5
Industry–PSR Linkage in Biotechnology

5.1 INTRODUCTION

The material presented in this chapter comes from two studies.[1] The main one is our study of industry–PSR linkage in biotechnology related RD&D in four pharmaceutical companies, conducted in 1990/1. The earlier study, conducted in 1983–4, looked at five pharmaceutical companies working in the field—three of these overlapped with the later study. There is striking agreement between these two studies over the nature of linkage activity and channel use, to which we draw attention in our account. Differences, which relate chiefly to the extent and benefits of PSR linkage, are described at the end of this chapter (5.8) in order to provide some insight into how industry interaction with PSR can change over time.

As indicated in 4.7, our account first provides background on the technology and the study firms; it then presents our findings on the extent of external RD&D linkages, on PSR linkage activity, and on STI from PSR. After summarizing these findings, we review the results of the earlier study and identify the main changes in industry–PSR linkage in biotechnology over time.

5.2 THE TECHNOLOGY

5.2.1 *Biotechnology*

At its broadest, biotechnology involves the 'processing of biological agents', including microorganisms, cultured cells, and enzymes (Bull *et al.* 1982).[2] As such, biotechnology has been practiced since the earliest production of beer and wine. However, it was the development of genetic engineering techniques in the mid-1970s which brought the term 'biotechnology' into widespread usage, and sparked interest in the field. The earliest genetic engineering included *recombinant DNA* techniques (invented at Stanford University in the US) by which genetic material is transferred from one

[1] Readers should note that industry–PSR linkage in biotechnology has probably been studied more than any other field. As a supplement to our evidence on large established companies, see Krimsky *et al.* (1991) for a quantitative study of links involving new biotechnology firms.

[2] The term biotechnology excludes medicine and agriculture, except where these involve the application of cellular or molecular biology.

organism to another, such that the 'host' produces proteins (and so performs reactions) which occur naturally in the 'donor' (Sherwood and Atkinson 1981). *Hybridoma* techniques (invented at the Cambridge Laboratory of Molecular Biology in the UK) are used to fuse different cell types to produce monoclonal (i.e. antigen specific) antibodies; by their very specificity, they enormously simplify and speed up the tasks of analysis and extraction.

The main disciplinary inputs to conventional industrial biotechnology are microbiology, biochemistry, and biochemical engineering. Molecular biology is a new strand; it originated and was developed substantially from within PSR, and spawned the new techniques of genetic engineering. There were several scientific discoveries and technical developments in molecular biology during the 1980s, mostly from PSR. Protein engineering uses new techniques for *site-directed mutagenesis* which provide the ability to alter the DNA sequence of a gene, and to express a protein in living cells. Another area of enabling technology which has seen important development is receptorology, the study of how molecules recognize and 'dock' onto specific surfaces. From industry has come the *polymerase chain reaction,* which enables a specific gene to be duplicated a million times or more in a simple test-tube procedure; this is expected to have major implications in diagnostics, epidemiology, and human genetics as well as in basic research (ACOST 1990: 4–5).[3]

5.2.2 *Likely applications and bottlenecks*

A striking feature of developments in the new biotechnology is the proximity of discovery and invention, and the speed with which commercialization has followed on the heels of breakthroughs in some areas. Yet, alongside the obvious dynamism of this field, there is considerable uncertainty. It remains extremely difficult to make realistic predictions concerning economic targets and time frames for the applications of the new biotechnology. The field is still very embryonic in terms of innovation.

The greatest impact to date has been in pharmaceuticals. Fourteen first generation biotechnology based drugs had been brought to market by 1992; these are natural therapeutic proteins, produced by recombinant DNA techniques. Second and third generation biotechnology drugs, based on interdisciplinary developments in pharmacology and biotechnology, offer the potential not only to improve the targeting of drugs, but also to stimulate or suppress the immune system as required, to detect genetic defects and for viral diagnosis. This said, our interviews revealed that the value of

[3] More specific applications are suggested by the discovery (from PSR) of the processes by which the genetic defects underlying cancers, oncogenes, often function. This discovery was awarded the 1989 Nobel Prize for Medicine. Other developments will be helped by programmes to map and sequence the human genome.

genetic engineering techniques is seen as lying more in their general use as a research tool than for their potential to yield new biologically produced products. Conventional empirical procedures for developing new drugs, by synthesizing new chemicals and conducting large-scale screening trials for potential therapeutic effects, had been reaching their limits in terms of the cost and time taken to develop new drugs. Biotechnology techniques are expected to help pharmaceutical companies to institute new, less costly programmes of 'rational' drug discovery and design, based on extending fundamental understanding of the natural processes they seek to influence.

In any case, a number of barriers will have to be overcome before there is a significant stream of new biotechnology drugs. First, although scientists have made significant advances in understanding and in developing techniques for the application of genetic engineering, each advance tends to highlight gaps in scientific knowledge which delay further progress; the extent of our ignorance in the life sciences remains considerable. Second, first generation biotechnology based drugs are unsuitable for mass treatment because they cannot be taken orally but require intravenous injection, often by medical professionals. The development of novel delivery systems could overcome this problem and so extend the market for these products. Third, firms have no assurances of gaining monopoly profits should they bring new products to market, because of uncertainty over patent law relating to the products of biotechnology, and of difficulties in enforcing patent protection. The fourth obstacle is the lack of a regulatory framework to safeguard the public interest and protect the environment; some halting progress is now being made in this area (House of Lords 1993).

5.2.3 *Response to biotechnology*

Start-up firms, many of them academic spin-offs, were prominent in the early commercialization of the new biotechnology, particularly in the US (Kenney 1986). Whilst some of these companies have launched new products (e.g. diagnostic kits), many act as a bridge between public sector and industrial research in genetic engineering, supplying scientific techniques and expertise as well as intermediate products such as reagents (Oakey *et al.* 1990).

In general, large established companies were slower to respond to the developments in genetic engineering. Research strategies were directed initially towards accumulating knowledge about the new technology, rather than focusing on specific applications and production strategies (Orsenigo 1989), although some pharmaceutical companies worked on therapeutic proteins from the outset. By the late 1980s, the pharmaceutical industry began to build up in-house RD&D in the new biotechnology. Significantly, this involved gaining capability in previously unfamiliar research disciplines and techniques. Arora and Gambardella (1990) suggest that pharmaceutical companies are using linkages with small biotechnology firms and with universities as complementary strands in their strategies to increase in-house capabilities.

A number of developments indicated strong public–private research linkages in biotechnology in the early 1980s. In the US, the impassioned public debate over conflicts of interest which accompanied the development of commercial interest in academic biology was unprecedented (Peters 1984), as was the extent of academic entrepreneurship in that field (Kenney 1986). Many of the new 'campus laboratories' set up by companies to carry out biomedical or biotechnology research were associated with strategic research alliances between pharmaceutical companies and academic or hospital research centres (Webster and Swain 1991).

UK PSR made a significant contribution to early developments in biotechnology, but much of this work was carried out in Medical Research Council (MRC) Institutes and Units. The MRC had an arm's length relationship with the pharmaceutical industry,[4] and the universities were of limited use to industry, largely because of a comparatively low level of university research and postgraduates in the biotechnology area. In response to a growing national awareness that it was necessary to foster the public research base in biotechnology, the SERC formed the Biotechnology Directorate in 1981. Its role was to provide a national focus for academic and industrial interests in biotechnology, and to stimulate and coordinate research and postgraduate training. By 1984, in collaboration with industry, it had identified priority sectors for support and stimulated the interest of university researchers in centres of expertise. Numerous mechanisms were devised to build up links between the universities and industry, including Clubs,[5] Cooperative awards, CASE studentships, round tables, and workshops; industry constituted 50 per cent of the Directorate's Management Committee. The pharmaceutical industry took a particularly active role because it gave them access to the biotechnology techniques which previously had been the preserve of the MRC (Senker and Sharp 1988).

The activities of the Biotechnology Directorate did not diminish other Research Councils' support for biotechnology with the result that, at a time of general decline in research funding, biotechnology has been a growth area.[6] Other endeavours to support biotechnology include the DTI's Biotechnology Unit, charged with fostering the industrial development of biotechnology in the UK; and initiatives in the European Community's Framework Programmes for research and technological development such

[4] By the late 1970s and early 1980s, when the pharmaceutical industry wanted to access the new biotechnology expertise, the MRC was not interested in establishing industrial links (Senker and Sharp 1988: 57–8).

[5] See Sharp 1987 for an evaluation of the Protein Engineering Club.

[6] Because of differences in the definition of biotechnology, it is difficult to estimate total Research Council expenditure on this technology. One attempt suggested that £53.5m was spent in the financial year 1985/6 (Senker and Sharp 1988: 46).

as BAP (Biotechnology Action Programme), BEP (Biomolecular Engineering Programme), and BRIDGE (Biotechnology Research for Innovation, Development and Growth in Europe).

5.3 THE STUDY FIRMS

5.3.1 *Firm profiles*

Four global pharmaceutical companies participated in this study; all are involved in RD&D related to the new biotechnology. Three are UK owned and also took part in the earlier study; the fourth is a US subsidiary which established research facilities in the UK during the 1980s. Pharmaceuticals is the main activity of three of the firms; the fourth is part of a chemicals group. The figures in Table 5.1 relate to the companies' pharmaceuticals interests.

