between science and technology, and between the academic community and industry. This may not in fact be the case, as has been pointed out the main users of the term strategic research have in the main been those science policy bodies representing the interests of the scientific community. However, analogous terms do seem to exist in industry. A likely candidate for the industrial equivalent of 'strategic research' is what US research mangers call 'directed basic research' (DBR). This has been described in the following way:

> Original scientific or technical work that advances knowledge in relevant (to corporate business strategies) scientific and engineering fields, or that creates useful concepts that can be subsequently developed into commercial materials, processes or products, and thus make a contribution to the company's profitability in the foreseeable future, (Fusfeld, 1986).

The term is now also used interchangeably with 'pre-competitive' research. The European Strategic Programme for R & D in Information Technologies (ESPRIT) is based around this concept, which means that it focuses on long lead-time R & D in basic technological and on precompetitive technical areas of fields like advanced microelectronics, data and knowledge processing, and office and factory automation.

2.4 Strategic research: examples from the US

2.4.1 Introduction: the academic-industrial complex

The most significant examples of the new type of relationships based upon strategic or pre-competitive

research, appeared in a series of seven articles on the "academic-industrial complex", that were published in Science journal during 1982 - 1983. Short indicative summaries of the series are provided below.

1. The Academic-industrial complex, the nature of several of the new research agreements emerging in the USA were examined by Barbara J. Culliton and their ethical and other implications were critically examined. In particular it draws attention to the academic "soul searching" that took place when the presidents of five universities convened a small, private conference at Pajaro Dunes in 1982, to develop guidelines that will permit collaboration to take place without seriously compromising "traditional" academic values. The article points out that although the recent agreements reviewed, are in the several million dollar range, the fact is that they are relatively few in numbers and highly specialised as to the area of research undertaken. The bulk of them are concerned with the healthcare applications of biotechnology. A warning note is also given that the emerging academic-industrial complex could give industry a significant influence over academic science.

2. The Hoescht Department at Mass. General. This article explored the $70m arrangement entered into in 1981 between Hoescht AG, the West German chemical company and Massachusetts General Hospital (an affiliate of Harvard). It was pointed out that this arrangement, the largest of all university-industry arrangements to date, was the object of interest in both university and the industry research world. It was widely seen as a new, strategically significant move.

The article points out that as a consequence of Hoechst's extensive funding of the molecular biology department, its scientists are generally precluded from seeking National Institute of Health grants, and are therefore taken out of the peer review process. Concern was also expressed about the question of 'open communication' with their colleagues, as a whole department has been funded exclusively by Hoechst.

3. Monsanto gives Washington University $23.5 million. This was another highly publicised interaction that differed from some of the others. It was an 'institution to institution' agreement, quite deliberately drafted to deviate from the majority of arrangements in which corporate funds are earmarked for research by one or two senior investigators of the company's choosing. The second feature that separates this arrangement from the others is the extent of constant, intimate collaboration that is anticipated between the researchers of the two institutions. It is termed a 'true partnership'. Another significant part of the agreement is the decision to identify a field of research to pursue rather than specific products. The article points out that this is a real strategic investment on Monsanto's part.

4. Electronic firms plug into the universities. This article explored a 'second revolution' in university-industry relationships (the first being in biotechnology), where electronics firms have collectively begun sponsoring centres at universities. Many of the arrangements being worked out include provisions for industry scientists to spend up to a year working in university facilities that their companies have helped finance. The article points out

that some of these developments, where groups of companies are supporting facilities, represent a significant new trend in science policy:

> In effect, corporations and state governments are taking initiatives in areas that just a few years ago would have been considered the exclusive preserve of the federal government.

A case in point is the Center for Integrated Systems, at Stanford University. It was set up with $12 million from industry and $8 million from the Department of Defense. This article showed a different angle on the developing nature of university-industry relations that were taking place in a different technical field, in contrast to the large bilateral relations in biotechnology, in electronics there was a pooling of funds for centres of expertise.

5. Stanford doctors try consulting, inc.

This article looks at the Institute of Biological and Clinical Investigation; a novel mechanism that was set up to link the Department of Medicine of Stanford University with industry. The Institute had two corporate sponsors, each putting in $250,000 a year for three years. These funds are given as grants to junior faculty. The relationship differed from others where industry only selected individuals to help with very highly defined problems "usually related to the fine tuning of a product that had already been discovered". The institute was designed to satisfy another need, where industry wants to analyse carefully the developing edges of biology in relation to the industry's particular product lines and scientific strength. They wanted to fund a fundamental university-based research projects with no obvious product connection. The reasons the sponsors Syntex and Hewlett Packard give for teaming up

with the Institute is purchasing "a window on science".

6. German firms move into biotechnology.

This article focuses on the export of the US corporate strategies outlined in previous articles in the series. It looks at how three German chemical giants are increasing their domestic support of basic research in molecular genetics. However unlike the US, the academic science is not being performed in the university sector but in research institutes, reflecting the different nature of the German research system.

A summary of the major corporate agreements with universities is given in table 2.3.

An analysis of the above literature also highlights another trend in university-industry relations. This is the recent development of research agreements linking a number of (potentially) competing firms with a university. This emerged in article no. 4 in connection with microelectronics and information technology (IT). The Semiconductor Research Corporation established in 1982 pools funds from member firms to sponsor basic research in the universities (Sumney, 1986). The Microelectronics and Computer Technology Corporation, a private R & D consortium, is another example of industrial research co-operation based on pre-competitive research. MCC is in the business of:

> advance long term R & D in fields of microelectronics and computer development. It is not engaged in product or process development; rather its role is to supply 'technology packages' to its members who will then convert MCC research into commercial products and processes through further R & D in their own organisations, (Peck, 1986).

Table 2.3

Ref: Kenney, 1986

As already mentioned in the context of the reports produced by science policy advisory bodies, the UK had developed a cooperative programme in the area of Information Technology; the Alvey programme which involved 53 companies, 46 universities and polytechnics and 5 research establishments in a wide range of consortia, (Arnold and Guy, 1986). The significance of universities to these new networks of technical cooperation is outlined in the US Office of Technology Assessment (OTA) report on Information Technology R & D (1986):

> The university today is in a special position. Universities are being courted by all of the principle actors and many are initiating programs of their own. Most importantly, they are the linking element in multi-institutional settings, (OTA, 1986).

The existence of such programmes such as ESPRIT and MCC, provide a science policy body like ACARD with a working model, as their report Exploitable areas of science shows. In it they too equate strategic science with pre-competitive research:

> Government programmes with emphasis on pre-competitive research involving collaboration between university departments and industry are one, measure which may find wide application in a policy of strategic support, (ACARD, 1986).

There are some indications that group activity had started to take place in biotechnology, the report on the Institute of Biochemical and Clinical Investigation at Stanford, and Engenics were an indication of a new trend in research funding that has come to be expanded, including in the UK.

The analysis of bilateral and multilateral university-industry consortia form the basis of the case studies for this thesis. An analysis of these developments is given in the concluding chapter.

2.5 Government and the new science policy

Reports like those produced by advisory groups such as ACARD, have had an affect on government policy towards science policy, in the UK. The White Paper on Civil Research and Development, (the government response to the First Report of the House of Lords Select Committee on Science and Technology 1986-1987 Session), published in 1987, gave a response to the ACARD recommendation in its report Exploitable areas of science, that a process should be established for identifying exploitable areas of science for the long term health of the country. This idea was applauded by the private sector and the government will set up a new national Centre for Exploitation of Science and Technology (CEST), led and primarily funded by industry and the city. The government will provide start up funds of £1 million. The White Paper also reported that the DTI was reviewing its role in supporting and encouraging innovation.

The governments new policy for technology innovation, which has major implications for science policy, was unveiled in its White Paper: DTI: The Department of Enterprise. The DTI objectives are stated simply as " We will encourage the transfer of technologies and cooperative research". The result of the DTIs review of its role in encouraging innovation is that the balance of existing policies should be changes to move away from near-market R&D support:

> The Government considers that companies are best placed to assess the balance of risks and rewards of their own projects in open and competitive market conditions. The focus of government funding should therefore be on research and technology transfer which spans companies and not on projects in single companies. (p37)

The policy is based on the following actions:

> give greater emphasis in collaborative programmes to longer term research between companies, and to encourage collaboration between higher education institutions (HEIs) and companies;
>
> give greater emphasis to encouraging and facilitating the many different aspects of technology transfer;
>
> end the general scheme for providing innovation grant assistance to individual companies; end the Microelectronics Industry Support Programme; the Support for Software Products and the Fibreoptics and Optoelectronics scheme; but continue small high-technology companies.

The White Paper places a major emphasis on collaborative research and encourages participation in programmes at the European level and at the national level. In the case of the latter it gives special mention to the LINK initiative aimed at encouraging the performance of pre-competitive research by companies, HEIs and Research Councils. The other major initiative it promotes is the National Research Programme. This is a longer term industrially led collaborative project between UK companies in advanced technologies. The role of the DTI is to help establish the collaborative links both between firms and between firms and the research community at the pre-competitive stage. The exemplar of this approach is the national programme on superconductivity, launched in autumn 1988. The programmes

core R&D has two lines of input. One is the academic research programme which is directed towards applications through an understanding of the basic mechanisms and material. The other input is the industrial programme, while including more basic research, concentrates on materials and their fabrication and on research into potential applications. The result of this coordinated mix is a national programme in strategic research, which encompasses applied research to "the most basic research eg. the search for new materials, is not pre-constrained to specific areas". Here we have the government giving its support to basic research, albeit in an area of science considered by industry and academics, to be 'exploitable'.

2.6 Conflict

Although the potential commercial benefits have been widely acclaimed (e.g. Langfitt et al, 1983) this penetration of industry into campus has provoked a major debate in the USA on the potential risks to academic and scientific values and practices (N. Wade, 1984). The source of these tensions can be summarised as;

- conflicting missions;
- a decline in basic research as researchers devote more attention to applied, short term research with immediate pay off;
- a decline in the quality of basic research as scientists become reluctant to share their findings;
- misuse of government funds.

Despite the worries the process has continued and seems to have followed the conclusions of the National Commission on Research (NCR) report that "Hazards to university academic freedom from university-industry relationships are manageable". The 1988 OECD report Science and Technology Outlook has expressed concern that the high priority given to industry's research needs may impede the freedom of access to scientific information, which has historically produced many benefits. It says industrial companies which sponsor academic research are insisting on delays in publishing the results for as long as one year until the companies have applied for patents. The OECD is concerned that such practices will become widespread. It argues that an assessment of developments in this area is urgently needed.

It is noticeable that there has not been the same kind of intense debate in the UK concerning the same issues. The debate being largely confined to editorials in journals such as Nature, (Nature, 1980 and 1983) and the debate has not been over the norms of the academic community but more about the balance of basic versus applied research and the marginalisation of research that cannot be (re) interpreted as being strategic.

2.7 A summary of the science policy literature

In this necessarily selective review of the burgeoning literature concerned with university-industry cooperation, I have sought to identify some of the underlying trends and issues regarding the increased interest and importance ascribed to university-industry relations.

From the literature reviewed above, and from the reports of the large agreements occurring in the US, there is a widespread belief that the increasing ties with universities are taking on forms that differ in character from earlier relationships. The reasons for the proposition regarding the novelty of these current university-industry interactions comes largely from the analysis of the major agreements listed above.

Several basic conclusions have been derived from an analysis of these agreements. The main points are given below;

* Many are of a long term nature;

* The size of investments indicate a strategic role for the interaction. Monsanto view their investment as part of a major diversification strategy into biotechnology, (see Kenney, 1987, and Dickson, 1984);

* There is the apparent contradiction that although most agreements emphasise that the linkage is at the level of basic research, the negotiations over patents and intellectual property, suggest that there is at least some expectation of patentable products or processes;

* The main public policy reason for supporting university basic research, is that it is unappropriable, (Nelson, R, 1961). Therefore some critics view these agreements as conflicting with public purpose. This worry was expressed in the US

National Committee on Research report on Industry and the Universities, (NCR, 1980) which stated that the less basic the research, the more difficult becomes the determination of whether the use of public funds for university-industry research relationships is proper;

* They focus on strategic or pre-competitve research;

* There is a growth of research consortia of universities with two or more (potentially competing) firms,

The other major factor associated with the new university-industry collaborations that were being set up, was the preoccupation with a narrow field of core/generic or broad spectrum technologies. These technologies all share a common dependence on fundamental science. The closeness of the science - technology interaction is put forward as the explanation as to why the universities have such a crucial role to play in their development.

The central role of the university in the promotion of new technologies has echoes in Daniel Bell's concepts concerning the post-industrial economy:

> What is true of technology and economics is true, albeit differentially, of all modes of knowledge; the advances in a field become increasingly dependent on the primacy of theoretical work which codifies what is known and points the way to empirical confirmation. In effect, theoretical knowledge increasingly becomes the strategic resource, the axial principle of a society. And the university, research organisations and intellectual institutions, become the axial structures of the emergent society, (Bell, 1974).

For Bell, the nature and kinds of state support for science, the sociological problems of work by science teams all become central policy issues in post industrial society. In the post industrial society, the chief problem is the organisation of science, and the primary institution the university or the research institute where such work is carried out.

The contemporary question of organising science echoes debates regarding the planning of science that can be traced back to J.D. Bernal's book The Social Function of Science, published in 1939. Bernal's book argued the case for the planning of science. Bernal's ideas were seen as an attack on academic freedom. Intellectual opposition to the concept of planning was organised, the most well known opponent was the philosopher of science, Michael Polanyi. His argument was that basic research should be controlled and directed by the academic community, this he denoted the 'Republic of Science'. This autonomy was justified because any interference would halt or slow the benefits arising from pure science. The debate was overtaken by events, the outbreak of the second world war and the need to establish priorities for research scientists at war. The debate today seems to have been overtaken by the confluence of the linkage between science and technology.

One immediate consequence of the new science policy focusing on strategic research is the way decisions about funding are made. The new organisation of science requires a mechanism for reorienting academics research away from the autonomous 'republic of science'. Because of the more complex information requirements defining the performance of

strategic research (See for instance Masons quote above):

> The task of identifying national basic research priorities cannot be devolved to the scientific community in the shape of its professional organisations, (Irvine and Martin, 1984).

In other words the promotion of strategic research requires new implementation structures that take account of external or demand side criteria. ACARD has explicitly recognised this:

> In allocating funds for strategic reasons internal scientific judgements remain indispensable but are no longer sufficient, and have to be supplemented by judgements of commercial and technological relevance, that is, by judgement of the external worth of the particular scientific area, (ACARD, 1986).

The science policy response to the promotion of new technologies through the performance of strategic research has meant decision making and funding has had to move away from crude customer contactor or science push approaches, towards new implementation structures, based on research cooperation, a strategy outlined in the government White Paper on the DTI; the Department of Enterprise. This means decision making is no longer just left to the scientists. Some of these new mechanism are the subject of empirical research in Chapters 7 - 10.

Chapter Two: Notes

1. This research was facilitated by extensive bibliographies in the following texts: NSB University-Industry Research Relationships. Selected Studies (US Government Printing Office; Washington D.C. 1983.
Stankiewitz, R. 1984. University-industry relations. Report to the Six Countries Programme, Delft, TNO.
Baldwin, D and Green, J. University-Industry relations: A Review of the Literature. Society of Research Admistrators. Spring 1984/5

2. The Haldane doctrine - the notion that research is most fruitfully applied to the needs of government when the agency responsible for research is separate from the government department most directly concerned.(See Rose and Rose,1977)

3. The Richards report states that: In general, there are fewer impediments to collaboration in the newer industries. These are in fact often referred to as 'science-based', or more accurately as 'research-led', which emphasises that the results of research are quickly absorbed into production practice.

4. Whether it is transferable to other areas of science is a moot point as the special nature of chemistry has to be taken into account:

> What might be called the first "modern" industry, because of its intricate linkage of science and technology, is chemistry, since one must have a theoretical knowledge of the macromolecules one is manipulating in order to do chemical synthesis - the recombination and transformation of compounds, (Bell, 1974)

5. The Council for Scientific Policy (CSP) was set up in 1964-65 to advise the Secretary of State for Education and Science on the science budget and other matters concerning science policy.

6. In the first report (1965), the CSP made it clear that exponential growth in research expenditure could not continue, and that research support must be expected to level off in the years ahead. More careful forward planning and discrimination among researcher projects would thus be required in future. the research councils were notified that they must hereafter justify their support programs on a broader range of criteria, including social, economic,

educational, and political objectives, as well as intrinsic scientific merit. The council announced that its first task was to demonstrate how criteria for the development of science can be formulated and applied in practice.

7. " This form of research activity, drawing together the excitement of discovery and the supposed glamour of a new, highly specialised industry, has its own mythology, which says that to be a genetic engineer is to be a pioneer in business and in science", (Yoxen, 1983).

CHAPTER THREE : University science and industrial technology: An innovation perspective

3.1 Introduction

From the literature reviewed, including those outlining a public policy for science, it would seem that it has become axiomatic that science is the source of technological innovation. There is however, no certainty that university research or basic science, is linked directly to technology and if it is whether it is the only input into the process of innovation. If we define innovation as " the whole process of analysing and developing a new idea, designing a product and a production route, setting up for production, and making the product a commercial success in the market place" (ACARD, 1978), information could be gathered from other parts of the innovation process such as development and marketing. The question of how science is linked to technology, which obviously has implications for the institutions which produce and use science, (the universities and industry) has been an area of much debate. This debate has primarily taken place in the context of theories of the innovation process, (Price and Bass, 1969). Important contributions to this debate have come from various disciplines such as economics, sociology, political science, research mangement and economic history.

In theories concerning the determinants of innovation, a dichotomy has emerged which represent the extremes of the debate. These two models regarding the determinants of technological innovation are usually categorised as the science push model and the demand pull model.

3.2 The science push model of innovation

The science/technology push model. The main determinants of innovation are supply-side factors. In this model, the first thing that happens is that a new scientific development occurs, this gets applied and ultimately leads to a new product. The basic policy implication is that in order to get more innovation you have to increase spending on R & D.

It is this model that is implicit in the immediate post-war policies for science. The literature of the history of science policy shows that the large expansion of support for academic research following the second world war was due above all to the lesson of war itself: the demonstration that research could be useful:

> It was the second world war and such developments as the atomic bomb which demonstrated to many for the first time, what could be achieved by harnessing the efforts of scientists within R & D programmes oriented to meeting national goals. In the case of the bomb, the research that made it possible - namely the work on splitting the atom- had at the time it was carried out, no apparent practical application. This example, perhaps above all others, helped establish the still strongly held notion that technological innovation is 'driven' by advances in curiosity-oriented science, (Irvine & Martin, 1984).

Such a view was most clearly expounded in a politically influential book by prominent American scientist, Vannevar Bush:

> Progress in the war against disease depends upon a flow of new scientific knowledge. New products, new industries, and more jobs require continuous addition to knowledge of the laws of nature and the application of that knowledge to practical purpose, (Bush, 1945).

Vannevar Bush set the original strategy for support of basic science. It was a strategy based on the following assumptions:

> New knowledge is a necessary condition for economic growth and progress;
>
> New knowledge can only be derived through basic research. The supply of new knowledge is unlimited but not predictable, and is not subject to diminishing returns;
>
> The government should provide resources for basic research, because of its direct stakes in national security, general health and commerce;
>
> Industry will not provide the support necessary for basic research because expected profits are perceived to be too low;
>
> As Bush stated:
>
> We cannot expect industry adequately to fill the gaps. Industry will fully rise to the challenge of applying new knowledge to new products. The commercial incentive can be relied on for that. But basic research is essentially non-commercial in nature. It will not receive the attention it requires if left to industry, (Bush, 1945).

A similar view was being propounded in the UK by P.M.S. Blackett, then president of the Royal Society. He submitted a memorandum to Parliament on what he considered to be the wisest placement of research funds. By way of introduction, he set out a "simplified schematic form of innovation in technology: pure science, applied science, invention, development, prototype construction, production, marketing, sales and profit" (Blackett, 1968).

Through the 1950s and 1960s scientists had little difficulty in convincing society and its political leaders that there

should be a substantial national commitment to research including fundamental research. Technological (and thence economic) development was coming to be seen as dependent upon a stock of basic discoveries which was in need of continuous replenishment. The science-push view of innovation dominated policy, this theory of innovation had obvious attractions to basic research scientists in that it provided a ready argument to support their claims in the post-war years for substantially increased public funding, and for those funds to be distributed according to the scientific community's own criteria. However, in the 1960s this view became increasingly under challenge. The growth of this concern was reflected in a resource crisis throughout the 1970s which led to a drastic reduction in the availability of funds for university research and higher education (see e.g. OECD 1981, Blume 1982).

3.3 The demand - pull model of innovation

In this model, the flow of influence is reversed and demand side factors such as a 'need' in the market-place calls forth the necessary scientific and technological R & D. The basic policy implications of this model meant that it has found favour with economic determinists and government officials. It simplifies decision making when faced with financing research projects that do not appear to have 'practical relevance'.

The work of economist Jacob Schmookler, is widely interpreted as providing support for this model. Schmookler provided an important contribution to the economic understanding of the determinants of technical change. He

attempted to bring technology within the scope of economic analysis by demonstrating that technical change is responsive to economic forces of demand. Schmookler examined variations in numbers of patents both within individual US industries over time, and between industries. In the industries studied it appeared that it was economic forces which determined the rate of innovation. Whether scientific developments were utilised depended decisively on demand. Schmookler's model of demand-led innovation is shown in figure 3.1.

Schmookler's work has received some criticism which has tended to focus on the methodology he employed. It has been argued that his approach was not designed to detect science-push effects (Wiseman, 1983).

Figure 3.1 Schematic representation of Schmookler's model of demand-led invention.

Ref: Freeman, 1974

Wiseman claims that:

> Science-push effects in the main would not be expected to arise from rather specific discoveries in a particular science, and to affect a spcific sector of the technology in the industry... In highly aggregated data such as that used by Schmookler, changes in inventive activity on specific issues will tend to be lost in the overall noise... Effects of supply side technical factors on inventive activity are most likely to be evident when narrow technological regions are examined, (Wiseman, 1983).

The science push model also has many limitations: it assumes that science itself is a 'disinterested pursuit of knowledge' unaffected by factors such as funding (Yoxen, 1984 , Kohler, 1976). It assumes that there is an uncomplicated difference between 'science' which happens first and 'technology' and 'application' which follow. The parameters of the debate questioning the linkage between science and technology can be found in a major text of the debate "Inside the black box", by Nathan Rosenberg. He asks the question 'How exogenous is science ?' The core thesis of Rosenberg's text was that technological advance largely determines the scientific agenda. He explains:

> ..technology is itself a body of knowledge about certain classes of events and activities: it is not merely the application of knowledge brought from another sphere. It is a knowledge of techniques, methods, and designs that work in certain ways and with certain consequences, even when one cannot explain exactly why. It is therefore, if one prefers to put it that way, not a fundamental kind of knowledge, but rather a form of knowledge that has generated a certain rate of economic progress for thousands of years. Indeed, if the human race had been confined to technologies that were understood in a scientific sense, it would have passed from the scene long ago, (Rosenberg, 1982).

Several empirical studies, using a wide range of methodologies have addressed the issue of this linkage, the most important ones are described below.

3.4 Schumpeter and technological innovation

To overcome the drawbacks of the two previous models, more complex models of innovation, involving a coupling or linking of some kind of social, military or economic need with scientific and technological knowledge, have also been proposed. The more complex models view the innovation process as a process whereby knowledge of market needs and scientific/technical knowledge are brought together. This generally involves a series of "actors" in various institutional settings. One of the major figures in the innovation debate has been Joseph Schumpeter, his models have mirrored the organisational changes in the nature of business that occurred during the inter-war years with the rapid growth of large corporations, and their ability to manage their own R & D functions. His work has been revitalised in a number of studies of high-technology industries, (see M.Kenney, 1986, Rothwell & Zegveld, 1985, Freeman, Clark and Soete, 1982).

Joseph Schumpeter developed essentially two models of how this coupling of market information and scientific/technological information can occur:

- Mark I, a model of entrepreneurial innovation
- Mark II, a model of large firm innovation.

In the entrepreneurial innovation model (Schumpeter, 1934), Schumpeter focused his attention on the first production of a new product, process or system into a commercial or social activity of a country. Schumpeter views the role of the entrepreneur as decisive, in that it is through the mediation of such an individual that invention is translated into an innovation. The entrepreneur brings innovations into the economic system. Schumpeter call this "the gale of creative destruction". It is through the introduction of radical new ideas into the economy that whole new industrial sectors can be generated. Schumpeter's ideas are of considerable interest to those now promoting radical generic technologies such as biotechnology and information technology.

Figure 3.2 shows the entrepreneurial model. In it we see that the entrepreneur is able to tap an autonomous sphere of scientific and inventive activity (referred to as exogenous science) which is not directly linked to the needs of the market. The entrepreneur makes this linkage, which involves a series of complex activities: investment, new production, marketing and profit making. Schumpeter's model also postulates a change in the primacy of time between demand pull and science push as industrial innovation grows to maturity. Exogenous science and technology tend to be important in the early stages of the innovation while demand becomes more important as the innovation becomes established in industry.

This model fits some of the characteristics possessed by the specialist New Biotechnology Firms (NBFs) that were spawned in the US. The model also shows why it was possibly

mistaken to conclude that we are witnessing a straightforward science-push situation in biotechnology. Advances in genetic manipulation can be seen as vital to the areas of current commercial interest but they also need entrepreneurs who made the link and coupled knowledge with what they perceived to be market needs.

Schumpeter developed the Mark II model in his later work (1943), it concerns the role of large firms in innovation. In this model (see Figure 3.3) the firm creates its own in-house research activities - labelled endogenous science and technology. The role of the traditional entrepreneur is taken over by managers of investment activity who combine

Fig. 3:2 Schematic representation of Schumpeter's model of entrepreneurial innovation (Mark I).

Ref: Freeman, 1974

Fig. 3.3 **Schematic representation of Schumpeter's model of large-firm managed innovation (Mark II).**

Ref: Freeman, 1974

new knowledge with the firms production and marketing. In this case the coupling process is institutionalised and socially more complex. Importantly, and despite the internalisation of R & D this model has the endogenous science and technology acting as a mediating agency for interacting with "exogenous science and technology", i.e. outside the firm. This model could possible tie in with the currently observed phenomenon of university-industry research interaction.

Schumpeter's later model reflects the change in the nature of business that occurred in the inter-war years with the rapid growth of large corporations and their ability to manage their own R & D functions. This model reinforces the view that inventive activity is increasingly controlled by large corporations, and ignores the contribution made by smaller organisations. It reflects the growth in the closer coupling together of science, technology, innovative investment, and the market, by larger organisations. This same process has also been recorded by business historians who in recent years have published several histories of the rise of the industrial R & D laboratory, that give us some insight into the strategies behind the internalisation of R&D activity, an activity long considered exogenous to mainstream business activities and indeed the province of the 'lone inventor'. These works (see Dennis, 1987) draw heavily upon the work of A.D. Chandler. Chandler, in The Visible Hand (1977) provides a historical approach to the development of large managerial hierarchies or vertically integrated firms. Whereas some writers on organisation (e.g. Williamson, 1975) treat this as instances of 'market failure', Chandler interprets it as consequences of

technological and marketing economies of scale. A key insight from these historical studies is that this move towards integration occured in certain industrial sectors and developed in response to technological changes in both the production and distribution of goods. The visible hand of corporate management replaced the invisible hand of market forces in allocating resources and distributing finished goods. According to these recent accounts of the emergence of industrial R & D ,the founding of corporate laboratories was another step in the development of the centralized firm by "integrating backwards into another of their raw materials: Knowledge ", (M. Dennis, 1987). By financing research laboratories, companies partially insulated themselves from the problem of external technological change. Technology as a major factor affecting organisational behaviour is made explicit and , I believe offers us an insight into the behaviour of firms today when facing the strategic challenge of rapid technological change.

> The giant firms which dominated the electrical and chemical industries pioneered in placing research work in industry on an organized basis. In doing so, they sought to institutionalize the foresight of those men who had laid the scientific foundations for the new industries, to transfer what hereto had been the result of random discovery of ingenious inventors into the routine product of a carefully managed process ... the research laboratories, above all, gave to the corporation command over the flow of scientific investigation. (Noble, 1980)

This model of innovation would seem to fit large firms who are beginning to incorporate, for example, genetic

engineering skills into their own research laboratories and develop special relationships with, and perhaps incorporate to some extent, centres of "exogenous science and technology", such as university departments, academic research labs or New Biotechnology Firms (NBFs). It is important to note that Schumpeter did not rule out the possibility of Model I mechanisms continuing to operate within a climate increasingly dominated by large scale corporate R & D. The present structure of the biotechnology industry consists of:

1. Research institutions;

2. Established major companies;

3. New biotechnology firms that develop specific applications or provide specific support functions.

This diverse environment could incorporate both Schumpeter Models I and II.

3.5 Empirical studies of technological innovation

3.5.1 Introduction

Current interest in innovation has spurred increased awareness of interrelationships among science, technology and economic growth. During the 1960s, two well known and detailed attempts were made in the US to determine empirically the role that fundamental, 'non-mission oriented' research, plays in technological innovation. The studies were Project Hindsight (Sherwin and Isenson, 1967)

and TRACES (Illinois Inst., 1968). Both studies have been criticised for lack of statistical reliability and for a partisan approach but they can be used as valuable complementary sources of information on science and technology links.

3.5.2 Project Hindsight

Project Hindsight (1966) investigated 20 major US weapon systems developed since 1945. Among these were weapons such as Polaris and Minuteman missiles, nuclear warheads, C-141 aircraft, the Mark 46 torpedo, and the M102 Howitzer. The report found that the contribution of university research was minimal: "undirected" research played no noteworthy role in the development of the 20 weapon systems. It contributed only 0.3% of all the R&D events, while applied research contributed 7.7% and technology 92%. In institutional terms only 9% of all R & D events came from universities (most of this evidently, was applied R & D), 46% came from industry, and 39% from government laboratories.

This report had important policy implications and presented a damaging argument to a scientific community still mobilising the science - push arguments put forward by Bush and Blackett for scientific autonomy. The results of this study influenced - and partly biased - the discussions on science-technology links (1). The results of Hindsight were being interpreted as supporting the demand pull theory of innovation. This model proved to be popular with economic determinists and government officials who are provided with a justification for not funding projects that do not appear to have 'practical relevance', (2).

Project Hindsight has been critcised on two major points:
1. An arbitrary cut off of 20 years was used in tracing back the science and technology events, thereby excluding from consideration any significant basic research arising before this time and inevitably reducing the apparent relative importance of basic research. Keith Pavitt, in the OECD report on The conditions for Success in Technological Innovation (OECD, 1974), pointed out that the apparent modesty of the universities collaboration was mainly due to the very short time period which the Hindsight investigation took into account. They started in 1940 and stressed that they had deliberately excluded the "pool of basic knowledge" assembled before 1940. In spite of this warning Hindsight conclusions have sometimes been misused, (3).

2. The fact that the 20 weapon systems chosen for the study had been selected by Department of Defense staff inevitably created suspicion among some that the sample was biased in order to provide support for those arguing in favour of increasing funding for in-house applied research.

3.5.3 Project TRACES

The conclusions of Project Hindsight were in part challenged by a report produced by the National Science Foundation in 1968: Technology in Retrospect and Critical Events in Science, (Illinois Inst., 1968, 1968). This study looked at five innovations that were regarded as very much 'high technology'; from oral contraceptives by way of electron microscopes to videotape recording. The conclusion of TRACES provides an interesting contrast to Hindsight.

* In all the case studies, pure research provided the origins from which science and technology could advance toward the innovations that took place.

* Of the key events documented, approximately 70% were classified as non-mission (pure) research, 20% were mission oriented (strategic and applied) and 7% were development and application.

Furthermore, universities appeared to have played a far more important role than might have been expected on the basis of the findings from Hindsight, having been responsible for 3/7 of non-mission and a 1/3 of all mission-oriented research. The TRACES study apparently provides evidence to support the 'science push' model of innovations.

Both of these studies have their critics, with most criticisms focused on the methodologies they both employed (see Mowery and Rosenberg, 1979): a linear model of innovation is imposed retrospectively upon a very complex interactive process; it attempted to identify all important discoveries or breakthroughs which made possible successful development of the weapon systems; technological events are arbitrarily assigned identical weights, and the suspicion that the interest of sponsoring agencies influenced results, (Layton, 1977).

3.6 Citation studies of technological innovation

While the particular methodologies of the two most widely known studies has been heavily criticised, other methods have been used to try and understand the interaction between

technology and science, one such method is the use of citation studies (Rabkin, 1981). One of the most widely known is the study carried out by the historian of science and pioneer of scientometrics, Derek. de Solla Price (Price, 1965). He questioned the proposition that scientific advance is a necessary pre-requisite of technological innovation. His methodology was based on science and technology literature citation studies, from which he proposed a model which regards science and technology as two autonomous and independent streams. Price argued that contact between these "essentially two separate worlds", is spasmodic and occasional, and that technology 'feeds on itself' for long periods without any major influences from science". Price also pointed out that the 'actors' associated with these two activities, science and technology, are different, as are their aims. He developed the theme of Lavoisiers plea for pure science by distinguishing between 'papyrocentre' science - for science is published papers and the scientists property is his publications - and 'papyrophobic' technology - for the technologists is keen to patent and then produce his artefacts or process without disclosing material that may be helpful to his peers and competitors before his claim can be established. It is this issue that has largely dominated the debates on the growth of university-industry relations in the US, (Wade, 1984).

The model developed by Price has provided a useful model for the debate. Many, perhaps most, technologies fit this model quite well, but in certain areas - including electronics and possibly the new biotechnologies - the science -technology coupling would seem to be much stronger than Prices model

implies. Indeed, Price acknowledges this by classifying these technologies within the body of science:

> By definition it should be remembered there is considerable part of such subjects as electronics, computer engineering, and industrial chemistry that must be classified as science in spite of the fact that they have products very useful to society, (Price, 1965).

In a study on information flows in various R & D laboratories, Marquis and Allen have elaborated on Price's analysis by inserting additional linkages between science and technology, concluding that under certain circumstances a communication link can exist between the science and technology sectors and that given these circumstances, the communication is bilateral direct and quite rapid. Marquis and Allen call the science which is transmitted in this process 'gap-filling science' since it occurs in response to a strong technological need and can consist of either 'new science' or 'old science', (Marquis and Allen, 1966). Marquis and Allen also proposed that "the degree to which specific technologies advance independently of the sciences underlying them is variable". Their study shows that some technologies such as electronics may be more closely coupled to frontier science than others, such as mechanical engineering.

More recent work, using citation studies, has been carried out by Marvin Lieberman who looked at science-technology coupling in electronics (Lieberman, 1977). As indicated by the work of Price and Marquis and Allen, the primacy of 'old' science seems to be the general rule, transmitted via the educational system and scientific literature. It also appears that under certain conditions some technologies may

become more closely linked to 'new' science than the general pattern suggests. Electronics is one such case.

Lieberman has developed a model of science - technology interaction developed for his study. It differs from the 'linear' model in that the innovative stimulus is not limited to basic science but can originate within any section of the chain, e.g. a discovery of a new physical phenomena can initiate a sequence of innovative activity; so can the appearance of a new user demand = feedback. A stimulus introduced in any one sector may thus impact through all or part of the chain. This corresponds to the kind of coupling that is suggested by the work of Schumpeter.

On the basis of science and technology literature citation study of the electronics components sector which produces transistors and integrated circuits. Lieberman found that the technology tends to interact with new science and also that the links between the scientific and components sectors are normally transitory. Discovery of a new phenomenon in basic research may initiate close ties with the component sector, but these ties gradually die away as the relevant science is assimilated by the component sector. Similarly the component sector may be induced to search the domain of basic scientific knowledge in order to better understand the operation of existing devices, or to identify physical phenomena useful for the design of new devices. If relevant scientific information is obtained, that information may be put to use either directly or after it has passed through an interim stage of applied research activities. In either case, the coupling between the science and technology

sectors will ultimately weaken as the scientific information becomes codified in technological form.

These findings also appear to support Rosenberg's model of science - technology interactions, mentioned earlier. Where in certain situations the advent of a promising new component technology may feed back to generate a pool of fundamental scientific knowledge potentially useful for refining the new technology and developing ancillary technologies. An example of this is the impetus given to solid state physics research by the development of the transistor, (Gibbons and Johnston, 1974). The result of this process is that the various couplings between the components and scientific sectors proceed over time like a series of overlapping waves, as old ties between the sectors decay and new ties are established. As a specific technologies mature they normally became more remote from basic science. What is interesting about some of the contemporary university-industry research agreements in biotechnology, described in Chapter two, is the length of time of some of the (renewable) agreements which are often five or more years.

Another study emphasising the transient nature of university-industry research interactions was carried out by John Langrish. He carried out a study on the institutional origins of abstracts in the Journal of the Royal Society of Chemical Industry. He found that the relative contributions of the university decreased over time, while that of industry, particularly in America, clearly increased. He proposed two explanations:

> After the original breakthroughs which establish a new discipline, the interest of the industrial and the university research tend to diverge. A new branch of science is only useful to industry in its early days.
> The relationship between university research and industry may well be a function of the degree of development of the area concerned. Once a new area has been established, the aim of science is to understand; the aim of technology is to make things work, and industry has been very successful at making things work without too much reliance on understanding.
>
> Industry has increasingly taken over its own research. Once the industry has built up its own R&D organisation its dependence on academic scientists gradually diminishes.

His conclusions were that industry makes use primarily of the trained manpower supplied by universities. It also uses new techniques such as chromatography, developed in universities. Echoing Rosenberg, Langrish found that the new products and processes of industry seem to depend on a combination of existing technological concepts, economic processes and empirical research with scientific understanding not being very relevant. These findings regarding the relevance of a particular part of science being dependent on its degree of development seems to be in agreement with the findings of Lieberman and indeed some of the commentators on the recent increase in university - industry relations, seem to suggest that this may be the case with the new connections (see Williams, 1984, and Stankiewitz, 1984).