Table 5.1: *Profile of pharmaceutical companies (turnover, employment, and R&D), 1989 (£M)*

Company (Date of entry)	Turn-over	R&D spend	World Employment Total	World Employment R&D	UK Employment Total	UK Employment R&D	UK Employment Biotech*
Firm A (1981)	2,570	323	38,000	5,000	11,500	2,400	3–400
Firm B (1986)	1,334	202*	12,800	3,000	4,500*	1,500	45
Firm C (1988)**	3,640	417	37,500	NA	1,500	275	50
Firm D (1980)	4,300	390	62,800	5,000	13,200	2,000	82

* 1990
** Date of entry in UK

5.3.2 *New product development and skill profile*

New product development work in all the companies is dedicated to drug discovery and conducted in-house. There are external collaborations but very little research is contracted out, except for toxicology tests. The three UK companies carry out research and development; the US subsidiary is involved in basic research only. All the firms separate research from both production and development work.[7] Lead time between an original idea for a new drug and its emergence in the market was estimated by our interviewees as between eight and fifteen years and, in the words of one,

[7] Such contacts as do occur are limited to seeking the help of people with specific expertise or for scaling up the production of compounds in research. One company has devised a formal procedure for speeding promising new products through to development.

'getting longer all the time'. All the companies organize research in interdisciplinary teams, with senior management generally making decisions on research projects to be pursued. Research directors perceive that ideas for research projects can come from researchers at any level. The experience of some junior researchers would suggest otherwise,[8] although one company has a system which allows 'the brightest and best' researchers some freedom to undertake exploratory projects of their own choosing which, it is claimed, often leads to new ideas.

The companies recruit technical staff at all levels. For research staff they prefer career scientists with first-class degrees from leading universities, a relevant Ph.D., and post-doctoral experience abroad. In-house training is generally related to career development or management skills. None of the companies was recruiting in biotechnology at the time of the interviews, but all reported specific and differing skills shortages—natural product chemists, virologists, protein scientists (for purification, analysis, and modelling), biochemical engineers, and traditional pharmacologists.

The companies have a variety of methods to overcome skills shortages, each of which involves some form of linkage with universities (see 5.4). At the lowest level, informal links are built up with relevant university departments. Placements are provided for sandwich students: it is hoped industrial research experience might encourage them to undertake postgraduate training in relevant areas. One firm sends staff for retraining to its campus laboratory. Others provide bursaries for staff to take Ph.D.s. Three of the companies provide financial support to university departments which train doctoral students in areas of interest.

5.3.3 *Age and scale of involvement in the technology*

Table 5.1 indicates firms' judgement of the number of staff involved in the new biotechnology and the date of entry (i.e. first significant in-house RD&D) in the field. These figures are necessarily impressionistic because of the difficulty of distinguishing new and old biotechnology, and the lack of relevant company data. All the companies are alike, however, in that significant recruitment of specialist staff in biotechnology took place in the late 1980s. The scale of in-house effort is in the range of 50 to 80 staff for all but one firm (A), whose efforts dwarf its competitors.

Firm A gave 1981 as the date of entry, but this was at a very low level. A major expansion of biotechnology capability took place towards the end of the 1980s, through both acquisition of a small research-intensive company and recruitment; laboratory equipment was also modernized including

[8] 'Junior people can put forward proposals for feasibility studies . . . or to explore new ideas. Such projects are high risk in terms of long term survival and, while the mechanism still operates, it has become very formalized in recent times. . . . Management has become more multilayered over time which is introducing a sort of rigidity . . .'.

'wall-to-wall NMRs' (Nuclear Magnetic Resonance). Until 1986, firm B's involvement in biotechnology was focused entirely on its corporate laboratory and on the external research it sponsored. It had planned to build up biotechnology expertise through acquisition of a small company but, when none was available on acceptable terms, it acquired biotechnologists from the corporate laboratory and from a group diagnostics company which had been wound up. Firm C established its UK laboratory in 1984; this was the company's first basic research facility outside the US. In 1986, an academic scientist was recruited to bring biotechnology into the laboratory, but it took two years for research to develop to a state where it was considered useful to apply biotechnology. Firm D's considerable expertise in antibiotics and fermentation technology somewhat blinkered it initially to the potential of genetic engineering. In 1988, however, a Biotechnology Management Group was formed which drew together biotechnologists already working elsewhere in the company and recruited others to join them.

5.3.4 *Strategy for the technology*

None of the study firms had yet launched a new biotechnology product. However, biotechnology is regarded as having central importance for future innovation and growth in all the companies, albeit primarily through its general use as a research tool. Typical remarks include:

> Any company trying to produce traditional drugs which does not use biotechnology will get left behind. It has become indispensable. . . . Companies which do not have this capability will be forced out of business. It is very quick and efficient. There are some subtleties . . . where you cannot use animal models any more. You have to use genetic products expressed in cells. It's a necessity.

> Pharmaceutical companies which do not employ biotechnology will be at a serious disadvantage by the year 2000.

Two of the companies have continued to work towards the development of therapeutic proteins, but all are applying the techniques of biotechnology to drug discovery: to identify particular pathways, transmitters, or receptors involved in specific targeted diseases, as a basis for deciding how to design remedies.

The goal of all four companies is to gain sufficient capability in biotechnology to be able to apply it wherever appropriate, or at least to cope with expected future developments in the technology. All the researchers interviewed have a high regard for the excellence of their companies' scientific base, both in terms of the numbers and competence of the research staff, and of the equipment provided. Only one of the companies has fermentation expertise and associated pilot plants; its researchers regret their lack of *large-scale* fermentation facilities.

5.3.5 *Perceptions of PSR strengths and weaknesses*

Despite the growth in public support for biotechnology research, there is general agreement that the major weakness of university research is its lack of funds:

> Biological research has become expensive and government does not realize, and so PSR laboratories are grossly under-funded. Relative to some years ago, the university system has deteriorated and is becoming worse all the time. It is under-equipped and under-funded and will gradually slip behind the work done by other countries.

Two specific examples of deterioration were mentioned: neurological molecular biology and gene expression.[9] Industrial researchers think that the lack of adequate equipment and technician support in the majority of universities has resulted in academic researchers not getting the best out of their research efforts. By comparison, some well resourced centres of excellence in the UK have been able to surge ahead. Providing PSR with expensive modern equipment is very important to companies because

> the expertise in PSR is all in areas in which industry itself would never have invested. Instrumentation for NMR, X-ray crystallography is the sort of equipment which industry does not possess.[10]

Apart from the lack of funding, British PSR is thought to be poor at understanding industry's needs, especially in the capabilities that support manufacturing, and in microbial physiology where it is described as 'light years behind what is happening in industry'.

The perceived strengths of UK PSR are the novelty of its ideas, plus the ability to carry out research across a wide spectrum, and to follow any discovery through to its logical conclusions. Despite the lack of funding, very good scientists are produced. Indeed, one research manager thinks that the UK has the world's best molecular biologists. Three centres of excellence were mentioned by the majority of those interviewed: University College, London, Department of Chemical & Biochemical Engineering; MRC's Laboratory of Molecular Biology, Cambridge; and Oxford University. Leicester University's Biocentre and Dundee University's Department of Biochemistry are also regarded highly. The 'also-rans'—groups mentioned once or twice as having specific expertise—include several departments at Cambridge University, the Medical Research Council Institutes, and nine other universities.

[9] The MRC in Cambridge was once the only group in the world involved in neurological molecular biology. Now, at a time when the rest of the world is pouring money into the area, the MRC is pulling out. This withdrawal will diminish the UK's knowledge base and affect the ability to train research scientists in this field. In the gene expression field, PSR has now been overtaken by small biotechnology companies.

[10] This interviewee clearly did not know about the 'wall-to-wall' NMRs in firm A.

Some judge US PSR, which is well funded and attracts good researchers, to be miles ahead, particularly in molecular biology and receptorology. However, US public research is perceived to be less accessible than that in the UK because 'there is a tendency for academic groups with anything to offer to hive off into small companies'. Moreover, better funding is not the panacea it may seem. Laboratories tend to 'put money into solving problems through the use of superfluous equipment', while difficulties in recruiting junior research staff limit progress. Researchers also think that UK PSR compares badly with Switzerland and Germany, which are better provided with essential items of expensive research equipment.

5.4 EXTENT OF EXTERNAL RD&D LINKAGES

5.4.1 *Relative contribution to STI used in innovation*

The overall responses of biotechnology company researchers on the relative contribution of various STI sources to new product development are shown in Figures 5.1 and 5.2. The majority view is that in-house sources make a greater contribution than external sources, and that accumulated internal knowledge comes more from collective RD&D than from individuals' existing knowledge. Externally, PSR sources make a greater contribution than other companies. Within this, two-thirds think the academic contribution is greater than, and one-third believe it equals, the contribution from government laboratories.[11]

These overall assessments mask some variations. The source of STI tends to vary by project area:

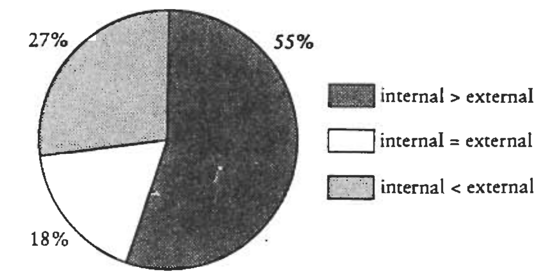

Fig. 5.1 *Relative contributions from internal and external sources in biotechnology*[a]
[a] *Percentages of responses (10)*

[11] These are Research Council links (mostly MRC). However, little subsequent reference was made to these laboratories in the interviews.

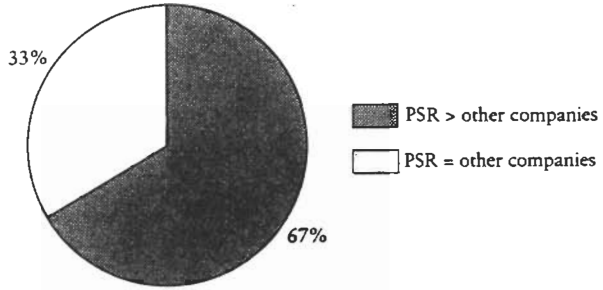

Fig. 5.2 *Relative contributions from PSR and other companies in biotechnology**
* *Percentages of responses (10)*

In systemic antibodies the majority of STI comes from in-house. In HIV most comes from outside, with very little from internal sources. There are extremes like that in almost every therapeutic area. Once you have developed a product, you have also built up company expertise, and external knowledge has become incorporated within the company.

Also, external knowledge is often more important when moving into a new field. One junior researcher, who currently benefits equally from internal and external sources of STI, identified occasions in the past when external sources had been more important for precisely this reason.

Research managers are unanimous that collective knowledge and teamwork make a much greater contribution than individual knowledge. Researchers at bench level tend to disagree; some think collective and individually held knowledge make equal contributions and others that individual knowledge makes the greater contribution. Further questioning revealed considerable variation between project and research areas:

On one occasion, the knowledge which someone brought into the company was crucial. In another case, someone's knowledge built up over twenty years in the pilot plant was important. You cannot divide the two.

It depends on the maturity of the project but in the development of systems it tends to be the in-house personally held which is more important. . . . [in] the more integrated project teams . . . [it] would tend to be the in-house generated knowledge which is more important.

With respect to biotechnology,

In some areas of molecular biology there is now a bias towards people bringing in knowledge, but that is short term.

Over the past year the number of scientists with genetic engineering skills has grown to quite a sizeable number. . . . The interesting thing is that their knowledge is spreading through the laboratory.

Thus we have evidence that personally held knowledge becomes diffused by the mechanism of interdisciplinary project teams.

The general importance of internal sources was also stressed in the earlier study: 'if research is worth doing, it is worth doing well.' This may be explained in part by the crucial importance of proprietary knowledge in pharmaceutical innovation. However, the comments above remind us that by employing qualified scientists companies acquire the expertise not only to generate new knowledge internally but also to access and 'import' external knowledge.

5.4.2 Sources of new product ideas

Our questioning here focused on ideas for new research projects. There is a consensus that the main source of such ideas is in-house research, but 'occasionally a paper which appears might trigger off new ideas if it suggests a significant advance in knowledge'. It was further suggested that there are qualitative differences between internal and external sources of STI:

In drug discovery external knowledge suggests new lines of work, but a great deal of internal knowledge is required to get quick solutions.

What happens in-house is the decision on what to go for, not the generation of the idea.

On the other hand,

it is usually the case that other major pharmaceutical companies and other academic groups are all pursuing the same ideas. It is so difficult to know where ideas come from and probably they develop at large in the scientific community.

Thus, whilst in-house activity is dominant, firms do not operate in isolation: idea generation is shaped by developments in the wider research community.

5.4.3 Links with other companies

Researchers have numerous links with other companies, including competitors and scientific instruments companies. Intelligence about competitors' RD&D efforts is a vital input to strategic planning. All the research managers report that they get a great deal of knowledge and ideas from the results of clinical trials of their competitors' drugs, reported in Scrip (world pharmaceutical news) and by the US Food and Drug Administration. Also, 'before drugs come to market companies provide samples to lots of academics and other investigators to run trials, and results of these tests become generally known'. Patent applications are another important source of external knowledge about competitors.

Bench level researchers value the occasional opportunities to meet informally with opposite numbers from other companies, such as seminars and other events run by academic or professional bodies. Such meetings enable industrial researchers to 'get a feel' for what each other are doing, to check that they are 'on the right tracks', or simply to exchange information of a 'neutral' nature. Several researchers mentioned the closeness which exists between researchers working in different industrial laboratories. They report that where basic research is concerned, there is not the hostility and secrecy which might be expected. Indeed, there is often a free exchange of ideas on 'scientific matters'—for instance, on matters related to equipment and safety, especially the containment of genetically engineered organisms, or on animal models for disease (which animals to use for investigating particular diseases). Pharmaceutical companies sometimes collaborate formally in such areas through government schemes.

There are several formal links between companies. Two companies have licensed in products from other firms or are actively involved in a search for products to license in. Another has a 'very productive' research collaboration with a small US biotechnology firm. Representatives from research equipment suppliers are a 'not insignificant source of information'. In one case, a local instruments firm has provided access to its instruments, allowing company researchers to try out their ideas: 'They provide the expertise with the instrumentation, we obviously have the expertise with handling the proteins.' Access to instruments is provided free of charge but is advantageous to both parties.[12] One bench scientist has informal links with friends and colleagues working in small companies. She is able to discuss pre-competitive aspects of the technology and instrumentation with them, but steers clear of discussing specific project work.

5.4.4 *Search activity*

All the companies have libraries or information science departments with a remit to keep researchers up to date on relevant information. All hold databases and a wide range of scientific journals, as well as reports of clinical trials and patent searches. Staff are encouraged to spend time scanning such publications. Company information scientists are used variously, to scan databases and compile personalized lists of relevant references for each researcher; to compile literature abstracts and carry out specific searches on request; and to produce a regular company bulletin of developments around the world. Researchers differentiated between knowledge search in ongoing areas, where researchers know the key journals to scan, and in new areas, where it is more appropriate to access information through databases.

[12] In order to persuade management to purchase new equipment, 'usually you have to generate a certain amount of data to prove to management that its worth their while. And very often these instruments are just at the prototype stage so you would never have them in-house . . . The instrument companies see it as advantageous because they want to advertise what they can do and so anything they generate with your particular proteins if they have the freedom to publish this, or if you're keen to publish, they're obviously very keen to help you out. . . . we get access to the technology and get results much faster than we would otherwise.'

Another route for getting into a new area is to use a consultant, who may be an academic:

> Initially when you are setting up a project in which no-one in the firm has expertise, it is really good to have a consultant. As you get further in, the need for a consultant decreases.

Scientific conferences are a valuable means to keep abreast of current developments. Each researcher usually attends at least one conference annually, in addition to any at which they present papers. They are expected to write up and disseminate conference highlights to their colleagues. All the companies invite academics to present papers at in-house seminars, including people deemed to have published exciting papers or given interesting presentations at conferences. Researchers are also encouraged to belong to relevant learned societies.

The earlier study showed that the stronger the internal communication between researchers, the greater the benefit of externally sourced knowledge to the company. We found a number of ways in which researchers are encouraged to exchange any new information they have acquired.[13] When research problems arise for which researchers do not personally hold the answers, colleagues can usually help—either by providing advice or recommending an appropriate external expert. If this fails, researchers use the literature to identify external experts.

It is difficult to get a clear idea of how much time researchers spend outside their companies to gather new knowledge, information, or ideas. Time allocated to knowledge gathering trips tends to vary depending on the researcher and project. In some project areas there are better people externally than in-house; in others the company is 'state of the art'. All but one of those interviewed estimate that they spend 5–10 per cent of their time outside the company gathering information; the exception, a research director, commits 10–20 per cent of his time on this activity.

Three companies have no formal mechanisms for monitoring search and knowledge gathering procedures. In the fourth, project teams have to review external scientific developments every six months, and look at alternative ways to achieve their goals:

[13] One company has 'Journal Clubs' where staff exchange information gathered in the literature. Another has formal quarterly meetings for research managers to discuss specific topics. Group meetings designed to review work also present opportunities to exchange information. Two companies have a regular programme of scientific seminars by staff, which help researchers to find out what colleagues in other research teams are doing. Another had tried to develop a handbook of company expertise where researchers could rapidly find a colleague with relevant knowledge, but it proved difficult to keep the information up to date.

Sometimes we feel we have done an inadequate job if a new development has occurred and we ask 'why didn't we know about this six months ago?' and this sometimes leads to new ways of doing things.

The research directors in two other companies believe that so many of their researchers are actively scanning that nothing of importance is likely to 'fall through the net'. Clearly all the pharmaceutical companies consider it vital that they keep up to date with the latest external developments in biotechnology.

5.5 PSR LINKAGE ACTIVITY

Here we look first at formal linkage with PSR, including company policy, the range of mechanisms, and examples which illustrate different types and uses of PSR linkage. Section 5.5.4 describes informal linkage in biotechnology, and 5.5.5 concludes with a discussion of the benefits of both formal and informal links with PSR.

5.5.1 *Company policy*

Three of the study firms have explicit policies to invest in links with PSR, backed by specific budgets. In two companies this amounts to several million pounds per annum; one operates a 'slush' fund of £300,000 per annum for projects costing below £10,000, which allows it to direct money quickly into interesting things which crop up. The third company, the US subsidiary, spends only £245,000 and cannot enter high cost schemes without prior approval from the parent. In the fourth company, PSR linkage happens on merit, rather than as an explicit part of company strategy.