3.7 Biotechnology: The science-technology linkage

There is a considerable amount of anecdotal reporting concerning biotechnology that suggests that at least in this area of technology, science and technology are very closely coupled. Typical comments include:

> The eagerness with which other small research companies have seized on monoclonal antibodies as the basis for commercial products like diagnostic kits alerted other universities to the way the gap between "basic" research and commercial application has narrowed almost to invisibility, (Turney, 1983).

> Increasingly the term "technology Transfer" is losing its meaning, since there is no motion or transfer, conception is capitalisation, (Yoxen, 1983)

> The time lag between research results in the academic laboratory and application in biotechnology-based industry is very short relative to the time lag for applications of other areas of academic research.
> (Evidence given by Glaxo)

It is because of this reported closeness that university-industry relations are deemed to be of such importance to the commercialisation of this technology. This 'closeness' has been tested using citation and referencing data from recent biotechnology patents and papers a study by Narin and Noma (Narin and Noma, 1985) has provided empirical evidence of a changing relationship between science and technology. They claim that in the area of biotechnology science and technology are more closely linked today than is normally perceived and that in fact the division between the leading

edge biotechnology and modern bioscience has almost completely disappeared:

> This leads directly to a very remarkable conclusion: namely that the science being relied upon in patented biotechnology, at least in biotechnology type patents, is quite recent. It is, in fact, just as recent as the technology (patents) referenced in those patents. Furthermore, if one allows for an extra year or two to prosecute a patent, the cited papers are just about as recent as the papers cited by papers. These biotechnology patents are not just the old, codified science found in texts and reference books; rather, they are using current science just about as quickly as it emerges from the research labs (Narin and Noma, 1985).

3.8 Research management and innovation

Most studies of innovation are implicitly or explicitly concerned to specify the conditions for successful innovation from the perspective of industrial management. Of interest to the research problem of this thesis is whether university -industry linkages are strategically important in a firms ability to produce innovative technology. The literature has some implications for public policy and some results of interest to the theme of university - industry relations do emerge.

Stuart Blume, in a review of the literature (Blume, 1974) summarised the main identifiable characteristics of firms successful in innovating :

> The organisations should stimulate the commitment to science, by demonstrating the appreciation of scientifically valuable work, write papers etc;
>
> A participative style of management;

Communication external and internal-gatekeepers;

Individuals encouraged to diversify -disciplines and functions.

In his book The Economics of Industrial Innovation Christopher Freeman summarising his findings from a number of case studies of science related industrial sectors, lists the following as characteristics of successful innovation:

Strong in-house professional R & D;
Performance of basic research or close connection with those who perform such research;
The use of patents to gain protection and to bargain with competitors;
Large enough size to finance fairly heavy R & D expenditures over long periods;
Shorter lead times than competitors;
Readiness to take high risks;
Early and imaginative identification of market potential;
Careful attention to the potential market and substantial efforts to involve, educate and assist users;

Entrepreneur ship strong enough effectively to coordinate R & D, production and marketing;
Good communications with the outside scientific world as well as with customers.

These generalisations were tested by another well known empirical study of innovation has been concerned with the conditions necessary for a firm's 'success', Project SAPPHO, (Scientific Activity Predictor from Patterns with Heuristic origins). Project SAPPHO's results emphasised the

importance for success of several factors, of interest to this study is the fact that one of these factors was communications with the outside scientific world as well as customers (SPRU, 1982) (4).

Some of these conclusions, especially those that emphasise the importance of external communication is consistent with the interest in university - industry relations. Similar findings emerge from Nystrom's work on R & D strategies in Swedish firms (Nystrom, 1978).

> Companies emphasising outside contacts in their R&D,that is with an external orientation, were more successful in developing new products with a high level of technological innovation than companies that relied predominantly on internal resources and competence for R & D, (Nystrom, 1978)

The findings of Blume, Freeman, Nystrom etc, have all found that external relations have played some role in a successful innovation strategy. The university-industry link seems to generally to enable a firms in-house R & D department to plug into fundamental research. Freeman has conceptualised this in strategic terms:

> The advance of scientific research in many different fields is constantly throwing up new discoveries and opening up new technical possibilities, which are to a large extent independent of any particular market pressure. If a firm, or a country, can monitor this advancing frontier, by one means of another, it may be able to gain both a technological and a market lead over its competitors by the speed of its response, as the Japanese example has shown, strong in house R & D, as well as close contact with potential users and markets, will usually be needed to convert this first awareness of the new potential into a competitive advantage.

> If innovation is a complex coupling process of communication, then structural problems both within and outside the firm are of central importance, (Freeman, 1974).

The importance attached to firms maintaining contacts with fundamental research at the universities is summarised by Price and Bass, (1969):

> 1. Although the discovery of new knowledge is not the typical starting point for the innovative process, very frequently interaction with new knowledge or with persons actively engaged in scientific research is essential.
>
> 2. Innovation typically depends on information for which the requirement cannot be anticipated in definitive terms and therefore cannot be programmed in advance, instead information is often provided through unrelated research. The process is facilitated by a great deal of freedom and flexibility in communication across organisational, geographical and disciplinary lines.
>
> 3. The function of basic research in the innovation process can often be described as meaningful dialogue between the scientific and technological communities. The entrepreneurs for the innovative process usually belong to the latter sector, while the persons intimately familiar with the necessary scientific understanding are often part of the former.

3.9 The work by Gibbons and Johnston Study

The previous studies have tended to indicate that the main way firms can make use of universities is to 'plug in' to the fundamental research that they perform.. The question of exactly how firms actually use university science in their problem solving has been addressed in a study by Michael Gibbons and Ron Johnston, (Gibbons and Johnston, 1974).

The study focused on a set of recent or current industrial product innovations. The history of each innovation and the identification of all the technical problems to be overcome were analysed. All of the types of information which were used in problem solving were then identified. They found in no case could an innovation be said to have been brought about by scientific discovery, yet scientific information made a major contribution to the innovations.

Of all information obtained from outside the company and used in problem solving, over 33% could be described as originating from scientific activity, the rest being technical. 1/3rd of all the scientific inputs were in the form of scientific literature reporting the results of original research. These research literature inputs were of major importance particularly in large scale innovations. As well as literature personal contacts with scientists in universities were also important. This work shows clearly that scientific research is important to the invention/innovation process, but that the coupling is extremely complex and takes various forms. They concluded;

> ...It is apparent that the relationship between science and industrial technology is more complex than previously assumed by either scientists or economists; there exists a wide variety of potential forms of interaction. While this settles the issue of whether science contributes to technological innovation, and provides a justification for maintaining an effective research capability, the very complexity of the relationship precludes simple calculations of the optimum size or distribution of the science budget.

The conclusions of Gibbons and Johnston are potentially very significant in improving our understanding of the complex

role of science in the innovation process. From their analysis of information flows the innovation process can be seen as a complex set of interactions between basic and applied, in-house and external, research. They also concluded that the basic research infrastructure in universities and government installations contributes to commercial innovation in ways other than those simply providing the private firm with exploitable scientific discoveries. Thus a complex, non-linear relationship between basic and applied research is indicated in Gibbons and Johnston's work, far more than is the case in Hindsight.

3.10 Policy implications of the innovation literature

This thesis is primarily concerned with innovation in the field of biotechnology. The biotechnical innovation process is not well understood and because of its significant commercial potential there is much speculation from policy makers, both public and corporate, about what linking mechanisms will most effectively stimulate rapid growth.

This chapter shows that our current conceptual understanding of the innovation process derives from the empirical study of technologies developed in fields other than the life sciences e.g. electronics. Because innovation in biotechnology lacks the systematic empirical understanding that is present in other fields, it is difficult to do more than speculate about mechanisms and/or conditions that provide a favourable climate for such innovation or industrial application and growth. The work of Noma and Narin, and the reality of the various corporate investments, there is reason to believe that innovation in the life

sciences has characteristics that are unique relative to those in other fields. In the life sciences basic research activity may be particularly important to development efforts.

Despite the heterogenous nature of the studies that make up the literature on innovation, some common themes do appear. The major consensus is the increasing role (at least in this century) of scientific inputs into the innovative process. Although the exact nature of this input is still unknown. Indeed the scientific input has to be seen in context as one of many inputs into the innovation process. The view of innovation has become more sophisticated than the original "science push" and "demand-pull" models that have influenced science policy over the years. A typical example of the contemporary view of the innovation process is given by Blume:

> Although the output of innovative activity is typically a new product or process technology, the activity itself, it is now understood, is primarily about the selection and control of information, (OECD, 1984).

John Child also takes this perspective:

> Most commentators agree that innovative capability depends on effective information processing: including access to sources of concepts and ideas; the integration of internal specialist contributions to the development and commercialisation of those concepts; and the ability to achieve sufficient operational flexibility to support new and evolving product specifications. The organisational contribution here turns on the integration of inputs to innovation from a range of sources (some external to the enterprise) and the facilitation of speedy implementation attuned to commercial needs." (Child, 1987)

From a policy point of view it is clear that some of this information lies in the universities.

Rothwell and Zegveld have developed a 'interactive model' that is indicative of this new perception of the innovation process. See figure 3.4. According to this model innovation is regarded as a logically sequential, though not necessarily a continuous process, that can be subdivided into a series of functionally separate but interacting and interdependent stages. The overall pattern of the innovation process can be thought of as a complex set of communication paths, both intra-organisational and extra-organisational, linking together the various in-house functions and linking the firm to the broader scientific and technological community and to the market place. In other words the process of innovation represents the confluence of technological capabilities and market needs within the framework of the innovating firm.

Fig 3.4

Ref: Rothwell and Zegveld, 1985

Although there is still some debate, many of the studies from the innovation literature discussed above seem to agree in ascribing considerable importance to links between firms and outside research performers for successful innovation. In so doing they substantiate the frequent stress laid in the science policy literature, reviewed in chapter two, upon the importance of university-industry links, for universities are of course the major performers of basic research in most countries.

Mowery and Rosenberg, in a review of most of the studies mentioned in this chapter, conclude that the studies taken together point towards the importance of institutionalising contacts between users and producers of research:

> intelligent policies must be directed at institutional aspects of the innovation process, working to encourage the interaction of users and producers, as well as the iterative interactions between more basic and applied research enterprises. We do not yet understand the characteristics of the innovation process sufficiently well, nor do we posses the necessary knowledge base in certain areas of substantial social utility. Useful policies would be those directed at the provision of information, from basic research institutions in the non-commercial sector to private firms and laboratories, as well as from users to producers concerning desired products and characteristics, (Mowery and Rosenberg, 1978)

They point out that policies directed toward increasing both the frequency and the intimacy of interactions among these separate participatory groups may prove to be successful in terms of encouraging innovation. The reports reviewed in this chapter, and produced by public bodies with an influence on science policy seem to increasingly reflect the views given by Mowery and Rosenberg.

Notes

1. There was a change in attitude to science policy in the US by the Johnson administration 1966. The position of the Johnson administration on basic research was bolstered by preliminary report of a study Project Hindsight. The conclusions:
   1. the contribution of university science was minimal.
   2. Scientists contributed most effectively when the effort was mission-oriented.
   3 The lag between initial discovery and final application was shortest when the scientist worked in areas targeted by the sponsor.
   This report helped popularise a new set of terms such as:
   Research in the service of man;
   Strategy for the cure of disease;
   Targeted research;
   Mission-oriented research;
   Disease oriented research;
   Programmatic research;
   Relevant research;
   Commission initiated research;
   Contract supported research
   Pay-off research (Comroe and Dripps, 1977).

2. The Rothschild reorganisation of science funding in the UK was an expression of this demand-pull view of innovation:

   > It was no longer a question of doing good research and ensuring that potential users were aware of it. By the middle seventies it had become a question of industrial representatives and officials together (in the industrial field), or officials and scientists togther (in the health field), or middle ranking civil servants alone (in many other fields of government activity), themselves deciding what research needed to be done, and looking for someone to do it., (Blume, 1981).

3. The study also carries a passage that seems to have been overlooked by many of the interpreters of the findings of Hindsight:

   > It is emphasised that this study identified only those incremental contributions to existing bodies of scientific and technological knowledge that were utilized in the analyzed military equipment. The strong dependence

of these contributions upon the total base of science and technology must be recognized.

4. The other conditions SAPPHO identified included 1. strong in-house R & D, 2. the use of patents to gain protection and to bargain with competitors, 3. careful attention to the potential market including substantial efforts to involve. educate and assist users, 4. entrepreneurship strong enough to effectively coordinate R & D, production and marketing.

CHAPTER FOUR: University-Industry Interactions: Organisational Strategy

4.1 Introduction

If science policy is becoming increasingly engaged in a process of encouraging technological innovation, it is important to look at the forms of organisation, and organisational strategy that might be available to translate the research carried out in HEIs into marketable technology. The previous chapters have shown an increase in the use of cooperative research as a mechanism. In this section I wish to review some of the literature concerning the ways of organising economic activity, and the way it is being perceived to have changed in order to face new strategic challenges, of which technological innovation is one. Through investigating this strategic management literature, I wished to see if there might be a useful overlap between the interests of science and technology policy analysts and those studying strategic management. For instance, are their trends in strategic management that may be used by those who seek to promote linkage between firms, and between firms and HEIs.

4.2 Technology and the role of the firm

The underlying theme of my research is the commercialisation of the biosciences. How (bio) technology enters into the economy of a modern industrial state like the UK. The complex multi-stage process by which this is done is through the process of "innovation", described in the previous chapter. In a capitalist economy such as the UKs, private sector firms are generally thought of as the institutional

means of applying technology. Although firms can be considered as the locus for the introduction of technical change, and that competitive theory conceives of firms as atomistic organisms, they are by no means completely independent agencies as the previous two chapters have shown. Indeed it is posited in this thesis that inter-dependency between organisations, particularly between universities and industry, now represents a key ingredient for success in innovation and in competitive business activities.

Some idea of the firms role can be gained by considering the process of developing and successfully marketing a new pharmaceutical product arising from genetic engineering. It is a multistage process involving:

* Identifying a need and identifying appropriate knowledge.
* Synthesising the product on a laboratory scale.
* Scaling up development.
* Clinical testing.
* Obtaining clearance from regulatory authorities.
* Marketing.

Each of these discrete stages itself involves many stages and an appropriate institutional structure and organisation. The firm operates within an environment which affects what it can and cannot do. The business environment is normally divided into the following main spheres 1. Technical, 2.Market, 3. Political, 4. Sociocultural. Firms vary

greatly in their ability to adjust to or manipulate this environment. In these terms the area of focus in this thesis is the firms interface with the technical environment.

The organisational strategy adopted by the firm can be seen as an organisation acting upon its environment to create circumstances favourable to continued existence and independence. From this perspective university-industry links can be conceived of forming part of a firms strategy. The empirical part of this thesis examines the mechanism and objective of such an interation.

4.3 Organising for competition

Competitive behaviour is normally seen as the domain of a single atomistic company, implying a strategy of independence (the rise of the vertically integrated firm seems to promote this view). Howver, there are many ways of organising economic activity and that in today's high technology areas, typified by biotechnology, a successful strategy (one based on technological innovation) may involve clear inter-organisational collaboration, national and international. Recently studied examples are; "mutual organisations" created to share costs and risks of advanced technologies necessary to remain internationally competitive; "Networks, a network arrangement is an organisational form which has undergone considerable development in our economies, particularly in the form of joint ventures, consortia and other corporate structure

prevailing in the European Aerospace industry." (Koenig & Thieart, 1987). These organisations "represent new design models created by and reflective of a collaborative network" (Child, 1987). These collaborative or network arrangements can be seen along the spectrum of organisational forms in the figure 4.1.

Figure 4.1, shows the arrangements in terms of a spectrum ranging from arms-length bargaining to total integration. At one end we have the 'open market', and at the other we have the firm which is relatively self-sufficient and is vertically integrated. This distinction is roughly parallel to Oliver Williamson's markets and hierarchies, (Williamson, 1975). Williamson has been a major influence on the debate about organising economic transactions. He is generally associated with an approach known as transaction cost economics. He views the market and the hierarchy as alternative transaction control mechanism. His analysis proceeds by outlining the conditions under which the mechanism will fail to provide this control for a focal organisation. The transaction cost approach is designed to determine whether the boundaries between market forms of coordination (e.g. buying in components or services) and administrative or hierarchical forms of coordination (by doing it in house), are most efficient. The approach therefore analyses factors which alter the boundaries between organisations and can be used to explain the integration strategies of firms, why some activities are coordinated within an hierarchy. Williamson suggests that

Figure 4.1

Continuum of macro-organizational designs

Ref: koenig and Thieart, 1987

hierarchies emerge as a system to reduce the costs associated with monitoring and controlling exchanges when markets fail. Markets are said to fail as a control mechanism as a result of two related factors. One is opportunism due to small numbers, and two is bounded rationality due to uncertainty and complexity. The transaction cost approach does have its critics (see Whitley, 1987) and it is seen by others as just one of many theoretical approaches that can be used to analyse inter-organisational collaborations such as consortia and joint ventures. Kogut lists strategic behaviour theory and organisation theory as other, not necessarily mutually exclusive, forms of analyses (Kogut, 1988). He concludes that " most motivations for joint ventures are reducible to three factors: evasion of small number bargaining, enhancement of competitive positioning (or market power), and mechanisms to transfer organisational knowledge", (Kogut, 1988). From among these approaches it is strategic behaviour, that I have found most useful in analysing the commercialisation of the biosciences and the role of public policy.

From figure 4.1 above, it can be seen that between the two extreme forms of organisation postulated by Williamson, there is an intermediate zone that corresponds to the sort of collaborative arrangements that are now receiving a lot of academic attention in publications such as the Strategic Management Journal. The key idea that runs through these articles is the suggestion that to be economically effective (i.e. competitive) it is not necessary to operate at either

of the two extremes of markets and hierarchies. Many transactions are taking place between these two points. This then leaves space for inter-organisational cooperation; cooperation that is compatible with competition. Most of these studies use a more strategic behaviour approach than the microanalytical perspective of market failure applied by Williamson.

4.4 Networks and joint ventures

Within the strategic management literature ideas are now emerging that place inter-organisational co-operations and networking at the core of new competitive strategies. One such author is H. B. Thorelli (1986), who conceives of networks as a way of organising economic activity that lies between markets and hierarchies. The network consists of two or more organisations involved in long term relationships. In some cases even competitors may form a network (which has anti-trust implications although it has now been overcome in cases of cooperative research which is very relevant to biotechnology). Thorelli, suggests that the network be viewed as consisting of nodes or positions (occupied by firms, households, strategic business units inside a diversified concern, trade associations and other types of organisations) and the links manifested by the interactions between them. "The links constitute a reflection and recognition of interdependence as opposed to the autonomy postulated by the classic theory of the firm". The positioning of the firm in the network (which depends upon economic base, technology, trust etc) "becomes a matter

of as great strategic significance as positioning its products in the market place". Power, information, money and utilities flow along the links of these networks. Importantly he points out that the network concept connotes a special type of system, whose internal interdependencies change over time (I will discuss later this in relation to the debate over the 'permanence' of new university-industry arrangements).

Thorelli, sees networks of interacting firms as an important new organisational form in the modern market economy and he warns that in its strategic planning companies should "not only keep one or several theories of the firm in mind, it should also think in network terms to open new perspectives of structure, strategy and performance". That this does seem to be the case is documented by K.R. Harrigan in her study of joint ventures (something Teece, 1987, refers to as 'strategic partnering') - a key networking activity that is currently very popular in the so called high technology sectors. Harrigan notes; "the willingness of firms to use cooperative strategies where previously they would not do so represents a watershed in their way of thinking about competitive strategy", (K.R. Harrigan, 1988). As she states: "By the mid 1980s domestic Joint Ventures had become an important means of supplementing strengths and covering weaknesses of firms in mature economies". Harrigan points out that past studies have devoted little attention to the use of joint ventures as competitive weapons in a mature economy. They overlooked the use of joint ventures as a new

approach to global competition, technology transfer, or other strategic challenges.

Conceptually a joint venture is a selection among alternative modes by which two or more firms can transact (Harrigan has provided a typology, see table 4.1 reproduced below, Harrigan, 1987). A theory of this behaviour, of why a particular mode of transacting is chosen over others needs to be developed. I have already made a brief reference to the work of Oliver Williamson, whose transaction cost approach provides a major theoretical approach to this issue. Both Harrigan and Thorelli seem to take a more strategic behaviour view, i.e. that organisations are not necessarily driven (exclusively) by cost-minimising considerations, but also by maximising profit through competitive positioning:

> Joint ventures (and other forms of alliance) are used with increasing frequency to restructure industries, create new products, keep abreast of rapidly changing technologies, and ease problems of worldwide excess productive capacity. Since they will be such an important tool in global strategy, savvy managers are taking aggressive, but methodical steps to meet the new challenges of joint venturing, (Harrigan, 1987).

I would suggest that interactions with HEIs in areas like biotechnology could be interpreted in this strategic framework; as enhancing a firms competitive position in the longer terms rather than doing research cheaper than it could be done in-house.

Ref: Harrigan, 1986

The strategy point of networking has been elaborated by R.E. Miles and C. Snow, who looked at networking in sectoral terms, where a sector is made up of a mix of firms following different strategies, the most common ones have been labelled 'Prospectors', 'Defenders' and 'Analyzers'. Prospectors are first to the market and use innovative technology and products; defenders develop on the basis of value/cost; and analyzers are second to market but have improved on the first product. Miles and Snow argue that new organisational forms arise to cope with new environmental conditions, and they suggest that the competitive environment of the 1980s is pushing many companies into the innovative mode. The signs of this new organisational form include, the increased use of joint ventures, subcontracting and licensing activities across international borders, new business ventures spinning off established companies. This new competitive form they refer to as "dynamic networks". The name is intended to suggest that the major components of the network can be assembled and reassembled in order to meet complex and changing competitive conditions (Miles and Snow, 1986). The concept reiterates the transient nature of networks as described in Thorelli's scheme and also echoes the temporary nature of the directorate and club mechanisms designed to help companies exploit an area of science and technology.

The mixture of strategic roles required for industry synergy changes as the industry evolves, for instance embryonic industries such as biotechnology are heavily populated with firms pursuing the prospector strategy. Within the dynamic

network structure prospectors essentially play the designer role within an industry, analyzers play the marketing/distribution role and defenders perform the producer role.

J. Jarillo is another author that has stressed the strategic importance of networks, indeed he refers to them as 'Strategic Networks', (Jarillo, 1987). In his view networks allow firms to specialise in those activities of the value chain that are essential to its competitive advantage, reaping all the benefits of "specialisation, focus and possible size (Jarillo, 1987). Its a situation where other activities are farmed out to members of the network, that carry them out more efficiently than the "hub" firm (this is very close to the 'dynamic network' mentioned above) since they are specialized in them. Jarillo views such 'deintegration', provided by the existence of a network that "takes care of the other functions", as being an extremely powerful competitive weapon especially in environments that experience rapid change, due to increasingly rapid technological pace, globalisation of competition, or the application of new flexible, deintegrated competitors.

These new organisational forms for economic activity have been termed by the journal Business Horizons as the forms for "Post-Industrial corporation". An organisational model for businesses in the post-industrial era. They pointed out that even many big companies that continue, for now, to do most of their own manufacturing are edging toward disaggregation: "Forced by the high cost of developing

products and penetrating world markets, many are turning to foreign sources for finished products. Others are forming joint ventures and temporary alliances overseas. General Motors Corp., a prototypical vertically integrated co. does all of the above", (Business Week, 1986). They go on to speculate that "the network model, if it is broadly adopted, would be only the third real organisational innovation since the corporation evolved in the mid-19th century. Now network companies may have their day". These remarks are speculative and there is obviously some dispute as to their significance. Teece for instance warns against the danger of moving too much into such 'strategic partnering' leaves corporations vulnerable, and in the Business Horizon issue referred to above, other articles warn against the "hollowing out" of US industry, (Teece, 1987).

4.5 Research and development networks

In order to bring a product to market ("to innovate") the firm has to perform numerous functions. The literature referred to above has attempted to conceptualise and explain a highly visible contemporary trend that shows that the business system delivering technological innovation can in fact involve a network, the relation between producers and consumers is one part of the network that has been investigated (see e.g. Von Hippel, 1976, Nystrom, 1978). Networking, or other collaborative arrangements could cover any part of the business chain, for instance Thorelli gives us an example of marketing and international consulting, others give examples in production (Miles and Snow, 1986),

the whole business chain, (Koenig and Thierart, 1987). My focus, because my primary concern is with biotechnology and university -industry relations, is with that part of the innovation trajectory concerned with research and development.

Chapter two showed that there is a growing literature focusing on joint activities at this part of the business spectrum. Although the 'networking' literature cited above concentrates mainly on inter-organisational collaboration between similar organisations (i.e. private firms), networking in R&D, because of its link with science and therefore the institutional structures that support it, involves organisations of different institutional structures and cultures and this gives the relationships extra complexity.

This point is well made in the study by R. Nelson and S. Winter of the "rapidly increasing literature on the nature of the R & D process, the links between science and invention, the sources of invention (large firms, small firms, private inventors), the
kinds of organisational and other factors associated with successful choice and carrying out a project, etc". They note that such " microcosmic studies" have shown:

> that the institutional structure for innovation often is quite complex within an economic sector, and varies significantly between economic sectors. Thus in agriculture, there is considerable public subsidization of research done by predominantly non-profit institutions (largely universities) and a subsidized federal-state extension service for the dissemination of info regarding new

technological developments to farmers, interacting with the network of private farms, and industries that produce and sell farm equipment, fertilizers,etc. The commercial aircraft industry is equally complex but must be described in quite different terms.

Innovation in medicine involves a set of institutions different from either of these. This institutional complexity and diversity would seem to be where the focus of a policy attention should be.

They go on to conclude;

If there is to be any hope of integrating the disparate pieces of knowledge about the innovation process, a theory of innovation must incorporate explicitly the stochastic nature of innovation, and must have considerable room for organizational complexity and diversity.

In many sectors there are a complex of R & D organisations, some profit oriented, some governmental, some academic, doing different things, but interacting in a synergistic way. In particular, in medicine, agriculture, and several other sectors, private for-profit organisations do the bulk of R & D that leads to marketable products, but academic institutions play a major role in creating basic knowledge and data used in the more applied work, (Nelson and Winter, 1977).

It is becoming clear that many of the new organisational forms are specifically geared to resolving technological issues; "Joint ventures, their has been a rise in the formation of R&D joint ventures as a means to offer firms a window on promising technologies such as robotics, genetic engineering, and solar energy", (Harrigan, 1987). An indication of the extent of these changes is given by

Carmela Haklisch who has studied technological alliances in the semiconductor industries;

> Changing patterns of technology transfer are defining a new contour on the R&D landscape of the semiconductor industry -- an increasingly dense network of industrial technical linkages occurring both within countries and across national boundaries. Some are wholly within the private sector; some are joint efforts of Government, industry, and/or academic partners. Perhaps the most pronounced topographical feature of the activity is the coupling of technology and research co-operation with competitive strategies. Put another way, patterns of technical cooperation that are evolving are part of the growing intensity of competition, (Haklisch, 1986).

Once again we see the apparent paradox of increasing competition leading to increasing cooperation. These increasingly involve what Schumpeter (1943) has called exogenous science and technology, that is science and technology that lies outside the firm. An important part of both Nelson and Winter's and Haklisch's analysis, and one central to my thesis, is the new role attributed to the academic sector as a source of science and technology exogenous to the firm. Network or cooperative relations with institutions like universities may now be viewed, in some cases as being directly related with a companies competitive strategy.

Table 4.1 above listed the types of cooperation that can occur, Haklisch refines this typology further by examining the R & D part of the spectrum:

> Technical cooperation can be distinguished

> in two forms: research and technology. Research cooperation is a joint undertaking in which an R & D project or goal is established and partners collaborate by sharing resources to achieve their objectives. Technical cooperation is a joint undertaking in which completed R & D is shared or exchanged. Some co-operative arrangements may involve both. These mechanisms may be public such as the Alvey Programme, or private company-to-company agreements, or in the case of universities, some of each, (Haklisch, 1986).

4.6 Conclusion

In this chapter I have taken a preliminary look at the recent strategic management literature to see if it offers any insights into subjects of science and technology policy interest. In particular the interactions of university research and indutry. The literature shows an awareness of increasing network formations and strategic partnering and has started to conceptualise their meanings. At present the focus tends to be on interactions between firms. However, from a policy point of view it is important to understand the circumstances under which the firm will form networks. An analysis of joint venturing and strategic partnering in the area of R&D could make a useful contribution to developing a relevant science policy, one that fits in with the strategies of firms. This may be particularly important if a policy is being developed that is based on cooperation, such as the ones emerging in UK science and technology policy.

One of the major conclusions is that technology today is

related to science, despite the useful insights provided by citation studies and studies of information flows, the actual nature of this linkage needs elucidation. However, business historians and economists have shown that firms have responded to the growing 'scientification' of technology by altering their organisational structure, firstly by establishing an in-house R & D department:

> As however new chemical firms grew up and consolidated their new markets they made an extraordinarily important social innovation - the captive R&D laboratory. This meant that they were no longer so vulnerable to "creative destruction" brought about by exogenous science and technology through new entrepreneurs. They themselves learnt the trick of institutionalising this process. By earning exceptional profits on their major innovations they were able to finance scientific and technical activities on such a scale as to retain the ability to generate successive new waves of invention and innovation or at least to keep fairly close behind the leaders. (Walsh et al, 1984).

The innovation literature also indicated that this was often a transient measure, that the nature of university-industry relations within a given area is in some sense a function of the stage of development of that technology (see Langrish, 1974, and Meyer-Thurow, 1982). The developments in biotechnology, for example, have been so rapid that industry has had no chance of building up its own R & D resources - hence its dependence on academic science. It is quite possible that their dependence will

diminish as the companies' own laboratories are built and staffed. The possibility of such temporary organisational arrangements are given in the networks of Thorelli, and the dynamic networks of Miles and Snow.

However, there is some evidence that there may be limits to the ability of firms to 'internalise' such science and technology:

> Beginning approximately in the late 1970s and continuing today, a subtle appears to have occurred in industrial research. Many corporations realising they can longer be self-sufficient technically. This is in part because the areas to be covered are increasingly beyond the funds and personnel available, and in part because the efforts of any single corporation are becoming smaller in relation to the growth of R & D in all sectors and in all but the poorest developing countries. This is a natural consequence of continuous growth in science and technology. Even the richest multi-national corporation may not find it economical to pursue technical self sufficiency. It can, however, identify the technical areas which cannot be pursued within the firm but which are relevant to the firm's strategic growth plans. They are very likely to be related to, or to feed into, some ongoing internal technical program, and certainly to potential growth plans which could not be implemented within the corporation itself. These pressures have led to university industry linkages involving far more substantial sums of money than were to be found even 10 years ago, (Fusfeld, 1986).

A major indication of this possible restriction on internalisation is the rise of co-operative research organisations like the Alvey programme; 'the technology

is intrinsically and complex. No single organisation has the know how to make sufficient scientific progress on its own (Alvey, 1982). Little is known about research-research links between producer firms and eventual economic success. If these new linkages, external to the firm, are now a prerequisite for success in areas of 'high technology' then cooperative research can be seen as introducing a new discontinuity into the industrial economy; to be successful it is becoming increasingly necessary to have access to the benefits of shared R & D. As pointed out in Chapter two, a growing feature of R & D today in high technology areas is the combination of two or more firms collaborating on basic or precompetitive research. Arnold (Arnold, 1987) who refers to these new organisational arrangements as 'meta-firms' views them as

> " a significant innovation in their own right, which may have as profound an influence on the future characteristics of industrial structure and competition as did the introduction of industrial R & D laboratory in the 19th century," (Rothwell, 1987).

Chapters two and three outlined some of the possible motivations for university-industry linkages. The strategic management literature shows that external linkages can be used to implement changes in a firms strategic position. Motivations given for such linkages in the strategic management literature include:

- access to new technology
- reduction of project risk

- technology too expensive to afford alone

- saving firms costly and unnecessary duplicate R & D efforts

The forces bringing about such a discontinuity can be summarised as;

the rising costs and complexity of R & D (technical convergence);

intensive competition for both domestic and foreign markets;

limited resources; and
accelerating pace of technological advances.
In this review of the strategic management literature I have outlined the growing awareness of the use of resources outside the firm. In particular I have focused on the strategic importance of such linkages regarding a firms ability to innovate. There seems to be a growing consensus emerging:

> Better understanding of the innovation process and organisational research are leading to a realisation that greater flexibility and finer tuning of the organisational structure to particular circumstances are necessary. New organisational forms may emerge, (Twiss, 1980).

Twiss in his book The Management of Technological Innovation (1980), provides a speculative picture of hybrid or multistructure organsations in the large firm, to deal with the growing uncertainty in the business environment (including the technical environment): joint ventures are seen as integral part of this new

organisation, see figure 4.2.

In the following empirical research I will investigate further the strategic implications of university-industry connections, and the new organisational forms that have appeared.

Fig 4.2

Fig. A suggested multistructure organization for the future

Ref: Twiss, 1980

CHAPTER FIVE: UK Biotechnology industry questionnaire survey results

5.1 Introduction

The analysis of the results of the responses to the questionnaire consists of a simple aggregated tabulation of the various responses, and a determination by visual inspection of the opinions and perceptions of each group. At this point the first comparisons could be made between the results of the survey and the conclusions which one would normally deduce from the literature search.

5.2 Responses

The questionnaire was sent to 90 biotechnology firms based in the United Kingdom (UK). From this a total of 40 useable responses were obtained. This gives the survey a response rate of 44.4%.

5.3 The company sample

A summary of the sectoral classification of the sampled firms is shown graphically in figures 5.1 and 5.2. It shows how the term 'biotechnology industry' in fact does not refer to an homogenous industrial sector. In fact the 'biotechnology industry' is emerging within a number of existing industrial sectors.. Biotechnology is a generic technology, in that it is a collection of techniques/tools which through a process of 'horizontal' technology transfer can significantly affect a wide range of traditional industry classifications.