Firms' expenditure on R&D is shown in Table 5.2; the PSR proportion refers to total company expenditure on PSR across a wide range of disciplines, including biotechnology. This table should be treated with caution since the data are not strictly comparable between companies. For instance, the table does not include PSR expenditure made by company laboratories outside the UK. Nor does it include expenditure on activities such as toxicology, pathology or clinical trials, many of which are conducted in PSR. Another complication is that in some companies extra-mural research is funded out of project or programme budgets and not accounted for centrally.

The range of formal links which each firm has with PSR is indicated in Table 5.3, and described more fully in 5.5.2 and 5.5.3 below. It can be seen that, with the exception of campus laboratories, companies are doing broadly similar things, and differences in expenditure relate to the scale rather than the type of investment. The vast majority of these links are with academic rather than government laboratories.

Table 5.2: *Pharmaceutical company expenditure on PSR as a proportion of R&D, 1989*

	Expenditure (£M)		
Company	R&D	PSR	PSR Spend as % R&D Budget
Firm A	323	4–6	1–1.5
Firm B	202	2.5*	1–1.5
Firm C**	9.5	0.25	2.5
Firm D†	390	NA	2.8

* Corporate HQ spends an additional £2.5M on PSR linkage
** UK
† 1990

Table 5.3: *Range of formal company–PSR linkage mechanisms in biotechnology*

Type of PSR Link	Firm A	Firm B	Firm C	Firm D
(*a*) BILATERAL				
Consultants	x	x	x	x
Postdoctoral fellowships			x	
Company studentships	x			
Sandwich students	x	x	x	x
Research contracts:	x	x	x	x
UK		x		x
Europe		x		
US				
Campus laboratory		x		x
(*b*) GOVERNMENT-SPONSORED				
CASE/MRC studentships	x	x	x	x
Biotechnology Directorate				
Clubs and LINK programmes	x	x		x
SERC Cooperative grants			x	x
EC BRIDGE programme		x		

Companies generally collaborate with academics who have specialist expertise they lack in-house. Research excellence is a vital criterion in selecting potential collaborators. One bench researcher looks for 'someone . . . who's been steeped in the area for six or seven or eight years in academic life. It demands that degree of immersion in the subject'. Another looks for researchers whose supervisors have good track records and come from good laboratories. Willingness and ability to collaborate is another vital criterion, as one researcher volunteered:

the interpersonal side actually becomes a factor when you're making the contacts, so not only would you say 'is it the best academic lab?', you'd actually look at their track record of interactions with the lab and industry. . . . so if you went and said 'how did you get on with Firm X or Y?' and they said 'Oh we had an awful time' . . . you'd probably think oh-oh.

Many of our interviewees emphasized that they make links with people they know and trust, and prefer to interact with individual people than with specific universities or departments.[14]

5.5.2 *Formal collaborations*

As shown in Table 5.3, all the companies are involved in direct contracts, CASE studentships, and sandwich student placements, and all use academic consultants to some extent. The distinction between consultancies and research contracts is generally one of size; also in the latter case the agreement is usually made with the academic institution rather than the individual. Such agreements are characterized by the requirement for confidentiality: companies retain the right to delay publication of interesting results for long enough to file a patent application.

All the UK companies are involved in LINK programmes and Biotechnology Directorate Clubs for pre-competitive research collaborations with other companies and universities; the US subsidiary is experiencing difficulties negotiating entry to such programmes.[15] Participation in other government schemes is more patchy, but each company has its own programmes for linkage. Most of these linkages are with UK universities, although one company has a project in Belgium and another is funding projects in Germany and the US.

In these higher cost linkages, the decision on whether to opt for government collaboration programmes (which can provide up to 50 per cent of the costs of a project) or a bilateral contract appear to be related to the potential application of the resulting knowledge. Government programmes are felt to be appropriate in fast-moving fields, where companies want to keep an ear to the ground in order to see what might be relevant to them. As one research manager explained:

[14] Similarly, 'centres of excellence' were described by one of those interviewed as ephemeral: 'They have to do with a group of people at a particular point of time; groups undergo constant change and this can affect the excellence of a place.'

[15] This is because the cost is higher than an individual laboratory can authorize and has to be approved by the parent company. Intellectual property rights are another stumbling block, since the UK laboratory does not have a legal department and the US legal experts cannot understand the terms of the agreement.

Research is about 90 per cent people-related. Government schemes mean you can use more people on a project. We also get involved as a charitable thing, so people can get experience of working in an industrial laboratory.

The fact that government sponsored collaborative programmes involve company researchers in a lot of work, and that the process of applying for government support is long and uncertain, is another important determinant. Thus, if a piece of work is urgent or important, or has left the pre-competitive phase, it is more appropriate to fund university research on a bilateral basis.

The use of low cost links, such as CASE studentships, illustrates two important general features of the personal interaction associated with formal PSR linkage. First, the academic or department involved is one in which the company already has an express interest and at least some previous contact. Industrialists rely heavily on prior knowledge before making a new contact. So, for example, academic consultants are rarely 'brought in cold'; industrial researchers often seek out information about a potential collaborator from existing contacts. Similarly, many interviewees reported instances when an informal interaction, for instance requests for sections of DNA, led to more substantial formal linkage. Second, low level linkages are a valuable means of relationship building, and can therefore lead on to lasting informal contacts and, at times, larger scale linkages. Successful CASE studentships sometimes result in the academic supervisor being retained as a consultant to the company, and one has resulted in a major collaboration.[16]

Large-scale research agreements are generally preceded by a history of interaction, in which initial informal contacts have led in an incremental, 'step wise' fashion to small and then progressively larger forms of collaboration. At each stage the relationship is tested, in what amounts to a trust building exercise. So vital is this process, that high level linkages imposed without a history of smaller but growing relations can prove unrewarding. These comments from a bench researcher are typical:

But a lot of the cases where a lot of money is spent . . . it's a senior management decision and . . . scientists are told 'this is who we perceive as the best centre in the UK . . . and now, you guys, get on with it.' I don't think that's a beneficial way to approach it.

It is clear that most is gained scientifically from formal contracts where there is a good relationship between the industrial and academic researchers *at the bench level*. This demands care over setting up the formal contract: long before a contract is drawn up, the researchers who will actually

[16] The student had built up a close connection with the company during the time he spent in their laboratories. The company now supports his academic supervisor's research group for work connected with NMR and proteins, because the university has the NMR equipment and the expertise to interpret results, which is crucial.

collaborate must be allowed to interact informally—to explore areas of mutual interest, and to establish the basic trust and understanding that will enable them to collaborate effectively.

5.5.3 *Specific linkages*

Here we describe the two campus laboratories, since this form of linkage is most prevalent in the field of biotechnology (Webster 1994). We also illustrate the range of bilateral research linkages including company studentships.

Firms B and D have both established research centres on university campuses. Company B's links are with a joint laboratory established inside a university department in 1980 to bring biotechnology expertise into the company. Initially this laboratory was funded by and reported to corporate headquarters, and its research was in fields of general interest (see 5.8.1). Now it works directly for the pharmaceuticals business and its research programme has become more structured. The company wholly funds approximately twelve researchers to work in the joint laboratory at a cost of £400,000 per annum. Other company researchers are seconded there from time to time. Company researchers at bench level perceive that researchers in the joint laboratory

> tend to have a lot more freedom, so they tend to be almost an ideas generation sort of factory there . . . I guess in a way its actually both cheaper [for the company] because the overheads and the actual cost of running that sort of group is cheaper within the university, but it means that those people are not constrained like the rest of us working here.

Company D has established two university research centres in the last two or three years. In the first of these, the company paid for the costs of refurbishing a laboratory in a department of medicine and committed themselves to meeting the running costs. In return they decide on which projects will be funded. The research staff are university employees on university salary scales, and are free to look for funds to carry out research in addition to company projects. It appears to run more or less like a normal academic laboratory, although the company funds the majority of the research projects. The second university research centre was set up in a derelict part of a university hospital which the company refurbished. The company has committed itself to meeting all the costs of the programme of research which it determines. Staff are company employees on industrial salaries. Basic research, not immediately relevant to company interests, is carried out at both of these research centres, whose main purpose is to act as 'listening posts'.

Both companies also have a wide range of other formal collaborations with PSR. Company B has a strategic research fund to which staff submit

proposals for pre-competitive PSR research projects. Projects funded under this scheme result in very good relationships between the industrial and academic researchers because there are no strings attached, unlike contracts where the company is paying for specific expertise or the solution to a specific problem. One successful project under this scheme funded four people over three years at the National Institute of Medical Research (NIMR). Some of the gene expression technology it developed was brought in-house very quickly by putting company people into NIMR, establishing parallel research in-house with the help of NIMR's Principal Investigator, and arranging regular meetings between the two groups.

Researchers in company B characterize the pre-competitive work undertaken in these formal collaborations as 'enabling technology' related to techniques and methods. On rare occasions it is connected with specific company projects, usually when the academics have approached the company because it has specific expertise or patents. Such collaborations can be difficult because the academics do not feel constrained by the rules and regulations imposed by the project teams, and because academics tend to be less open when a patent is involved. Researchers feel that 'the more fruitful collaborations are going to be the ones where there are free and open discussions of all of our work, all of their work and [we] actually go out and publish'.

Firm A has set up a scheme of company studentships for doctoral research; eight to ten are awarded each year. The company covers all the costs of the studentship—fees, enhanced grant, and materials costs. The studentships are publicly advertised, inviting applications in any discipline from students with a project and a supervisor; applications are reviewed internally. The scheme has been developed to promote the company to university students as an organization willing to support first-class research.

5.5.4 *Informal linkage*

It will be clear from the discussion at the end of 5.5.2 above, that informal contacts are both a precursor and a consequence of successful formal collaboration, and that much of the scientific value of these arrangements depends on good inter-personal relationships with the academic researchers concerned. This explains in part why informal links are very important to all the companies. But our interviews showed that informal interaction is also very important *in its own right*. It takes place much more frequently than formal linkage and, combined with reading the literature, undoubtedly contributes a high proportion of knowledge flows from PSR into pharmaceutical companies (see 5.6.3 below).

Informality offers major advantages. In particular, it avoids any restrictions on the flow of ideas and information which may accompany formal arrangements. It also facilitates important two-way flows of both STI and technical assistance, for example in the use of equipment or the exchange of research materials. We have experience of researchers in collaborative government schemes using formal meetings to exchange strains of cells and microorganisms. Companies are keen to use the same biological materials as academics in order to be able to replicate results reported in the literature.

Such 'mutual back-scratching' or barter is often not formalized, for internal reasons. First, it is not always realistic to account for the service provided in the normal way (i.e. a cash value attributable to a single project). Second, the exchange can appear unbalanced because industry generally has greater resources for equipment and the like; the knowledge and opportunity for discussion which it gets from PSR in return is not sufficiently tangible to be easily recognized by company accountants. Yet, corporate goodwill in this form is reportedly very important in strengthening the climate of trust and mutual respect between colleagues in industry and PSR. And the benefits can be real enough. Thus, informal interaction can be a source of valuable research materials, e.g. a piece of DNA or plasmid which has been reported in the literature and has potential use for the company. Existing contacts provide such materials quickly, without any fuss, although there is sometimes a small charge. By contrast, 'academics you don't know expect a signed agreement with promises of a percentage of the profits for something you may only ever look at for a week or two'.

The sources of informal contacts in PSR tend to reflect the work histories and specialisms of industrial researchers. Contacts dating from the period of doctoral and post-doctoral research are especially durable and important of doctoral and post-doctoral research are especially durable and important early on in a career. Bench researchers also build on the personal contacts of their colleagues. The 'old boys network' is useful for information about who is good; alternatively they use post-doctoral researchers whose supervisors have a sound reputation. The main way to meet new people is going to meetings and reading published papers: 'When you read something interesting, you make a mental note of the name and if you come across them at a meeting you make a point of contacting them'. Alternatively, researchers telephone or write to the author directly. Academic scientists contacted in this way are sometimes invited to the company to present a seminar. On occasion, this has led on to a direct contract, or to the academic becoming a company consultant.

Researchers stress that they need to find additional contacts when they move into new or unfamiliar technological areas. Project leaders in two companies reported that they are engaged in an active search for contacts with expertise in a variety of novel specialisms (e.g. signal transduction, baculo-viruses). This activity is described as

> part of getting my act together, so to speak. . . . If it was an area I only had a cursory knowledge of, it would be doing my homework properly, and perhaps contacting other people I knew to ask their opinion of other people if I thought they had a wider knowledge of the area. Then perhaps I'd try and make a short-list and then after some preliminary discussion here as to who was perceived by management as a good person to contact I think I'd just plunge in . . . and make a phone call.

This comment throws light on another use of informal links; they provide an entrée to other networks of contacts. From this point of view, researchers find that personal contacts in large university departments can be most fruitful:

> The most productive work happens in larger places. For instance, if there is a problem your contact does not know about, someone close at hand will know the answer. Once you have established a contact with someone you have established a network of contacts in the same university. It is much easier to deal with networks of this sort. Sometimes a major research investment may grow out of low level contacts of this sort.

Again we see the tendency for minor interaction to lead on to more substantial linkage.

In all our study firms, staff are encouraged to make and maintain personal contacts in PSR.[17] One company has recently sought to increase the number of contacts between company and university researchers at bench level. Despite giving large sums of money to the universities each year, it feels that it is not being approached often enough by innovative groups which have come up with interesting ideas, and suspects that this is due to outsiders not understanding how the company is organized and how to go about contacting relevant people.

5.5.5 *Benefits of linkage*

The reasons given for linking with PSR vary considerably. Nevertheless, it is possible to summarize the picture which emerges with respect to high and low cost formal linkage and to informal interactions.

One common factor associated with higher cost linkages is the tendency for companies to spend money on PSR in areas where they do not have the expertise in-house. Perhaps the most telling comment on this was made by a project leader who had been recruited from PSR to bring her expertise into the company. She perceives that PSR linkage is used by companies as a way to access

> new areas we want to get into or where we don't have the requisite level of expertise in-house. If it was relevant enough we'd find the expertise and bring it in-house.

So linkage can be a prelude to recruitment in areas where companies wish to build up capability in-house. Significantly, we found that many strategic

[17] Informal contacts are judged of such importance in one company that the contacts researchers maintain is one criterion for staff promotion.

research collaborations with PSR are aimed at acquiring skills in the techniques of biotechnology—skills which the company lacks, especially in new, specialist areas. These collaborations contain provisions for the post-doctoral researcher to work first in the academic and then in the company laboratory, or for company researchers to go to academic laboratories for training:

> [Academics] can talk to us about something on the telephone or send particular papers but doing it is different from reading about it. Very often what you need is to send someone out to spend some time in the lab or have them come here and comment on what you're doing.

Secondments of this type facilitate the transfer of academic skills and techniques to the company. They also enable academics to become familiar with industrial research, and some are subsequently recruited as permanent members of staff.

Specific knowledge acquisition is not normally the main objective of formal linkage with PSR; these links tend to be more about acquiring experimental techniques and skills in the enabling technologies. Knowledge does play a role, however. PSR linkage is often undertaken to develop underpinning knowledge, for instance, related to routes to discovery. It is also common for companies to use formal links with PSR to investigate areas peripheral to mainstream company research—areas which emerge during in-house project work, but cannot be pursued because the need to focus on clear objectives means a 'lack of freedom in our own research [which] leads us in a fairly blinkered way'. Interesting and useful results can be gained from PSR work on these low priority topics.

Our evidence in 5.5.2 suggests that collaborative projects funded through government programmes will tend to be more exploratory and peripheral than those funded bilaterally. Perhaps for this reason, our interviews reveal considerable ambivalence about the scientific benefits of participating in government supported schemes. Some use these linkages, like bilateral ones, to alleviate a skills shortage or build up new expertise. One bench researcher mentioned that academics in several LINK programmes had developed techniques relevant to company research interests. The company had subsequently entered bilateral contracts with these academics, outwith LINK, to develop the work further. For others, the benefits of government sponsored collaboration were thought to be minimal—fostering a sense of community and generating contacts. One bench scientist who had been involved in two LINK programmes remarked:

> collaborations have not made a great deal of difference to my work at all. *It has just been to keep up with what is going on.* It is a source of potential recruitment, general education, and contributes long-term to improvements in the background technology (our emphasis).

Notice, however, the emphasized remark which confirms the general impo tance of PSR linkage as a means of keeping abreast of external develop ments in a fast moving field.

Many of our interviewees stressed the public relations role of PSR link ages. For example, three research managers reported that PSR interaction used partly because 'the universities expect it of us', but mainly to ai recruitment or the flow of new ideas into the company. This is not a cyn cal observation: academics will only recommend their best students to see employment in a company when they are familiar with the company research and respect its scientific worth. One company provides compan studentships for doctoral research, in order to promote the company to un versity students as an organization willing to support first-class research Public relations is a particularly important factor influencing the PSR link of the newly established US subsidiary:

> When the laboratory was first established we had to compete for attention with . . [major British competitors]. We did everything we could to foster university link and spread knowledge about our activities so we could get access to the scientifi community. We will not be able to recruit and retain very good career scientist unless we give them the opportunity to go to scientific meetings, publish, and ge involved in the general process of refereeing papers and presenting papers. It give them the chance to measure their worth through the assessment of external peers We try to attract the best academic minds and therefore want to assure them tha working for us will not mean being cut off from the academic sector. We encourag them to arrange collaborations or offer visiting post-docs the opportunity to worl in the lab.

There is a general hope that the goodwill which ensues from such linkage will encourage academics to approach the company, rather than its competitors, with any interesting ideas of projects which crop up.

The public relations benefits of PSR linkage seem to be especially prominent in low cost linkages, such as sandwich student placements and CASE studentships, where the scientific benefits are generally marginal. Whilst student placements provide a pool of cheap labour, it is considered a bonus when CASE studentships provide scientific benefits. These activities are a useful mechanism for building relationships with the academic supervisors. One project leader reported that CASE student supervision also provides useful experience in managerial training.[18]

The benefits of employing individual academics as consultants vary enormously. In general, if companies have a specific question or problem, they want to be able to contact the appropriate person directly. Researchers in our first study emphasized that PSR contacts tended to help more with the 'testing of a proposed solution' than 'providing or describing the basic

[18] 'Because of the stability connected with studentships—ongoing research as opposed to shorter term in-house projects—it is a step up the ladder. I can keep my science going while doing administration.'

elements of the solution'. Several researchers use consultants as a sounding board for new ideas. Academics are also relied on

> for the more general observations which are often the things that actually lead to quantum leaps—in understanding anyway, because they are not predictable.