Figure5.1 Number of firms by sector (A)

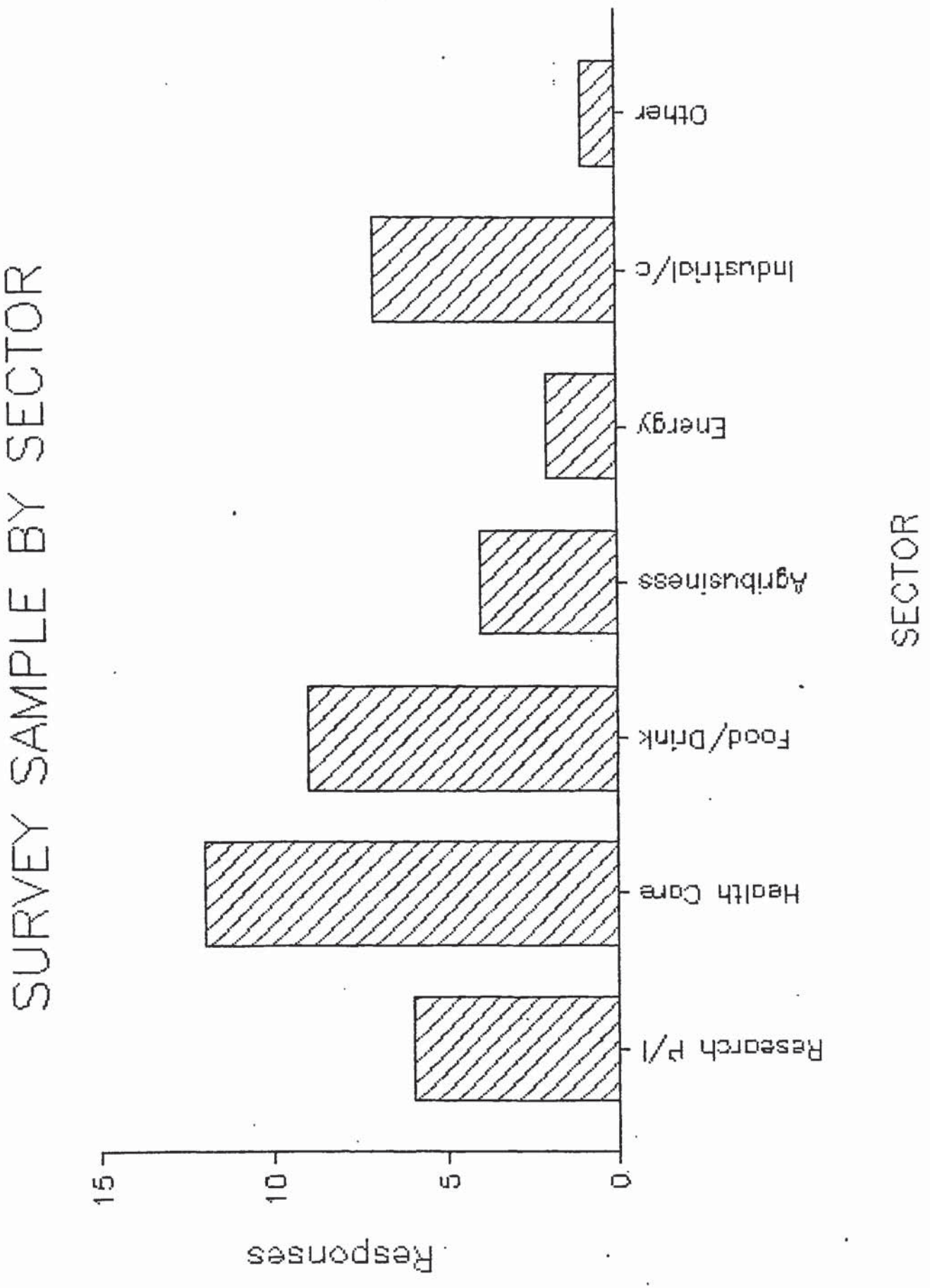
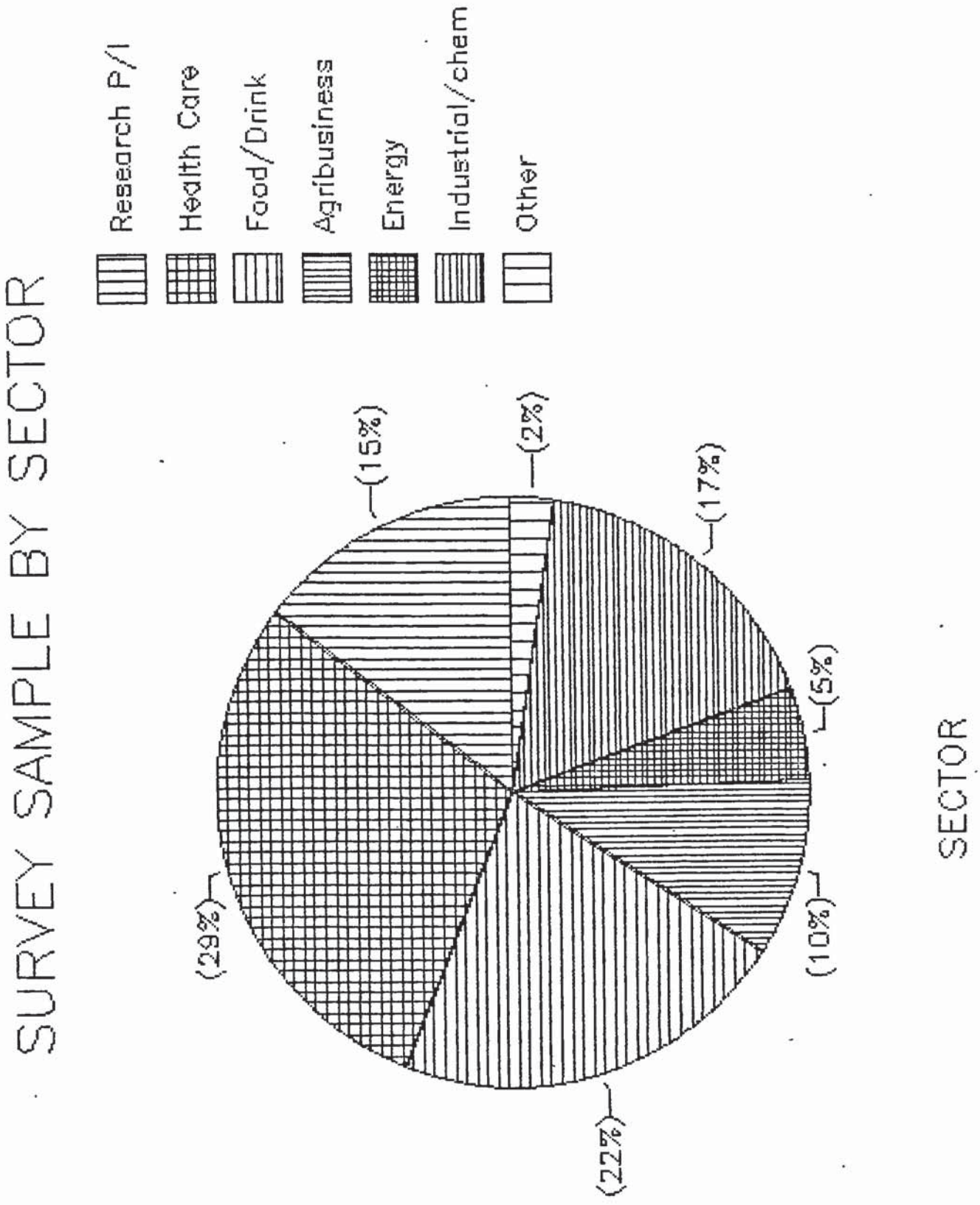


Figure 5.2. Number of firms by sector (B)



The survey sample also encompasses firms which range in size from under fifty employees to over 300,000. British companies with an interest in biotechnology are usually divided into two main categories; established firms who wish to make use of the new tools of biotechnology; and small new enterprises, (Dunnil and Rudd, 1984). The sample contains representatives from each of these categories.

The results have been divided into two parts:
Part One: academic - industrial collaborations in biotechnology; and part two: technology linkages in biotechnology.

5.4 Part One: Academic-industrial collaboration in biotechnology

5.4.1 Research networks and the externalisation of research

The R&D process whereby knowledge is generated and transformed into new production processes and products involves the cooperation of various elements and can be located in various places. One place is to have the R&D process completely contained within the boundaries of the firm (as in the case of in-house laboratory). Other places (either partially or not all within the firms boundaries) to locate the R&D process involves various combinations of joint firm (or firms), university and government organisations.

There are a number of organisations that can form an external R & D market. The survey question (Question 1, section 2) was intended to help determine whether university research linkages are part of a wider strategy that draws upon resources external to the firm. The relationship of the sampled firms with the various external organisations is given in Table 5.1 below:

Table 5.1 Institutions with industry research relations (n=39)

Rank	Respondents	%
1. Universities, Polytechnics	39	100
2. Government Research Establishments	31	79.5
3. Contract Research Companies	24	61.5
4. Established Companies	24	61.5
5. New Biotechnology Firms	23	59

The most significant result in Table 5.1 is that all industrial respondents support academic-industrial research relationships. Although the primary object of this research is the study of academic-industrial research relationships, it is nevertheless interesting to note that the survey data shows that the academic-industrial collaborative axis is just one element in a network of external cooperative arrangements used by the respondent firms. This is reinforced in the results shown in Table 5.2.

Table 5.2 Multiple industry external research relations

No. of Organisations	Respondents	%
5	14	35.9
4	11	28.2
3	1	2.6
2	11	28.2
1	2	5.1
0	0	0
Total	39	100

It is important to note that biotechnology firms interests are not confined to in-house research or just one external connection, these firms have "multiple positions" in biotechnology. From these results we can see that this involves combining in-house research and sponsorship of biotechnology research in universities. Other studies include equity interests in new biotechnology firms (NBFs) as a strategy used by large firms (1). The purpose of the university-industry linkage is tested to section 4 of the questionnaire.

The results in tables 5.1 and 5.2 indicate the following;

1. All members of the British biotechnology industry who responded have research relationships with higher education institutions.

2. University - Industry relations are the primary external research relationship. That is, those respondents that had just one external research relationship, had it with a higher education institution.

3. The majority of respondent firms have research relationships with two or more external organisations. So although previous results showed that all of the surveyed firms carried out in-house research, there was still a market for external research services. No firm satisfied all of its research requirements through its own internal resources. The most popular external source of research according to these results were the higher education institutions and government research laboratories. These organisations are the main components of the 'public sector' arena of research performers. The biotechnology industry appears from these results, to have a strong linkage with research performed in the public sector. This close interaction has clear public policy implications. That is, the areas of research carried out in the public sector that are of interest to these companies, may be of significant strategic and industrial importance and as such their health (in terms of manpower, funds, facilities etc) may need close attention by the research funding agencies.

Overall the results show that there is a strong propensity in the biotechnology industry to engage in external research relationships.

5.4.2 Academic-industrial collaboration; location

The previous results showed that higher education institutions represent a widespread source of external research to the biotechnology industry. Having established this the following question identified the geography (i.e.

whether the contracted research is a domestic service or whether there is a significant imported component) and the future intentions, of this part of the network.

Table 5.3 location of HEI, (n=39)

Location of HEI	Respondents	%
UK	39	100
Overseas	15	39.5

Table 5.3. The results concerning the location of the collaborating institutions seems to indicate a strong preference for collaboration within national boundaries, that is the research services are domestic. It should be noted that a significant number do have research links with institutions which lie outside the United Kingdom. However the major part of this (12.8%) is accounted for by the fact that five of the sampled firms with oversea university links, are themselves owned by foreign parents.

These questions have implications for those concerned with the 'decline' of UK science. This school of thinking is expressed in the Office of Health Economics book Crisis in Research:

> ...there exists a widely held view that research in Britain has reached a point of crisis. The scientific journal Nature for example, carried a two page leading article in one of its 1984 issues examining the reasons for what is described as the 'Dead end for British research', (Nature, 1984). Later that year Martin and his colleagues (1984) wrote an article entitled 'The writing on the wall for British science' that 'international

> comparisons suggest Britain's basic science is rapidly declining in quality and quantity. More recently the chairman of ICI, is reported to have said that growing concern about the status of British research has 'led us to start increasing our links with oversea universities that we see as centres of excellence' (Guardian, 1985). And New Scientist, in a final editorial for 1985, proclaimed that the preceding 12 months had witnessed 'the final passing of Britain as a leading member of the world of science', (New Scientist, 1985), (OHA, 1986).

As can be seen the remark attributed to the chairman of the UKs major science based company has caused some alarm. In Germany, science policy underwent a period of reappraisal in the early 1980s following the highly publicised decision by one of its leading companies, Hoeschst, to fund basic research in molecular biology at Massachusetts General Hospital, in the US (see also chapter 2). It is important from a policy point of view to see if there is a trend towards increasing international contacts. Already ICI has plans to build a 'high technology research centre' for electronic materials to use in the electronics industry. Glaxo is participating in cooperative research at the Centre for Monoclonal Lymphocyte Technology in the US.

5.4.3 Trends in university-industry interaction

Table 5.4, below, outlines the survey results covering trends in the domestic and importation of research services attributed to the higher education sector.

Table 5.4 Interaction trends

Results. Increase in research relationships in the next five years.

Location of HEI	Respondents	%
UK	32	80
Overseas	18	45

The results outlined in table 5.4 show that the majority of biotechnology firms in the survey will be increasing the number of research relationships they have with higher education institutions, over the next five years (i.e to the end of the decade, 1990). A sizeable number of the firms (just under half) suggest that they will seek to increase (or establish ?) research relationships with overseas academic institutions. Again most of this can be accounted for by the fact that six of the firms that indicated that they are likely to increase relationships with non British universities, were owned by foreign parents (they were therefore 15% of the respondents). Nevertheless, this does give an indication of a possible trend for at least some firms to start looking at the possibility of oversea connections. These results seem to indicate that despite widespread concern about the health of British science, the majority of respondents were satisfied with the current outcomes from relationships with the domestic higher education system. This is reinforced by the interest of oversea companies in UK research, for example Japanese companies have ongoing research programmes with Warwick University and Edinburgh University; there is oversea involvement in the

Plant Gene Tool Kit consortium; and oxford University has contracts with Monsanto ($1.8 million over five years) and with the pharmaceutical company Squibb, (£20 million).

The results are also relevant to the concern expressed about the possible long term damage that may result from any prolonged direct interaction between universities and industry in biotechnology. There are some commentators who have touched upon the question of whether in fact the nature and duration of university-industry relationships within a given area of technology are a function of the stage of development of that technology. It has been claimed that the prominent role played at present by academic scientists in developing biotechnology, will soon be over as firms establish their own in-house research competencies (2).

The fact that 80% of the respondents were planning to increase their research collaboration over the next five years, indicates that the period of interaction may well be of the order of at least five to ten years.

A final point also needs to be made regarding the Question 3 and 5 in section 2 of the questionnaire. The original intention was to obtain details of the academic departments taking place in these collaborations. From this information it would have been possible to get a clear idea of what the research interests of the firms involved were. This was intended

as part of a strategy for identifying 'strategic research areas', on the assumption that 'where organisations carry out or support university research, they do so for strategic reasons', (Rothman, 1985). - However, the results have proved to be disappointing, in that there had been very little response to this part of the questionnaire and so consequently I have not been able to extend the research along these lines.

5.4.4 Potential outcomes of research collaboration

Industrial support of academic research in biotechnology has been the subject of lively discussion. The potential commercial and scientific benefits of such research relationships have been widely acclaimed and the potential risks to academic and scientific values and practices widely deplored. This study focuses on the demand side part of the equation. In the previous section the results have shown a propensity of the biotechnology industry to make use of external research services, in this part of the study the results of the Industrial perception of the outcomes anticipated from research relations are given. These perceptions are coded on a Likert-type scale of 1 to 4 to rate the importance of 11 possible outcomes:

1=Extremely important;
2=Considerably important;

3=Somewhat important;

4=Not at all important.

The results are displayed in tables 5.5, 5.6 and 5.7 below.

Table 5.5

POTENTIAL OUTCOMES OF RESEARCH COLLABORATION

GOAL	1	2	3	4	%	Rank
Develop Commercialised Products	53.9	20.51	15.4	10.25	100	1
Develop Patentable Products	35.9	25.7	25.7	12.8	100	2
Improve Manufacturing Processes	23	41	20.5	15.4	100	3
Development of New Research Projects in Company	20.5	30.8	35.9	12.8	100	4
Improve Instrumentation	12.8	10.25	20.5	56.4	100	5
Improved Access to Faculty Scientists	12.8	46.15	28.2	12.8	100	5
General Expansion of Knowledge	10.8	17.9	41	30	100	6
Access to University Facilities	10.8	46.1	28.2	15.4	100	6
Enhance Industrial Research	7.7	48.7	23	20.5	100	7
Enhance Student Training	7.7	23	33.3	35.9	100	7
Better Personnel recruitment	7.7	20.5	43.6	28	100	7
Redirect Uni Research	5.12	23	30.8	41	100	8
Enhance student understanding of industry	5.12	23	35.9	35.9	100	8

Importance of Project Goals/Potential Outcomes

1=Extremely Important
2=Considerably Important
3=Somewhat Important
4=Not at All Important

Table 5.6

POTENTIAL OUTCOMES OF RESEARCH

Importance of Project Goals/Potential Outcomes

Aggregate table of Extremely Important & Cons4 (%) Rank

GOAL	1&2 (%)	RANK
	64.1	1
Develop Commercialised Products	76.4	1
Improve Manufacturing Processes	64.1	2
Develop Patentable Products	61.5	3
Improve Accessibility to Faculty Scientists	59	4
Gain Access to University Faculties	56.4	5
Enhance Industry Research	56.4	5
Development of New Research Projects in Company	51.3	6
Enhance Student Training	30.7	7

Table 5.7

POTENTIAL OUTCOMES OF RESEARCH

Those classified as NOT AT ALL IMPORTANT

Goal	4 (%)	Rank
Enhance Quality of University Research	64.1	1
Improve Instrumentation	56.41	2
Redirect University Research Towards Industrial Problems	41	3
Enhance Student Understanding of Industry	35.9	4
Enhance Student Technical Training	35.9	4
General Expansion of knowledge	30.8	5

If we take the results of the strongest opinion, that a particular goal is extremely important, we get the ranking order of goals displayed in Table 5.5. The major priorities of the industrial participants in these research relationships with academia is;

a) commercialised products;
b) patentable products;
c) improved manufacturing processes.

The goal of general expansion of knowledge comes a joint sixth in the ranking. This goal is of course most usually associated with the aim of academic research. Here then is a possible incompatibility of goal congruity between academia and industry. The high ranking given to patentable products, by industry, may also provide an incompatibility with academic norms and values such as the rapid communication of results.

The general ranking of goals, if we take extremely and considerably important perceptions together, does alter slightly, see table 5.6. It does however reaffirm the primacy of the three major industrial goals;

a) commercialised products;
b) improved manufacturing processes;
c) patentable products.

Behind these major goals four other 'second division' goals emerge;

1) Improve accessibility to faculty scientists;
2) Access to university facilities;
3) Enhance industry research quality;
4) Development of new research projects in company.

Even in this second set of figures the goal of general expansion of knowledge is very low, with 30% of the respondents stating that they thought it not at all important. Another interesting result is industries perception of the goal of redirecting university research to industrial problems. Only 28% of respondents felt strongly positive about this as a goal and 41% perceived it as not at all important. The potential redirection of academic research to be more relevant to industrial needs is often cited as a possible risk to the health of the scientific enterprise, and manifested in a general move away from basic to applied research.

Another worry to the future health of the academic research community is the problem of the 'brain drain'. The pessimistic scenario often put forward is that the higher salaries of the private sector companies will attract academic talent away from the institutions of higher education. Some observers have viewed closer academic-industrial collaboration as a mechanism used by companies to help recruit personnel. The results in Table 5.5. Indicate that this is not a very significant goal in this survey sample, rated significantly by 28% of the respondents. Rated extremely important by only 7.7%. However there is no doubt that a significant number of

companies while engaged in research collaboration primarily for other reasons does keep the recruitment of personnel in mind, this is demonstrated in table 5.5, where 43.6% of the respondents deemed it somewhat important.

The final table 5.7. ranks the goals by the strength of the negative response attributed to them by the respondent firms. Some of these results have been touched upon above, but it is clear that firms have no reported desire to enhance the quality of university research nor redirect university research towards industrial problems. So in a more general sense the firms seem to indicate that the quality of university research is good, and that the research agenda in general is the province of the academic establishment itself, while at the same time it is able to build productive linkages around specific contract research projects.

5.4.5 Comparison with US industry/university cooperative research programme study

A study carried out in the US provides an interesting comparison. The study was carried out by Elmima Johnson and Louis Tornatzky, of the Productivity Improvement Research Station of the National Science Foundation, (NSF). Their study was an assessment of the NSF Industry/University Cooperative Research Program, (IUCR). The objectives of the IUCR were:

> to strengthen the fundamental research in science and engineering in order to enhance future industrial technological opportunities, and to improve the linkage between universities and industrial firms.

The program had participants from 88 companies covering all the major industrial sectors. The results of the assessment concerning the importance of project goals/potential outcomes was as follows:

Importance rated as extremely important by industry:

Develop patentable products	66%
Improve manufacturing processes	59%
Develop commercialised products	58%
Instrumentation development	33%

The results regarding the top three aims of cooperative research programs are very similar to those of my own study. It is interesting to note that there is a general expectation, across industrial sectors, that university-industry research collaboration will provide benefits in terms of new products and processes. The next research step would be to test the outputs of such relationships to see whether they fulfill these expectations.

5.4.6 Types of research performed

In Chapter two of this thesis I outlined the emergence of strategic research in science policy discourse during the 1980s. Strategic research has increasingly come to represent a common ground of research interests between the academic sector and industry and increasingly more and more science and technology policy has come to be

based around the concept. These range from national programmes such as Alvey, to international programmes such as ESPRIT, RACE and BRITE. All of these programmes operate on the premise that there is some 'feasibility' area upstream from competitive products and processes in the innovation chain, where academics and industrial scientists can cooperate. The idea of the performance of this type of research as providing a bridge or coupling of the research system (of the academic community) and of the industrial system is tested in the survey.

If we consider innovation as a linear chain linking basic research to applied research to development and prototypes, that is it is an axis linking several types of research. Then these types are often associated with specific institutional locations. The academic sector is traditionally associated with the performance of basic or pure research and strategic research. Whilst applied research and development, considered 'upstream' R&D activities closer to the market, are usually associated with the corporate environment.

For the purposes of this study it was necessary for me to obtain a profile of the types of research carried out by the sampled companies. A body of literature already exists that links elements of such a research profile with particular corporate characteristics. These include:

Success at innovation. Many case studies of innovation show that direct access to original research results was

extremely important (see for example Illinois Inst, 1968; Gibbons and Johnston, 1974, Comroe and Dripps, 1977). The results of Project SAPPHO (1974), although not strongly differentiating between success and failure on the basis of fundamental research performance, did suggest a marginal advantage to fundamental research performers. A study by E. Mansfield (1980) also suggests that the composition as well as the magnitude of an industry of a firms R&D expenditure, affect the rate of productivity increase. His results indicate that there is a statistically significant and direct relationship between the amount of basic research performed by an industry, or by a firm, and its rate of total factor productivity, when its expenditure on applied R&D is held constant.

Interaction with universities. Price and Bass (1969) in their analysis of a number of US empirical studies of innovation indicated that access to the results of fundamental research is partly related to the degree of participation. The idea has gained wide acceptance (see for instance the OECD report 1984), and the point has been made by Irvine and Martin:

> Large science-based firms typically choose to devote a limited (but probably growing) proportion of their own R&D budget to those areas of basic research felt most likely to provide the new knowledge required to develop the products and process of the future. Many firms use such research to develop links with the relevant academic research communities. Such links are generally essential if the firm is successfully to monitor and take advantage of the latest scientific results. They are also necessary to

> develop within the company the skills and techniques required to mount rapid R&D programmes as new research possibilities as and when they occur, (Irvine and Martin, 1984).

In his book The Economics of Industrial Innovation (1974), Christopher Freeman describes how innovation and the strategy of the firm can manifest itself at the level of its research profile, that is the type of research it performs. In his analysis, the performance of fundamental or basic research is linked to the firms operating an 'offensive ' strategy. An 'offensive' innovation strategy is one designed to achieve technical and market leadership by being ahead of competitors in the introduction of new products. Since a great deal of the worlds science and technology is accessible to other firms, such a strategy must be based upon a 'special relationship' with part of the world science-technology systems, or a strong indigenous R&D, or on a very much quicker exploitation of new possibilities, or on some combination of these advantages.

The results show that the primary emphasis of corporate in-house scientific activity is on the applied and development end of the spectrum, although there is a sizeable focus on strategic research. This is a type of research that could possibly act as a bridge between the two value systems of academic and industrial science, and have the functions suggested by the literature outlined above.

The question of bridging or the nature of the research carried out in cooperative interactions is tested in the results given below, table 5.8.

Table 5.8. Type of collaborative R & D (n=38)

	1	2	3	4	
Pure Research	2.6	7.7	18	69.2	100%
Strategic	10.25	25.6	51.28	15.4	100%
Applied research	10.25	56.4	25.6	5.1	100%
Development	12.8	15.4	30.8	38.5	100%

1 = completely, 2 = mainly, 3 = some, 4 = not at all

These results show that for:

1. Pure research the most significant response was 69.2% for non performance;
2. Strategic research, the most significant response was 51.3% for some performance;
3. Applied research, the most significant response was 56.4% for mainly performed;
4. Development, the most significant response was 38.5 for non performance.

To get a more general research profile of the type of research performed at the academic-industrial interface, the activity table was constructed. This showed the proportion of companies who are active in each particular category of research. The results are graphically displayed in figure 5.3.

Figure 5.3. Number of firms performing each type of research at the university-industry interface

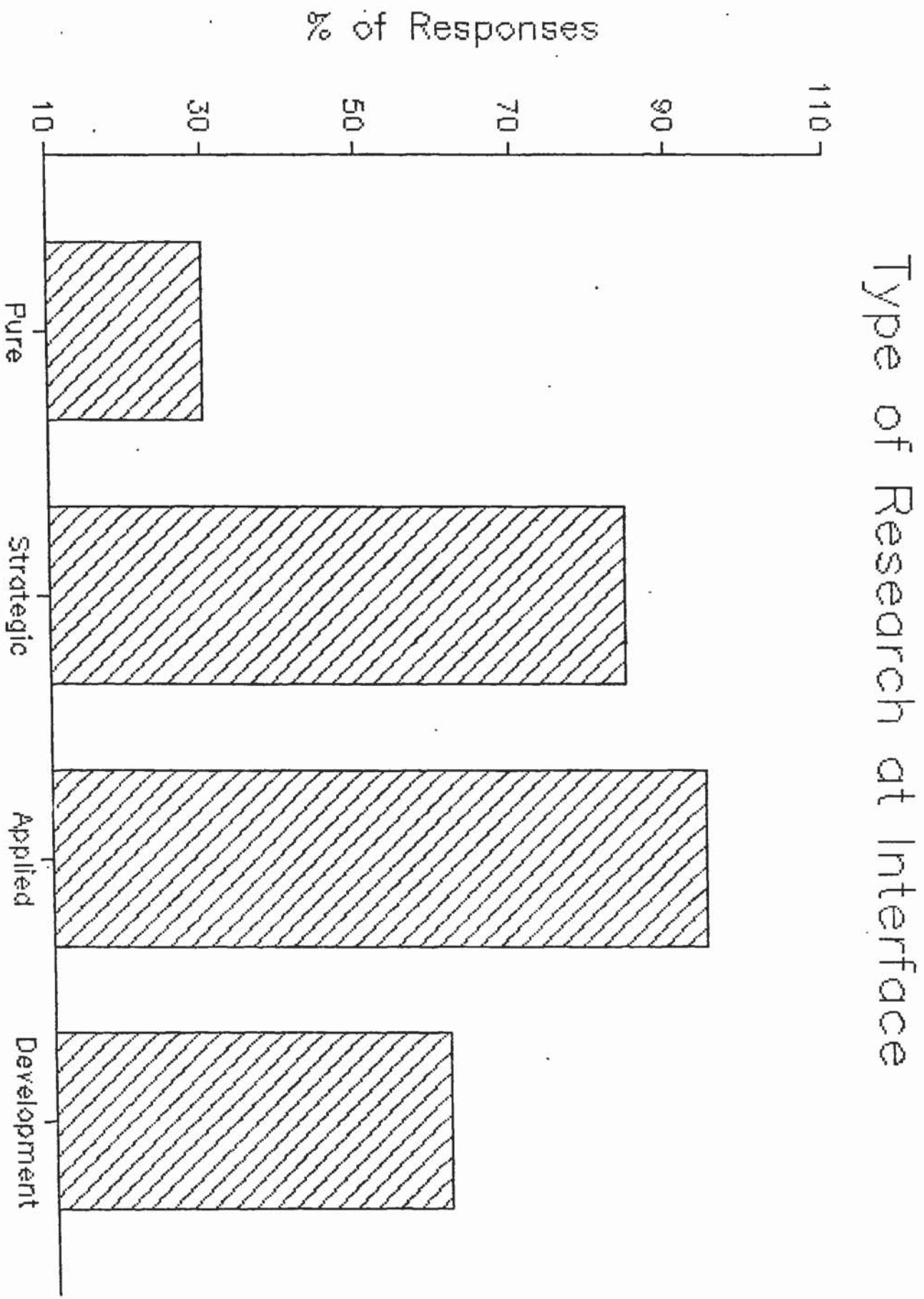


Figure 5.4 Comparitive breakdown by type of research of in-house and university-industry R&D

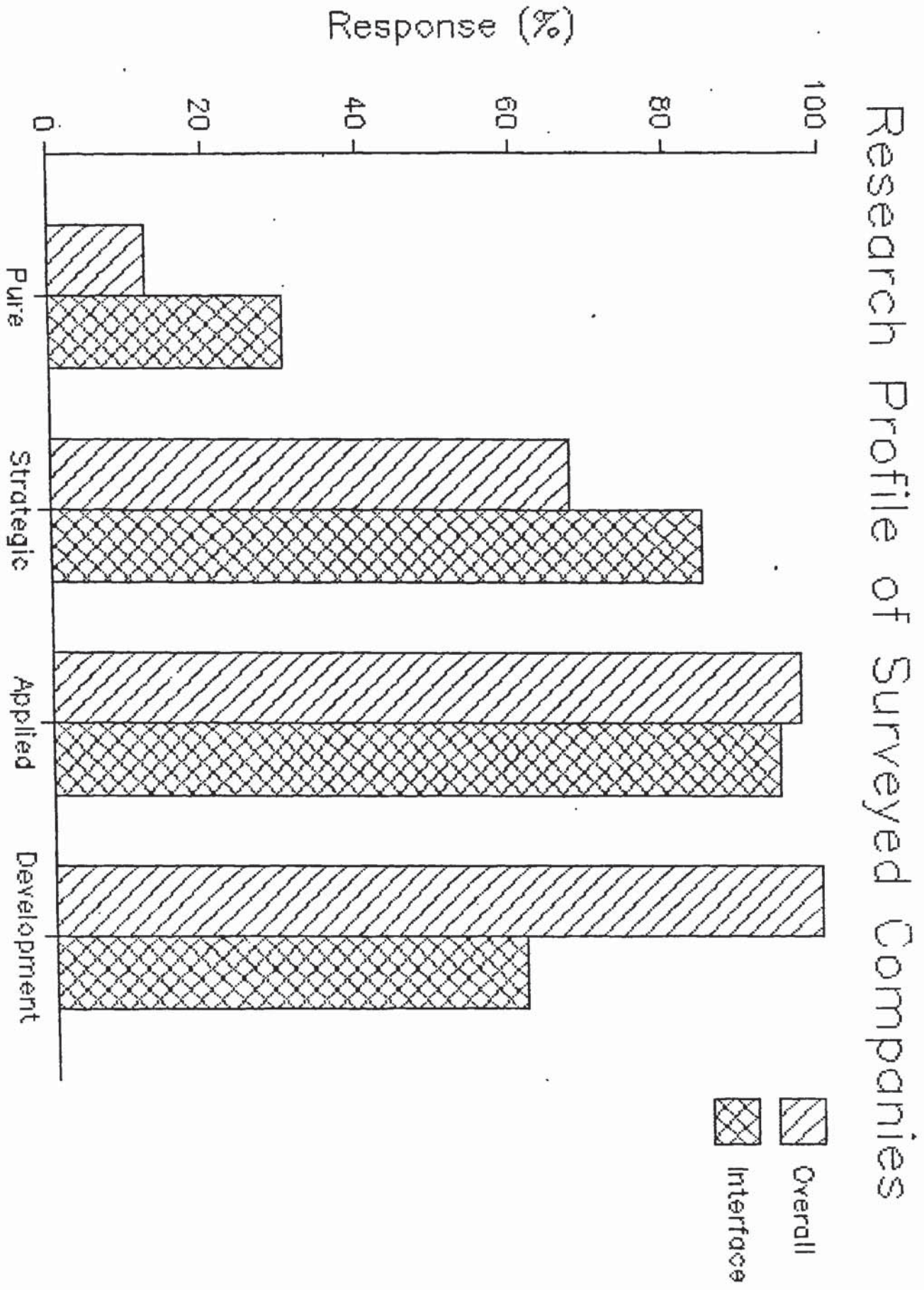


Table 5.9. The number of firms performing each type of research at the U-I interface

Research	Active at interface (% of responses)
Pure	30
Strategic	84.6
Applied	94.9
Development	61.5

These results do differ from the aggregated data for the types of research involved in-house research. For comparative purposes the research profile for both in-house research and cooperative research are displayed together in figure 5.4.
The results clearly demonstrate a shift to 'upstream' activities. An increase in pure research and strategic research at the expense of development work in particular, but also with some diminution of applied research.

These results seem to confirm that there is an intermediary zone between applied and basic research where academia and industry can cooperate. The more expensive, more proprietary parts of the innovation process appear to be internalised within the firms.

5.4.7 Mechanism for collaboration

Results on the major mechanisms used for research cooperation, (section 3 of the Questionnaire). The table 5.10 below outlines the survey results concerning the mechanisms used for academic-industrial research collaboration.

Table 5.10

Mechanisms for Research Cooperation. Survey Results.

Mechanism	1	2	3	4		Rank
Contract Research	37.5	27.5	20	15	100	1
Individual Consulting	32.5	37.5	20	10	100	2
Grants:studentships,Fellowships	20	22.5	50	7.5	100	3
Research Council Co-op Schemes	20	37.5	20	22.5	100	3
Joint Research Programmes	17.5	30	35	17.5	100	4
Grants without fixed timescale	15	5	5	75	100	5
Informal Cooperation,co-authors	15	27.5	32.5	25	100	5
Loans or Gifts of Equipment	7.5	12.5	35	45	100	6
Research Consortia	5	22.5	25	47.5	100	7
Endowment of Chair or University Post	2.5	12.5	10	75	100	8

Table 5.11

Mechanism of Research Cooperation. Survey Results
Opinions 1 & 2, Extremely and Considerably Important >30% Resp

Mechanism	Response	Rank
Individual Consulting	70	1
Contract Research	65	2
Research Council Co-op Scheme	57.5	3
Joint Research Programme	47.5	4
Grants/Studentships,fellowships	42.5	5
Informal coop, co-authors	42.5	5

Table 5.12

Mechanism for Research Cooperation. Survey Results

Those classifoed as NOT AT ALL IMPORTANT >30%

Mechanism	Response	Rank
Grants without fixed timetable	75	1
Endowment of Chair or University Post	75	1
Research Consortia	47.5	2
Loans or Gifts of Equipment	45	3

The results show that the mechanisms considered extremely important were contract research tied to specific projects and individual consulting. This result is confirmed when we look at the ranking when both strong positive opinions, extremely important and considerably important are added (table 5.11). Top of the list is individual consulting. This is primarily seen as a 'knowledge transfer' mechanism (see Brodsky, 1980) dependent on personal interaction. These sorts of personal contacts are thought to be the precursors of longer term more formal relationships, (Peters and Fusfeld, 1983).

The second most popular mechanism was contract research. This is a more formal relationship than consulting, and is tied project by project and year by year. It appears to be the basis for most university-industry research cooperation. The specific limited nature of such contracts makes it easier to negotiate than broader based joint research programmes. These more formal contract research projects require some degree of joint technical planning but also require matters of a non technical nature to be considered. These agreements must take into account university procedures and policies and industry's objectives and proprietary concerns. This may go some way to explaining the fact that Research Council support schemes for encouraging university-industry research collaboration are ranked lower. Government funded schemes (such as those developed over the 1970s by the Science and Engineering Research Council) have until recently (1987) presented problems regarding the intellectual property rights over the

outcomes of supported cooperative research. The inhibitory effect of this for both individual academic institutions and company partners were outlined in two ACARD reports (ABRC/ACARD/RS, 1980, and ACARD, 1983). In recent years there has been an increased effort in all Research Councils towards finding ways of using government funds to facilitate university-industry research cooperation. The intellectual property rights of these new programmes (such as the LINK programme) are assigned solely to the participating organisations. This may well create a more favourable opinion in industry towards government funded cooperative research schemes.

Table 5.12 shows the ranking with regard to the negative response - not at all important. These results show two very clear negative responses for;

a) endowment of chair or university post (75%) and;
b) Grants without a fixed timescale (75%).

Both of these can be categorised as general research support, where the major objective is to provide support to maintain university research excellence, rather than to strengthen research ties. Both take a longer-term perspective. A somewhat more surprising result is the low priority given to Research Consortia as a mechanism for research cooperation, this is discussed more fully in my case studies of research consortia.
The table 5.13 below shows which mechanisms the respondents seek to increase over the next five years. Unfortunately

there were not many respondents to this question. Of the sample of 40, 25 responded. Two of the 25 said that they would not be increasing any particular mechanisms. The results of the remaining 23 are given below:

Table 5.13 Mechanism likely to be used over the next 5 years

Mechanism	%
Contract research	65
Individual consulting	43
Joint research	26
Research consortia	26
Res Council co-op schemes	26
Informal cooperation	22
Studentships	13

The results indicate that no new trend in mechanisms has appeared, and that most companies will seek to carry out research interactions in the future with the mechanisms they currently find most useful. From a public policy point of view, it is interesting to note that Research Council schemes appear to represent only a small part of the flow of the collaboration between the two sectors, and that most cooperation takes place without the intervention of third parties.

5.4.8 Optional responses

The final part of the questionnaire, section five, had two optional open ended questions which respondents could answer if they wished. As expected this section received very little response; 16 out of 40. Some indication of the type of comments made are reproduced (anonymously) below.

One respondent, which had no research interactions with universities, made the following comment;

> Academics are academics and have no knowledge or understanding for industry.

A number of foreign owned companies made comments:

A German company stated that it was "actively seeking cooperation with universities and other institutes to increase the growth rate of new products".

A Swedish company stated that is had "exceedingly strong links with many institutes (being a Swedish company - very largely in Scandinavia). This will undoubtedly expand in future".

Many of the comments directly addressed the different culture and working practices of universities as being impediments to increased university-industry interaction:

> Universities must recognise that except where fundamental research is being funded, industry often has to work to critical time schedules and that if universities want a share in the applied work they must also introduce the disciplines of time and cost control. (Major food company).

> 1. Important for goals to be set by industry but within the sphere of interest of academia.
> 2. Greater appreciation of industrial cost structures by academia would help to improve understanding between both camps.

3. greater emphasis should be placed by universities on academics consulting/interfacing with industry. (An academic 'spin-off' firm).

Industry needs to be profitable to expand. It is therefore important that there is a sensible and realistic cost relationship between industry and academia for any joint research programmes and related to the likely commercial value of the work to the company.

Universities prime function is to train the future young scientists for industry in addition to strongly supporting industry through basic scientific discoveries which can be commercialised. (Diagnostics firm).

Universities must learn to package their ideas to industry so that product potential is clear and the commercial and technical risks can be assessed. They must also learn to construct terms with a commercial partner which is practicable for the company but which gives good returns to academia in the event of a successful exploitation, (New bioetchnology firm).

Other criticisms of the academic side were also made:

Many university staff have a departmentally parochial outlook. "If its not my Department, I don't need to promote it". The interfaces between university departments could be more fertile if they (the interfaces) actually existed. (A multinational chemical firm).

Many academics have the impression that industrialists have a bottomless pit full of money, and find it difficult to accept that a research project costing £25,000 per annum requires justification in terms of success. We favour the direct approach via a consultancy, which through collaboration generates ideas which can be tried out quickly and cheaply and form the

basis for a more rational and firm proposal to

senior management for the expenditure of larger sums. (Foreign pharmaceutical firm).

A few comments were received on the question of the type of research universities should perform:

Industry is likely to seek increasingly narrow goals for university research. (Brewing company).

It is important to allow and recognise universities independence in research terms. Their job is basic research from which hopefully ideas for new products will emerge. Industry is best at applied research. The trick is to integrate the two approaches. (Multinational pharmaceutical firm).

5.5 Summary of part one

The main results of Part One of the survey can be summarised as follows:

1. The biotechnology industry is emerging within a number of existing industries. This is reflected in the make up of the sample.