More importantly:

> If you are involved in research at the cutting edge, PSR is an effective means of analysing the field for you. It serves as an information science facility with a strong element of judgement, which is useful in terms of knowing which direction to go in-house.

Academic experts are often contacted as a follow-up to reading something in the literature—to comment on or to clarify the significance of new scientific breakthroughs, to indicate the ways in which such new knowledge might be exploited, or to provide further related information (e.g. where to find specific research equipment).

Given the continuum which exists between informal and formal contacts, it is not surprising that similar types of benefits derive from both types of link. The main difference is that with formal contracts the expected benefits are more specific. To summarize the wide range of benefits derived from informal contacts, these include specific help, advice, and information; a perspective on the latest findings reported in the literature; an entrée into academic laboratories; an opportunity to meet people which may lead on to recruitment; training in new techniques; and access to research equipment and materials. Interaction with PSR researchers also has the additional (incidental) benefit of catalysing the flow of information between companies because, in the words of one researcher, 'academics are leaky and you find out what other companies are doing'.

One matter warrants further comment, with respect to the general use of PSR contacts to keep up to date with scientific advance. Bench level researchers place particular importance of what several called 'being on the unpublished grapevine', e.g. through refereeing papers for journals or participating in closed seminars which enable them to hear of scientific advance prior to publication. In the earlier study, researchers complained that abstracts and digests represent 'old knowledge' by the time they reach the libraries. Such comments suggest that, in spite of their heavy reliance on the results of basic research, pharmaceutical researchers feel themselves to be on the periphery of the informal communication networks which connect academic scientists in any one specialty.

5.6 STI TO INNOVATION

5.6.1 *Types and sources of STI*

Researchers in the four companies have similar views about the importance of the various types of STI inputs required for their work. Knowledge of specific fields, plus skills, account for the majority of the inputs; STI relating to technical information and to artefacts were mentioned only occasionally. In this latter category, the STI identified by researchers were connected with research not production equipment. The importance of the various types of STI and its source is summarized in Table 5.4.

Table 5.4: *Types of STI by source in biotechnology*

	Sources of STI		
Type of STI	Internal	Other companies	PSR
Knowledge of particular fields			**FORMAL**
Technical information		Formal	Formal
Skills	**TACIT**		
Artefacts	Tacit	Tacit	Tacit

Note: Boldness of typeface indicates importance of STI

Knowledge of particular fields. This is mainly codified. It derives from formal education and training in PSR, and from the published literature. Basic research conducted in-house also makes a small contribution. The knowledge of specific fields required is extremely wide, and companies rely on individual employees for expertise and sources of knowledge abour particular fields. Table 5.5 contains a composite list of all the scientific areas which researchers think relevant to their work; this is grouped according to whether researchers consider the fields of core importance, or useful only occasionally.

Technical information. Most researchers could not think of any STI which contribute to their work under this heading. The only example mentioned was information on the availability and suitability of materials such as different strains of micro-organisms or vectors. This is usually available in the catalogues of companies which market molecular biology materials.

Table 5.5: *Relevant disciplinary fields in biotechnology*

Core Disciplines
biochemical engineering
biochemistry
chemistry
clinical medicine
molecular biology
organic chemistry
pharmacology
toxicology

Other Relevant Fields
cell biology
cell culture
computer applications
electronic control
fermentation
genetics
haematology
membrane proteins
modelling active sites of enzymes and receptors
neurobiology
new screening methods
physiology
protein biochemistry
protein purification
protein structure
rDNA techniques
separation techniques
small molecular weight compounds
statistics
transgenic animals

Note: Compilation of all the fields which interviewees reported they used

Skills. These are largely based on tacit knowledge. They are acquired in part during doctoral and post-doctoral research in PSR, and in research collaborations described in 5.4.3 above; but, in the words of one interviewee, '99 per cent is acquired from learning on the job'. Many directors and project leaders stressed the importance of firm-specific expertise built up over time, for instance in fermentation. Skills also relate to setting up experiments, interpreting the results, and understanding why an experiment will or will not work:

The most important input is the things you have picked up about what is likely to work, and what is not.

I need to know what might have gone wrong and what questions to ask my colleagues when they have problems with an experiment. If you have not done it yourself, you do not have the assurance that it can be done or know why an experiment does not work.

You couldn't do your research unless you knew how to set things up. Many results can be interpreted in different ways. If you know what you are looking for, it is easier to see something, but that's just experience.

There are also skills associated with managing research—knowing how to work as a team, to share knowledge, and to train colleagues in specific expertise.

Artefacts. Research equipment and materials were described as a necessity, but most researchers are not aware of related STI inputs. One researcher's reaction was that research equipment tends to 'speed things up rather than add any knowledge'. There were exceptions, with examples of STI derived from PSR and other companies. The company which uses NMR equipment and related expertise in PSR occasionally pays for company researchers to be trained in new techniques at an academic laboratory. Another purchases molecular biology products from PSR because of greater confidence in the reliability of these products than those purchased from some commercial organizations. Scientific instruments companies provide STI relating to the great number of machines and methodologies available, especially advice on which is appropriate for a specific application. However, the main source of STI relating to research materials and equipment derives from in-house sources. All the companies have technicians to look after the equipment, but the researchers themselves require the expertise to analyse the results produced.

Bench researchers and project leaders are emphatic that tacit knowledge and related skills make a much greater contribution to their research than does theory or published knowledge. They believe that they could not carry out their work without formal training, but they also require the expertise built up through work experience. Although there is a great deal of information available in written form, it lacks value judgements, for instance, about the best method to use for an experiment. This type of knowledge can only be gained through experience, or from talking to experts:

The knowledge I need comes from reading the literature, plus doing, plus finding out from other people.

In the early days of their careers researchers rely mainly on their formal knowledge base, because that is all they have; over time the tacit knowledge and expertise acquired on the job becomes more important.

Some of the bench researchers suggested a change in the nature of STI to RD&D in biotechnology since the early 1980s. At that time, very little information was formalized or available in published form, and companies needed to send their researchers to PSR to be trained in recombinant DNA techniques. Now, new recruits have learnt these techniques through experience and example during their undergraduate education.

5.6.2 *Impact of STI by source*

Figure 5.3 shows the impact of STI from various sources on company innovative activities, in terms of the percentage of researchers interviewed.[19] PSR appears to make the greatest relative contribution in three areas: 'scanning the research frontier', 'underpinning knowledge', and 'skills in experimentation and testing'.

In-house RD&D and staff are considered to be the sole source of STI related to 'articulation of user needs' and 'routine problem solving', and the main source for 'feedback on existing products'. The only activities on which external sources have a significant impact are search activity ('scouting for new applications' and 'scanning the research frontier'), 'underpinning knowledge'—where roughly half of those interviewed thought PSR had the greatest sole or joint impact—and activities classified by us as instrumentalities. Within this latter category, other companies are particularly important for 'new research equipment', and PSR is important for 'skills in experimentation and testing'.

These aggregate findings mask differences between the views of research managers and researchers at bench level. They agree about the activities on which PSR STI impacts, but researchers at bench level placed greater emphasis than research managers on the impact of in-house activities on search activities and underpinning knowledge.

5.6.3 *Channels for STI from PSR*

In Table 5.6, data on the impact of STI from PSR is summarized in terms of the channels through which researchers obtain these STI. This shows that the literature is the most important channel overall, and is particularly important for RD&D procedures (as a share of all channel use for this activity). Further questioning revealed that company researchers often use multiple channels to acquire STI from PSR. Specifically, most researchers at bench level use the literature and contacts in tandem for accessing information

[19] The reader should be aware that the data presented here is based on relatively small numbers of responses, so Fig. 5.3 should be taken as indicating broad trends only. This impact chart was intended to indicate the relative contribution of individual sources to each area of activity, and should not strictly be used to provide a measure of the *overall* knowledge contribution of each source. Nevertheless, it does appear to confirm the primacy of in-house STI for most activities.

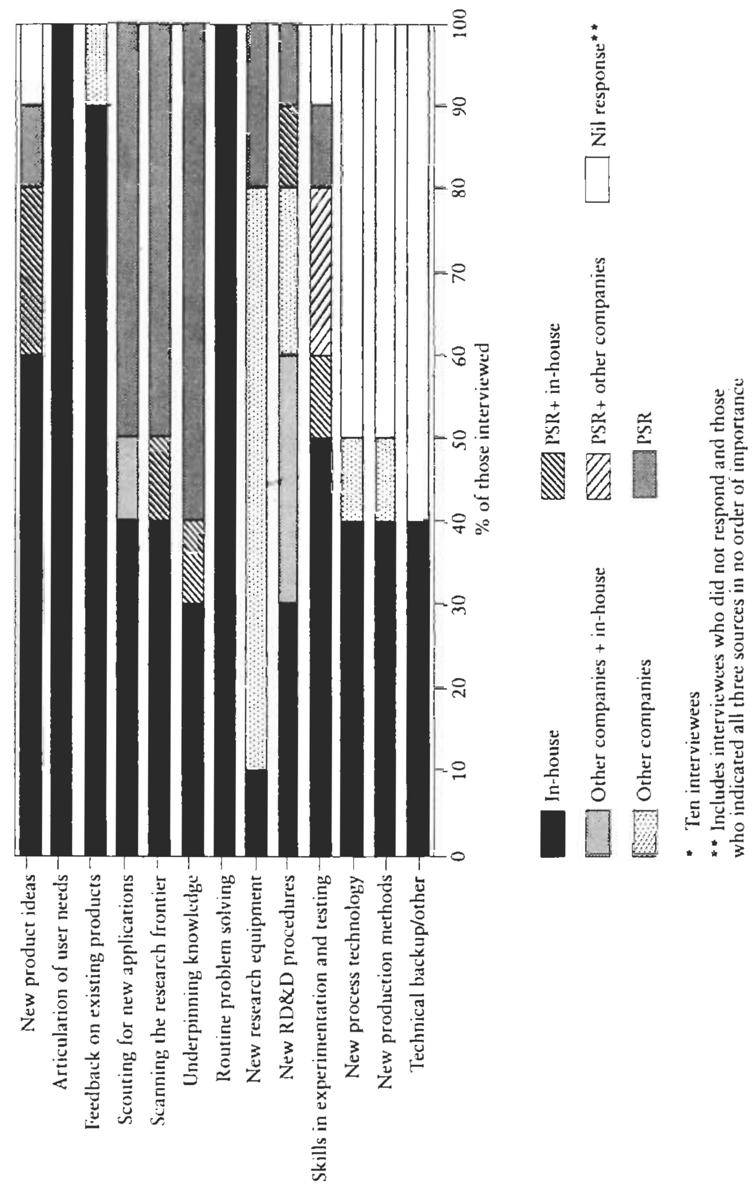

Fig. 5.3 *Impact of STI by source in biotechnology**

* *Ten interviewees*

** *Includes interviewees who did not respond and those who indicated all three sources in order of importance*

Table 5.6: *Impact of STI from PSR in biotechnology, overall and by channel use*

Activity	Overall	Literature	Contact	Recruitment
Future Innovations	9.1	4.5	2.3	2.3
Search	45.5	25.0	16.0	4.5
RD&D	22.7	13.6	9.1	—
Instrumentalities	22.7	9.1	9.1	4.5
Overall		52.2	36.4	11.4

* percentage of responses (10)

from PSR; they follow up papers of potential relevance to the company by contacting the author. By contrast, research managers tend to rely more on a single source—either the literature (by far the most common) or contacts.

Researchers noted that the scientific literature and personal contacts differ as information sources in important respects. The literature is hard and fast, tried and tested. It has been vetted through the refereeing process, but does not provide the context or the tacit knowledge available from informal contacts.

Personal contacts are the only way to find out what things went wrong during an experiment, and why. They tell you what is worth following. . . . Often the most important part of a paper is cited as 'personal communication'.

The literature is also three to four months out of date. Researchers, therefore, reported that they would be very disappointed not to be aware of significant research before it appeared in the journals—hence the importance attached to being on the unpublished grapevine.

If you are trying to get an edge on things and be absolutely up to date, you rely on personal contacts.

Contacts are therefore more useful for information about new directions in research, even though knowledge from personal contacts is less reliable than STI from the published literature. At least one of the companies likes its researchers to referee papers submitted to scientific journals, as this is an excellent way of picking up information on recent research.

The earlier study produced very similar findings. All those interviewed reported that the published literature was the most frequently used external source of STI, describing the literature as 'essential' to company R&D, 'the major form of scientific and technical assistance' used routinely, and 'the largest single mode of information transfer into corporate R&D'. They were also similar to their contemporaries in using the literature and personal contacts as complementary inputs to company R&D: in the words of one interviewee, 'breadth of knowledge comes more from what you read that from what you hear' but 'what you can't get from the literature is the intellectual stimulation which comes from personal interaction'. Similarly, when searching for new contacts, 'it is important to know more about people one might wish to contact than simply what they publish'.

Returning to the current study, research managers alone identified recruitment as a channel for STI from PSR. (Presumably they are responsible for the decision to appoint.) New recruits from PSR make a small contribution to future innovations, search activities, and instrumentalities. Scientists recruited at Ph.D. level and beyond are generally expected to bring new knowledge and skills into the company, particularly skills in experimentation and testing. On occasion recruitment has been pursued deliberately in order to fill a specific gap in in-house expertise, particularly in areas of new and scarce expertise.

5.7 SUMMARY

5.7.1 *Context of industry–PSR linkage in biotechnology*

Large pharmaceutical companies have traditionally invested heavily in RD&D. Their initial response to biotechnology was to keep a watching brief on external developments worldwide, with the aim of identifying where the new technology might pose opportunities or threats. They did this by forging links with university research and, to a limited extent in the UK, with small research-intensive biotechnology firms. By the late 1980s, they recognized that their main opportunities lay not in biotechnology products, but in applying biotechnology tools and techniques to radically decrease the cost and time for drug discovery and development. Techniques such as recombinant DNA, protein engineering, and the use of monoclonal antibodies carry the hallmark of Price's instrumentalities (see 3.2.1) in that they are research tools with the potential to open up new opportunities in both innovation and research. All the companies interviewed believe that biotechnology is crucial to continuing competitiveness, and have recruited large numbers of staff with genetic engineering skills. All reported skills shortages in some areas.

UK PSR in biotechnology is relatively well funded compared with other fields. Its main strengths lie in producing very good scientists, novel ideas, ability in research, and in its accessibility for industry. Compared with other countries, particularly the US, it suffers from lack of funding and equipment.

5.7.2 *To what extent do companies interact with PSR?*

All the companies interviewed spend 1–3 per cent of their R&D budgets on links with PSR. The absolute sums amount to several million pounds in three of the companies, which reflects the high R&D expenditure in the pharmaceutical industry. Companies differ in the scale and range of their linkage activities, rather than in the type of investment.

Despite this PSR expenditure, in-house sources make by far the greatest contribution to STI used in biotechnology research, especially the collective knowledge which companies have accumulated over time. By employing researchers qualified in biotechnology related disciplines, however, companies are able not only to generate new knowledge internally, but also to access and import knowledge from outside. Of this, the contribution from PSR far outweighs that of other companies. Surprisingly, the input from this latter source comes mainly from competitors and instrument manufacturers, not small biotechnology firms.

5.7.3 *How do companies interact with PSR?*

Companies use a wide range of formal and informal mechanisms to interact with PSR. Formal contracts include those subsidized by government and other bilateral arrangements fully funded by the company. Two of the companies have invested in laboratories on university campuses. Less costly forms of linkage are consultancies for academics and studentships. All the researchers maintain wide networks of informal contacts (in PSR as well as other companies) through which there is a two-way flow of STI and technical assistance. Building up trust in informal relationships is a necessary precursor to formal contracts, which in turn can serve to strengthen informal ties.

Researchers use multiple channels to access knowledge from PSR. The scientific literature is most widely used because it provides indications of where interesting developments are taking place as well as information on research techniques. Scientific papers seldom provide the depth of information required—for instance, the precise nature of a new technique or its potential applications—so researchers often make direct contact with the author or discuss individual papers with existing contacts. Informal contacts can also identify papers which provide the answer to specific problems. Thus, it is quite common for the literature and personal contacts to be used in tandem. Moreover, it appears that so much importance is attached to being aware of the latest developments on the research frontier that researchers make strenuous efforts to find out about research before it is published.

5.7.4 *Why do companies interact with PSR?*

Biotechnology researchers are emphatic that they could not do their work without the (largely scientific) knowledge acquired during their formal education in PSR. However, because biotechnology is a fast-moving field progressing across a broad front, they also need to keep up with and acquire the *new* techniques and knowledge emerging in PSR. This is reflected in our evidence on the benefits of linkage activity and on the impact of STI.

The most significant impact of STI from PSR is on underpinning knowledge and scanning the research frontier. This corroborates the importance researchers attach to being on the unpublished grapevine, and the use of some large-scale links to provide a window on the research frontier.[20] More generally, firms set up formal links with PSR in new scientific areas where they are trying to build up in-house expertise, using government schemes only when little importance or urgency is attached to the results. STI from PSR also make a significant impact on skills in experimentation and testing. Accordingly, companies in biotechnology have made extensive use of PSR linkages to access new techniques as these are developed. Some strategic collaborations and secondments are undertaken to acquire enabling technologies and specific skills which a company lacks; and informal links can give access to research materials or equipment. Strong informal interaction and small-scale linkages both contribute to public relations and image building, which it is hoped will facilitate the flow of new recruits from collaborating laboratories and contribute to goodwill in future interactions.

Reliance on external knowledge sources is expected to be short-term since new specialisms are rapidly integrated. However, the prospects for PSR linkage activity continue to be high because new knowledge and techniques are emerging all the time.

5.8 INDUSTRY–PSR LINKAGE IN BIOTECHNOLOGY 1983/84

The earlier study of PSR linkage[21] in biotechnology involved interviews with ten researchers working in five pharmaceutical companies.[22] The main findings of this earlier study are summarized here to establish whether industry–PSR linkage has changed over time. It should be stressed that the collection and analysis of data on STI from PSR was less systematic than in the later study, although the broad research design was similar.