2. The firms surveyed ranged in size from small new firms with less than 50 employees, some span off from academic departments, to large multi-national corporations with over 300,000 employees worldwide.

3. All of the firms performed in-house research.

4. All of the firms supported university (or another higher education institution) research.

5. Most of the firms had more than one external research relationship. The majority were with public sector research agencies. This has important policy implications.

6. For all sizes of firms and all sectors, activity in biotechnology research requires some degree of external research services and these are primarily located in the public sector of universities and Government research establishments.

7. The results showed only a modest projection of increased importation of these research services from 1986 to 1991.

8. A closer analysis of the demand side factors - the industrial perception of goals and outcomes from university-industry research, shows that in biotechnology there is a clear expectation of technology transfer. The development of products and processes is a major priority. University research in biotechnology fields may be more closely allied to product development than in other fields.

9. When we look at the type of research undertaken in university-industry interactions it can be seen to differ from the in-house research profile. University-industry interaction is focused around the performance of strategic and applied research, an increase in pure research and a significant decrease in development.

10 The most favoured mechanisms for academic-interaction are:
- Individual consulting and;
- Contract research for a specific project.

5.6 Part Two: Technology linkage in biotechnology, an analysis of the biotechnologies involved in university-industry research relations

5.6.1 · Introduction

Biotechnology is defined in the Spinks report as:

the application of biological organisms, systems and processes to manufacturing and service industries.

Biotechnology in this general sense can be said to have progressed through three major stages. The first phase stretched from B.C. up to the 1930s where microbes were used in brewing, baking, wine and cheese making and some other processes. The second phase occurred in the 1940s and up to the 1960s with the manufacture through fermentation of antibiotics and the application of this knowledge to food and drink and in the treatment of waste

and sewage. The third phase resulted from a series of discoveries made in the 1970s in the field of molecular biology. The restraint on biotechnology up to this point was the difficulty in identifying and isolating the microbe that produces a useful product and adapting it to provide commercially acceptable yields. The discovery within molecular biology of recombinant DNA (rDNA) has opened up dramatic possibilities in overcoming these problems by enabling scientists to directly manipulate genetic material. The discovery of gene splicing or rDNA is the most important and pervasive discovery made in the new era of biotechnology. However there are other technologies, the new biotechnology can be taken as a general term for a cluster of technologies. The individual technologies are looked at in more detail in this section.

Table 5.14 the technologies used by companies

Technology (n=40)	Respondents	%
1 Fermentation technology	26	65
2. Downstream processing	24	60
3. Recombinant DNA	18	45
4. Monoclonal antibodies	16	40
5. Waste treatment/biodegradation	14	35
6. Biocatalysis	12	30
7. Animal cell culture	10	25
8. Biosensors/bioelectronics	9	22.5
9. Protein engineering	9	22.5
10. Plant genetics/biochemistry	8	20
11. Plant cell culture	7	17.5

Table 5.14 above, derived from survey data, we can see that the most widespread technologies in the sample are process technologies, these are areas of traditional strength in the United Kingdom (i.e Food and drink, pharmaceutical industry). These are followed by the two fundamental techniques (so called "first generation" techniques of the 'new' biotechnology) recombinant DNA (rDNA) and monoclonal antibodies (Mabs) both of which are products of academic research in the 1970's and led to a renewed interest in academic-industrial collaboration and academic spin off firms.

There is also less representation in the more advanced technologies (some of these are looked at in more detail in the case studies). These rely on the combination of several techniques, and are multidisciplinary in their requirements.

To assist in data reduction these technologies can be grouped together into two basic groups.

5.6.2 Grouping the technologies

Table 5.15. Corporate activity in the various technology groups.

	Respondents	% (n=40)
Group One. Bioscience/technology Categories 3 - 11 above	37	92.5
Group Two. Biochemical engineerring Categories 1 and 2 above.	33	82.5
Group One and Two.	30	75

The results above show that there is a significant overlap in the interest in these general technology categories, 75% of the respondent firms are active in both. There is a strong implication in these results that there is a strong linkage between science and engineering disciplines involved in 'biotechnology'. In this section I have taken a more detailed look at the technology profiles of the respondent companies. A technology matrix for each company was compiled to see what technologies tend to be clustered together.

Table 5.16 below shows the number of biotechnologies each company is involved in and the number of companies that are interested in them.

Table 5.16. Number of technologies per firm

No. of Technology Areas	Companies
11	-
10	1
9	-
8	2
7	1
6	4
5	4
4	7
3	9
2	2
1	2
0	-

The table shows that not every firm is involved in the same number of technological areas and that involvement in the 'biotechnology industry' does not necessarily depend on expertise in a single technology. Those involved in the highest ranges (7 to 10) are the largest and most diversified firms in the sample. In the following analysis the various combinations of technologies are detailed. This involves a disaggregation of the two main technological categories into their component technologies.

5.6.3 Fermentation technology and downstream processing links

Fermentation technology and downstream processing dominate the survey, in terms of technological activity of the firms. The growth of microbial cells within a culture medium is an activity which has been carried out in the food and drink industry for many hundreds of years so there is a good basis of expertise in this technology,

and the higher education sector has well established 'applied' departments of chemical engineering to service this area of technology.

Yeast, fungi and bacteria are usually put to work on an industrial scale in fermentation systems which provide optimal environments for containment, growth and production of the desired end product. The development of more sophisticated fermentation systems is, however, seen as critical to the commercial exploitation of rDNA. The novel techniques of rDNA bring with them novel problems for the biochemical engineers. eg. the use of immobilised cells and enzymes, new types of continuous 'bioreactors', the use of genetically modified organisms bring new biological problems (shedding genes) to fermentation. The scale up from the test tube at bench level to industrial scale up involves a large change of dimensions and brings with it a whole set of engineering, biochemical and economic problems that do not exist with bench experiments. So conventional expertise is unlikely to be alone capable of scaling up biotechnology processes. Fermentation and downstream processing is therefore likely to require additional inputs to chemical engineering.

The survey results in table 5.17 shows a strong linkage between the genetic manipulation tools (often laboratory scale) and the fermentation technology (75% of the sample), thereby covering the spectrum from laboratory size activity to industrial scale up technologies. With this combination biotechnology enters a new phase; scale

up from an academic laboratory activity to an industrial process.

It is not enough just to grow the required cells in a culture, extraction and purification of the desired end product (so called 'downstream processing') from the culture soup is crucially important. Downstream processing expertise is needed to move the product from the laboratory into commercial production with the required purity. This is born out in the strong linkage shown in the survey between Fermentation and Downstream Processing.

See Tables 5.17 and 5.18. Because of the new problems modified biological material brings to fermentation and downstream processing external expertise, outside the traditional chemical engineering disciplines is required.

rDNA-Fermentation/Downstream processing: From table 5.19, 78% of the firms linked rDNA technology to Fermentation(and 67% to Downstream processing). These companies have covered the basic axis referred to above,linking the basic bioscience tools of the laboratory to the capability to industrial scale up and to purification and product recovery.

Table 5.17 Fermentation technology linkags

FERMENTAT/s

	DStream.P	rDNA	MAb	Waste.Tr	Biocat	A.C.C	BioS	ProtEng	P.Gen	P.C.C.
ABM	1	1	0	1	0	0	0	1	0	0
G.B.	1	0	0	0	1	0	0	0	0	0
P&S	0	1	0	0	0	0	0	0	0	0
G.C	1	1	0	0	0	0	0	0	0	0
HAH	1	1	1	0	0	0	0	0	0	0
BeP	1	1	1	0	0	1	1	1	0	0
GXR	1	1	1	0	1	1	0	1	0	0
PFZ	1	1	0	0	0	0	0	0	0	0
FIS	0	0	0	1	0	0	0	0	0	0
CELL	1	1	1	0	0	1	0	1	0	0
CS	1	1	0	0	0	0	1	0	1	1
EFG	1	0	0	1	1	0	1	1	0	0
AB	1	0	0	1	0	0	0	0	1	0
BASS	1	1	0	0	0	0	0	0	0	0
RHM	1	0	0	1	1	0	1	0	0	0
UNI	1	1	1	0	1	1	1	1	1	1
BTc	1	0	0	1	0	0	0	0	1	0
MON	1	1	1	0	0	1	0	1	1	1
PBT	1	1	1	0	0	1	1	0	0	0
BiC	0	1	1	0	0	0	0	1	0	0
CDA	1	0	0	0	1	0	0	0	0	1
FT	1	0	0	0	0	0	0	0	0	0
IB	0	0	0	0	1	0	0	0	0	0
BIS	1	0	0	1	0	0	0	0	0	0
EC	0	0	0	1	1	0	0	0	0	0
CAS	1	0	0	0	1	0	0	0	1	0
TOTAL	21	14	8	8	9	6	6	8	6	4
%	81	54	31	27	35	23	23	31	23	15

Table 5.18 Downstream processing technology linkages

D.Stream P

	Ferm T.	rDNA	Mab	Waste.t	Biocat	A.C.C.	BioS	ProtEng	P.Gen	P.C.C
ABM	1	1	0	1	0	0	0	1	0	1
G.B.	1	0	0	0	1	0	0	0	0	0
G.C	1	1	0	0	0	0	0	0	0	0
HAH	1	1	1	0	0	0	0	0	0	0
BeP	1	1	1	0	0	1	1	1	0	0
GXR	1	1	1	0	1	1	0	1	0	1
PFZ	1	1	0	0	0	0	0	0	0	0
CELL	1	1	1	0	0	1	0	1	0	0
CS	1	1	0	0	0	0	1	0	1	1
EFG	1	0	0	1	1	0	1	1	0	0
AB	1	0	0	1	0	0	0	0	1	0
BASS	1	1	0	0	0	0	0	0	0	0
RHM	1	0	0	1	1	0	1	0	0	0
T&L	0	0	0	1	1	0	1	0	1	1
UNI	1	1	1	0	1	1	1	1	1	1
BTC	1	0	0	1	0	0	0	0	1	0
MON	1	1	1	0	0	1	0	1	1	1
B.CAT	0	0	0	1	1	0	0	0	0	0
CTDS	0	0	0	0	1	1	1	0	1	0
PBT	1	1	1	0	0	1	1	0	0	0
CDA	1	0	0	0	1	0	0	0	0	1
FT	1	0	0	0	0	0	0	0	0	0
BIS	1	0	0	1	0	0	0	0	0	0
CAS	1	0	0	1	0	0	0	0	1	0
TOTAL	21	12	7	9	9	7	8	7	8	7
%	88	50	29	38	38	29	33	29	33	29

Table 5.19 rDNA technology linkages

rDNA

	DStream.P	Ferm	Waste	Mab	Biocat	A.C.C	BioS	ProtEng	P.Gen	P.C.C
ABM	1	1	1	0	0	0	0	0	0	0
ANG	0	0	0	0	0	0	0	1	0	0
P4S	0	1	0	0	0	0	0	0	0	0
G.C	1	1	0	0	0	0	0	0	0	0
HAH	1	1	0	1	0	0	0	0	0	0
BeP	1	1	0	1	0	1	1	1	0	0
GXR	1	1	0	1	1	1	0	1	0	1
AMER	0	0	0	1	0	0	1	0	0	0
PFI	1	1	0	0	0	0	0	0	0	0
MDIA	0	0	0	1	0	0	0	0	0	0
CELL	1	1	0	1	0	1	0	1	0	0
GENI	0	0	0	1	0	0	1	0	0	0
CS	1	1	0	0	0	0	1	0	1	1
BASS	1	1	0	0	0	0	0	0	0	0
UNI	1	1	0	1	1	1	1	1	1	1
MON	1	1	0	1	0	1	0	1	1	1
PBt	1	1	0	1	0	1	1	0	0	0
BiC	0	1	0	1	0	0	0	1	0	0
TOTAL	12	14	1	11	2	6	6	7	3	4
%	67	78	6	61	11	33	33	39	17	22

Table 5.20

(ref: Dunnil & Rudd, 1984)

Table 5.21

Technologies by Sector TABLE 7

Technology	SECTOR						
	Res Po	Health	F&D	Agri	Chem	Energy	Other
Fermentation Technology	75	50	75	50	85.7	100	
Downstream Processing	50	42.8	87.5	75	71.4	50	
recombinant DNA	75	71.4	35.5	25	28.6		
Monoclonal Antibodies		71.4	12.5	50	28.6		
Waste Treatment/Biodegradation	25	21.4	50	50	14.3	100	
Biocataiysis	25	14.2	50	25	42.8	50	
Animal Cell culture		35.7	12.5	50	28.6		
Plant Cell Culture		7.1	50	25	14.3		
Biosensors/Bioelectronics		21.4	50		28.6		
Protein engineering	50	21.4	25	25	14.3		
Plant Genetics			50	50	14.3	50	
(sample size)	4	14	8	4	7	2	

5.6.4 Linkages within biosciences

5.6.4.1 Recombinant DNA (rDNA)

On the bioscience side rDNA technology provides the most active area in the survey. rDNA has very widespread applications (see table 5.20). The survey sample reflects this diffusion of rDNA technology across traditional industry sectors, see table 5.21.

Following on from the strong linkages with the process engineering described above, the other closest link is with another major 'new' biotechnology that emerged from academic laboratories in the 1970s; monoclonal antibody/hybridoma technology.

5.6.4.2 Monoclonal Antibodies

From table 5.14, it can be seen monoclonal antibodies are another major biotechnology. Hybridoma technology was the second major discovery of the new biotechnologies. The technology resulted from attempts to improve antibody production in cell cultures. Normally antibody producing cells, following exposure to an antigen, produce several types of antibody, each differing in their specificity to the antigen. These cells cannot be grown under controlled laboratory conditions because they only perform a limited number of cell divisions before they die. The solution to this problem was discovered in 1975 by G. Kohln and C. Milstein, working at the Medical

Research Laboratory at Cambridge. They demonstrated that antibody producing cells can be fused in the test tube with blood cell tumours known as myeloma cells. These fused cells are known as hybridomas and the antibodies they produce have certain key characteristics:

- Hybridoma cells divide and can be grown in culture as an essentially immortal cell line;
- Each hybridoma line produces a single antibody of defined specificity. It is called a monoclonal antibody;
-a single antibody can therefore be produced in bulk with no batch to batch variation and no contaminating additional antibodies.

By looking at the technology matrix, linkage to other technologies from both generic categories was analysed, (Table 5.22).

16 Companies (40%) of the respondents were active in this area. Of these 11 were also active in rDNA. It should be noted that rDNA subcellular technique that can assist with the development of monoclonals, genetic engineering may be able to replace cell fusion in monoclonal antibody production. Also DNA probes, directly made by rDNA technology, represent an alternative technology to monoclonals in some diagnostic applications. So there are clear scientific and commercial reasons for this linkage.

Fifty percent of the firms active in this technology were linked to fermentation (and 44% for downstream processing). However it is not clear, because of the aggregated nature of the survey data, whether this

linkage is due to the monoclonals or to the other major technology in the matrix, i.e. rDNA, (rDNA & MAb = 7 cases, 44% of sample). However, by using additional sources of information it would seem that some of the companies in the sample are linking the technologies to develop the ability for large scale production of monoclonal antibodies. The initial products involving MABs to be commercialised were ultra-high value products, (perhaps $1000/lb). There commercial production could be achieved with big laboratory equipment with little need for process efficiency or capital cost reduction, i.e. it was really still at bench level. The survey data appears to indicate a move towards larger scale production of monoclonal antibodies. This may also explain the strong technological linkage in the sample with Animal Cell Culture (56%).

Another interesting feature of the results is the technology profile of the five firms in the sample that show no linkage to fermentation/downstream processing. This lack of emphasis on traditional 'scale up' technologies would seem to indicate that they are interested in producing low volume/high value products. A strategy with lower barriers to entry in terms of capital cost and technology.

These five are linked to the following technologies; Animal cell culture (3) Biocatalysis (1) Biosensor (1), Waste treatment. They are all concentrating on the specialist bioscience end.

5.6.4.3 Biocatalysis

Biocatalysis is another technology on the bioscience category that could be linked to manipulation and fermentation needs.

Table 5.22 Monoclonal antibody technology linkages

MAb	DStreamP	Ferm	Waste	rDNA	Biocat	A.C.C.	BioS	ProtEng	P.gen	P.C.C
HAH	1	1	0	1	0	0	0	0	0	0
BeP	1	1	0	1	0	1	1	1	0	0
GXR	1	1	0	1	1	1	0	1	0	1
AMER	0	0	0	1	0	0	1	0	0	0
MDIA	0	0	0	1	0	0	0	0	0	0
CELL	1	1	0	1	0	1	0	1	0	0
BSCOT	0	0	0	0	0	1	0	0	0	0
IG	0	0	0	0	1	1	1	0	0	0
S.DIA	0	0	1	0	0	0	0	0	0	0
GENI	0	0	0	1	0	0	1	0	0	0
UNIP	0	0	0	0	0	0	0	0	0	0
UNI	1	1	0	1	1	1	1	1	1	1
PREM	0	0	0	0	0	1	0	0	0	0
MON	1	1	0	1	0	1	0	1	1	1
PBT	1	1	0	1	0	1	1	0	0	0
BiC	0	1	0	1	0	0	0	1	0	0
TOTAL	7	8	1	11	3	9	6	6	2	3
%	44	50	6	69	19	56	38	38	13	19

Table 5.23 Biocatalysis technology linkages

BIOCATALYSIS	DStreamP	FERM	WASTE	rDNA	MAB	A.C.C	BioS	ProtEng	P.Gen	P.C.C
G.B	1	1	0	0	0	1	0	0	0	0
GXR	1	1	0	1	1	1	0	1	0	1
IG	0	0	0	0	1	1	1	0	0	0
EFG	1	1	1	0	0	0	1	1	0	0
RHM	1	1	1	0	0	0	1	0	0	0
T&L	1	0	1	0	0	0	0	0	1	1
UNI	1	1	0	1	1	1	1	1	1	1
BiC	1	0	1	0	0	0	0	0	0	0
CTDS	1	0	0	0	0	1	1	0	1	0
CDA	1	1	0	0	0	0	0	0	0	1
IB	0	1	0	0	0	0	0	0	0	0
EC	0	1	1	0	0	0	0	0	0	0
TOTAL	9	8	5	2	3	5	5	3	3	4
%	75	67	42	17	25	42	42	25	25	33

Traditionally enzyme use has predominantly been in the food industry (e.g. dairy products) and these enzymes have been obtained from natural sources, (e.g. renin from calf stomachs). Enzymes in this context are linked to fermentation processes. In such processes it is technically very difficult to recover active enzymes from the reaction mixture for re-use. As a result, there is a loss of active enzyme during each reaction cycle. These disadvantages can be overcome by the use of immobilised enzymes. They can be re-used and are usually more stable and can make a continuous process possible. Since enzymes can catalyse reactions under mild conditions including normal temperature and pressure, the applications of immobilised enzymes in the chemical industry may reduce their energy requirements.

From the table 5.23, it can be seen that biocatalysis is linked to fermentation in 8 cases (67%) and downstream processing in 9 cases (75%).

The use of immobilised enzymes or immobilised cells in continuous reactors is a field identified in the Spinks working party on biotechnology, as a field showing great potential, 'limited often only by present competitive costs and the stability of the catalyst under the conditions of optimum use'. There is a clear linkage then between fermentation/downstream processing and biocatalysis to try and develop novel bioreactors and fermenters.

Another possible technology linkage with biocatalysis is through the production of enzymes, to develop new productive sources, and better enzymes. The technology inputs to achieve this are rDNA technology to engineer cells to produce enzymes and protein engineering to design tailor made enzymes. In this sample these technological routes do not seem to have been taken up, (protein engineering 25%, and rDNA 17%).

Biocatalysis,then, is relatively independent of the two basic biotechnologies of rDNA and Monoclonal antibodies with just three exceptions, (25% of the sample). Two of these were in large multi national companies who are active in all areas of the 'new' biotechnologies, and in the other case a specialist company which was linking biocatalysis technology with monoclonal antibodies in biosensor technology, (enzyme diagnostic kits).

5.6.4.4 Waste treatment/biodegradation

The survey identified 14 active companies. The possible applications of biotechnology to waste treatment are given in table 5.24. The major technologies linking into waste treatment can be seen from table 5.25. By far the largest combinations with fermentation (50%) and with downstream processing in particular (64%). The survey indicates that at present waste treatment technology is very much linked to process technologies.

On the science side there was linkage with biocatalysis (36%), (enzymes being of use in isolating specific molecules) and plant genetics (29%).

5.6.4.5 Animal cell culture

The survey identified 10 companies active in this technology. Table 5.26, indicates the linkage profile obtained. The biggest linkage was with Monoclonal antibody technology (90%). Producing monoclonal

Table 5.24 Waste treatment/biodegradation technology linkages

WASTE TREATMENT,BIODEGRADATION

	DStream	Ferm	rDNA	MAB	Biocat	A.C.C	BioS	ProtEng	P.Sen	P.C.C
ABM	1	1	1	0	0	0	0	1	0	0
S.DIA	0	0	0	1	0	0	0	0	0	0
EFG	1	1	0	0	0	0	1	1	0	0
AB	1	1	0	0	0	0	0	0	1	0
RHM	1	1	0	0	1	0	1	0	0	0
T&L	1	0	0	0	1	0	0	0	1	1
BTEC	1	1	0	0	0	0	0	0	1	1
Bic	1	0	0	0	1	0	0	0	0	0
BIS	1	0	0	0	1	0	0	0	0	0
EC	0	1	0	0	1	0	0	0	0	0
CAS	1	1	0	0	0	0	0	0	1	0
THORN	0	0	0	0	0	0	0	0	0	0
TOTAL	9	7	1	1	5	0	2	2	4	2
%	64	50	7	7	36	0	14	14	29	14

Table 5.25

antibodies is intimately linked with mammalian cell culture techniques as their production process. For scaling up production of monoclonal antibodies much research will be needed on large scale animal cell culture processes.

There is also a strong linkage with fermentation (60%), animal cells will need special fermenters, and downstream processing (70%), purifying the products (often made in small quantities,ie interferon from human fibroblasts) requires sophisticated downstream processing techniques.

On the bioscience, other than monoclonal antibodies, there are also some strong linkages:

rDNA 60%. This technology can be used to modify what the cultured cells actually produce.

Protein Engineering, 50% animal cells can be used to express the novel proteins designed via this technology.

Biosensors, 50%, this technology makes use of some of the grown cells, in particular monoclonal antibodies.

Table 5.26 Animal cell culture technology linkages

ANIMAL CELL CULTURE

	DStreamP	FERM	WASTE	rDNA	MAB	BIOCAT	BioS	ProtEng	P.Gen	P.C.C
BeP	1	1	0	1	1	0	1	1	0	0
GXR	1	1	0	1	1	1	0	1	0	1
CELL	1	1	0	1	1	0	0	1	0	0
BSCOT	0	0	0	0	1	0	0	0	0	0
IB	0	0	0	0	1	1	1	0	0	0
UNI	1	1	0	1	1	1	1	1	1	1
PREM	0	0	0	0	1	0	0	0	0	0
MON	1	1	0	1	1	0	0	1	1	1
CTDS	1	0	0	0	0	1	1	0	1	0
PBT	1	1	0	1	1	0	1	0	0	0
TOTAL	7	6	0	6	9	4	5	5	3	3
%	70	60	0	60	90	40	50	50	30	30

Table 5.27 Biosensors technology linkages

BIOSENSORS

	DStreamP	FERM	WASTE	rDNA	MAB	Biocat	A.C.C	ProtEng	P.Gen	P.C.C
BeP	1	1	0	1	1	0	1	1	0	0
PBT	1	1	0	1	1	0	1	0	0	0
IB	0	0	0	0	1	1	1	0	0	0
GI	0	0	0	1	1	0	0	0	0	0
CS	1	1	0	1	0	0	0	0	1	1
EFB	1	1	1	0	0	1	0	1	0	0
RHM	1	1	1	0	0	1	0	0	0	0
UNI	1	1	0	1	1	1	1	1	1	1
CTDS	1	0	0	0	0	1	1	0	1	0
TOTAL	7	6	2	5	5	5	5	3	3	2
%	78	67	22	56	56	56	56	33	33	22

5.6.4.6 Biosensors

The survey indicates that nine companies are active in this technology. The technology draws upon several separate technologies. It involves the immobilisation of biological molecules directly to the surface of microelectronic sensors. The potential advantage being that biosensors, using biologically sensitive material can be used, (e.g. enzymes to monitor specific substances like glucose in blood). It could find uses in medical diagnosis, and in process control in the food and drinks industry and in waste treatment.

Table 5.27 indicates the linkage found in the survey. The major link appears to be with downstream processing (78%) where biosensors might find use in process control. Following this it appears strongly linked (although the very small sample size may distort this) with fermentation (67%), rDNA (67%), monoclonal antibodies (67%) and biocatalysis (56%).

The most significant finding here may in fact be that so few firms are actively involved in this area of technology.

5.6.4.7 Protein engineering

The survey indicates that there are nine companies active in this technology, which aims to genetically engineer specific protein structures. Table 5.28, shows that the major linkages in the small sample are with the following technologies:

- fermentation (78%);
- downstream processing (67%);
- rDNA (78%).

This linkage is understandable as rDNA technology is a major tool in protein engineering which brings together various disciplines under its auspices. This may explain why so few firms in the sample are actively involved in this area, as it requires many technological inputs.

5.6.4.8 Plant genes/plant cell culture

Plant genetics provides the underlying science base for plant biotechnology, of which plant cell culture is a major production technology. Plant genetics furnishes the information regarding vectors for transferring genes, the molecular biology of seed development and composition. Some of these genes can be used to produce high value chemicals such as drugs, flavourings, colours etc, by using the large scale cultures of plant cells.

The survey identifies eight firms active in plant genetics and seven in plant cell culture. Table 5.29, suggests a strong technological linkage between plant cell culture and downstream processing (86%), fermentation technology (71%), rDNA technology, biocatalysis and plant genetics, (all 57%).

Table 5.30 suggests a strong linkage between plant genetics and downstream processing (100%), fermentation

(75%), waste treatment and plant cell culture, (both 50%).

In both cases, it is significant to note that the sample size is very small. Plant cell culture is an advanced technology like animal cell culture and protein engineering that requires many technological inputs.

Table 5.28 Protein engineering technology linkages

PROTEIN ENGINEERING

	DStreamP	FERM	WASTE	rDNA	MAB	BIOCAT	A.C.C	BioS	P.Gen	P.C.C
ABM	1	1	1	1	0	0	0	0	0	0
ANG	0	0	0	1	0	0	0	0	0	0
BeP	1	1	0	1	1	0	1	1	0	0
GXR	1	1	0	1	1	1	1	0	0	1
CELL	1	1	0	1	1	0	1	0	0	0
EFG UNI	1	1	1	0	0	1	0	0	0	0
MON	1	1	0	1	1	0	1	0	1	1
Bic	0	1	0	1	1	0	0	0	0	0
TOTAL	6	7	2	7	5	2	4	1	1	2
%	67	78	22	78	56	22	44	11	11	22

Table 5.29 Plant cell culture technology linkages

PLANT CELL CULTURE

	DStreamP	FERM	WASTE	rDNA	MAB	BIOCAT)	A.C.C	BioS	ProtEng	P.GEN
GXR	1	1	0	1	1	1	1	0	1	0
CS	1	1	0	1	0	0	0	1	0	1
GALL	0	0	0	0	0	0	0	0	0	0
T&L	1	0	1	0	0	1	0	0	0	1
UNI	1	1	0	1	1	1	1	1	1	1
MON	1	1	0	1	1	0	1	0	1	1
CDA	1	1	0	0	0	1	0	0	0	0
TOTAL	6	5	1	4	3	4	3	2	3	4
%	86	71	14	57	43	57	43	29	43	57

Table 5.30 Plant genetics and technology linkages

PLANT GENETICS

	DStreamP	FERM	WASTE	rDNA	MAB	BIOCAT	A.C.C	BioS	ProtEng	P.C.C
CS	1	1	0	1	0	0	0	1	0	1
AB	1	1	1	0	0	0	0	0	0	0
T&L	1	0	1	0	0	1	0	0	0	1
UNI	1	1	0	1	1	1	1	1	1	1
BTc	1	1	1	0	0	0	0	0	0	0
MON	1	1	0	1	1	0	1	0	1	1
CTDS	1	0	0	0	0	1	1	1	0	0
CAS	1	1	1	0	0	0	0	0	0	0
TOTAL	8	6	4	3	2	3	3	3	2	4
%	100	75	50	38	25	38	38	38	25	50

Notes

1. An example of the 'multiple positions' taken by firms in biotechnology is given below:

Monsanto's investments in biotechnology

In-house investment
$185 million invested in biological sciences research centre

Biotechnology companies (equity investments and important contracts)
Collagen - artificial bone materials
Biogen - tissue plasminogen activator
Genetech - bovine growth hormone
Genex - venture capital investment
Biotechnica International - B. Subtilitus protein expression

University contracts
Harvard University - biomedical research ($23 million)
Washington University - biomedical research ($23 million)
Rockefeller University - photosynthesis research ($4 million)
Oxford |University - sugar chains ($1.5 million)

Drug companies
G.D. Searle - purchased for £2.7 billion, manufacturer of aspartame and has major biotechnology research facilities in the US and UK.

Seed company subsidiaries
Jacob Hartx Seeds, Monsanto Seeds.
Hybritech Seeds Co. Farmers Hybrid Co.
(Source, Kenney, 1985)

2. A leading exponent of this view, Bruce Williams warns;

> before jumping to the conclusion that there has been a decisive change in the nature of the innovation processes, and that those countries in

which universities and polytechnics seize the opportunities to become primary institutional sources of innovation will gain an advantage and perhaps a cumulative advantage in industrial innovation and rates of growth, past fluctuations in the relations between the direct and indirect contributions of academic scientist and engineers should be considered, (Williams, 1984).

CHAPTER SIX: UK Science Policy: The Science and Engineering Research Council and the Development of Biotechnology 'Clubs'

6.1 Introduction

The Science and Engineering Research Council (SERC, formerly the Science Research Council - SRC), is one of the five Research Councils operating under the aegis of the Department of Education and Science (DES). The Council's broad responsibility is to sustain a fundamental capacity for research and advanced training in the United Kingdoms institutions of higher education. In the context of this study, regarding support of biotechnology, the responsibilities of the SERC do not extend to the application of biotechnology in agriculture and medicine (the domains of the Agricultural and Food Research Council (AFRC) and the Medical Research Council (MRC) respectively).

Over the years of its operation, the SERC has developed a number of mechanisms to both increase university-industry collaboration and to single out specific fields for special support, (often these were of industrial interest). The development of the directorate and club structures as a means of organising science for industrial relevance, can be seen as the latest in a series of mechanisms devised by the SERC policy of selectivity; providing extra support for a limited number of research areas, which are interpreted as being strategically important. An analysis of the evolution of these mechanisms shows that the criteria by which these

areas of research are judged is by their perceived industrial relevance. In this section I will briefly review the mechanisms, placing case studies in the context of the evolution process in selecting and organising areas of science by the SERC.

6.2 Selectivity and concentration - 1969-1970

The SERC introduced a policy of selectivity and concentration in 1969/70, (SRC, 1970). This policy was designed to select areas of research for priority treatment and to concentrate available resources into fewer 'centre's of excellence'. The reasons for this original policy was a combination of fiscal restraint; of not spreading resources too thinly; and of industrial relevance. However, the problems of attempting a more dirigiste approach were outlined by a study carried out by Farina and Gibbons (1979), on the selectivity policy of the SERC. Farina, through the analysis of the grant allocations made by SRC demonstrated that neither of these policies had any effect on the distributions of these grants. Grant distributions remained substantially the same before and after the policy intent was adopted, in the majority of cases variations were not statistically significant. The level of concentration over the decade remained constant. The conclusion that Farina draws from this is that SERC produced many public statements regarding policy aimed at appeasing those outside forces in government and industry which were exerting pressure on the SERC to cater more readily to

national needs. The research community to whom the SERC was also answerable, however, experienced no change in policy they still received the same distribution of research grants. An interesting point made by Farina was that the peer review process is incompatible with any attempt to instigate new criteria for funding if the initiative arises from outside the scientific community (see comments in Chapter 2). These findings seem to have influenced the structure of subsequent mechanisms such as the directives and clubs.

The SERC mechanisms can be usefully divided into two main types;

1. Bilateral 1:1 agreements in the Cooperative Research Grants Scheme (CRGS);

2. Specially promoted areas of research, as represented by the directorates.

These groups are not mutually exclusive and I will discuss the role of the CRGS as an instrument of the directorate policy later.

6.3 The Cooperative Research Grants Scheme (CRGS)

The CRGS seems to have emerged from the desire to search for more effective means of encouraging academic-industry collaboration in research and continues to be an important element of the SERCs strategy to encourage

university-industry research collaboration. The roots of the concept for CRGS emerged from the findings of the Richard report, which called for a pre-development grant. It was conceived as a research analogue to the SERC CASE studentships scheme. This scheme is aimed at training a postgraduate in the methods of research, and typically leads to a PhD degree. In CASE, the student works on a project devised and supervised jointly by representatives of the industrial and academic partners and the project is often of commercial significance to the company.

The scheme itself formally resulted from the SERC working group set up under the chairmanship of W.E J Farvis to advise how best to develop the arrangement for supporting research in which involves academic industrial collaboration. Their work was completed by 1978. The report urged the SERC to support:

> Research by universities and polytechnics in partnership with employers in the UK. The research should advance understanding and assist the improvement of significant industrial and commercial operations and processes and also enable university researchers to make additional contributions to the well-being of the UK economy. By this means research and training in academic institutions will derive general benefit and the results of the SRC-supported researchers will be better used by industry.

The analysis of the scheme performed by TCC categorised the CRG as follows:

> The Cooperative Research Grant Scheme aims to increase the level of understanding between academia and industry, the industrial relevance of academic research, and the technological advance of industry,

by bringing together educational establishments and industrial firms working as partners in joint projects, in particular it seeks to achieve one of the following things:

a. improve the understanding of the science underlying an industrial process or product:
b. advance technology in a way likely to lead to a new process or product:
c. encourage multi-disciplinary work and the joining of different technologies;
d. improve the standard of R&D in industrial laboratories;
f. provide an industrial input to reinforce and influence basic research in areas of industrial value;
g. orient academic researchers at PhD or post-doctorate level towards careers in industry.

(Source: Kennedy et al, 1984).

The Council accepted the proposal of the working group, that a trial cooperative Research Grant scheme should be launched in March 1979. Grants under it were able to be made in any field of the biological, engineering and physical sciences.

The report on the CRGS produced some interesting results. Two thirds of the projects sampled by the TCC team were predominantly, or wholly applied:

> In view of the industrial purposes of the scheme, and because our analysis suggests that applied projects yield better overall benefits than fundamental ones, we feel that the proportion of applied projects could be increased with advantage to (say) 75 or 80 per cent. We would certainly

not wish to see a shift in the other direction. In future, where a hard choice has to be made (for example in the current unfunded-alphas situation), preference should be given to the more applied work.

Despite the investigators opinion that CRGS should be a mechanism for applied research, their analysis indicated another type of relevance, another type of research market, it could address. This stems from the needs of large science based firms. One of the reports conclusions is that the scheme is dominated by large firms, with small and medium sized firms under-represented. The large firms were asked why they participated in CRGS projects, three reasons were identified:

1. the company sees a clear need to have access to, or acquire, some special technique or expertise;
2. where good work is going on in a university, the company wishes to evaluate its relevance to their own research;
3. the company scientists wish to make and maintain contact with leading workers in selected fields.

In the first case, as the report points out, it is difficult to see why the company could not have got the work done by a direct research contract without SERC funding, there is a question of opportunism and additionality.

The others reasons, however, are more long term and speculative; and can be funded by large companies. Despite their earlier conviction that the CRGS should focus more on applied work they see the CRGS as having a role to play in the more basic research area:

> Large science-based companies can afford to adopt a long-term attitude to their research. In these firms much of the industrial scientist's thinking is concerned with the future changes likely to take place in the industry. But this forward-looking attitude is still very much market driven and one aim of research is to provide an insight into the science of some possible future product range so that the company can be prepared to enter that market from a position of technical strength should the opportunity occur. Much of this work is concerned with exploring some topic with a view to gaining understanding, and there are many parallels between such in-house work and work going on in universities. Provided the academic will accept a certain amount of guidance, university work can be a valuable adjunct to the in-house effort. The CRGS has a clear role to play here.
>
> On a broader front still, this looking ahead process not only involves seeking better understanding of selected topics but also involves knowing which topics to select. Here the industrial scientist needs a wide range of contacts in the academic world so as to be up-to-date on what is happening, and in order to couple this academic information with his own industrial acumen in reaching a decision. Here the CRGS can be important. The existence of a CRGS project, with the SERC stamp of approval, gives the firm an entry to the university department and opens the way to meetings and discussions where the range of subject can be far wider than the project itself and can lead to further collaboration. We believe that this effect, perhaps unintended or unforseen when the scheme was set up, is one of the more important features of CRGS in its basic science role, as distinct from the part in plays in

technology.

There are seeds in these later statements to the role of the directive mechanisms. Instead of picking out individual topics, areas of research are selected in conjunction with industry. Within this field of strategic research there are elements of research spanning the spectrum from basic to applied work.

6.4 The SERC Directorate programme

6.4.1 Introduction

In its annual report for 1974-1975 the SERC outlined organisational developments in the methods it was using for supporting research. Certain areas of science and engineering of special promise or national need were selected by the Council for more favoured support, e.g. Astronomy and Manufacturing technology. A few areas of national importance had not attracted sufficient academic workers to provide the capacity for the programme of basic research which the Council judged to be needed.

The classical way in which the SERC supported research was simply to respond to applications that came in and these were then assessed according to their quality and timeliness. In engineering and the applied sciences the SERC came to realise that it was necessary to take a more active view and the first way in which this was done was to have Specially Promoted Programmes, where a coordinator was appointed to encourage good applications

to come forward. Such a full time director was thought of as necessary in order to get universities and industries together to produce ideas, to produce grant applications which could be funded. It was considered by the SERC as being a very effective way of getting an area of research going, albeit an expensive way of doing it. Because of the costs the SERC would only apply this mechanism to particular areas:

1. Where the area is of great national importance;
2. That without someone taking an entrepreneurial view; there is a danger that the universities and industries together will not come fully to realise the potential that there is in their skill, time and ideas.

The most comprehensive organisational mechanism devised by the SERC for promoting a special area of science is the directorate programme. The directorate is essentially a mechanism for designing and implementing research policies in areas of perceived national need. Each directorate is aimed specifically at areas where existing mechanisms such as research grants, studentships, fellowships etc, are regarded as insufficient to provide an adequate basis for the development of activity and where a more comprehensive and active approach to R&D is thought to be necessary.

However, each directorates existence is intended to be transitory. From the outset, the research programme is developed from inputs from the customer (ie the

industrialists on its management committee) and, as the programme develops, it is expected that the balance of funding will shift in the direction of the user thereby freeing resources for the establishment of another directorate. The intention of the directorate is to build up university and polytechnic resources to a stage where they could be recognised by the relevant industries as capable of providing them with expert assistance in maintaining the highest possible level of technology. It was intended that once this had been demonstrated the continuation of academic activity at its peak level should depend on a progressive increase in the funds contributed by industry, with the engineering board funding being reduced to the level needed to maintain viability. The first such directorate was set up in polymer engineering.

6.4.2 The case of polymer engineering

The model for this new policy approach took place in the field of polymer engineering. In 1969 polymer science and technology was selected as a priority area for concentrated SRC support to encourage useful research and postgraduate training. By late 1973 it was clear that while the programme had been successful in polymer science, the scale of activity in polymer engineering fell short of the national needs. The Council accepted recommendations of a working party that a Polymer Engineering Directorate be set up to initiate and oversee a closely coordinated programme of research and post graduate training in selected higher education

institutions, with the active involvement of industry. The Council approved specific proposals to enable an effective collaborative programme in polymer engineering to be launched as quickly as possible.

In February 1976 Dr A. A. L Challis was appointed Director of the Polymer Engineering Directorate and he prepared a detailed programme of research and training; the need was for further fundamental research to provide the basic underpinning upon which the industry can build its development work to ensure that within five years the training and research project established in higher education institutions have attracted the active collaboration and financial support of firms in the polymer engineering industry.

The Director of the programme was to work with the management committee, consisting of industrialists, academics and Department of Industry representatives. The programme mechanism was designed to give more comprehensive support for identified extra cost than is normal in research grants and it hoped that staff would be encouraged to move into the selected centres. The funding for the programme over a period of five years was £2.5 million.

The Polymer Engineering Directorate was set up as the first phase of a possible two phase activity, and was expected to satisfy the working party's objectives for four or five years. However, even when polymer

engineering in the universities had become established, it was thought that there may still be a need for a facility which is directly geared to take on industrial R&D work and the universities may not be ideally suited for this type of work because their traditional constraints which cannot be completely removed. Hence there was felt to be a need for an Institute (the second phase) to take over the middle areas of training and R & D, i.e. those areas which may not be fully catered for by either universities or industry, or those which may grow out of the research partnership between university and industry. In addition, an Institute would provide a facility for training industrial staff seconded by industry in a realistic environment and over a short time scale. It would also take on R & D under contract to industry. The SERC in introducing this mechanism pointed out that its usefulness may be limited and may not be applicable to other fields. At this time the SERC was also designing support mechanisms for manufacturing technology and marine technology.

6.4.3 Marine technology

The second directorate was set up in 1977 in marine technology. The sea was considered vital to UK economic interests (oil/gas). The Engineering board of the SERC first examined the field in 1970-72 and published a report in 1973. The response from the academic community was disappointing and early in 1975 the Board began further consultations. In October 1975 a Marine Technology Task Force set up to advise the board on the

desirability of developing a co-ordinated programme of research and training. and to advise on priorities and funding requirements of the field. The Task Force reported in April 1976. It recommended support should be provided for a major coordinated programme of research as chiefly concentrated in a limited number of centres. Priorities were allocated to the various research topics identified. In marine technology, industrial development and technology were often in advance of academic interest and the need was to create university centre's that would command respect of industry.

6.4.4 Biotechnology

Following the publication of the Spinks report (ABRC, ACARD, RS, 1980) biotechnology was identified as an area requiring the support and coordination of a directorate mechanism. It was reçognised as being a key technology to a number of industrial areas. It was also an area which drew on different academic branches, in biology, in engineering and it was an area where both university and industry were seen as having a contribution to make, but the community was very scattered and it was felt that it needed to be brought together, and that is what the directorate was set up for.

The directorate was set up in 1981, jointly between the Science board of the SERC, through the Biological sciences committee and the Engineering Board. The panels first task was to define a research programme which was appropriate for this important field. The strategy of

the biotechnology directorate operated at three levels:

(i) basic underpinning to support an adequate amount of fundamental research in any of the contributing disciplines;

(ii) priority sectors where it is essential to maintain a national capability;

(iii) priority targets for research on specific products or processes, which could only be carried out effectively if in cooperation with industry. This strategy therefore mainly evolved the use of the CRGS.

As mentioned earlier, the directorate mechanisms were intended to be transitory, both polymer engineering and marine technology, have been hived off from the SERC. So in some respect they are intended to become private sector concerns. The process has not proved to be so smooth with the biotechnology directorate. One of the main reasons for this is that the range of research areas covered is very large, it can be subdivided into a lot of subgroups, some of which are more speculative than others.

Biotechnology constitutes a large area of research and the directorate originally identified eight priority sectors that could be covered under the remit of the SERC. After some deliberation the management committee decided to support six areas only. Details of the

membership of the Biotechnology Directorate's Management Committee are given in table 6.1. Selectivity was given to those sectors that were likely to bring benefit to British industry, and therefore to the UK as a whole. The club concept can be seen as an extension of this selectivity. The participation of companies at an early stage of establishment of a research area legitimised the sector as a priority, important to industry. Addressing the question of the transitory intention of the directorates existence the report of the biotechnology panel recommended that:

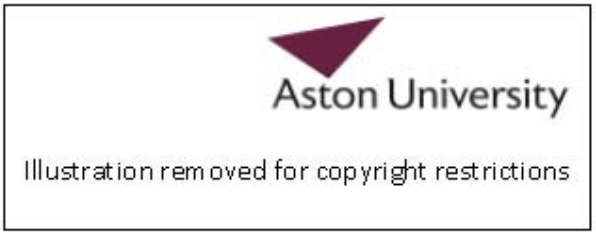
> The kind of transition of support from SERC to DTI practised in the case of other Directorates is not appropriate, since for biotechnology the transition to industrial practice often lies well into the future. However, the panel recommends that special attention should be paid to the coordination of SERCs and DTIs activities. (SERC, 1986).

By narrowing it down to small sectors (ie clubs), the transition may well be on the agenda: a micro directorate concept. In the next four chapters case studies are provided of clubs set up to organise science in specific sectors of biotechnology. These sectors are protein engineering; animal cell culture; antibiotics and recombinant DNA and plant genetics. Because of the recent nature of the use of these mechanism the analysis is provisional, it is too early for an exhaustive evaluation of their effectiveness and impact. However, because of the innovatory nature of the research club

concept in the UK, an analysis of the origins and organisation of such clubs provides a useful history of the establishment and the early development of the initiatives and of the changing nature of a science policy whose objectives are increasingly linked to technological innovation and economic success.

Ref: Seneker and Sharp, 1988

Table 6.1 Membership of Biotechnology Management Committee



CHAPTER SEVEN: The Protein Engineering Club

7.1 Introduction

The Protein Engineering Club (PEC) was the Biotechnology Directorate's first experiment with a new organisational implementation structure, designed to both support and coordinate an 'exploitable area of science' and to facilitate technology transfer between academic research and industry. The innovative character of the club was that it sought to achieve its aims by creating a structure whereby a group of companies were involved at the inception of a research programme and were involved collectively in outlining the strategic problems with academics in the area. This way of organising research for exploitation has proved to be a model structure for other areas of biotechnology, as the other case studies in this thesis go on to illustrate.

7.2 History of the programme (See Table 7.1)

The SERC Biotechnology Directorate held one of a series of 'Round Table' discussions between academics and industry on the theme of immobilised enzymes, when the subject of protein engineering emerged as an area of importance. The Directorate, having established a series of priority research areas, thought that the research targets within each of the sectors needed to be further defined.

Table 7.1 Development of the Protein Engineering Programme

November 1983	:	Preliminary meeting SERC and academics.
February 1984	:	Prospectus circulated to companies.
April 1984	:	Meeting with industrial representatives.
May 1984	:	Project definition drafted and circulated to academic laboratories active in the field.
July 1984	:	Outline proposals submitted by 10+ academic groups considered at meeting with SERC, academic and industrial representatives. Six projects selected for further development.
September 1984	:	Full grant applications submitted by six groups; total sum requested £3.7 million.
October 1984	:	Applications considered by group of academics, SERC representatives and representatives of six companies. All proposals recommended for support, many at considerably reduced rates; total sum recommended £1.17 million.
November 1984	:	Recommendations endorsed by BSC and BTMC.
January 1985	:	Programme Manager appointed.
March 1985	:	Form of contract between SERC and companies finalised; two of six sponsoring companies fail to sign and drop out.
April 1985	:	Grant award letters issued for first round of grants. Steering group for programme formally constituted. First meeting of Steering Group. Programme Manager in post (3 days/week).
July 1985	:	Steering Group strategic discussions.
October 1985	:	First six-monthly reports due. Formal meeting of Steering Group.
January 1986	:	Two day discussion meeting of all participants in programme.

The 'Round Table's' were the instrument devised to achieve this. They were seen as 'an opportunity to bring together academics and industrialists for frank and open discussions on specific topics where confidential matters could be aired. It was hoped that the meeting would act as a catalyst to interaction between academics and industrialists', (Senker and Sharp,1988).

At about the same time as this round table, Dr Geoff Potter, head of the Directorate, read a paper presented by Professor Blundel (of Birbeck College) which outlined the potential commercial and scientific significance of protein engineering (Blundell, 1983). Dr Potter then discussed the subject with his industrial contacts and discovered that there was some interest in carrying out cooperative research in this area. Discussions then progressed between the Biotechnology Directorate, the Biological Sciences Committee of the SERC and industry with a view to developing a programme.

The meeting that proved critical to the use of a research 'Club' concept as an implementation structure for running a programme in the area of protein engineering, was held in November 1983. This was referred to as the Programme Definition meeting. Eleven companies were present at this meeting and two possible models for a co-ordinated programme were considered.

1. The first model was proposed by Celltech. This envisaged " a tightly managed programme in which

Celltech became de facto managing agents with a research programme subcontracted by them to various university groups." (Sharp, 1988)

2. Dr Potter, of the Biotechnology Directorate proposed a looser club structure organised by the Directorate, and jointly funded with industry which would sponsor work at universities. It was this model that was preferred by the majority of those attending the Programme Definition meeting and eventually became the organisational format for the club.

Following this successful meeting the Directorate drew up a prospectus for a Protein Engineering Club, to circulate to all of those who attended the November meeting. The prospectus described the proposed co-ordinated programme in protein engineering to be carried out in UK institutions with support from public funds and from industry (SERC, 1984). The aims of the Programme at this early stage were as follows;

1. The structure of over 100 proteins have been determined to date although many of these proteins are of limited industrial importance. There is a need to extend this base of knowledge by carrying out structural studies on proteins which are representatives of families of proteins such as interferon, plasminogen activators and certain viral proteins, and enzymes of potential industrial importance such as carbohydrases, lignases, lipases, glycosidases and isomerases.

2. The high conservation of tertiary structure implies that detailed knowledge of one protein structure can be used to predict the structure of another within the same family. There is a need to develop expert systems for predicting protein structure both from a knowledge of homologous protein and, more fundamentally, from the amino acid sequence. The construction of such predictive algorithms will require detailed analysis of structures already determined together with, where appropriate, additional structural studies on appropriate model systems.

3. Site directed mutagenesis, amongst other techniques, may be used to make specific changes in the amino acid sequences of proteins. There is a need to use these techniques to develop predictive algorithms for structure/function relationships. Work on model systems would elucidate for example the governing principles which determine the effect on specificity of action of a change in the amino acid sequence in the active cleft of an enzyme. Similarly, studies could provide general rules for altering the thermal stability, ph optima etc of proteins.

In order to meet these aims, the prospectus outlined the need for a coordinated research programme which should be developed to:

1. elucidate the structures of selected representative proteins;

2. establish expert systems for the prediction of protein structure (both by hology and ab initio);
3. establish rules for predicting the effects of protein modification.

The following sub-objectives were also set;

a. to provide greater understanding of the science of crystallisation;
b. to generate robust software for molecular modelling and expert systems;
c. to provide a framework for the coordinated development of molecular modelling hardware and software in the UK.

The prospectus explicitly pointed out the need for a co-ordinated programme, and the need for central management.

7.3 The balance of research

A particular feature of the co-ordinated programme was the range of contributing disciplines, covering structural studies and computer graphics through to the study of genes (molecular biology) and the biochemistry of the protein products. As each of these represented distinct academic disciplines, there was a clear need to bring these groups together to interact productively on a common programme. This also represented a range of research activities that covered the spectrum from basic

to more applied science. The prospectus made clear that to make progress in such a multidisciplinary field as protein engineering, high levels of expertise are required in all of these areas. It was noted that groups in UK academic institutions already possessed great expertise in the disciplines which contribute to the field of protein engineering. But if the UK was to benefit to the maximum extent from this expertise then the research effort has to be enhanced and co-ordinated and industry must be closely involved with the co-ordinated programme.

The prospectus for the club envisaged that the aims and objectives could be achieved by developing a core research programme based on a small number of academic groups. In order to encourage industrial participation this programme would provide participating companies with privileged access to enabling technology and results of general significance. Hence the prospectus set the basic parameters for the operation and significance of the club format, and outlined some organisational objectives that were deemed necessary to achieve the scientific aims: these were the performance of pre-competitive research, basic science focused on model systems and the co-ordination of work from several disciplines.

The later literature produced by the Biotechnology Directorate, discussing the activities of the club, described it as an organisational structure for performing strategic or pre-competitive research.

However, at the early stages of its formation there was at least some ambiguity as to what type of research was appropriate, or what constituted a particular type of research.

The original protein engineering club was seen as having two components. Overall it was set up to coordinate, to bring together various research groups that could contribute to the enabling technology of protein engineering. This enabling technology was of interest to industry, but before it became a routinely useful technology, several basic scientific questions needed to be solved, hence the Directorate was able initially to bring together three groups who, at least theoretically, were involved in specific parts of the innovation pipeline. The Biological Science Committee of the SERC, who look after funding basic or fundamental research, the biotechnology directorate who look after the more applied research, and industry whose interests are applied research and development i.e. product and process innovations.

In the original vision of the programme, the core programme, outlined above, was to focus on model systems, essentially basic research and pre-competitive research but in addition - and separate from the core programme - it was thought that individual companies may seek to exploit developments in the core programme by carrying out research on so called target systems. The prospectus, in paragraph 4.4, points out that " It is

foreseen that such strategic research would be carried out by companies either in-house or by way of contract with academic groups, but taking due account of any exploitation rights and arrangements concerning the results of the core programme under section 8". The programme at this stage was divided into two phases:

Phase 1. Multi-lateral core 'pre-competitive' programme suitable for the type of organisational structure that the club represented:

Phase 2. "Strategic research", bilateral target system/development work, this was work that was thought to be closer to the market and therefore inappropriate on two counts; firstly the SERC does not fund product development work and secondly industry is unlikely to want to carry out proprietary product development work in external laboratories, and is even less likely to do this when other industrial companies are involved in the research arrangement. Consequently SERC suggested that support for such competitive work could be sought through SERCs Co-operative Research Grants.

7.4 Implementation of the club concept

The prospectus invited companies to declare an interest in the proposed programme. The progress of the club depended on the response to this call. Following this, academics would then be invited to give a brief submission. A Programme Definition Group (PDG) would be set up to screen these submissions. The PDG would

comprise of representatives of those companies who had declared an interest, plus expert representatives from public funding agencies. The PDG would then select a small number of groups (perhaps 4 or 5) to draw up detailed proposals in collaboration with each other. The PDG was to have an active steering role and would consider the research plan for the core programme, suggesting modifications if necessary. It was envisaged that an agreed programme would emerge from such negotiations.

Once this stage had been reached companies would then be asked to confirm their membership of the club, this would require an agreed annual financial contribution over a fixed number of years. Public funding agencies would also be required to approve their support for the programme.

7.5 Project organisation

To supervise the implementation of the research programme, a programme steering group would be established, comprising of representatives of the participating companies and the public-funding agencies involved. In order to provide an active role it was envisaged that the group would meet at regular intervals in line with programme requirements, perhaps biannually, to discuss progress with academic groups. The club concept put a high value on the feedback from sponsors in these meetings which could then lead to recommendations.

for a change in the emphasis of aspects of the research programme. It was emphasised that an active and effective steering group was considered of the utmost importance to enable the joint industry-academic institution approach, as SERC intended, to work.

7.6 The role of the Project Manager

One of the essential characteristics of the club concept was the appointment of a manager. The Project Manager was to be responsible for the day-to-day coordination of the research programme and would liaise between the academic institutions, the industrial sponsors and the public-funding agencies. Other important roles were to liaise between the academic groups to ensure effective coordination of effort; to establish and report progress on the programme to the different industrial concerns and to the SERC. It was anticipated that an overall written progress report would be provided bi-annually using reports and results provided by the academic groups. The Programme Manager also had the responsibility of arranging and administering the meetings of the steering group, and monitoring project costs.

7.7 Programme results and reports

For the programme organisation to achieve its operational aims, the dissemination of the results of the research teams was of the utmost importance. The provision of suitable project documentation and results and reports

presented in a way that can be effectively used by industry, was seen as essential to the effective running of the club. The information dissemination was to be achieved via the following instruments;

* Six-monthly progress reports
Sponsors would have the opportunity to input to the work and, if appropriate, suggest amendments to subsequent studies at Steering Group meetings.

* Relevant Project Data
Particularly relevant project data generated or obtained during the programme would be distributed to sponsors as it becomes available in the form of technical notes and reports.

* Computer Programmes
Sponsors would have preferential access to the computer programmes developed, either through special purchase or usage.

7.8 Terms and conditions

In a programme concerned with the development of enabling technology, the question of intellectual property rights (IPR) and privileges is a sensitive one for industry, where proprietary concerns are a priority. This question is also a site for possible conflict with the academics interest in publishing research results. The prospectus addressed the issue in the following way;

Whilst it is not possible to legislate for

> every eventuality, those involved in the programme would be expected to adhere to the following principles;
> a. to promote as far as possible a free and open exchange of in formation between participants in the programme;
> b. to avoid divulging information of possible commercial benefit to third parties;
> c. academic groups should be prepared, as far as possible, to take part in contracts proposed by sponsors and allow some minimal prior access to sponsors to carry out pilot experiments.

The protein engineering club, turned out to be less generous in this respect than the clubs that followed it, probably because it was breaking new ground and erred on the side of safety. Under the protein engineering club, which involved 20 per cent industrial funding, the intellectual property rights were vested in the universities concerned and the firms had rights to favourable licensing terms and a share of the royalties. Copyright and other property rights, including those in respect of computer programmes, arising from the Programme, were to rest initially in SERC.

> Results capable of commercial exploitation would be assigned to an agency selected by SERC which will be charged with the responsibility for exploiting the results on the basis of a revenue sharing agreement between the agency and the sponsors preferential arrangements for licensing are made with sponsors to reflect their participation in the project, (SERC, 1984).

The legal position in fact was not at all clear, at the

time the Clubs patent agent was the British Technology Group (BTG). However the BTG was itself undergoing a change in status, where it was about to lose its first option rights to exploitable university research. If the BTG declined to handle the exploitation of any of the Clubs results (there was some doubt whether there would be any intellectual property), the Club did not have a clear route to exploitation. The Club itself could not own any industrial property rights. These were owned by the universities involved, and without the BTG it seemed that it would be up to the individual universities to protect and exploit any valuable results generated within the Club framework. The rules of the Club require only that members have privileged access to any patents.

Disclosure and access to the results generated by the programme is confidential to the participants and is given on an exclusive basis on the understanding of no wider dissemination to third parties. Publication or other wider dissemination of results was not to be made for a period of six months from the date of disclosure to sponsors. Beyond this period publication of the results would normally be expected unless further delay is necessary in order to protect the results for the purposes of commercial exploitation.

In some ways it is surprising that this clause did not cause more anxiety amongst the academics. At the first meeting of the Steering Group in 1985 this stipulation was modified to mean that there would be a six month delay following the date of a formal Steering Group

meeting where the results could be presented.

7.9 The formal establishment of the club programme

Following the proposal phase where the programme structure and intellectual property rights were defined, companies were invited to join the project definition phase, of the eleven firms initially involved in the discussions, eight joined the PD group. These were - Celltech, Glaxo, ICI, Shell, Sturge, Tate and Lyle, Unilever and Wellcome.

Following the establishment of a Project Definition group another document was produced: Coordinated Programme in Protein Engineering. Project Definition (SERC, 1984). The negotiations with the participating companies had resulted in a slightly modified programme. By this time the target element instead of being dealt with by a separate 1:1 relationship, had now been included into the concept of the club. The programme was to comprise of two major elements;

1. To improve methods of predicting the three dimensional structure of proteins from a knowledge of the amino acid (or cDNA) sequence.

   This involved the construction of predictive algorithms involving analyses of structures already determined together with additional studies on appropriate model systems.

In the longer term the industrial members of the group felt that such work would enable them to develop more efficient ways of;

a. studying receptor-ligand interactions leading to more rational drug design.

b. determining the topography of bioactive molecules leading to more effective proteins in cases where the proteins themselves are intended for use as therapeutic ones;

c. improving enzyme performance by extending or modifying substrate specificity, ph optima, temperature stability, resistance to proteases etc (relates to objective 2).

Several model systems were discussed by industrialists as systems for aiding the improvement of present predictive methods including;

i) dihydofolate reductase.
ii) tyrosyl t-RNA synthetase
iii) IFN analogues
iv) cytochrome C or Insulin
v) hen egg white lysozyme
vi) antibody systems

The second major objective for the programme was

To establish rules for predicting the effect of changes in the amino acid sequence on the properties of proteins. Thus site directed mutagenesis, amongst other techniques, were suggested means that might be used to make specific changes in the amino acid

composition of a protein in order to probe structure/function relationships. Work on model systems could provide rules for effecting the following changes in the properties in the properties of proteins;

a. enhanced thermal stability
b. changed ph optima
c. enhanced organic solvent stability
d. enhanced resistance to proteolytic degradation
e. altered substrate specificity

The industrial members of the group felt that the most rapid progress could be made by working on systems where the gene structure was already well understood, where the expression of mutant genes could be predictably obtained and where the relationship between the function of the normal gene product and its three dimensional structure was well established i.e. areas not normally considered basic research. However, in addition to wishing to encourage the rapid formulation of 'rules' on well developed model systems the industrialists, in a significant change in the composition of the programme, were reported as being "anxious to encourage the development of systems of more direct commercial importance (including the determination of high resolution structures) on which rules may be tested" (SERC, 1984). In this connection the following systems were discussed;

1. Penicillin acylase
2. Glucose isomerase

3. Amypglycosidase
4. Foot and mouth virus
5. Lipases
6. Cellulases

The industrialists felt that academics should be invited to consider the merits of using the above commercially significant targets and other systems.

The project definition group also included two subsidiary objectives that related more to basic 'underpinning' science that could appeal to funding from the Biological Sciences Committee.

These sub-objectives were;

1. To increase understanding of the basic science which underlies the production of large single crystals of a protein suitable for crystallographic studies. Apart from enhancing the basic science, it was expected that contributors to this area would advise members of the sponsoring companies on the crystallisation of specific proteins whose structures might then be solved on a 1:1 collaboration between a company and a crystallographic laboratory. Advances in the particular problems associated with the crystallisation of glycoproteins and proteins active at lipid interfaces were deemed by the industrialist as being desirable.

2. To collect and maintain a suite of compatible polypeptide and protein modelling and display programmes. The file structures should be compatible. These programmes should be as user friendly as possible, although the full development of robust software was not seen as part of the university-based programme.

This Project Definition document was then circulated in the Summer of 1984 to 19 individuals in 12 universities. During the period May-July 1984, discussions had been held with a number of research groups which resulted in six groups being invited to submit detailed applications in certain areas to meet the objectives of the programme. These applications were considered at a meeting on 2 October 1984 attended by industrialists from the contributing companies and from representatives of the SERC Biological Sciences Committee and the Biotechnology Management Committee. The outcome of these meetings were recommendations to both the Biological Sciences Committee and the Biotechnology Management Committee on scientific merit and requesting levels of funding. The summary of the first two funding rounds are given in table 7.2.

Table 7.2 Work supported by the protein engineering programme

Work supported by the protein engineering programme

TOPIC	LOCATION	POSTS	COSTS
Enabling technologies:			
Structure prediction	Birkbeck/Leeds	6	
Crystallisation methods	Imperial/Sheffield	2	£1 million
Computing methods for 2D NMR data	Leicester/Oxford	2	
Solution conformation methods	Newcastle	1	
Studies on model proteins:			
Phosphoglycerate kinase	Bristol	2	
Isocitrate dehydrogenase	Glasgow	2	
Multifunctional *arom* enzymes	Glasgow	2	
Subtilisin	Imperial College	2	
Barley protease inhibitor	Imperial College	1	£700,000
Dihydrofolate reductase	Leicester/UMIST	2	
Chloramphenicol acetyl-transferase	Leicester	2	
Anti-lysozyme loop antibodies	Oxford	1	
Antibodies as catalysts	Sheffield	1	
Myoglobin haem-binding pocket	York	1	
Studies on target proteins:			
Glucose isomerase	Imperial College	5	
Methanol oxidase	Leeds	1	£600,000
Penicillin acylase	York/Newcastle	5	

An insight into the science policy "novelty" of the Protein Engineering Club arises from an examination of how these funding decisions were arrived at (Freedman, 1986). In the original funding applications to the Club many of the academics stressed the industrial connection of their projects, but it was clear to the referee's that in a few cases there was almost a one-to-one relationship between sponsor and academics. The application from York was a case in point. The referee's noted that the benefits to Glaxo would be very considerable if the project was a success "and one wonders whether it is right to pretend that it is an academic exercise" (SERC, 1984). Support for the York project had to be renegotiated from the original application. The same connection was seen between Imperial college's application and ICI, who had a definite interest in it. ICI itself encouraged the build up of Imperial College work. It was felt by ICI that it could afford to do the work by itself but was pleased to see a facility being built up (Sheard, 1986). ICI, as a UK company was interested in supporting an initiative aimed at building up a useful scientific and training infrastructure.

The Leeds and Birbeck projects illustrate an active 'steering' approach taken by the steering group. The panel were disappointed with the original separate applications from each university group because they had not been better integrated. Leeds had proposed a relational database whereas Birbeck had proposed a hierarchical database. It was considered by the panel

that the groups should be 'encouraged' to take professional advice on database structure and agree on a common database design.

With the submission from Leeds, the industrialists felt that methanol oxidase was a very important enzyme commercially and that high priority should be attached to its further study. However rather than fund the original programme it was agreed to support a feasibility study to concentrate on obtaining good crystals.

The proposal from Imperial College brought to light other issues. They had proposed to carry out work on the enzyme subtilisin, while it was agreed that the proposal had considerable scientific merit, but there was some concern that similar studies were well advanced by the US company Genentech. It was further noted that the applicants proposed to work closely with the company Novo, and that this non-UK company was likely to be the major beneficiary of any research. On this first analysis no money was recommended but a further application was to be considered on the following conditions;

1. if it could be shown that the work did not duplicate that already carried out by Genentech;
2. if it concentrated on those aspects independent of Novo collaboration.

Imperial also proposed research work on the enzyme glucose isomerase. The industrial representatives attached high priority to this enzyme. ICI had been active in this area but said that they considered this a long-term project and did not propose to enter into direct collaboration with Imperial 'at this stage'. ICI indicated that they would endeavour to provide assistance, including the provisions of oligonucleotides.

The limits to what constitutes a suitable model for the programme was illustrated by Imperial's suggestion for work on liginase, which has had some commercial speculation surrounding it (Milgrom, 1985). This was deemed a 'speculative proposal unsuitable for support under the club programme'.

York's proposal for work on penicillin acylase was considered appropriate for the club as it would yield much information of wider relevance. Glaxo offered assistance with the molecular genetics of this project, again giving an indication of a two way flow of assistance between the academic groups and industry, that was encouraged by the club mechanism.

Another part of the steering groups involvement was to 'steer' cooperation between groups in the same university. The Oxford proposal disappointed the review panel because of the lack of collaboration between groups at Oxford.

From this initial round of funding recommendations the steering group showed a clear and active steering role in bringing different groups together, both from different universities and within individual ones. The selection criteria focused both on scientific and industrial criteria. Worries about benefits going to non club members, and dealing with the problems of integrating expertise that already has some other commitments regarding industry. It was also apparent that the club encouraged firms to do more than just passively 'watch' research developments, they were prepared to put some of their research capabilities into the programme.

The discussion amongst the steering group of this original selection of research work concluded that the proposals were of both high scientific merit and of industrial relevance.

> A critical look had also been taken at the resource requirements of the programme and in a number of instances support for feasibility studies had been provided which could require substantial support at a later date. It was felt imperative, for the club programme, that support be only provided for well thought out programmes which met the objectives of the club. At this round, and taking into account of the limited funds available for expenditure in 1985/86, this has led to a recommended commitment of up to £1.7m. The meeting considered that it made strategic sense to hold back on some of the resources potentially available until evidence of progress was available to allow consideration of further proposals which the Programme Manager would be active in stimulating, (SERC, 1987).

Following the first round the programme still had money to spend and the Project Manager was still having to stimulate further proposals.

7.10 Funding bias

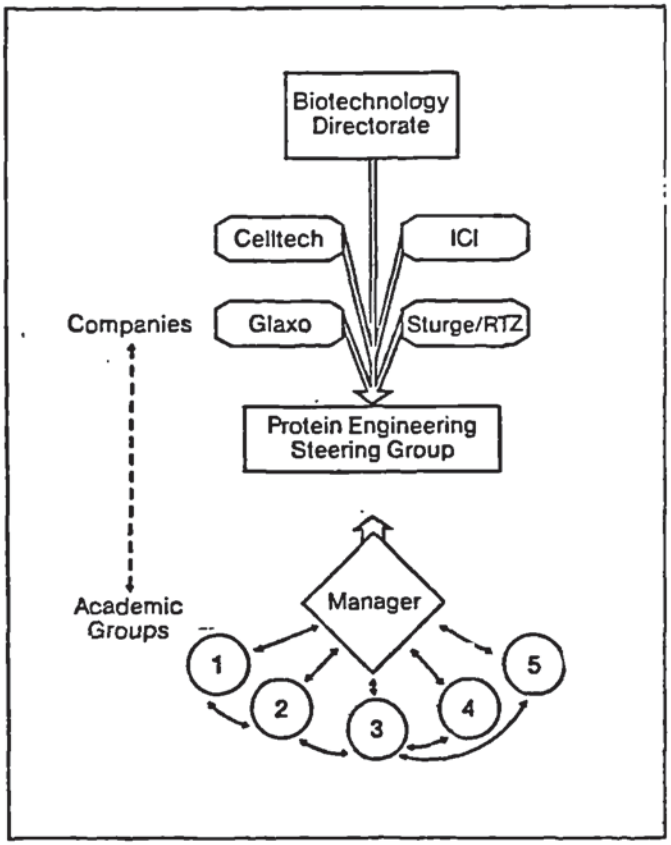
The result of the first round led to some criticism of the club. From table 7.2 it is clear that certain components of the protein engineering programme had received the bulk of the funding. Critics of the programme, within the scientific community, found it easy to criticise the programme as favouring the crystallographers. This also led to the suspicion that in order to please industry, beta quality science was being funded. The argument of the critics was that the club was taking money away from basic research to subsidise applied work that the companies should be funding themselves. The original funding, it was acknowledged by the manager of the programme, did appear to have a bias particularly towards the crystallographers and 'folders'. This group did see the initiative as a rare chance (in view of a static or declining science budget in real terms) to get the hardware which they needed to remain competitive, they were largely successful in this endeavour, because they managed to organise themselves well. It became obvious to some of the outside referees involved in refereeing the proposals, that some groups were making substantial bids for hardware as a consequence of some years of 'getting by' with equipment that had become obsolete (personal

communication, 1986). A case in point was one request for very expensive hardware for making oligonucleotides, when much cheaper facilities existed.

That these criticisms arose was not surprising. This was part of an experimental phase, the Biotechnology Directorate itself, was set up in response to the identification in the 'Spinks' report of the funding problems associated with 'strategic' research and the 'pre-development gap' in biotechnology. The PEC represented an explicit micro approach to funding a very particular subset of biotechnology research. Because of the novelty of the organisational idea, the club was careful to maintain scientific credibility through peer review (this was also critical to some of the company participation in the programme, notably ICI and Glaxo). Many of the critics had ignored the fact that the funding decisions required the same peer-review procedures as normal Research Council grants, and that the academic community were well represented on the PDG and that the decisions of the Group (and subsequently of the Programme Steering Group) had to be reviewed by both the Biological Sciences Committee and the Biotechnology Management Committee (M. Sharp, 1987).

Following the discussion of the Steering Group the recommended proposals were presented to the Biotechnology Management Committee and the Biological Science Committee, to maintain peer review standards.

Fig. 7.1 Organisation of the protein engineering club



7.11 Analysis

The final structure of the operational programme is shown in figure 7.1. The corporate membership now consisted of just four companies, Celltech, ICI Pharmaceuticals, Glaxo and Sturge. From a sectoral perspective, three of the companies come from the health care sector and Sturge was an industrial enzyme manufacture, owned by Rio Tinto Zinc.

Glaxo had been involved in genetic engineering since 1980-81, its focus was on vaccine design, and its primary products were low molecular weight conventional drugs. They were predominantly interested in that part of protein engineering club that was associated with 'substrate engineering', analogues of enzymes, receptor proteins and drug design. These areas are increasingly tied up with manipulating proteins and the use of specialist software for simulating and testing such manipulations. Dr Williamson, Glaxo's research director, stressed that the most important factor for their participation in the protein engineering club was the quality of the science. They were interested in state-of-the-art science. Although they carried out major development work in-house the programme represented a major input; a 'non-trivial' contribution to their in-house research.

Within the programme, however, some areas were of more interest to Glaxo than others. Particularly interesting

to them was the database/graphics work. From the programme, it was felt that they could get useful 'hands-on' experience. While products would be a nice benefit, at the pre-competitive level it is lead time that they were after. They were particularly interested in the software and handling system of the Birbeck/Leeds project (the Glaxo panel member helped steer this collaboration).

Dr Williamson pointed out that it was difficult to find a pre-competitive area; it was generalised as one to do with general rules/laws that are still some way from products. This was made difficult by the academic propensity to try and be relevant by guessing what the industrial targets might be. Glaxo did not want products, product development was seen as a company job.

For Glaxo, the protein engineering club was most usefully employed filling a gap, supporting 'strategic research', it did this by bringing together multi-disciplinary research at universities. Their criticism of the club was that it had failed to bring together all of the national expertise in protein engineering. Of particular note was the absence of the expertise of the Medical Research Council.

On the question of additionality; Glaxo pointed out that if the SERC programme had not existed it is likely that they would have worked on a one-to-one basis with two of the groups involved in the club.

ICI also had some initial reservations about the programme because they felt that the academics, encouraged by the SERC, were trying too hard to be relevant by trying to promote research on products. Research on product development, as far as ICI were concerned was confidential and was not suitable for external research cooperation, or for industrial consortia. While accepting that academics were under a lot of pressure to be useful, Dr Sheard stressed that ICIs needs are different, academics could be relevant without having to move too far away from traditional basic research. ICI were relatively keen on cooperative schemes and on representation on committees, they did not seek to direct research, but liked to indicate fields e.g. plant biochemistry (see chapter 8 on PGTK consortium), that they would be interested in and could perhaps get involved in, in the future. Having identified the general field then it would be up to the peer review process to sustain scientific excellence.

Part of their interest in the PEC was in building up a good scientific infrastructure, they encouraged the build up of expertise at Imperial college as they saw it as beneficial in the long term; both in terms of manpower and data.

In contrast to the interest of the large R & D intensive companies, one of the smaller members of the club was much more interested in products and was reported as being disappointed that there had been so little success

in this aspect.

It is clear that in the minds of the contributors the achievable outcomes over a given period were perceived in different ways. The large firms did not see the organisation as appropriate for product development. The inclusion of the 'target' proteins (once thought of as 'near market') indicates the long term nature of the benefits to accrue from the field. The club had aims in addition to completing the scientific objectives. It was possible to do a lot of the research via one-to-one contracts. This became clear from interviews I carried out with the industrial participants. As the programme has progressed several one-to-one collaborations have emerged:

> The Oxford NMR group and ICI collaborated on the NMR structure determination of human epidermal growth factor and the human tumor growth factor (TGF), and with Glaxo on interleukin 2.

The other 'structural' function of the Club was to coordinate the research. It's multi-disciplinary nature required different groupings to come together, interdisciplinary cooperation was vital. The importance of this trend of organising knowledge 'for action' and not sticking to traditional disciplinary boundaries was pointed out to me by one of the participants, Glaxo, who viewed this as an important structural innovation. One that was fundamental to the clubs set up to develop other

areas of biotechnology.