5.8.1 *Summary of findings*

The aim of the earlier study was to investigate whether linkage with academia was stronger in research related to the new biotechnology than in other

[20] Using campus laboratories as 'listening posts' is perhaps the most ostentatious means of doing this.

[21] In fact the study only looked at linkage with academic research but, since the later study found only a small minority of PSR linkage to be with government laboratories, the two are broadly comparable.

[22] This study also looked at seven new biotechnology firms; these results are not reported here but see Faulkner 1986 and Oakey *et al.* 1990.

more established areas of pharmaceutical RD&D and, if so, whether this was due to the newness of the field. There were a number of reasons for expecting that such linkage would be particularly strong in biotechnology at that time, not least: the emergence of new instrumentalities with great promise for both research and innovation; the fact that these emerged from within PSR, and that industry had no previous capability in the main underpinning discipline, molecular biology.

Evidence collected from the study firms took four forms: first, an audit of the level of linkage activity; second, comparisons of linkage in different fields, specialisms, and projects; third, analysis of cross-company differences; and fourth, analysis of the knowledge obtained from PSR.

The audit of linkage activity suggested that involvement in government backed formal collaboration was higher in research related to genetic engineering than in more routine areas of pharmaceutical research, whilst the level of privately arranged collaboration was at least comparable with other areas. Significantly, the level of informal interaction was unusually high, even for the pharmaceutical industry. Researchers in all of the companies were spending considerable time and effort seeking out and 'courting' specialists in molecular biology and areas like immunology; new contacts were being pursued in a particularly purposive manner.[23]

When asked directly, interviewees were ambivalent about whether PSR linkage (formal and informal) was stronger in biotechnology than in more established areas, although most thought it probably was. Comparison of academic linkage in new biological fields with the more established areas of organic chemistry revealed that academic inputs to biological research are less visible than in organic chemistry, but academic contacts have to be pursued more purposively in biology. Investigation of differences between projects pointed to three factors affecting the extent and nature of industry–academia research linkages. First, the more open-ended the project, the more likely is academic linkage. Second, academic linkage tends to be associated with projects near the research end of the RD&D spectrum; projects geared to discovery or idea generation tend to 'cast the net wide' in terms of sources for STI, and academia is particularly valued for the breadth of expertise it contains. A third and somewhat distinct factor is the availability of academic expertise relevant to the specific project. Some areas 'lend themselves to strong academic relations' simply because they are well represented within academia.[24] In general, there was considerable overlap between industrial and academic research in the new biotechnology but this did not guarantee a perfect match. In the words of one interviewee, the objectives of academic and industrial research tend to 'criss-cross' even within broad areas of common interest.

[23] One company had recently established a molecular biology department which, it emerged, was dramatically more extrovert than older departments in terms of relations with the external research community. This was attributed to the fact that all of the molecular biology staff were very new recruits. Other longer serving research staff tended to feel more constrained by line management; they were reported to feel less free to go out of the company, and to be less interested in and knowledgeable about academic research.

[24] For example, a contrast was drawn between research on anti-bacterial agents, which was well represented, and work on the production of growth promoters, which was not.

Since at that time most of the industrial RD&D in biotechnology involved research rather than design and development, and was rather open-ended in nature, and since PSR was the major locus of research related to the new techniques, these observations indicated a strong basis for academic research linkage. They also suggested a connection between the strength of industry–university research links and the newness of the field. Marked inter-company differences in the extent of linkage in biotechnology pointed in the same direction. These differences were related in part to disparities in companies' general propensity to linkage (see 4.5.1), but in part also to differences in the strength of companies' involvement in the new field. Thus, the cross-firm analysis revealed that those firms which had gone furthest in building up in-house capability in biotechnology were also those which had made the greatest use of academic research.

The earlier study identified three broad types of STI accompanying academic linkage in pharmaceutical research related to the new biotechnology: (*a*) skills and training in the new techniques; (*b*) fundamental knowledge relevant to their application; (*c*) specific assistance with problem solving. Of these, the first two appeared to reflect the early stage in the development of a technology in which new techniques and opportunities are emerging all the time. Also, the use of linkage to acquire key skills and training was commensurate with the strategic concern of companies to build up expertise in a promising new field in which they had no pre-existing capability. Precisely because of the dynamism and uncertainty associated with the new field, it was not possible for them to predict how it would unfold or to pursue all possible lines of development—hence the desire to 'cover the technological waterfront' by plugging into academic research. Even where targets were relatively clear and companies had moved beyond the exploratory stage in research, there seemed to be a continuing need to maintain strong communications with the external research community—to ensure that company efforts were underpinned by good basic research. In short, academic linkage in the early day of biotechnology enabled companies to hedge their bets in terms of potential opportunities and, at the same time, to maximize their effectiveness in terms of the knowledge and techniques necessary to exploit those opportunities.

5.8.2 Differences between 1983/4 and 1990/1

The first study of biotechnology demonstrated that linkage between the pharmaceutical industry and academia was unusually strong in research related to the new biotechnology (compared with the industry norm), and concluded that this could be attributed in part to the newness of the field. Comparison with our more recent study identifies changes which have taken place during the 1980s.

The single largest change to emerge from this comparison is the growth in the scale of biotechnology related research throughout the pharmaceutical industry. Even in those companies which had only just begun to think about genetic engineering in 1983/4, there has since been a sizeable recruitment of specialist staff skilled in the new techniques—some from PSR and some through the acquisition of new biotechnology firms. Corporate commitment to the new technology is now significant, even though considerable uncertainty remains, and even though company researchers in the mainstream chemistry disciplines are still reportedly reluctant to recognize the potential application of biotechnology to their work.

Comparing the audits of linkage activity in the two studies, we find that search activity is less intense now than it was in the early 1980s. For the most part, company researchers now know 'who's who' and have established networks of personal contacts in the field. This provides some support for the idea that informal linkage, geared to searching for and making personal contact with external experts, might be particularly strong in a nascent technology. Formal linkage activity has clearly increased, though we cannot say whether this is more or less proportional to the increase in company RD&D effort in biotechnology. Company data on extra-mural research, though not strictly comparable cross-company, indicates an overall increase in expenditure on PSR during the 1980s. For example, company B reported an extra-mural research spend of less than 1 per cent of the R&D budget for the whole group in 1984 compared with between 1 and 1.5 per cent in 1991. In this time, involvement in government backed linkage continued to be strong as programmes like the SERC Biotechnology Directorate became more established. Where, in the early 1980s, such programmes provided a mechanism for companies to test the water, now they allow companies to engage in peripheral research not undertaken otherwise.

Comparison of the STI flows indicates that PSR linkage is still used by all companies to acquire skills and training in instrumentalities, and to access fundamental knowledge. However, the intensity of efforts to acquire skills has diminished somewhat. This reflects the extent to which knowledge about the new techniques has been incorporated in the education system (and can thus be acquired through recruitment), or is codified in the literature. Also, with respect to underpinning knowledge, we detect a slight shift in emphasis whereby the concern to hedge bets in terms of potential product applications has been displaced by a greater concern to keep up to date with the new techniques and the knowledge necessary for their application.

In research the differences between reported benefits from linking with PSR in the earlier and later period tend to reflect the growth in in-house

biotechnology capability over the period. The increased familiarity of company researchers with the new field has diminished the use of PSR contacts to find out about specialist facilities and services, or to make new contacts. The efforts of all pharmaceutical companies to build in-house biotechnology expertise explains why recruitment and public relations are now significant benefits of PSR linkage but were not so in the early 1980s.[25] Then as now, however, it is clear that much uncertainty remains; there is a continuing proliferation of new knowledge and new techniques across a broad range of disciplines.

It is clear that the increase in company RD&D in biotechnology has been accompanied by an increase in PSR linkage. The sharp differences in linkage activity between companies revealed in the first study are not perceptible in the more recent one; all companies are now interacting strongly with PSR in this field. Evidence from the first study had suggested that differences in company 'propensity to linkage' are a very enduring feature of companies' RD&D organization and innovation strategy. During the early 1980s, there were also marked differences between some of the large US chemical companies in terms of their willingness to 'export' long term research interests in biotechnology by funding extra-mural research.[26] As with our UK study firms, however, such differences have diminished subsequently (Kenney 1986). It seems that an 'introvert' strategy is simply not tenable in the commercialization of the new biotechnology.

In sum, industry–PSR linkages remain a prominent feature in biotechnology, even though all companies have now recruited new staff with requisite expertise. A recent Office of Technology Assessment study (1988 cited in Feller 1990) points to suggestive evidence that the current level of industrial interest in academia in biotechnology is a temporary phenomenon which will decline as industry builds up its own capability, but we have yet to find evidence of this. New knowledge and techniques in the field are emerging so rapidly, and across such a broad front, that companies need to maintain close contact with government and academic researchers working at the frontier if they are to make sense of, and take advantage of, these developments. It seems likely that the innovation cycle in this field, as in other major new technologies, may be some 30–40 years. If so, we will not know the outcome of company strategies for biotechnology until well into the twentieth century.

[25] In any case, such companies have become more concerned now about the need to ensure adequate supplies of skilled personpower—across the range of specialisms.

[26] Monsanto, for example, was involved in several multi-million dollar collaborations with academic institutions (NSB 1983) and had sizeable investments in a number of new biotechnology firms, whilst Dupont concentrated its resources on building up in-house capability in the field (Horwitch 1982).