However the PEC can be seen to have failed in one very important aspect in its attempt to bring together, the national protein engineering community. A certain amount of national expertise was left out of the programme, this was essentially due to the different philosophies of the different Research Councils regarding the mechanisms for exploiting science and the way industry can involve itself in science policy. The AFRC did eventually join the programme as an observer, but the major omission, and one which undermined to some extent the credibility of the club, was the expertise of the Medical Research Council (MRC). The MRC had already been carrying out protein engineering research in its Laboratory of Molecular Biology in Cambridge, where it was given a priority in 1980. The reason for their failure to participate in the protein engineering club was due to a difference in their perception of how science should be funded and exploited. They carried out research in various aspects of protein engineering under a programme budget and did not wish to submit individual project proposals to the Biotechnology Directorate. Industrial concerns, Dr Bremmer, Director of the laboratory, pointed out could approach the MRC directly to undertake collaboration and training. They were interested in carrying on with their established programme and entering into bilateral agreements with firms who may be interested in some aspects of their research (Bremmer, 1986).

The disappointment of not having the MRC expertise participating in the PEC has forced a rethink for the setting up of other clubs that the MRC could contribute to, and much more consultation was sought to bring the MRC in right from the start. The end of the exclusive relationship with the Celltech for the reasons outlined above would also have assisted this process of integrating the MRC into collaborative programmes. In the post PEC follow-on programme;

> The future evolution of the PEC is already under discussion within the Directorate and the Club itself, in conjunction with DTI. In addition, the Biotechnology Advisory Group is discussing with all research councils the possible co-ordination of a general programme in protein engineering, (SERC, 1988).

It was announced in April 1989 that the PEC will continue as part of the LINK programme and will involve the SERC, DTI, MRC and AFRC.

CHAPTER EIGHT: The Plant Gene Tool Kit consortium

8.1 Introduction

The Plant Gene Tool Kit (PGTK) consortium, was an academic industrial collaborative grouping, set up in 1986 to strengthen the commercial exploitation of Britain's expertise in plant genetics. The objective of the research consortia was the creation of an enabling technology that would allow the user of the PGTK to make gene transfers in crops of commercial significance. The consortium programme was set up for three years with a budget of £3 million.

8.2 The context of agricultural biotechnology

The applications that biotechnology has opened up in agriculture, were discovered a few years after its application to medicine and health care was recognised. This was primarily due to the fact that the new techniques of biotechnology, such as genetic manipulation, emerged mainly from medical research. There was not such a rapid application of new biotechnology applied to plants, in part because less was understood about plant genetics and physiology than about bacteria and viruses, on which the early genetic engineering principles and techniques were worked out. Rapid corporate funding, particularly in the US, of academic groups expanded the biotechnological applications in the health care sector as it was perceived as the quickest route to commercial

exploitation of the new techniques.

Once the basic techniques of genetic engineering had been established academic research scientists working on plant science did begin to apply the molecular biology techniques to plants, partly out of intellectual curiosity but also from the awareness of the radical possibilities that this technology could bestow upon agriculture. An early recognition of the commercial possibilities of plant biotechnology were outlined in the influential US Office of Technology Assessment (OTA) report (OTA, 1981). Firms with interests in the agrochemical sector also began to realise, in the early 1980s, the significance of the opportunities presented by agricultural biotechnology and began to develop strategies to counter these threats (Kenney, 1987). The PGTK consortium represents one of the ways the UK has sought to meet the challenge of developing new technology for agricultural biotechnology. This case study examines the circumstances surrounding the founding of the PGTK consortium; its organisational arrangement; its objectives; and its role as a model for organising science for exploitation.

8.3 The techniques of plant biotechnology and areas of application

Plant breeding is a form of biotechnology that has been practised for centuries. Plant breeding via natural selection, is a form of genetic manipulation in which there is random combining of genes from the parent

plants. The production of a new hybrid via this process is a very time consuming and laborious process. The aim of the new biotechnology techniques is to develop technology which will circumvent this process and allow plant breeding to be developed more rapidly:

> ...to speed up the development of new strains of plants (it took 50 years from 1930-1980 to increase the yield of corn by 70% through a long process of genetic selection; the same improvement could now be obtained in a few years or less, (EEC, 1988).

The enabling technologies or tools biotechnology can bring to plant breeding are:

> Production of hybrid plants by fusion of modified cells, known as protoplasts;
> Transfer of genetic information in and out of species using rDNA techniques.

The potential applications of these tools include:

> Production of a wider range of varieties from which genetic selection for yield and quality can take place;
> Introduction of characteristics, such as disease resistance or tolerance of unusual soil or climatic conditions;
> Transfer of the ability to fix nitrogen to plant species not capable of doing this;
> Engineer a plant to become a source of various chemicals (expression of high value products);
> Transfer out of plants of synthetic capabilities into bacteria or other micro-organisms;
> Development of new types of pesticides and other agricultural chemicals by application of rDNA techniques to biochemical processes. (Shaw, 1984)

8.4 Plant Genetics Research

8.4.1 Introduction

The discovery of new biotechnology techniques in the mid 1970s allowed the transfer of cloned DNA between micro-organisms to be performed routinely in many laboratories, the absence of a convenient vector system had inhibited similar experiments with higher plants such as cereal crops (monocots); the ones of most commercial interest.

Another bottleneck in the advancement of plant biotechnology was the problem related to the question of what genes need to be transferred into plants in order to give rise to specified improvements in particular crops. Despite the acknowledged importance of the need for transforming vectors, it became apparent to all concerned that success in achieving plant improvements would rely on a thorough knowledge of the genetics and regulatory mechanism of the traits to be transferred. For plant biotechnology to advance, basic research on the molecular biology of plants needed to be performed.

8.4.2 UK research in plant biotechnology

The PGTK consortium, as a coordinating mechanism and research funding organisation, involves two universities and two Agricultural and Food research Council (AFRC) Institutes, with the funding coming exclusively from the

corporate members and the Department of Industry (DTI). This funding approach differs from the standard public support for plant research. The primary responsibility for agricultural research in the UK lies with the AFRC, formerly the Agricultural Research Council (ARC). It has run a coordinated programme in biotechnology since 1977. In that year an internal priorities working party set up by the AFRC, identified genetic manipulation as a priority area, as a source of techniques that could usefully be applied to plant and animal research. In 1978 the Department of Education and science (DES) provided special funds to set up a co-ordinated programme in plant gene manipulation, the funding being divided between three AFRC Institutes (John Innes/Plant Breeding Institute/Rothampstead). Within the AFRC, several ad hoc working groups had been convened to discuss developments in specific areas, and this led to the establishment of a programme on photosynthesis research; a Monoclonal Antibody centre; programmes on immobilized cell systems and the consideration of genetic manipulation of animals.

The developments of the research strategy of the AFRC had made a significant shift away from its traditional research that meant that it had benefited the farmer directly, toward the new molecular and cellular technologies and food processing research. This type of research favoured those firms that possessed the internal R & D capabilities to assimilate externally funded research and to filter this knowledge for commercially relevant technologies.

8.5 History of the PGTK consortium

Table 8.1 Development of the PGTK consortium

* 1983 Agicultural Genetics Company established

* September 1983 Unilever/ICI Report on fundamental plant science

* AFRC/SERC/DTI Study Group set up to oversee three Steering Groups

* 1984 Call for proposals for AFRC/SERC/DTI Initiative

* SERC and AFRC drop out due to insufficient funds

* Early 1985 PGTK discussions underway

* End 1985 Programme agreed

* Early 1986 organisational framework established

* April 1986 PGTK Launch Symposium

* Mid - June 1986 PGTK established

* Autumn 1986 Research underway at four academic centres

* April 1988 SERC/DTI Plant science initiative call for proposals

* 1989 Programme end of PGTK consortium

* September 1989 discussions between sponsors about a PGTK II programme

The PGTK consortium emerged from an ambitious attempt by the Research Councils to coordinate and promote research jointly in the area of plant biotechnology. This approach reaffirms biotechnology as one of the 'generic' technologies, which because of its broad applications,

from energy to health care, spans the interests of most of the Research Councils, co-ordination is consequently seen as key to success. This point, originally made in the 1980 'Spinks' report, was reiterated in the Third Report to the Heads of Research Councils (HORC), presented by the Inter-Research Council Coordinating Committee on Biotechnology (IRCCCOB) report, which was set up to assist with the coordination recommended in the Spinks report. The terms of reference of the Inter Research Council Coordinating Committee on Biotechnology: The Committee shall advise the Heads of the Research Councils on:

(i) The development of the biotechnology research programmes within the Research Council system;

(ii) Any coordination or rationalisation that may be desirable between the programmes of different Councils;

(iii) Any new work that should be initiated as a consequence of inadequate coverage or recent discoveries.

The IRCCCOB report (IRCCCOB, 1986) identified a number of areas where an increased research effort was required to underpin the needs of UK industry. Following discussions, involving industrialists as well as academics, they developed the concept of creating joint Research Council programmes in two areas; microbial physiology; and plant molecular biology and biochemistry. It was believed that a sufficient programme could not be developed within existing resources and they brought this

requirement for additional funds to the attention of HORC in January 1984. In the event the bids were unsuccessful. This IRCCCOB responded as follows:

> We now seek the views of HORC on the merits and desirability of IRCCCOB developing inter-Research Council programmes. We had felt the joint approach to the funding of programmes in subjects that were important to a number of Councils was a unique development in collaboration between Councils, and as such we believed it would receive a warm welcome. However there does seem to be a danger that such joint bids of each Council, as discrete and identifiable items. We would welcome the advice of HORC on whether, and if so how, we should develop and seek funding for joint Research Council programmes in the future, (IRCCCOB, 1986).

In the absence of additional funding, the Research Councils had nevertheless proceeded to try to provide sufficient resources for the two areas mentioned above. In plant molecular biology and biochemistry the AFRC, SERC in collaboration with DTI and Natural Environment Research Council (NERC), attempted to coordinate their respective research programmes, funded from within existing budgets, and also sought to make the research more relevant to the needs of industry. In order to ascertain what industry wanted in the area of plant biotechnology a report was commissioned from ICI and Unilever on the needs of UK industry for underpinning research in this area. This report Guidelines for SERC supported research in Plant Science relevant to Biotechnology. Proposals from Unilever/ICI to the academic community and AFRC Institutes, completed in September 1983 (Unilever/ICI, 1983), was extensively

circulated to both industry and academics. Views on the report were considered by a new organisational structure. In order to provide a central focus for overseeing the research and initiating new proposals, the SERC, AFRC and DTI established in 1984 a study group. The study group identified three key areas where there existed a need for better co-ordination of existing activities and stimulation of further research. The areas identified were:

- tuning and use of seeds in plant genetic manipulation;
- molecular biology/biochemistry and seed development/composition;
- pathogenicity and symbiosis.

Steering groups were then set up in each of the three research areas; each group identified UK research expertise in the area and the main problems which required further research and requested research proposals be submitted. As a result of this effort many research proposals were received. The steering groups then made their recommendations for funding to the Directorate, expecting that they would be processed in the normal way. In the event a major obstacle appeared, the Biotechnology Directorate of the SERC, acting alone, did not have sufficient funds to support the programme. It had hoped for contributions from AFRC, the DTI and the Biological Science Committee of the SERC. The AFRC backed down and the DTI was uncertain about its participation.

At this point, Dr Ed Dart, from ICI (also Chairman of the Biotechnology Directorate Management Committee and later head of ICIs seed division) approached the DTI to see if they were interested in funding proposals being put forward in the first steering group (on vectors) in which there was a good deal of industrial interest (a necessary factor for DTI funding). The Biotechnology Directorate was not involved in any of these discussions and were " rather surprised" when the DTI took over the project to create the Plant Gene Tool Kit consortium, (Seneker and Sharp, 1988).

Although much of the work in designing a research programme on vectors had already been done under the auspices of the original AFRC/SERC/DTI Study Group, one of the industrial secondees to the DTI Biotechnology Unit (Mr Keith Cowey), sought ideas from academic scientists for research in the area of the genetic manipulation of crop plants. Professor Donald Boulter, of the Department of Botany University of Durham, put up the original ideas that, about a year later, and after "much discussion and revision", emerged as the Plant Gene Tool Kit (PGTK) Consortium, (Levi, personal communication, 1986).

8.6 The objectives of the PGTK consortium

The aims of the original joint Research Council plant science initiative were broader than the objectives set for the PGTK Consortium, based on a much narrower research programme. The cooperative focus of the consortium was on research that was defined as pre-competitive and the research programme itself was confidential. The consortium brought together several potential competitive companies and public sector universities and research institutes. The involvement of the DTI as one of the funding sources and organisers, indicated that this programme was nearer the market than the cooperative programmes such as the SERC/industry protein engineering club was; there was an area of academic research that was sufficiently relevant to industry to justify the involvement of DTI funds, thereby blurring the basic/applied dichotomy of the research funding mechanism.

The "tool kit"- the end product of this programme - was a gene transfer technology that would enable the consortium members to identify and isolate and transfer particular genes in a plants, e.g. those that control desirable characteristics.

The examination of the circulation and amendments of research prospectuses can provide a useful insight into the negotiated process of how research proposals develop as a result of the varying interests of those involved in

a cooperative enterprise. However because of confidentiality (once again giving rise to the view that

this work is much more closer to the market than other biotechnology initiatives), the Project Manager was unable to release them for the research of this thesis. However, the programme aims and objectives evolved during discussions over nearly a year, as new prospective members became involved. Each members special interests were taken into account by the academics and DTI staff in "massaging" the research proposals until a mutually satisfactory programme was agreed by about the end of 1985. At this stage, some eight companies were firmly committed and several others were interested. All were said to "have research capabilities and seeds businesses in the UK and span a wide variety of company size" (Levi, 1986).

8.7 Membership of the PGTK consortium

Due to questions of confidentiality, there was some reluctance on the part of the Programme Manager to identify all of the members of the Consortium, but in total there are 15 academic and industrial organisations. The companies known to be involved include multinationals like Shell, Unilever, Ciba-Geigy but also some start-ups, some of which are US owned, are also said to be involved (Fishlock, 1986). The academic contributors are the two AFRC funded Institutes; the Plant Breeding Institute (divisions which were to remain within AFRC on the privatisation of the National Seed Development Organisation) and the John Innes Institute. The major part of the funding was concentrated in these two establishments, but in addition Warwick and Durham

Universities were engaged on specialised aspects of the work, including targeting of genetic expression to specific organelles.

8.8 The research programme

The main thrust of the research was to attempt to develop methods for the tissue culture, redifferentiation and genetic manipulation of monocotyledous plants, specifically temperate cereals. At the time of the programmes inception no such methods were available, this was in contrast to the situation for dicots. The programme was looking for vectors that would carry genes into crops of particular commercial interest in Europe, wheat, barley, peas and oil seed rape. The research programme can be divided up as follows;

1. The establishment of transformation (vectors) and regeneration systems for wheat, barley, peas, and oil seed rape. This is the largest part of the programme, concentrated at the Plant Breeding Institute, John Innes Institute and Durham University.

2. Plant genetic engineering. This complemented project 1, and was carried out in the same institutions. The research aimed to isolate genes of interest to the sponsors, e.g. genes of genetic systems which control important processes like the storage of energy or the process of photosynthesis. These isolated genes would then be tested to ensure that the isolated

and reconstructed genes can be expressed (replicated) by biotechnology methods. The idea was to use the "gene cassettes" produced by this programme to transform the four crops using the technology developed in Project One.

The focus of the genetic engineering research was primarily on seeds, because it is seeds or grains which are normally harvested. The most important markets centre upon the seed, the package of genetic information that determines a plants agronomic characteristics. The seed is the vehicle for conveying the fruits of genetic engineering to the farmer and thereby realising a profit on the incorporated research.

3. The third research programme, was carried out at Warwick University and the John Innes Institute. The main component was carried out at Warwick University under the direction of Professor John Ellis, who also led one of the Steering Groups set up under the SERC/AFRC/DTI initiative. The research relates closely to project 2, but aims to put the genes more precisely into that part of a plant cell responsible for a particular function e.g. the chloroplast in order to control photosynthesis.

8.9 Organisation and management

The organisation of the PGTK consortium represents a novel structure for a 'club' involving the DTI. Much of the early part of 1986 was taken up with designing and agreeing the proper framework within which this research initiative would function. Solicitors for the DTI were involved in this process and produced a series of development documents entitled the Project Agreement (containing the technical programmes) and the Consortium Agreement. The latter describes the consortium which is not a legally-constituted body, but an ad hoc association of eleven members, four institutes and the DTI, coming together for the specific purpose of the PGTK consortium. Up to this point discussions had been technical but legal and patents experts then had to became involved. Finally, agreements were despatched in April and returned, signed, by mid June, to the DTI. Recruitment to the agreed plan then began. It was completed by early Autumn and the last of nearly 50, three-year contract employees were taking up their places at four institutes. In the UK the consortium gave the company members access to up to 70 % of the UK's academic expertise in plant biotechnology (Fishlock, 1986).

A distinctive feature of the DTI sponsored programme (not retained in future DTI collaborative arrangements) is the active participation of a Programme Manager. Co-ordination of the PGTK Consortium is the responsibility of the Programme Manager, Dr R. Levi. In the event these duties were performed by Dr Levi and his wife trading as Polmont Partnership. They reported to the Management Committee, comprising of a nominee from each

of the eleven member companies and a DTI representative. This Committee met quarterly to receive reports from the research leaders (who were senior permanent staff of the Institutes) and from managers. There was a launch symposium in April 1986, and the first round of company visits to the Institutes were completed in December 1986.

One of the Programme Managers main functions was to act as "honest broker" between the academic whose priority is publication, and the industrialist whose need is for proprietary protection of any useful information. The "mainly industrial" background of the Programme Manager and the provision for rewards to inventors were considered to be aids in the resolution of any creative tension that may be generated. Dr Levi, at the early stage of the PGTK Consortium, stated that " At present there is a great deal of goodwill on both sides to make the Consortium succeed and this must be maintained throughout the 3 years of the programme".

8.10 Intellectual Property Rights (IPR)

Property rights are critical issues to the industrial participation, and also are a source of possible conflict with academic imperatives. Property rights in the PGTK consortium are assigned to the consortium, for which one of the members will act. All members have equal rights to any patents and properties (e.g. gene cassettes) generated but can opt out if they wish. Property can also be licensed to third parties.

8.11 Consortium funding

Each company member contributes approximately £50,000 per year, the Government then matches the contribution. This gives each member access to a three year, £3 million programme for its subscription.

Budgets were enshrined in the agreements and the Institutes send the Project Manager quarterly invoices of their actual spend. Polmont Partnership then claim this, management fees and other expenses (e.g. auditor, symposium) from the DTI (50%) and the members (one eleventh of 50% each) and pay the Institutes invoices from moneys received. The Programme Manager, Dr Levi speaking in 1986 stated:

> We have just completed the first round and it seems that workable systems are being evolved to complement the framework provided by the agreements (Levi, 1986).

8.12 Implications for science policy

Plant biotechnology was originally financed from within the public science funding structure, notably through the AFRC and the SERC. Realising the commercial possibilities of tools/techniques that were being generated within this research infrastructure, and to cover the whole range of possible applications a joint research council programme was proposed.

Despite the encouragement of the IRCCCOB, a joint Research Council grouping designed to co-ordinate the

research in biotechnology, the science budget was unable to accommodate the original and more ambitious programme to exploit the 'area of plant science'. At this point plant science and plant biotechnology had been identified both by academics and industry as important both scientifically and commercially yet funds could not be found to support a comprehensive and coordinated programme in the area. These arguments were to do with larger arguments regarding science funding in general. Because of this lack of funding the DTI appropriated the enabling technology part of the programme and managed through its catalytic investment (pump priming) to attract eleven corporate sponsors; the largest for any biotechnology club arrangement.

The more applied and short term programme was able to attract more corporate contributions than any of the SERC biotechnology clubs. Essentially that part of the programme that could be linked to the market place or in the short term, was effectively 'spun - off'; transposed into a new mechanism to be exploited.

This does not mean that all companies are primarily interested in short term applied research. The original plant science initiative was largely based on the recommendations for a fundamental research programme set out by Unilever and ICI, both of whom have large R & D operations, (Unilever and ICI, 1983).

Their report presented an insight into the research requirements of such large and R & D intensive firms.

The programme they recommended sought to identify research areas in plant science where lack of basic understanding was limiting the development of technology. The reports intention was to indicate the areas of fundamental research required to allow further development and commercial application of plant biotechnology. It outlined some of the principle areas of commercial exploitation of fundamental plant science. Their further development was seen as being dependent upon a move forward from present base of physiological correlations into a much deeper understanding of the detailed molecular events involved in the genetic control of metabolic processes. The common ground in all the applications was the need for deeper understanding at the molecular level of the processes by which plants control their development and interact with their environment. The report went on to say;

> Relevant University research will provide the essential understanding of genetic, biochemical and physiological systems. Relevance does not consist of doing pseudo product development on a popular crop, (Unilever and ICI, 1983).

When funding for this programme was not forthcoming the balance of research changed to a focus on enabling technology of the PGTK.

The Plant Gene Tool Kit Consortium, in terms of UK science and technology policy, indicated a significant

change in Government policy towards science based technological innovation. It served as a prototype for an initiative that later became known as LINK (FT. 1988). It represented a qualitative break with the DTIs previous experiments with industrial 'clubs', which were essentially informational (DTI, 1988), to one where areas of research, carried out at universities and research institutes, can be supported through DTI and corporate funds.

8.13 Peer review

In appropriating part of a programme originally instigated by the Research Councils, the PGTK consortium has had some effects on the academic research community and has highlighted some of the tensions involved in academic-industrial collaboration. By effectively taking it out of the Research Council apparatus, the programme had been taken out of the normal peer review grant process; viewed by the scientific community as the ultimate arbiter of scientific quality (one which, despite the claims of its critics, the biotechnology directorate was strict to adhere to, see Seneker & Sharp, 1988). This has resulted in questions being asked, within the scientific community, about its ability to do first rate science.

The Programme Manager of the consortium has emphasised the importance of the quality of science:

> Present indications are that all parties should obtain good value for the expenditure

> of £3 million on this exciting area of biotechnology over the next 3 years, but this will depend critically on good creative science (Levi, 1986).

The policy question is whether good creative science can be maintained. The process of negotiation itself, with member firms, altered the original research programme. It may have shifted the research to shorter term, less fundamental objectives.

The DTI does not operate a peer review system for allocating grants, but decided to place its research funds into established centres of excellence; the John Innes Institute; Plant Breeding Institute; Warwick and Durham University. The academic composition of PGTK Consortium thus reflected industry's preference in the selection of groups. The original programme had succeeded in attracting proposals from many centres; many from 'New Blood' posts and other young unknown researchers, bringing new people into the area, an area concerned about the shortage of talent. When the original programme folded in disarray a lot of scientists who were prepared to enter the field found themselves unable to do so. This may well have detrimental effects in the longer term. The other effect, of placing grants exclusively in established centres may also have the effect of excluding other novel avenues of research.

The collapse of the original programme and the establishment of the PGTK consortium had a significant impact on the behaviour of the Research Councils in their approach to the support of plant science. The AFRC,

throughout the early 1980s, was undergoing restructuring and although it had a lot of expertise in the area was subject to cuts. The AFRC Corporate Plan for 1986 stated that its scientists had "a greater variety of exceedingly powerful research techniques than they ever had" (AFRC, 1986). Its problem was developing them as the governments spending on agricultural research was declining. Although the AFRC did not fund the consortium, AFRC institutes were involved, this was despite the fact that the AFRC had already established a vessel for commercialising its novel biotechnology innovations through its 'country cousin' technology translation company, Agricultural Genetics company.

It was reported at the time that the ARC was very much in favour of establishing a company like Celltech, as they recognised it as being providing an opportunity for an easy and financially beneficial way for the ARC to channel its discoveries of commercial potential in the domain of plant breeding, which at that time it did not have. At that time new strains of plant were developed by conventional techniques within ARC institutes, had to be given to the National Seed Development Organisation which then donated its profits to the Treasury. For discoveries involving novel methods, such as gene cloning and transfer, in improving plant varieties there existed no outlet from the ARC and therefore a company along the lines of Celltech would have suited them.

Despite the worries over the possibly long lead times the company Agricultural Genetics Company (AGC) was set up in

July 1983. Interestingly (unlike Celltech) the details of the companies contract with the ARC has not been disclosed, but the AGC will have exclusive rights to exploit ARC supported innovations in non-conventional plant breeding. Under the ARCs own definition of biotechnology, the AGC would appear to have had access to most of the research carried out under this description, including microbial innoculants and biological control products. In return for giving these rights the ARC will receive a royalty.

Within the SERC Biotechnology Directorate policy toward this area became confused. The whole question was aired at its 1985 Policy Meeting. Plant Cell Culture was removed from its priority area status - although this was not a unanimous decision. The industrial members took a short term view; that plant cell culture as a method for producing secondary metabolites could not economically out-compete traditional extractive methods, the academic members took a longer term view. At this point the industrial view prevailed. The whole issue of SERC support for 'Whole Plant Biotechnology' was further confused because of PGTK Consortium and the plethora of funding agencies supporting this sector which made it unclear what the Directorates role should be:

> There is substantial investment in both AFRC and DTI/PGTK programme in molecular biology of plant genetic manipulation and the regeneration of manipulated plant tissue to whole plants (SERC, 1985)".

The academics were arguing that these activities do not provide fundamental plant biochemistry and molecular biology which helps define the key genes that need to be manipulated. They pointed out that in the UK, no centre of plant cell biochemistry could be found. The academics pointed out that this was a crucial area of research on which much future work on plant biotechnology depended. They also argued that there was a global lack of knowledge on the control of metabolic pathways.

The EEC in its evaluation of the EC funded Biotechnology Applications programme (BAP), which funded some work in basic plant biotechnology reached these conclusions:

> It has become apparent world-wide that the bottleneck to progress lies less in the absence of adequate application technologies and more in large gaps in our basic understanding of key structures and functions within plants. European biotechnology has now reached a stage where the ability to manipulate plant genes has outstripped the knowledge of many underlying biological functions and metabolic properties.

> In order to make significant advances in biotechnology it is therefore essential to go back to the investigation of plant physiology, using all the new tools developed for molecular investigation. If major efforts are made now,(1988) it may be possible within 5-10 years to identify, for example, the 'quality molecules of many plants.
>
> Genetic and molecular techniques have attracted attention, they have become particularly precise and powerful, but they still can be applied only to the emerged side of the iceberg which represents living matter. The hidden principles regulating plant functions and metabolism now need to be elucidated, before useful work can proceed

> at a scale of macro-economic significance. Know-how has outstripped knowledge, so that technology will be limited in scope until technology has served the purpose of producing the necessary understanding of agricultural objects; what could also be called "new plant physiology". At present, the developed skills must be used for asking the fundamental questions of plant physiology, before meaningful applications can be further devised" (EC, 1987).

The PGTK consortium was seen by some in the academic community as being too applied, concentrating on 'gene jockeying' rather than on the fundamentals underlying such developments. These same criticisms were extended to the work carried out in AFRC; its scientists followed the molecular genetics route to plant research and lacked basic expertise in protein chemistry.

8.14 Plant science post-PGTK

The original joint Research Council programme illustrated the difficulties of creating and co-ordinating an organisational framework for developing a fundamental area of science underpinning a generic technology. In the event a short term 'enabling technology' route was taken. This approach has now changed, and the value of some of the more fundamental studies (envisaged as part of the original programme) are now being understood by industry. In April 1988, SERC launched its Plant Science Initiative. This new initiative plans to involve SERC, the DTI and a number of agrochemical and seed firms jointly to sponsor a coordinated research programme in the control of plant metabolism. It is aimed at

increasing the understanding of the basic molecular and biochemical mechanisms that control metabolic processes in plants. Such knowledge is vital for the logical design of new and improved agrochemicals such as herbicides and growth regulators and will be required before the genetic engineering of plants for such features as pest resistance and cold hardiness becomes a useful and commercially viable reality.

The SERCs Biotechnology Directorate and the Biological Sciences Committee identified a number of priority topics for a support after extensive consultation with industry. The priority areas are given below;

- pathways for the conversion of the products of primary assimilation, sucrose and glutamate to storage products of primary economic importance such as starch, lipid and protein;

- pathways of intermediary metabolism such as those involved in amino acid biosynthesis;
- the biochemistry of various aspects of plant development, particularly associated with growth and reproductive development, for example in flowering and pollen biology.

A call for proposals inviting research in this area was issued late in 1988, at which time it was hoped that sufficient funds might be raised to support a number of substantial academic research centres in Plant Science,

"possibly under the LINK scheme" (SERC, 1988). The PGTK Consortium is widely thought to be the precursor of the DTI LINK scheme and SERC had already earmarked funds to pump prime the initiative and discussions were underway to try to get AFRC involvement.

There are also discussions underway to try and set up a PGTK 2. This has some appeal for the small company members of the original consortium, who feel that the plant metabolism LINK programme is 'too general' for their needs.

CHAPTER NINE : The Animal Cell Culture Programme

9.1 Introduction

The main characteristics of the programme can be summarised as follows:

* It involves higher education institutions and industry;
* The focus is 'strategic research' into fundamental aspects of mammalian cell physiology and biochemistry;
* It is a four year coordinated multidisciplinary programme designed to promote further research and training in academic institution in the area of science;
* The corporate members represent the main commercial expertise in the field. They all have experience of animal cell culture.

9.2 Animal cell culture technology

Animal Cell culture technology is now playing an increasingly important role in the biotechnology industry. Its two main areas of application are in the manufacture of monoclonal antibodies (MAbs) and as an expression system for recombinant DNA (rDNA) proteins used for human therapy. Until recently, the main effort in cell culture for the purpose of expressing human and animal proteins, has centred on prokaryote hosts such as the bacterium E. Coli. It has now been realised that the

human and animal proteins expressed from such procaryotes are frequently in an insoluble

and denatured form. They require subsequent tedious and expensive procedures to make them soluble and active. For these reasons, greater interest is now being shown in mammalian cell culture.

Animal cells can offer important advantages over both yeast and bacteria for the expression of heterologous genes. These include post-translational modification of proteins (such as glycolysation, phosphorylation or proteolytic cleavage) and correct folding of the polypeptide including the formation of quaternary structures. Proteins without the correct secondary modifications may lack biological activity or they may be unsuitable for use as vaccines, due to differences in conformation compared with the native protein. Molecules intended for therapeutic use may elicit undesirable immune responses, due to inappropriate amino acid additions. Incorrectly folded proteins may be insoluble, and therefore not secreted and difficult to recover.

Despite these advantages, there are also a number of limitations to the use of mammalian cell cultures. It is considerably more expensive than microbial fermentation, due to much slower growth rates of animal cells, there is a lower final biomass concentration, and it requires more expensive and complex culture media. Another limitation is the shortage of suitable cell lines; either types which produce a useful natural cell protein or lines

which efficiently express genes introduced into the cell by gene transfer techniques.

The aim of the animal cell culture programme is to provide information on certain aspects of animal cell physiology and genetics which may be used by industry to develop more efficient processes for the manufacture of recombinant DNA products and monoclonal antibodies. In the latter case, the market for monoclonal antibodies is already established but in order to remain competitive there is a need for greater efficiency in their production. This bottleneck in productive efficiency is seen as one requiring additional basic research into animal cell culture.

Several studies (Institute of Manpower Studies, IMS, 1987) have indicated that there may be another bottleneck to the expanded industrial use of animal cell culture techniques. They have identified a shortage of skills in this area, so this programme also has an explicit training purpose.

9.3 Markets

It is widely agreed that for the next 30 years or so a number of human proteins produced in cell culture will be important in the treatment of life-threatening conditions (SERC, 1988). Animal cell culture is a production technique or enabling technology that could be utilised

to produce a wide range of protein products. Some idea of the range and markets is given in table 9.1.

TABLE 9.1 PROMISING THERAPEUTICS

Source: Robert Kupor, Cable Howse & Ragen

Ref: International Biotechnology Handbook. 1988

9.4 Background to the establishment of the programme

Table 9.2 Animal Cell Culture Research Programme timetable

February 1985	Round table meeting
July 1985	Programm Definition Group established
November 1985	Call for proposals
October 1986	Official Launch of programme
Early 1987	Appointment of Programme Manager

Before the establishment of the programme the SERC biotechnology Directorate had identified the field of animal cell culture as a priority sector. From June 1982 the work on animal cell culture was concentrated on the large scale culture of animal cells. It supported two major groups at the Universities of Birmingham and Surrey. The Directorate's largest commitment to the field was a grant of £125,655 at Birmingham which was carrying out research on the scaling-up of hybridoma cell growth and the improvement of antibody production. This research was being done in collaboration with Unilever Research via a SERC cooperative research grant (see Chapter six). A team of chemical engineers at Birmingham were also investigating how to improve the growth of hybridomas in suspension culture for monoclonal antibody production.

The joint development work with Unilever had enabled simple reproducible production of monoclonal antibodies at scales up to 30 litres. The Birmingham group has continued to direct its research effort towards improving yields of antibodies from their expensive raw materials bringing the concentration of antibodies closer to those obtained by in vivo methods using mice (SERC, 1984). The Directorate efforts in animal cell research had, up to 1985, been largely confined to these studies associated with the large scale growth of animal cells. It was with a view to ascertaining what further research in this area could benefit UK industry that talks with a number of companies were held during 1985.

Animal cell culture was the subject of a SERC Biotechnology Directorate 'Round Table' held in February 1985. These were discussion meetings where the Directorate invited academics to talk about what they were doing, to an audience of industrialists. The industrialists were then asked to respond by saying what they thought the academics should be doing that would meet their interests. This Round Table meeting was somewhat unusual as the subject set for discussion concentrated on the scale up of animal cell culture but in fact led to a programme on the physiology and genetics of animal cells in culture.

The Directorate discovered at this meeting that the industry representatives were not at all interested in

the scaling up work they suggested; they were more excited by the prospect of research in the basic physiology of animal cells in culture. This episode

illustrated the important effect industrialists had on the development of research programmes within the Directorate structure. Discussions held with a number of companies on the possible formation of a club in this area led in July 1985 to a 'Club' programme meeting (chaired by Dr John Birch of Celltech). A Programme Definition group composed mostly of industrialists but also including some independent academics was established. This group was responsible for defining more closely research objectives and for drawing up a call for proposals. A half page advert was issued in the journal Nature in February 1986, calling for research proposals. The call for proposal document, dated November 1985, was also circulated widely in academic circles.

9.5 The objectives of the programme

The club programme was established to improve the understanding of the physiology of animal cells in culture to underpin the design of more efficient industrial processes. The Programme Definition group outlined their strategy and research objectives in the following terms:

> The intention is to concentrate funding on a small range of cell types of interest to industry, thus the main emphasis of the programme will be on hybridomas, chinese

hamster ovary cells and other cells possessing potential for the expression of rDNA proteins in suspension culture, (SERC, 1986).

The proposed areas for study were;

a) factors limiting maximum population density of cells in culture;

b) energetics of cell growth;

c) physiology of product formation;

d) manipulation of cell phenotype to improve characteristics;

e) studies on immortalisation of cell lines;

f) comparison of cell types;

g) development of novel expression systems. (SERC,1985)

9.6 Funding and structure of the programme

Following its 'call for proposals' 27 applications were received from higher education institutions. The Programme Definition group were able to select five which met the aims of the programme and, where they felt there would be particular benefit in collaboration. The agreed details were released in October 1986 in a document entitled 'A Co-ordinated programme: Animal Cell Biotechnology', (SERC, 1986). The Programme was finally set up in early 1987 on the basis outlined in figure 9.1.

Fig 9.1 Shared Cost Programme

SERC Biotechnology Directorate	Beecham Glaxo Celltech Wellcome Foundation Porton International
50%	50%

The industry contribution was on the same basis as the SERC Cooperative Research Grants scheme, i.e. 50% of the funding. The five research projects were to be carried out in five higher education institutions, four studentships for training were also awarded.

The original call for proposals projected the size of the programme to be of the order of £1 million over four year period, commencing in 1986, and would concentrate support to two or three, multi-disciplinary teams for research. Research eventually got underway in June 1987, and it was distributed in five centres. The details are

listed in the table 9.3 below.

Table 9.3. Programme funding

Five companies each contributing £25,000 per year over four years:	£500,000.
Biotechnology Directorate:	£520,000.
Total:	£1,020,000

9.7 Coordination of the programme

The programmes is funded by contributions from the participating companies and the SERCs Biotechnology Directorate. A Programme Manager was appointed, Dr John Clegg (ex Wellcome Foundation). His role involved coordinating the activities of the academic research groups involved and ensuring that effective interaction with the sponsoring companies takes place. The Programme Manager reports to a Steering Group, comprising of representatives of the participating companies and the Council which supervises the implementation and further development of the programme. The Steering Group holds meetings every six months, or more frequently if required, in order to receive reports on the past progress and the future developments of the programme. The Steering Group advises the academics on future developments via the Programme Manager. As with the other club initiatives it is pointed out that it is likely that the funding of projects under the programme will require the acceptance by the Institutions involved, of special conditions to reflect the industrial

participation in the Programme. These consist of the following basic elements:

- regular progress reports to participating companies;

- some delay in publication following disclosure of results to companies;

- advantageous access by participating Companies to results capable of commercial exploitation.

9.8 Industrial membership

From the above figure 9.1 it can be seen that the programme successfully attracted five industrial members. Although they all come from the health-care sector, they are not directly competing concerns. The animal cell culture technology is generic and can be used to produce many types of products.

Porton International, has a focus on health care, vaccines and human proteins. Beecham, although originally focused on antibiotics is diversifying and is trying to develop its own mammalian cell culture system. The company considers that it will need one if it is to make any headway in producing from cells the glycoproteins that form a major part of the human body chemistry:

> If you look at the proteins of value in the clinic, the majority are glycoproteins. Since the carbohydrate won't be expressed in bacteria, we probably have got to go to a mammalian cell, which is why we are trying to acquire these cell culture skills, (Bryan, 1984).

Celltech is Europe's leading biotechnology company and as a group employs over 400 people. It has expertise in both recombinant DNA and hybridoma technology, and leads the world in large-scale mammalian cell culture. It also played a major part in setting up this programme. The Wellcome Foundation also has expertise in deep cell culture for manufacturing therapeutic proteins. Wellcome also has licensing agreement with companies that have cloned genes for products but need the firms deep cell culture expertise to develop them.

From this brief examination of the member firms it can be seen that the Club has attracted the involvement of all of the major UK firms which have expertise in this field. The one exception is Unilever Research, who had worked on the scale up of animal cells through a Cooperative Research Grant. My own survey indicates only a modest interest in this area of animal cell culture, so it would seem that the majority of those UK companies interested int his area are represented in the programme.

9.9 The analysis

9.9.1 The establishment of a focused fundamental research programme

The development of the animal cell culture programme is an interesting one in that it shows the influential role played by industry in the definition of the programmes technical targets. This programme was thought unusual even by those involved, (Lex, 1986), in that a meeting

was called to discuss a possible further extension into an applied area of enabling technology; the scaling up of animal cell growth. However, this was rebuffed by the companies present, who turned it back on the Directorate asking them to focus on research further 'upstream' from the market place. A collaborative programme on the more applied 'near market' research was felt to be incompatible with the club concept. This industrial view was in accordance with the club concept as articulated by the Head of the Directorate, Geoff Potter:

> Clubs are concerned with pre-competitive research and do not replace the Cooperative Research Grants where normally single companies collaborate with the Directorate to fund research that is often more applied in nature... Clubs therefore support enabling research. A natural progression is seen from research supported on a club basis through to one-to-one arrangements between companies and academic departments which lead to company in-house applied research and development, (Potter, SERC, 1987).

In the case of the animal cell culture 'club', industry can be seen to have directed the SERC Directorate upstream, into funding longer term fundamental studies. This puts the animal cell culture programme further away from the market than the antibiotic or plant gene programmes. It shares with the protein engineering programme a four, rather than three year programme, and because of its fundamental and long term nature, it cannot attract Department of Trade and Industry funding. The difference with the antibiotic programme is

emphasised in the antibiotic programme definition, (see Chapter ten):

> Whilst bioactive products might be made by animal or plant cells in culture it is probable that only the recombinant DNA technology of microorganisms is as yet at the stage where we can apply it widely. Recombinant DNA work on the secondary products of the higher eukaryote cells in culture should still be on the techniques rather than their widespread applications." (SERC 1985)

9.9.2 The relationship with the Medical Research Council (MRC)

The issue, however is not just one of moving the research upstream from being applied to being more fundamental, there is also the question of the area of study itself. This shift has started to blur the traditional lines of demarcation between the research responsibilities of the different Research Councils. In particular animal cell culture was considered to be the 'territory' of the MRC, particularly in respect of its major contribution to hybridoma technology. So what is surprising some researchers, is that SERC are active in this area at all.

It was reported in 1986 that the initiative had been discussed with the MRC (SERC, 1986, and IRCCCOB, 1986), but it appears that the MRC were very opposed to this

initiative because they considered that in entering this area, the Directorate had not taken account of the MRCs work. The dispute reportedly, delayed the establishment of the club for about a year. The club concept was established at the first Round Table discussion of 1985. The second one led to the creation of another club on recombinant DNA and Antibiotics, which actually became operational before the animal cell club. Dr Maurice Lex suggests that other factors may have also contributed to this delay, "Throughout all these deliberations, considerable effort was expended in attracting additional companies to join the Club. Even more time and effort has been put into reaching Agreements between the companies and SERC on exploitation, confidentiality, management of the programme etc", (Lex,1986).

The Directorate had run into 'territorial' problems with the Medical Research Council before with the setting up of its Protein Engineering Club (see Chapter seven). In the SERC report of the Biotechnology Review Panel of 1986, they outlined possible reasons for the inter-research council antagonism. In a review of the 'Club' concept the panel draw attention to the fact that:

> ...doubt has been expressed about this mechanism for conveying technology transfer from basic research to industrial development. Views for the MRC, especially, were strongly in favour of concentration on underpinning research which would lead to bilateral arrangements with individual companies for development in promising areas, (SERC, 1986).

The club mechanism represented a completely different approach to relations with industry than that of the MRC. It wanted to focus on basic research and if anything of commercial interest emerged it could be taken forward via bilateral relations, a concept already put into practice with the establishment of Celltech. Celltech struck a deal with MRC giving it first refusal to all of its research in the new biotechnologies such as genetic engineering and monoclonal antibodies. This exclusive relationship was curtailed in 1984 but Celltech firmly established the principle that an entrepreneurial venture could "exploit" a research centre successfully for commercial ideas. The Club mechanism, on the other hand, allowed industry to come in at a much earlier stage and help set the research agenda, ensuring a smooth technology transfer by ensuring that a field of interest was being worked on.

It has been suggested that the reason SERC seems to have found itself moving more into the research territory of other Research Councils is because it is being driven by the research interests of the firms that tend to dominate its management committees and clubs. Most of these tend to come from the health care sector and so tend to direct research to their area of interest. The assumption is that companies are keen to do this because they are allowed to direct research to a much greater level through the Directorate structures than they can with the Institutes of the MRC such as the Laboratory of Molecular Biology.

The animal cell programme would appear to give some substance to these views (see Seneker and Sharp, 1988). From the MRCs perspective the original SERC programme of research on the scale up of cell culture, the more applied engineering aspects necessary to turn cell culture into an industrial scale process, was well within the SERCs remit. Within the present programme, the industrial partners have established research further upstream in fundamental cell genetics and physiology which comes into the sphere of the MRCs basic underpinning activities. If the SERC had not entered the area it would seem that the health care companies would have to monitor the MRCs peer reviewed research and if promising research did happen to emerge from this basic science, they would individually, have had to approach the MRC.

9.9.3 Restructuring

It was stressed by the Programme Definition group that there was a strong feeling that in order to make progress in this area the problems should be tackled by multidisciplinary research groups possessing expertise in both physiology, genetics and biochemistry. Where such expertise was not already available within existing research groups, encouragement was to be given to develop collaborations between groups with complementary

expertise either within the same academic institution or within institutions elsewhere. This small number of multidisciplinary research teams would then carry out research in the areas identified by discussions with a number of companies.

The programme has succeeded in establishing a number of centres, bringing together the mixture of disciplines deemed necessary to progress work with this particular technology. The success of this is pointed out in the Biotechnology Review Panel Report 1988:

> The programme has been running for 18 months and is providing useful insight into various aspects of cell physiology. It has proved particularly valuable to involve groups whose previous experience was in microbial physiology and biochemistry, (SERC, 1988).

This phenomenon may bear further research in terms of the development of technological (or applied) science in response to external needs or demands.

It has been reported recently that a sixth company, ICI Pharmaceuticals Division has joined the club, (SERC, 1989).

CHAPTER TEN: A Coordinated Programme: Antibiotics and Recombinant DNA

10.1 Introduction

This co-ordinated programme represents a further development of the SERC Biotechnology Directorate club mechanism. The programme shares a number of common features with the other clubs, but also possesses additional, more distinctive features. The main features are as follows;

- Involvement of Higher Education Institutions (HEIs) and industry;
- A focus on pre-competitive research;
- A three year programme consisting of a series of individual projects.

Its more distinctive features include;

- The involvement of the Department of Trade and Industry (DTI) in its funding;

- The relationship with other Research Councils in particular the Agricultural Food Research Council (AFRC);

- The integration of existing research strands into a coherent industrially oriented programme together with the promotion of new projects;

- The integration into a cooperative research programme of the major UK pharmaceutical companies.

Prior to the formation of this club mechanism, antibiotics had already been the subject of technology transfer arrangements, notably through the activities of the British Technology Group (BTG, 1986). The club programme offers a new alternative to that route, and although it can be seen to evolve from previous organisational experiments (e.g. protein engineering), this club is significant in that it is a precursor to the DTIs LINK initiative (DTI, 1988).

10.2 The commercial importance of antibiotics

Part of the significance of this programme is that it provides a much clearer route to commercial targets than the other club programmes in biotechnology. This is because the initial impact of the programme is seen to be on improving the production of existing antibiotics. Products which have an established market. This is an area, therefore, where uncertainty may be significantly reduced (Freeman, 1974).

The worldwide pharmaceutical business is projected to pass $70 billion by the mid-1990s. Currently, antibiotics compose around 12% of that market (SERC, 1988). The world market for antibiotics is therefore already large and is expected to grow still further.

Antimicrobial agents for the treatment of infectious diseases have been the largest selling prescription pharmaceuticals in the world for the past three decades and it is believed that they will continue to form a significant sector for drug discovery and development, (ECN, 1989). More than 5000 different antibiotics have been isolated from cultures of fungi and bacteria. About 100 of these are used to treat human, animal, and plant diseases. Microorganisms of the species Streptomycetes are responsible for the formation of more than 60% of the 5000 known antibiotics; an additional 15% are made by members of the related actinomycetes species (Martin and Gill, 1984). The Actinomycetes, and more specifically the genus Streptomycetes, also produce a large variety of other industrially important secondary metabolites such as anticancer and anti-viral agents, antiparasites, coccidiostaties and animal husbandry products. These 'bioactives' present an opportunity for an increase in the contribution of micobial products to the overall health care market.

10.3 Technical aims of the programme

Clearly the antibiotic business is well established, it was initially dependent on academic research in the development of penicillin and cephalosporins, (Abraham, 1982). The UK pharmaceutical industry has developed a world lead in antibiotics largely through its own in-house research. This programme signifies a return to academic-industrial collaboration as the new techniques

of recombinant DNA, that have emerged from university science, may have an important role to play in future antibiotic innovation.

The survey results outlined in Chapter five, indicate a widespread interest in both recombinant DNA technology, and collaboration with higher education institutions, among the health care sector, some of which are antibiotic producers. This programme can be seen as linking (or horizontally transferring) those general 'genetic engineering' techniques to underpinning specific commercial programmes.

The reason for corporate interest in a programme on applying recombinant technology to antibiotic production, lies in the fact that despite their obvious commercial importance, the basic physiology and biochemistry of the industry's two major organisms, streptomycetes and filamentous fungi, is only poorly understood. At present there is no rigorous model to explain why these soil microorganisms make secondary metabolites. While knowledge of molecular details in metabolism have made some difference, not a single antibiotic has had its complex biosynthetic pathway elucidated. This is partly because there is no single gene that can be isolated to produce an antibiotic. It still remains to identify the cellular control signals which switch on production, and to understand how the pathways are controlled.

With the application of recombinant DNA technology to bacterial systems (e.g. E.Coli) there has been a very rapid increase in the understanding of gene expression and regulation. The initial exploitation of this knowledge has been the promotion of heterologous gene expression in these organisms (eg the production of human insulin in E.Coli). The application of rDNA technology to the antibiotic producing organisms should greatly facilitate the understanding of both primary and secondary metabolism and, furthermore, may give some insight into the factors required during metabolic switching. Such information would provide the enabling technology to be applied to the manipulation of these organisms for the overproduction of useful secondary metabolites. One of the major applications of recombinant DNA technology is expected to be the improvement of pre-existing strains of commercially important microorganisms.

Although in the shorter term it is unlikely that recombinant DNA technology will lead to entirely new antibiotics, it is virtually certain that improved strains of micro-organisms will be evolved which will both improve the production yields of existing antibiotics and lead to the industrial production of several known antibiotics which cannot at present be produced economically. In the longer term need for novel antibiotics is, however, certain since bacteria gradually become resistant to the effects of those to which they are exposed routinely, (ECN, 1989).

10.4 Development of the antibiotic the programme

Table 10.1 Antibiotics and recombinant DNA programme timetable

July 1985	Round table meeting
August 1985	Programme Definition Meeting
October 1985	Call for proposals
October 1986	Launch of programme
November 1986	Appointment of Programme Manager

From the chronology outlined in table 10.1, it can be seen that the origins of the current programme can be found in the Round Table discussion of July 1985, held by the SERC Biotechnology Directorate. The meeting held in July 1985 on antibiotic production succeeded in catalysing such interaction and led to the formation of this club programme. It was felt that the UK had a significant centre of excellence in recombinant DNA (rDNA) technology and antibiotics at the John Innes Institute, which came under the auspices of the AFRC (and whose commercialisation routes seemed to be well established through the BTG). Additionally, individual projects had been funded by the directorate in this area, under its Host-Vector priority scheme, which evolved out of the more general rDNA priority sector (SERC, 1984). The Host Vector sector supported a number of projects aimed at developing a range of specific and novel host-vector systems including bacteria, yeasts, filamentous fungi and animal cells. The work carried out on yeast will continue under the auspices of the LINK programme on Eukaryotic Genetic Engineering Programme,

(DTI, 1988).

The relevant expert (Professor David Hopwood from the AFRC institute) participated in the Round Table and acted (in an extraordinary inter-council cooperative gesture) as an adviser to the Directorate in subsequent developments connected with the programme. The general industrial bias in the setting up of the programme is indicated by the fact that only one academic spoke at the meeting, and that the companies present immediately asked that a coordinated programme should be set up:

> Following the Round Table discussions on Antibiotics production, there was a large response from both academics and industrialists urging us to launch a coordinated programme on the physiology/biochemistry of filamentous microorganisms that would complement the world lead on the genetics which had been obtained by David Hopwood and his group at the John Innes Institute, (Dr Maurice Lex, 1986).

It was agreed that the programme should concentrate on two consensus organisms and involve two to four centres. The companies together with one or two academics were asked to develop a Programme Definition, which was followed by an advertisement in Nature requesting research proposals.

10.5 Programme definition

The programme definition, under the title: The application of rDNA technology to the discovery and production of microbial secondary products, outlined the following aims:

1. The Antibiotics Industry needs patentable new fermentation products;

2. Whilst bioactive products might be made by animal or plant cells in culture it is probable that only the recombinant DNA technology of microorganisms is as yet at the stage where we can apply it widely. rDNA work on the secondary products on the higher eukaryote cells in culture should still be on the techniques rather than their widespread application;

3. We are therefore concerned with the application of rDNA technology to matters bearing on the discovery and production of secondary metabolites made by microrganisms often as multi-gene products;

4. Important secondary products are made by filamentous fungi and actinomycetes so that research should be concentrated mainly on these two types of organism;

5. To take advantage of the background knowledge of genetics and to promote the benefits of a concerted study of a limited number of species, it is anticipated

that most of the work will be carried out in S.Coelicolor or S.lividens and Aspergillus nidulans, (SERC, 1985) .

Approximately 30 academics responded, many with very high quality proposals. Many of these responses came from young scientists in 'New blood' posts and were consequently distributed quite widely across institutions. Because of the high quality the companies decided to support research at 11 universities and polytechnics.

10.6 The Research programme

The research programme, which got underway in October 1986, consisted of two parts;

10.6.1 Programme on streptomycetes

These organism produce a large number of secondary metabolites, including the majority of clinically and agriculturally useful antibiotics, as well as a number of other products of significant industrial value. Whilst considerable progress had been made in recent years in the development of DNA cloning systems to supplement the well established genetics of some of these organisms (an area in which the UK has a recognised lead), studies of the physiology, biochemistry and other aspects of Streptomycetes biology have lagged behind.

The projects in the streptomycetes programme have a central theme running through them; to obtain knowledge of those areas of steptomycete physiology, metabolism and biology that will be required to fully exploit the opportunity presented by the recent developments in gene cloning in these industrially important organisms, an area in which this country has a significant lead. The successful completion of these projects will make a major contribution to the development of this area of science both in industry and in academia. The programme is focusing on more basic biochemistry of the microorganism where host-vector systems have been developed, (by the AFRC John Innes Institute).

10.6.2 The programme on filamentous fungi

The B-Lactams, produced by filamentous fungi, form the single-most commercially important group of antibiotics, such as penicillin. The main objective was to gain a better understanding of the factors associated with the production of these antibiotics. The organism chosen for the study is Aspergillus nidulans. For antibiotic production the organism is not of industrial importance although it does produce penicillin. However, the genetic and biochemical information available for this strain made it an ideal model system. To concentrate on a commercially important organism would inevitably favour whichever company that uses that microorganism for making its commercial antibiotic. The Programme Manager, Dr Iain Hunter concluded that;

an extremely attractive and fully coordinated

> package of grant proposals has been assembled in which a largely physiological/genetic study of the factors involved in the regulation of secondary metabolism is combined with a number of investigations into gene regulation at the molecular level. Furthermore, as rDNA technology in filamentous fungi is very much in its infancy a number of projects have been integrated into the programme that further develop this basic technology thus enabling the studies to progress more rapidly, (SERC, 1988).

The programme can be seen as achieving structural aims by stimulating the development of multidisciplinary groups. The directorate has emphasised that some of the teams have achieved this e.g. the UMIST team combines expertise in physiology, biochemistry, fermentation technology and molecular biology, while at Glasgow: physiology, enzymology and molecular biology are collaborating. This seems to be a common feature of the new cooperative structures, it is not just a matter of encouraging cooperation between industry and the universities, but also the formation of new groupings between academic disciplines.

10.7 Organisation: structure and mechanisms

The organisation and management of the programme follows the plan set out for Protein Engineering Club (see chapter 7). The programme was funded by contributions from the participating companies, the Department of Trade and Industry and the SERCs Biotechnology Directorate and Biological Sciences Committee.

A Programme Manager, Dr Iain Hunter of Glasgow University (ex Pfizer), was appointed in November 1986 to coordinate the activities of the academic research groups involved and to ensure effective interaction with the sponsoring bodies. The Programme Manager will report to a Steering Group comprising representatives of the participating companies, the Council and the DTI to supervise the implementation and further development of the Programme. The Steering Group will hold meetings every six months or more frequently if requires to receive reports on the past progress and the future developments of the Programme. The Steering Group will pass back advice on future developments to the academics involved via the Programme Manager.

In the original call for proposals the special conditions associated with such a pre-competitive club were outlined. The funding of projects under the programme will require the acceptance by the Institution of some special conditions reflecting the industrial funding. These will include:

(i) 6-monthly progress reports to participating companies;

(ii) a delay in publication (up to 3 months) following disclosure of results to companies;

(iii) advantageous access by participating companies to results capable of commercial exploitation;

Products and processes arising from the cooperative research grants will be assigned to the consortium of companies involved. But net income generated by the programme will be shared between the companies and the university originating the research.

10.8 Financing of the programme

Industrial members contributions were on the same basis as SERC cooperative research grants, 50 % of funding, (In Protein Engineering it was only 20% of funding).

Table 10.2 Funding of the programme

Three Year programme total funding of Filamentous fungi	
Five grants costed at:	£375,966
Streptomycetes	
Seven grants costed at:	£962,310
P/T Programme Manager/travelling at £30,000 per year over 3 years	£90,000
Total cost of programme over three years	£1,428,276
Sources of finance	
Four companies at £20,000 per year over three years:	£240,000
Matching funds from DTI:	£240,000
Biological Sciences Committee (SERC):	£250,000
Biotechnology Directorate:	£698,276
Total:	£1,428,276

10.9 Corporate members of the programme

Figure 10.1 shared cost programme

SERC Biotechnology Directorate	Glaxo
Biological Science Committee	ICI
DTI	Apcel
	Beecham

50% 50%

The antibiotic club programme was primarily set up to service the UK Pharmaceutical industry, and it is an interesting feature that the companies themselves did get involved in such a novel cooperative research arrangement. Although the pharmaceutical industry is very R&D intensive, and while the pharmaceutical firms spend large sums of money on basic research in-house, figures collected in a survey carried out by the New York Centre for Science and Technology Policy indicate that a small percent of total R&D expenditures (0.5-1.8%) is spent in support of university basic research. The authors point out that, "there is a continuing compromise between the tendency of drug companies to cooperate in basic research and to draw back because of proprietary concerns", (Peters and Fusfeld, 1983). They go on to point out that:

> Since the effective life of a patent in the pharmaceutical industry depends on the relationship between the issue date of the patent and the date of the commercial introduction of the product, pharmaceutical firms tend to seek outside research help after they have established their patent rights or when the research is very far removed from the product. Thus, legal protection of proprietary rights is extremely important and hence may explain the smaller amount of cooperative research sponsored by this industry than one would expect from such a highly science-based sector, (Peters and Fusfeld, 1983).

However, there may be a growing tendency for pharmaceutical firms to support basic or pre-competitive

research at universities because of a growing interest in rDNA technology which originated in the academic sector. In addition the rising costs of research and its multidisciplinary requirements, may also provide impetus to collaboration in research. There is already signs of pharmaceutical companies around the world forming 'strategic alliances' and joint ventures (Dibner, 1985) also at the basic research end of the product cycle large bilateral academic-industrial alliances have been reported (see Chapter two). The antibiotic programme is different in that it is bringing together a number of competitors, that is a multi-lateral alliance focused on research carried out in a number of academic centres. But collaboration amongst such competitors doesn't come easy. Herbert Fusfeld writing in 1985 speculated that:

> The absence of collective industrial R & D in biotechnology is a clue to that industry's characteristics: It is in an early and highly competitive stage, in which patentable processes and know-how are of great importance. Even basic research can lead to commercial concepts that companies can quickly connect to practice. In this stage, companies may be unable to identify opportunities for cooperative activity in areas of common interest, (Fusfeld and Haklisch, 1985).

British pharmaceutical companies, prior to the antibiotics programme, seem to have followed this pattern. There are five significant antibiotic producers in the UK: the British companies, Beecham and Glaxo, and the UK subsidiaries of the American companies, Eli Lilly (Dista), Cynamid and Pfizer. A sixth British enterprise,

Wellcome, has a strong tradition of manufacturing other biological products such as vaccines, insulin and blood analysis reagents. These companies hold virtually all the UK manufacturing expertise in advanced microbial technology geared to pharmaceutical products. Of these major pharmaceutical companies both Beecham and Glaxo are participating in the programme together with ICI, which has had a strong interest in all areas of biotechnology since the early 1970s. Glaxo and Beecham were relatively latecomers to biotechnology. Beecham had already turned down an offer to join the Protein Engineering Club, which although defined as pre-competitive is far enough from the market to rule out any DTI participation, but the antibiotic programme is much closer to the company's more immediate interests. In 1984 Beecham was experimenting with methods of improving its antibiotic yields by modifying streptomycetes genes, (Bryan, 1984). Glaxo also has a clear interest in the type of research undertaken in this programme. Speaking in 1984, Alan Williamson, Research director at Glaxo, said that although he believed that Glaxo would inevitably continue to specialize in antibiotic design and manufacture, recombinant DNA technology is unlikely to form the main thrust of research. However he did concede that recombinant DNA technology may have something to offer to Glaxo's antibiotic production, by revealing new drugs that are currently transient metabolites during fermentation: "In any fermentation process involving antibiotics, the secondary metabolites of microbes producing penicillins or cephalosporins could be

manipulated through their genes, and some of these new metabolites could be very important" says Williamson. " At worst these techniques could simply improve on the production techniques for making currently available antibiotics, but at best we could get some entirely new products", (Bryan, 1984). It is interesting to note that this statement, made two years before the antibiotic programme was set up, accurately encapsulates its aims. Glaxo was already involved with external research via the British Technology Group.

Another participant in the programme is Apcel. Apcel were formed in November 1984 by Celltech (50%) and Air Products Ltd (50%), which is a subsidiary of Air Products and Chem inc USA. The R & D focus of the company is on harnessing advances in microbial genetics, specifically for industry, either to produce highly specialized microorganisms that can perform new functions or perform existing functions more efficiently and cheaply. The company plans to genetically manipulate industrially important microorganisms and improve manufacturing processes. These interests make it a useful technology transfer vehicle for the programme.

10.10 Technology Transfer and the British Technology Group

Before the development of the new club programme, antibiotic research had been exploited with some success in the UK. There was already a tradition of academic excellence and there had been a successful transfer of

this technology, via established companies, to the market place. The main vehicle for this in the past had been the National Research and Development Corporation (NRDC), which later became the British Technology Group (BTG). The function of the NRDC was to fill the pre-development gap and its replacement by the new organisational structure for coordinating strategic research is illustrative of a change in science policy thinking.

The cephalosporin antibiotics discovered by Professor Sir Edward Abraham and his colleague, Dr Guy Newton, at the University of Oxford in 1953 have been a major success for the BTG. The BTG has continued to support research at Oxford since 1953 to the present day, although its future is still in some doubt. Much of the work has helped to unravel the pathways by which fungi produce cephalosporins and also penicillins, which have a very similar chemical structure. Useful leads on novel penicillin have recently emerged and BTG filed two patent applications during 1984. BTG funding continues specifically to progress these findings and negotiations are in hand on commercial arrangements with a major (unnamed) pharmaceutical manufacturer. In another approach to the search for newer antibiotics, BTG has supported the development of a collection of 600 aquatic fungi. These are screened by Glaxo and ICI, who are both members of the new antibiotic research programme.

More closely related to the current cooperative programme is the fact that the BTG was also involved in the genetic

engineering of novel antibiotics. As early as 1977, BTG invested in a project at the John Innes Institute in Norwich to develop techniques for genetic engineering in streptomycetes. The John Innes Institute enjoys the highest international reputation in this field and in 1982 BTG funding was agreed for a project to use plasmids to introduce fragments of DNA from various sources into a number of streptomycetes species in the expectation that the hybrid clones would exhibit clinically useful activity not apparent in the starting strains. The agreement provided for screening using the laboratory resources of major industrial companies, who would also provide parent strains in confidence for hybridisation. ICI is collaborating in the project and providing screening facilities, and began to submit strains to the institute during 1983. Any products developed commercially by ICI will be subject to royalties payable to BTG.

BTG is also supporting a project in the Biochemistry Department at Cambridge to clone genes from a strain of bacterium that does not produce antibiotics into a strain of streptomycetes that does. The aim is to modify the normal biosynthetic pathways in the streptomycete, either to increase the yield of known antibiotic or to produce entirely novel antibiotics.

At least two of the club programme members, ICI and Glaxo, have established technology transfer mechanisms with academic establishments in the area of antibiotics.

I will now take a closer look at the significance of the new club programme.

10.11 Analysis

In this section I will be looking at the inter-relationship between the programmes organisational and management structure and its technical programme. The programme confers to the participant companies the following benefits attributed to cooperative research:

- the sharing of risk;
- each single company will have access to a more comprehensive research programme than its single contribution alone could achieve. Although this does have to put into the perspective of industrial R&D expenditures. In this case the sums are nominal when compared to the corporate R & D budgets as a whole. For instance Glaxo spent £220 million in 1988 on R&D, compared with a total contribution over three years of £60k.

On a more fundamental level the programme represents an attempt at structural change. The government and the member companies have been able to organise and promote a field of science that can be exploited by them, and often this involves restructuring in the sense of bringing together different disciplines to work on an area of significance to corporate interests. The need for the

establishment of new multidisciplinary groupings may also suggest another reason for corporate interest, the large number of academic inputs may put some of these research programmes outside the inhouse capability of a single firm. This may may be more true today in the pharmaceutical sector as it has been suggested that the research aimed at increasingly stringent regulatory requirements as diverted funds away from more basic research, (OHE, 1986).

The route for academic-industrial technology transfer followed by the British Technology Group (outlined above) differs considerably from this new type of organisation. The Steering Group, of which the company members are part, plays an active part in deciding upon research priorities and in commissioning and monitoring the research programme. BTG operated in an altogether more static environment, where it had a reactive role to support more applied research projects (as opposed to programmes) as they emerged from a science base whose research areas were largely defined by peer review.

The next question that needs to be addressed is why industry and indeed the Department of Trade and Industry have taken an interest in areas of basic research, far from the market place. Following on from this is whether the interest into more basic research is reflective of the relationship between science and technology.

Prior to the formation of the SERC biotechnology clubs, the research funding agencies followed a demarcation based upon perceived different types of the research that made up the innovation chain and their institutional locations. Basically the allocation was an institutional representation of the science leads to technology 'innovation pipeline'. The multi-source funding of the antibiotic programme gives some idea of the growing complexity of the innovation process. The fundamental principle is that the technology in this case, has become more dependent on basic science. As was pointed out in the earlier description of the aims of the research programme, the programmes purpose is to 'fill in' the gaps in scientific understanding that has produced a bottleneck in the development of both antibiotic production and in the development of new secondary metabolites. It also sought to develop some additional enabling technologies to assist this research (ie cloning vectors for filamentous fungi). There is a strong belief that biotechnology is essentially a science push driven technology, in the case of the antibiotic club research programme we have an established technology determining the scientific agenda. Even in a science based industry such as antibiotics, there would appear to be a need to go further into the fundamental knowledge base. As Rosenberg has pointed out ' there are many areas even today where technological progress occurs in the absence of a full understanding of the underlying scientific principles' (Rosenberg, 1982). The assumption behind the funding of this programme is that the gaining of the

basic scientific understanding of the technology will greatly enhance the scope and accelerate the pace of technical change. The programme would therefore seem to be a more sophisticated version of the customer-contractor principle. This has implications as to whether this type of club mechanism is suitable for developing truly new technologies and new applications.

It is because existing companies with existing products have largely determined the scientific agenda of the programme, that DTI funding has been attracted. This is because, although it will not fund clearly competitive/development work, it will also not fund speculative long term speculative research. This programme provides a clear route to commercial situation, so it is in the real sense pre-competitive. This involvement of DTI in this type of programme is a precursor to its own LINK programme.

The programme provides a clear demonstration of a change in the DTIs methods of supporting innovation. It represents a change in policy from its 'Support for Innovation' scheme which helped individual companies with demonstration projects, (this support scheme was abruptly halted in June 1986). There is now a government policy to transfer to industry the costs of what it defines as 'near market' research. This new approach is described in a recent White Paper The DTI the Department for Enterprise. During the setting up of the antibiotic programme the DTI had been thinking of setting up a club

in this area and decided to join in with the SERC initiative in this case. It had also decided to become involved in the Plant Gene Tool kit initiative (see chapter eight). Both of these allowed the DTI to try out its new and controversial innovation policy. Following on from this initiative the DTI went on to collaborate with the SERC in establishing two LINK programmes, one on Eukaryotic Genetics and one on Biotransformation.

10.12 Summary

The antibiotics programme is less speculative than other research clubs because the 'exploitable area of science' could be identified relatively easy. This was because the primary or initial aim of the three year programme was to work with existing organisms and products. As one of the SERC biotechnology Directorate publications pointed out:

> The combined impact of this coordinated research over three years will, it is hoped, produce results which can be exploited to step up production of known antibiotics and to begin to produce new ones. Perhaps other novel and valuable therapeutic compounds will result, (Hunter, 1986).

It has recently been announced that since the programme is due to end in 1989, the members wish to see this kind of coordinated research activity to continue and to expand. Discussions are now underway with the existing sponsors together with other interested partners with the aim of developing a new initiative. It is thought that

the next programme will appeal to sectors other than pharmaceutical companies and will most likely take the form of a LINK programme, (SERC, 1989).

CHAPTER ELEVEN: Conclusions

11.1 Introduction

In the previous chapters, I have described the nature of university-industry research relations in the UK and have given detailed accounts of the new club mechanisms established to couple state funded science with national economic development. What emerges is that the promotion of new technology is a central concern of public policy. A review of the reports produced by science and technology policy advisory bodies such as ACARD and ABRC, show how they have influenced the direction of public policy debate in the late 1970s and 1980s. In the ACARD reports Industrial Innovation, (1978), and Technological change: Threats and Opportunities for the UK (1979), ACARD drew the governments attention to the importance of technological innovation:

> The role of technological innovation in UK industry will need to increase if its products and manufacturing processes are to match those of our major competitors. This is a necessary condition for our future survival as a leading trading nation, (ACARD, 1979).

The report listed the new technologies that can fulfil these strategic opportunities: energy; materials; micro-electronics; information technology; and biotechnology. These are the technologies mentioned in Chapter 1, considered core or enabling by most governments of the advanced industrial nations.

These initial advisory reports of the late 1970s set the general economic arguments for a policy for encouraging technology. The early reports were followed by other reports which focused on specific technologies, advanced manufacturing, biotechnology; and on the specific mechanics of science and technology policy; the notion of university-industry relations, followed by a more innovative concept of an 'exploitable area of science' and a new science policy discourse of strategic research, pre-competitive research, generic technologies and research collaboration.

Although the initial response from the government to these reports has not been good (1), by the second half of the 1990s most of the points raised in a succession of reports appear to have been brought together to constitute the current science and technology policy of the government, as articulated through the White Paper issued for its lead department in these issues (and for biotechnology in particular) the DTI: the department of enterprise.

The fact that technology has to be promoted had long been taken as axiomatic (following 1945), what I have attempted to illustrate in this thesis is the difference embodied in the present mechanisms for promoting industrially relevant science and technology. These mechanisms embody a more sophisticated view of the innovation process involving the identification and establishment of exploitable areas of science through the

interaction of industrialists, academics and government.

The present governments technology policy now has as its emphasis the promotion of the research side of the R & D equation. It has chosen to promote collaborative programmes to perform longer term research. Public policy on exploiting science and technology, has moved the activity upstream into 'longer-term' research, previously the exclusive province of science policy. The new policy also depends on an organisational innovation; not only collaboration between HEIs and industry, but also between firms, some of which may well be competitors.

The DTIs role is to help establish the collaborative links between firms, and between firms and HEIs at the pre-competitive stage. The reasons for the development of this type of policy have been investigated in this thesis with regard to specific areas of biotechnology. We can see how models originally developed in the SERC clubs aimed at promoting strategic research, have been developed to form the central plank of the governments technology policy through both the LINK initiative and national research programmes, such as that on superconductors. However, if the SERC clubs provide immediate working prototypes, the genesis of the rationale for the government policy can also be seen as a fusion of science and technology policies that have been underway in our major competitors.

11.2 Cooperation as strategy

The organisational concept behind firms cooperating when they are basically used to competing is quite radical, but Japan has provided a model. In the 1970s Japan created a successful organisational mechanism for generating technological innovation. They set up R&D associations which established a new pattern in joint development. The main initiative was the Very Large Scale Integration (VLSI) semiconductor programme. It was government funded, and management of the programme was achieved by consensus of the participants rather than the dominant role of the government which occurred in previous government supported programs. By stimulating consensus amongst the participants avoids overlapping developments and maximise utilisation of R&D budgets. VLSI managed to attract 100 researchers from competitors in the same field and fostered over 600 patents; it provided an influential model of development through co-operation of competitors. A. M. Anderson points out the effects such developments as these had:

> Given the success of this project (VLSI) it is not surprising that the announcement of two new projects - the high speed computing system and the 5th generation computing project - had produced a state of near panic in western manufacturers and governments. Numerous committees have been set up to examine the new Japanese projects and to decide whether similar projects should be launched in the UK, USA and France. At the first western conference on the 5th generation computer, Japan's project was described as 'a computing apocalypse' and a 'technological mein-kampf'. In the UK a committee was set up under the chairmanship of J.

> Alvey, director of technology at British Telecom and recommended rapid reorganisation and concentration of the British effort. (Anderson, 1984).

The Japanese were not the first to utilise cooperative mechanism. The difference that separates these new waves of collaboration, which have now spread to US, EEC and the UK, is their concentration on high technology areas. F. Wolek in a study of Co-operative R&D in the USA (Wolek, 1979) found that 'in general industries which are high in cooperative R&D are not those which are R&D intensive'. The work performed by them was 'traditionally unexciting', and mainly concerned with the improvement of exiting technology. Developing new hardware was a very small part of the sample. Wolek, thus found that the hypothesis that cooperative research would facilitate the performance of larger, riskier, more complex and longer term projects redundant. The state of activity appears to have changed in the 1980s, the emphasis has shifted toward the promotion of cooperative (often long term) high technology research.

This transition to cooperative high technology research is amply illustrated if we look at traditional research organisations in the UK and see how this model was utilised by Japan. The UK has a well established system of over forty industry specific research associations. They tended to service mature or traditional industries, performing contract research to assist (usually small and medium sized) firms with technical problem solving. The

Japanese took these basic models into the 1980s. The Japanese research association are different in the following ways (following Goto and Wakasugi, 1987):

1. They carry out specific R&D programmes and are dissolved after completion of the programmes;
2. Their member firms are generally large and operate in areas closely related to their R&D projects. Thus, they come from those industries that are essential for the successful implementation of the project;
3. Research subjects are usually in high-technology areas (areas that are normally immature and fast growing).

Although Japan has to a large extent led the way in this new cooperative research, it now seems to represent the norm for science and technology policies in the 1980s. Chapter two of this thesis outlined the spread of such initiatives and the case studies indicate the evolution of such mechanisms applied to specific areas of biotechnology. The studies show that the clubs fit the criteria set out above for Japanese research associations and places them in with the current trends regarding research cooperation (see Fusfeld and Haklisch, 1987).

11.3 The role of New Biotechnology Firms

If the current initiatives focus on cooperation, the Spinks report on biotechnology also offered another model for commercialising biotechnology in the UK. This model was one borrowed from the US. The early growth of

biotechnology (1976-79) in the US is largely attributed to the actions of small venture capital backed new biotechnology firms (NBFs), who had no vested interests in existing products or the development of established technologies, (Smith and Fleck, 1988). In these very early stages neither large corporations nor banks exhibited great interest in investing in such an untested technology. The Spinks report responding to this activity in the US called for the government to support the establishment of an NBF in the UK. The company Celltech was set up in 1980 in response to this call (see chapter seven). The growth of NBFs in the UK has continued, but on a much smaller scale than in the US.

Commercialising biotechnology in the UK can be seen to have utilised both of the above mentioned routes. What seems to be happening today is that one is in ascendancy to the other, cooperation between established companies now seems to be favoured. The government however, does still see a role for new small firms in its technology policy:

> 8.26 ...the rise of new high-technology firms from small beginnings adds an extra element of rivalry and flexibility to the market's response to technology opportunities. This appears to be better developed in other economies, such as the US, than the UK. Funding innovation in start-ups, the growth of new technology-based small firms and innovation in small firms in regions with a limited technological infrastructure can add to innovation throughout the economy.

This shift to a policy favouring cooperation is explicit in the funding requirements of the new R&D programmes such as LINK. As a prerequisite for participation (and receiving support funding) is cooperation with either another company or a HEI. Cooperation in the joint venture mode is becoming a common organisational form in the high-technology sector. Most of the NBFs established in the US now have joint venture agreements with the established companies with biotechnology companies. The survey carried out for the research of this thesis shows a widespread propensity to cooperate with external organisations. However, one notable finding was the lack of interest shown in consortia or clubs. This indicates a potential limitation on the notion of cooperation; that joint ventures are acceptable but clubs involving many members are not. One of the respondents to the questionnaire gave their views on the emerging policy preference for clubs:

> Recently the trend has been to set up joint industry/academic or industry/government clubs. These tend to be expensive, diffuse and on the whole not very good value for money. We are coming to the view that we should set up interactions with selected academics in areas which are of direct relevance to our own needs, thus cutting through the club mish-mash. We will be looking to increase our direct contracts through SERC collaborative awards or by direct funding of projects of relevance to us, at the expense of the club approach (No.76, 1986).

With such apparent disinterest in the consortia or club approach, it is interesting that it has been so heavily promoted. In the case studies I examined the reasons for

the establishment of such clubs and outlined the expectations of the club members.

11.4 Science and technology policy for a generic technology

11.4.1 Introduction

This new public policy for technology has implications for all of the actors associated with the implementation of science policy. The fundamental reason for this knock on effect is that the technologies identified as presenting strategic commercial opportunities are all science-dependent. That is they require inputs from, or at least cooperation with researchers, who are usually located in HEIs. This is confirmed in the case of biotechnology, by both the empirical survey (Chapter 5) and the structure of the clubs analysed in the case studies. There is then the problem of organising cooperation between two types of cultural systems.

Since the discovery during the second world war, that organised science, ('mission oriented science') could achieve spectacular results, public policy towards science has shifted to funding areas less dictated by the internal scientific criteria of the academic community to allow external factors (such as industrial importance) to influence the direction of research.

The science funding system of the UK has responded (or in some cases resisted) in different ways to these influences. There is a stark contrast between the SERC whose polices are investigated in this thesis and the MRC. As outlined in chapter six, the SERC has welcomed industrial influences, but MRC has been much less keen as is described in Chapter seven concerning the protein engineering programme. The difference of opinion between the Research Councils and between the DTI and the MRC were publicly acknowledged at the 1988 conference on 'Biotechnology - Spinks Eight Years On', organised by the Royal Society. At the meeting Ron Coleman from the DTI criticised the inflexibility of permanently staffed research institutions devoted to curiosity-led research (i.e MRC and AFRC). He stated that the DTI was keen to cooperate with all of the Research Councils, but the task would be easier with a spirit of tolerance and compromise between them. Responding for the MRC, Dr Winter stated that the MRC Laboratory of Molecular Biology now had an effective strategy for identifying discoveries which could be applied, for patenting and exploiting them. Winter contrasted this approach, based upon performing basic research for its own sake and allowing any interesting results to be exploited, with the clubs and the DTI LINK scheme, where companies help decide the research agenda at a much earlier stage.

This overlapping of interests and the use of different mechanisms has brought the SERC and the MRC into conflict, particularly in the case of protein engineering.

The findings of this thesis suggest several reasons for these conflicts within the science funding mechanism of the UK.

1. The technology is science dependent, and because in a capitalist economy like the UK, the firm is the main agent for introducing new technology into the economic system, industry must cooperate with HEIs or HEIs must create firms to take their technology to the market place. The results of the survey of the biotechnology industry in the UK indicate that all of the respondent firms supported research at HEIs and all performed in-house R&D.

2. In biotechnology we can talk usefully of 'first generation technologies' which are in essence techniques or tools such as rDNA splicing and monoclonal antibody techniques, often artisinal in nature (see Mackenzie, Cambrosio and Keating, 1988). These techniques diffused rapidly across academic laboratories so that there were lots of contact points for industry to access expertise in these basic techniques. The survey carried out in this thesis shows that these techniques have diffused across almost 40 to 45% of the respondent firms. Also these techniques have allowed the creation of NBFs (some created by academics) producing standard products such as monoclonal cell lines, peptides, gene sequences and diagnostic kits based on these more basic techniques. It is becoming clear that the initial tools represent the first phase of the new biotechnology, they have opened up

the field for much more research that can produce information that can affect all sectors of the economy. The survey results show that the biotechnology industry is emerging from within a number of existing industrial sectors. In this sense biotechnology is a generic technology which, in order for all of its possibilities to be exploited, needs a wide variety of inputs, as in the case of a major second generation techniques protein engineering. The survey shows that there is far less corporate involvement in the more complex 'second generation' technologies (see Chapter five), which may indicate a lack of expertise and therefore could possibly represent an area for future university-industry cooperation.

Because the technology is both generic and multidisciplinary, questions were asked in the Spinks report as to whether the existing system of research support, based on four research councils with clear 'domains' and utilising researchers largely organised in traditional disciplines, was sufficient to promote the full use of biotechnology:

> The Research Councils should substantially increase their support for biotechnology. But because the subject cuts across their areas of interest and expertise and will point up gaps between them, The Councils should also, with the Advisory Board for the Research Councils (ABRC), set up a Joint Committee for Biotechnology...this Joint Committee should develop and co-ordinate a coherent programme of biotechnology research, (ABRC/ACARD/RS, 1980).

This was essentially rejected by the government with the result that each Research Council was allowed to carry on with its own distinctive approach, and despite the establishment of an elaborate inter - Research Council committee structure (see table 11.1. and note 2), friction and overlapping interests have not been avoided as I have pointed out in the case studies.

The literature review and the case study of the Plant Gene Tool Kit (PGTK) have also brought to light an additional source of conflict, confusing further the division of responsibilities. This additional confusion stems from the new technology policy in the UK where the DTIs involvement in technological innovation is one of 'backward integration' or upstream from 'near market' research. It is now active in the following pre-competitive areas; superconductivity; eukaryotic genetics; nanotechnology; and plant metabolism. Subjects that would previously have been the exclusive domain of the scientific community.

Table 11.1

GOVERNMENT COMMITTEES CONCERNED WITH BIOTECHNOLOGY.

Committee	Abbreviated Title	Terms of Reference	Chairman/Membership	Links with Other Committees
Inter-departmental Committee on Biotechnology	ICBT	To assist DOI in planning and executing action in those areas of biotechnology that do not fall clearly in specific Departmental responsibilities by providing the necessary co-ordination within the U.K. and internationally. To stimulate the exploitation of biotechnology in U.K. industry by actively identifying and encouraging support for specific projects. To provide biotechnology in Government with a visible focus for outside enquiries and suggestions.	CH Government Chemist Membership flexible including DOE, MAFF, DEn, DHSS, HSE, MRC, ARC, SERC, PHLS/CAMR, PHLS, MOD(PE), BTG, Scottish Office. Others attend as necessary.	Cross membership with IRCCCOB, MRCB, Links with UGC, BCCB, SCI, CBI.
Inter Research Council Co-ordinating Committee on Biotechnology.	IRCCCOB	To advise the Heads of the Research Councils on the development of biotechnology research programmes within the Research Council system. - any co-ordination or rationalisation that may be desirable between the programmes of different councils. - any new work that should be initiated as a consequence of inadequate coverage of recent discoveries.	CH MRC Membership; MRC, ARC, SERC, NERC.	Cross membership.
Materials and Chemicals Requirements Board (and its Chemical Manufacture and Biotechnology Executive Committee)	MCRB (CMBEC)	The DOI's research and development requirements boards determine the objective, composition and balance of the DOI research and technology programme. The MCRB covers mineral resources, mineral processing, metals extraction, chemical manufacture, biotechnology process plant, reclamation and engineering materials. CMBEC covers chemical manufacture and biotechnology.	CH Dr B C Lindley, Dunlop Ltd, Membership made up of senior industrialists, academics and government	Chairman of ICBT sits on MCRB AND CMBEC Director of SERC Biotechnology Directorate sits on CMBEC.
SERC Biotechnology Directorate Management Committee	BTMC	To advise and report to the SERC's Engineering and Science Boards on the development of the Biotechnology programme. To approve expenditure within the powers delegated to it. To oversee the programmes and encourage the participation of industry, academic institutions and government in both the research and training aspects of the programme. To guide the Director on the content, balance, implementation and exploitation of the programme.	CH: Dr A J James (Unilever) membership senior industrialists and academics and Government Chemist.	Director of SERC Directorate sits on ICBT, CMBEC and IRCCCOB. Government Chemist
Genetic Manipulation Advisory Group	GMAG	To advise research workers and others on the risks involved with recombinant DNA experiments and the appropriate safety and containment precautions.	CH : Sir R Williams, (Formerly Director of PHLS). Membership made up of senior industrialists, academics and government.	Contacts with HSE and Advisory Committee on Dangerous Pathogens

The research clubs studied in this thesis offer clear signs of the efforts aimed at reorienting the scientific enterprise to better respond to industry's needs, the conflict mentioned above results from the transition to a new enterprise system where science and technology policy are integrated, HEI research funded by the Research Councils and the DTI is relevant to industry, and to stimulate a real increase in industry's own investment in R&D. The technical enterprise will be a continuum involving HEI research and industrial R&D, something akin to what the OECD term a 'socio-technical community' which provides:

> opportunities for people with different backgrounds (large high technology firms, mature industries, small firms, regional and national governments, traditional as well as new universities, scientists of all disciplines) to become personally acquainted, to understand their respective motivations, interests and constraints, and to explore the possibilities and mutual benefits offered by co-operation, (OECD, 1984).

11.4.2 Rationale behind clubs - central R&D

The clubs and directorate schemes of the SERC studied here and the Alvey programme, appear to represent the most favoured form of organisation for this new type of technical enterprise that will unite industry, HEIs and government. A useful concept that emerged from my research for interpreting the development of the club mechanism, is provided by the idea of creating an 'academic' analogue of the centralised R&D function in

industry. The corporate central laboratory became popular in the 1960s as a tool to anticipate and counteract technological obsolescence. The corporate central laboratory was typically given freedom to pursue long-term objectives without interruptions, it helped avoid duplication of work relevant to more than one division, and gave the company the ability to build effective groups with a wide range of disciplines. It could also assign resources to investigate new technologies which do not fit into the existing divisional structure. Against these advantages can be set the following disadvantages: remoteness from market forces and the needs and experiences of the operating division; reduced profit consciousness; demarcation and communication difficulties between the central and divisional laboratories; a tendency for R&D for the medium term to be neglected by falling between the central and divisional labs, (Twiss, 1980). The disadvantages have tended to outweigh the advantages in the 1970s and corporate R&D came to focus more on strictly market led applied research, with a consequent cut back in spending on more fundamental research, (Praeger and Omenn, 1980).

After disenchantment in the 1970s with central R&D there now seems to be interest again. Several reports have indicated that research conscious companies are worried about how to embrace a sufficiently wide span of 'enabling technologies' to prepare fully for the future, (see Fishlock, 1988). Many companies were looking to

central R&D to fulfil this role. In addition to generating the technologies of tomorrow, central R&D will be the company's 'intelligence agency' for future market opportunities -another good reason for strengthening links with other research centres.

The forces that have brought about this renewed interest in central R&D are the same as those now influencing science and technology policy: the emergence of a series of science based generic technologies such as biotechnology. The question now facing science based companies is whether to perform generic or targeted research. Roland W. Schmitt, Vice President of Corporate R&D at GEC (US) captures the flavour of this debate:

> In many areas, it is entirely possible to stay at the forefront of technology by working on target developments alone, i.e. divisions closely linked to existing business; marketing etc. For technologies like the micron and submicron integrated circuit, however, targeted programs are not enough. When the rate of progress is especially rapid (and new discoveries and inventions are common), it is not possible to ensure forefront competence by concentrating on tightly focused programs alone. In these cases, it is prudent to carry out untargeted or generic research in areas of continuing pertinence to the business. the supreme example of such an area is biotechnology, where most of the ultimate applications are still highly speculative, (Schmitt, 1985).

In the light of my studies of the SERC clubs and biotechnology directorate (recent developments in science policy), it is interesting to look at the 'structure' of this corporate central R&D:

> Some observers view centralised R&D as trying to strike the optimum balance among basic research, applied research, and development. I do not think that these are operationally useful categories. For me, the key is whether a corporate laboratory is working at the forefront of technical areas centrally important to the parent company. Is it producing results of near-term value and laying the groundwork for future advances ?(Schmitt, 1985).

Rather than using the terminology of the traditional academic scientific community the objectives of industrial research are stated simply enough:

> To strengthen present products and processes;
> To develop new products and processes that will expand present business;
> To provide the basis for new business.
> (Fusfeld, 1986)

These objectives do not distinguish basic research from applied research or engineering. Nor do they mention disciplines, such as physics or chemistry or electrical engineering. Each company can identify specific missions that relate to its particular products or business interest. These missions then determine what know-how will be needed to pursue the goals. Thus industrial research is, by definition, interdisciplinary. The particular mix of physics, biologists, chemical engineers, and others that make up an industrial research

laboratory follow from the missions the parent company has established for the laboratory. The centralised corporate laboratory can be said to have as its emphasis the performance of what has been termed strategic research or pre-competitive research. The research moves out to the divisional laboratories in order to be developed, through 'competitive' research, into new products.

11.4.3 Directorates/Clubs and strategic research

This is a key point to understanding the radical transformation of UK science policy. The analysis of the research clubs indicates that the 'problem' of organising university research has moved to a more sophisticated level. The first approach was to create physical and administrative structures that companies could identify e.g. applied institutes, contract R&D. The requirement today is an exploitable area of science, a field of science and technology, made up of a mixture of disciplines, long and short term work; a mixture recognisable to industry. The current use of clubs and directorates may be seen as manifestations of this process. Michael Gibbons has provided an interesting analysis of the directorate mechanism of the SERC, that illustrates this type of process:

> The Directorate schemes if successful contain considerable potential for transforming the environment in which university research is carried out. The directorates are intended to change academics perceptions about their research
>
> activities...The directorate schemes are trying

> neither to provide more academic research per se nor to increase the range of contacts within industry or government per se. They are trying to promote what has been called in other contexts 'strategic research'; that is fundamental or basic research which is related to national needs or problems. The directorate schemes aim to break down the conventional division of research into short- and long-term in which short term research is regarded as applied research and long term as pure research. It is a mistake to think that all socially relevant research must be short term in nature, (Gibbons, 1982).

The directorate system, according to Gibbons interpretation presents a mechanism for establishing a scientific community that performs strategic research (where a national need is transformed into a set of research problems), which gathers support from several areas of science and engineering and creates an ethos of research with a practical orientation which overcomes essentially discipline-oriented problems.

> One of the key aspects of the Directorate scheme is that by reorienting university research under a national objective, a different type of research will be carried out. Implied in this is the loosening of the bonds which attach the academic to the international scientific community; or possibly a reduction of the quantity-though perhaps not the quality- of the research judged solely by reference to discipline-oriented peer groups. Further because problems so identified tend to be multi-disciplinary, a form of collaborative research not familiar to academics is required and if the research is to be really effective some commitment from universities or group of universities is often required, (Gibbons, 1982).

These conjectures have been borne out by the club case studies carried out in this thesis. After some initial attempted 'relabelling' particularly in the context of protein engineering which was due to researchers attending to discipline oriented problems, over time, a protein engineering community did appear to have been formed.

The directorates and clubs will provide mechanisms for performing strategic research that is of interest to science-based industry. They will be of interest to companies because they are recognisable as analogous to central R&D. The survey tested the recognition of 'strategic research' as a possible bridge between university and industrial research. Research undertaken in university-industry interactions was found to be focused around the performance of equal amounts of applied and strategic research.

The club mechanisms themselves indicated the flexibility of the terms of strategic and pre-competitive research. They were all multi-disciplinary, bringing researchers together from several disciplines (the clubs also had definite structural objectives to create such multidisciplinary groups). The overall research programmes were of different durations (ranging from three to four years), indicating that some strategic or pre-competitive research is closer to the market than others i.e. it is contingent on the nature of the specific technological area. Protein engineering was

further from the market than either PGTK or the antibiotics programme. The mix of research within a particular programme ranged from longer term exploratory research to work on specific targets. The existence of such a mix reinforces the analogy with corporate central R&D.

11.4.4 Selecting and steering areas of science

From the analysis of the clubs in this thesis it is clear that a certain model has emerged for exploiting carefully selected areas of science and technology. A major part of this mechanism, is the system for selecting areas and individual projects. This brings the argument back to the upheaval in the science policy agenda. The failure to implement the degree of coordination recommended in the Spinks report has led to friction between the Research Councils and the government (largely through the lead government agency in biotechnology, the DTI). In policy terms for supporting science and technology the government favours the collaborative arrangements such as the directorates of the SERC and clubs. We have seen in the clubs analysed in this thesis that the SERC through these mechanisms has moved into areas normally associated with other Research Councils, and the MRC in particular. It was suggested that the industrial members of the management committees of the biotechnology directorate and the individual club schemes favoured this route to performing research that might normally come under the auspices of the MRC, because it is not able to influence

the MRC so well. They do not allow for industry to help set the research agenda. The mechanism quite clearly gives its industrial members a wide birth in selecting areas of interest to them, and in steering individual projects towards those aims.

It was pointed out in the study of the clubs in this thesis that concern was expressed by both industrialists and academics that not all of the nations expertise in a particular club field was integrated into the programme. The government has realised that for the clubs to work to their maximum efficiency it is necessary to involve all the relevant expertise. We can now see that the MRC has had to modify its attitude and is participating in several of the new LINK initiatives, this could well have significant implications for UK science policy.

Throughout the 1980s in biotechnology the UK has been pursuing a 'dual track' policy on exploiting science. On the one hand we have the MRC performing its curiosity led research in its own institutes. They are quite explicit they perform basic research and if anything of commercial interest emerges from this research programme they will be exploited by the technology translation company Celltech or else companies can come and apply for licenses. Corporate influence is kept to a minimum. The implicit theory of innovation they are working on is the science-push model as espoused by Blackett in the UK and Bush in the US (see chapter 3). In contrast the SERC has first through the biotechnology directorate and then through the clubs, allowed industry to shape the research

programme itself. The theory of innovation is more of a mixture of demand pull and science push. In order to maintain the quality of science of the research carried out via these mechanisms, projects still have to go through the peer review process of the scientific community (as is the case for MRC). The most recent development, the backward integration of the DTI, may take some of the strategic science out of this quality control process and this effect (touched upon in the case study on the plant gene tool kit) needs further investigation, especially if the MRC also becomes involved in the DTI LINK programmes, where proposals are approved by the LINK steering group which consists of senior industrialists, government officials, and academics (3).

11.4.6 Problems with the club mechanism

The club initiatives are still at a relatively early stage of development, nevertheless it has proved useful to study their establishment and early development in order to see how each programme has been shaped by the participants and to assess the policy implications of these new mechanisms for supporting science. The clubs share similarities with centralised corporate R&D, and the policy trend seems to be in creating more of these clubs for more technologies. As these clubs come to the end of their planned life it will be vitally important to test the effectiveness of these mechanisms. Their structure is based upon several assumptions that need to be tested.

Firstly, there is very little information on whether cooperation is the best way of generating new technologies. The assumption that pooling together fragmented groups of researchers in a collaborative club such as that of protein engineering is the most effective way of exploiting research. Dr Williamson of Glaxo refers to the research community built up by the club system as 'dispersed centres of excellence', and compares them with the Institutes set up by the MRC. In this context its performance could be usefully compared with the MRC activity, which is based on the performance of research whose direction is set by the academic community and performed in single institutes. There are indications that the LINK programme favours the establishment of single centres of excellence.

Secondly, the quality of the science performed by the clubs is crucial to its legitimacy. As reported in the case studies most sponsors put as a priority that the research be of the highest order, it must be at the frontier of the science. However, my research has brought to light several factors that may impinge upon the ability of the club system to do top quality research. The club mechanism may be less 'efficient' in its science because of the organisational requirements demanded by its sponsors. The club communication patterns may be more couched in restraints and secrecy because of the proprietary concerns of the corporate sponsors. From a national point of view it would be useful to know whether there is any interactions between

both sides of the 'dual track' approach; the clubs and the MRC/AFRC.

Thirdly, the quality of science is also related to the question of peer review (see Section 11.4.4). The PGTK indicates the conservatism of the DTI/Industrial evaluation of centres of excellence, many "New Blood" applicants accepted by the *original SERC programme, were* rejected by the DTI PGTK programme. There is some indication that, at least in some fields significant new areas tend to be opened up by younger scientists (see Mullins 1980), to overcome the conservatism of the corporate steering groups there well be the need then for flexibility in funding of younger researchers.

Fourthly, there is the question of whether strategic or pre-competitive research programmes are attractive to industry. I mentioned above that the survey results indicate that industry carries out strategic research, and that this represents a sizeable part of the type of research that constitutes their university-industry research relations. The survey also shows that industry has a high expectation in terms of tangible pay offs from this research. It also shows a preference for particular types of mechanisms, in particular contract research and individual consulting. Government programmes, joint research and consortia do not appear to hold much appeal. This then could have serious implications on the usefulness of the current policy favouring cooperation. The clubs by their nature do not appear to appeal to companies whose strategy is more usually focused on

competition. There is a natural reluctance to share research or to cooperate with possible competitors. The clubs have as their focus pre-development or strategic research. This by its nature is upstream from the market place, and may be longer term research than companies normally deal with. Companies may be reluctant to take part on this count because there is no clear short term route to products, an objective the survey (Chapter five) found to be extremely important to industrial sponsors.

Finally, the question of appropriate public funding arises. The clubs carrying out strategic research show that the terms meaning is flexible. Each club has projects of mixed timescales and varying degrees of applied and basic research. Care will have to be taken to help identify what is pre-competitive, so that public funds are not being used to carry out research that industry, by itself or collectively in private consortia should carry out. The emphasis on pre-competitive research rather than on more applied research is because the government wishes to stimulate an increased level of industrial research in the UK and it believes that its funds are more likely to achieve this effect if they are concentrated on the more risky, early stages of R&D. This policy objective needs to be tested. Clubs should result in an increase by companies in that area of research. The research should be truly risky to ensure this, the term strategic and pre-competitive should not be allowed to cover research is essentially applied. In the club format there may be a natural balance preventing

this, as the corporate sponsors have tended to force the research agenda towards more fundamental studies to keep the work away from areas of conflict, where research is getting close to the market. They want to carry that sort of research in the secrecy of in-house research.

Despite these draw backs the clubs have proved to have a strategic significance for their members. The selection of the area indicates that it has such a significance. The question is whether the club mechanism is the best way of exploiting the strategic research. Clearly a company could enter into bilateral agreements with different researchers for different pieces of strategic research. The clubs have the added benefit of establishing a field. Once established, firms outside the club should be able to approach the new community to form bilateral research agreements. The success of the club scheme may well be in the structural innovation of establishing expertise and a community in a new field of exploitable science.

11.5 Planning: Science and technology policy in the future

The 'dual track' approach outlined above, represented a choice of approaches a multiplicity of decision makers in science and technology policy. The companies in the directorate programme, the club steering groups, and possibly the LINK programme, in totality represent a narrow range of commercial interests. The corporate

members and the number of SERC clubs that they are involved in is given below:

Table 11.2 Corporate membership of SERC- biotechnology clubs

Company	SERC Clubs
ICI	3
Glaxo	3
Beecham	2
Celltech	2
Sturge	1
Apcel	1
Wellcome	1
Porton International	1

The restructuring of the research system to fund exploitable areas of science has a crucial implication for the development of biotechnologies. One must be cautious in assuming that there is only one scientifically derived trajectory along which biotechnologies may evolve. The very diversity of biotechnologies implies that there are multiple paths that can be followed. The original diversity of products and techniques that proliferated in the US was due to small firms with no vested interests in established products and technologies. The programmes analysed in this thesis involve, in their decision making, large established companies such as Glaxo and Beecham, which were implicitly criticised for not taking full advantage of the new biotechnologies in the Spinks report. The clubs also do not appear to be too successful in attracting small new biotechnology companies. We may be

seeing a series of what Dosi calls 'technological paradigms' being established; a redirection of a significant portion of the UK scientific community towards the interests of a few corporate interests, (Dosi, 1982). From this perspective there may be some question about whether a programme in for instance antibiotics (research underlying a current technology) is as appropriate as a subject for pre-competitive research with public support, when compared with support for protein engineering; an enabling technology of potential interest to a wider range of companies.

Within the spheres of science and technology activities there is a wide variety of possible subjects that could be worked upon, but, according to Dosi, these are focused down to narrower problem areas through the operation of economic forces, together with institutional and social factors, that act as selection devices. Once the path has been selected and its boundaries established, it is considered to show a certain momentum of its own. An important aspect of Dosi's paradigms is their exclusion effects, such that organisations are often 'blind' with respect to other technological possibilities. For example the direction of biotechnology in agriculture was focused via a club format on a plant gene tool kit, there was no such support for an alternative multidisciplinary agroecological approach (Buttel et al, 1983). With the integration of MRC into clubs we may be able to assemble all of the nations expertise into a particular field, but

it may come at the cost of a plurality of research directions.

In chapter 3, I discussed the theories of Joseph Schumpeter (1964), in his model of innovation, model 2, he essentially argued that large capitalist organisations now control innovation. There is some indication that the new mechanisms described in this thesis as being in the vanguard for the new science and technology policy, could facilitate this process. However, Schumpeter does point out that established firms with farsighted management can also move into the 'new economic space', with new methods or commodities. They need not stifle innovation. If these established organisations are in the steering groups for selecting and exploiting areas of science and technology, it is important to monitor these firms to make sure that they are interested in the 'new economic space' opened up by radical technological innovations or technological discontinuities.

In conclusion this thesis has investigated the interest of UK industry in university research in biotechnology. More specifically it has analysed the formation and initial development of a series of club initiatives that are described as models for support in the new framework of an integrated approach to science and technology policy. It is suggested that further work could be done to see whether such arrangements are the most effective way for commercialising science based technology generally, and whether the widespread use of such a

mechanism may have a deleterious effect on the number of technological options the UK can exploit.

The findings of this thesis however are restricted by virtue of the analysis to the situation found in the UK, where there has been a long history of a 'pre-development gap' inhibiting the coupling of university science and industry. It is interesting to note that the phenomenon of clubs, of R&D consortia based on the performance of pre-competitive research is rapidly becoming an international one, with initiatives like the European Community programmes on information technology (ESPRIT and RACE) and biotechnology (BRIDGE) taking the idea of cooperation to a transnational level.

Notes

1. In March 1981, HMSO published the long awaited government response to Spinks which was generally greeted with disappointment by industry and academics alike. The White Paper (1981) showed the governments lack of enthusiasm for Spinks diagnosis and recommendations. It put the main responsibility for turning concepts underlying science into useful products and services lay with industry. The merging of science and technology can be seen at another level, the Advisory Council for Applied Research and Development (ACARD) is to be expanded into the Advisory Council on Science and Technology (ACOST). Acost will encompass academic science as well as technology.

The ABRC has recently called for the creation of a single research council, which shows just how far attitudes have changed since the more modest coordination called for by the Spinks report.

2. MRC officials held the posts of Chairman and Secretary of the Inter Research Council Coordinating Committee. Only a few large industrial organisation were well represented in the Committee structure in table 11.1.

3. The 'backward integration' of the DTIs intervention is also demonstrated by the recent establishment of the Biotechnology Joint Advisory Board (BAJB). The BAJB is the latest manifestation of a closer working relationship between the SERC and the DTI. It and the two committees that report to it ((the Project committee and the collaborative committee), will be made up from existing membership of the Biotechnology Directorate Management Committee and the LINK programme management groups. They will agree the future research programmes of both the SERC and DTI. Although the structure initially involves only the DTI and SERC it does allow for other Councils such as the MRC and AFRC to become equal partners if they wish. It is this latter arrangement that the government would seem to favour as this would encourage the formation of a national programme in biotechnology closely allied to the needs and interests of UK industry, (SERC, 1989).

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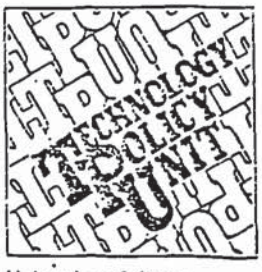
APPENDIX ONE

Academic-Industrial Relations
in the British Biotechnology
Industry
A study by I.Williams B.Sc M.Sc



University of Aston
Gosta Green,
Birmingham B4 7ET
Tel: 021 359 3611 Ex 4420
Telex: 336997
Director: Dr David Collingridge

Dear

I am conducting a study of the academic-industrial research relationships that exist within the British biotechnology community, in order to develop the basis for understanding how they developed and the importance of the role they play in the industrial development of biotechnology. I am a Ph.D candidate at the Technology Policy Unit (Management Centre) of the University of Aston, and I am writing to you in that capacity.

A good deal has been written over the past few years about the need for new and improved research relationships between academia and industry. Biotechnology is commonly cited as an area which would particularly benefit from such interactions. In the analysis of the influential 1980 "Spink's" report on biotechnology, significant importance was attached to the role of academic research in the generation of ideas and in the production of the skilled manpower necessary for the development of industrial biotechnology. However since the publication of this report, some six years ago, there has been no thorough science policy study in this country to determine the actual amount of industrial interest there has been in the transfer, from the academic sector to industry, of scientific knowledge, products and processes in the area of biotechnology. In this study, and with your assistance, I hope to provide such an overview detailing the extent, variety and the significance of current academic research interactions with industry across most of the disciplines relevant to biotechnology. The study aims to provide a clear analysis for science policy makers of the present and future role that the academic sector is likely to play in the development of the biotechnology industry.

Enclosed is a questionnaire directed to the above objectives. I would very much appreciate it if you would personally take the time (approx 15 mins) to respond to the questions posed. The validity of our study depends critically on the response of people like you. I am addressing the questions only to persons in the industrial community who are in a position to make an informed judgement on the issues discussed.

The specific information you and the others provide in response to this questionnaire will be treated as strictly confidential and safeguarded accordingly. Only the analytical results of the responses will be published and those results will be published in such a way to preserve the anonymity of each and every respondent.

I want to thank you in advance for your co-operation and assistance with this study. We hope to gain a much better perspective on how the academic community can assist in the development of this exciting industry and your responses should assist us, in a very significant way, in reaching this objective.

yours faithfully

I. Williams

3

I.D. NO. 79

INDUSTRY/ACADEMIC RESEARCH RELATIONS

A QUESTIONNAIRE FOR THE BRITISH BIOTECHNOLOGY INDUSTRY

This questionnaire is designed to provide an overview of industry/academic research relations in biotechnology. Your individual responses will be held confidential and will not be discussed.

Confidential

Instructions are provided with each question and if any question is inapplicable please proceed to the next question.

GENERAL INFORMATION

Name of Company: _____

_____

Is this company:

(a) Independent YES ____ NO ____

(b) Part of a group YES ____ NO ____

If your answer is (b). Then what is the name of this group?

Continued/Section 1

I.D No.__

SECTION ONE

RESEARCH AND YOUR COMPANY

Q.1.Does your company perform in-house research and development ? YES__ NO__

Q.2.If your answer is YES,what is the approximate distribution of effort amongst the following categories of R & D ?

NATURE OF R&D		Percentage
BASIC RESEARCH:	1.PURE, Basic research for advancement of knowledge only.No effort to apply results to practical problems.	_____
	2.STRATEGIC, Basic research carried out with the expectation that it will produce a broad base of knowledge likely to form the background to the solution of recognised current or future problems.	_____
APPLIED RESEARCH:	Undertaken in order to acquire new knowledge,and directed primarily towards specific practical aims.	_____
EXPERIMENTAL DEVELOPMENT:	Systematic work drawing on existing knowledge that is directed towards producing new or improved materials products etc,including design and development of prototypes and processes.	_____

Continued/Section

Q.3.Please list the areas of BIOTECHNOLOGY R&D in which your company is involved.Please tick below;

a.Recombinant DNA	☐	g.Animal cell culture	☐
b.Monoclonals/Hybridoma Technology	☐	h.Plant genetics & biochemistry	☐
c.Biocatalysis	☐	i.Biosensors/Bioelectronics	☐
d.Fermentation technology	☐	j.Waste treatment/biodegradation	☐
e.Downstream processing	☐	k.Protein Engineering	☐
f.Plant cell culture	☐	l.Any others;	☐

Q.4.Does Biotechnology represent a major part of your company's R&D at present ?

YES __ NO __

Q.5.Does Biotechnology represent a growing part of your R&D activities ?

YES __ NO __

Q.6.What is the major R&D activity of your company,if it is not biotechnology ? Please list below;

Continued/Section 2

SECTION TWO

ACADEMIC/INDUSTRY RESEARCH RELATIONSHIPS IN BIOTECHNOLOGY

Q.1.Does your company have research relationships with any of the following ?

a.Government research establishments YES __ NO __

b.Independent contract research companies YES __ NO __

c.New biotechnology companies YES __ NO __

d.Established companies YES __ NO __

e.Universities or Polytechnics YES __ NO __

Note; If your answer to Q.1 e was No, please go to SECTION FIVE.
If your answer was YES please continue;

Q.2.Does your company have research relationships with British Universities and/or Polytechnics ?

YES __ NO __

Q.3.If your answer to Q.2 was YES,what are the main institutions/departments involved ? Please list below;

_____

_____

_____

_____

_____

_____

Q.4.Doyou have research relationships with oversea Universities ?

YES ___ NO ___

Q.5.If your answer to Q.4 was YES,what are the main institutions/departments involved ? Please list below.

_____

_____

_____

_____

_____

_____

Continued/Section 2.

SECTION TWO contd

Q.6.Are you likely to increase the number of research relationships in the next five years with any of the following ?

a) British universities or polytechnics YES ___ NO ___

b) Oversea universities YES ___ NO ___

Q.7.How does your company identify specific academic research programmes or ideas that are of strong interest to it.On a scale of 1 to 4 please indicate the relative importance your company attaches to each of the mechanisms listed below;

Scale
1.Extremely important
2.Considerably important
3.Somewhat important
4.Not at all important

SECTION THREE

MAJOR MECHANISMS FOR INTERACTION WITH ACADEMIA IN BIOTECHNOLOGY

Q.1.On a scale of 1 to 4 please indicate the relative importance your company attaches to each of the mechanisms used by your company for interacting with Universities and Polytechnics in the field of Biotechnology;

SCALE
1.Extremely important
2.Considerably important
3.Somewhat important
4.Not at all important

MECHANISMS	Importance
a.Grants for research without fixed timescale or agreed programme	1 2 3 4
b.Grants for studentships,fellowships etc	1 2 3 4
c.Endowment of a chair or university post	1 2 3 4
d.Loans or gifts of equipment	1 2 3 4
e.Individual consulting arrangements	1 2 3 4
f.Contract research,specific to a research project or programme	1 2 3 4
g.Joint research programme	1 2 3 4
h.Membership of a research consortia	1 2 3 4
i.Informal co-operative interaction, co-authored papers etc	1 2 3 4
j.Researchcouncil co-operative research schemes	1 2 3 4
k.Any other mechanisms ? Please list below;	

Q.2.Do you see your company increasing,over the next five years,the use of any particular mechanisms described above.If so which ones are likely to be increasingly used ?Please list below;

Continued/section 4

SECTION FOUR

THE NATURE AND PURPOSE OF INDUSTRY/UNIVERSITY RESEARCH CO-OPERATION IN BIOTECHNOLOGY

Q.1.Howwould you classify the nature of your collaborative R&D with Universities/Polytechnics ? (Definitions as in section one).Please tick below;

COMPOSITION	Completely	Mainly	Some	Not at all
BASIC RESEARCH: a.PURE				
b.STRATEGIC				
APPLIED RESEARCH				
DEVELOPMENT				

Q.2.How important to your company are the following goals and potential outcomes of research collaboration ? On a scale of 1 to 4 please indicate the relative importance your company attatches to each in the field of Biotechnology;

SCALE
1.Extremely important
2.Considerably important
3.Somewhat important
4.Not at all important

GOAL / OUTCOME	Importance			
a.Develop patentable products	1	2	3	4
b.Develop commercialised products	1	2	3	4
c.Improve manufacturing processes	1	2	3	4
d.Redirect university research toward industrial problems	1	2	3	4
e.Improve instrumentation	1	2	3	4
f.Enhance quality of university research	1	2	3	4
g.Enhance quality of industrial research	1	2	3	4
h.Development of new research rojects in your company	1	2	3	4
i.Enhance student understanding of industry	1	2	3	4
j.Enhance student technical ttaining	1	2	3	4
k.General expansion of knowledge in this area	1	2	3	4
l.Better personnel recruitment	1	2	3	4
m.Gain access to university facilities	1	2	3	4
n.Improved accesibility to faculty scientists.	1	2	3	4

o.Any others,please list below

Continued/Section 5

SECTION FIVE

Q.1. If your company does not have research relationships with universities or polytechnics, please could you state the main reason for this below;

Q.2. If you would care to make any additional comments on the role or future of research relationships between industry and academia, they would be gratefully appreciated. Please use the space below;

Name;.....

Position in Company;.....

END

Thank you for your cooperation. Please place your completed Questionaire in the enclosed envelope and return to

Mr I.D Williams
Technology Policy Unit
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Birmingham B4 7ET