PATTERNS OF INNOVATION IN THE CHEMICAL INDUSTRY

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by

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Introduction: Innovation and technological economics

The analysis of innovation contained in this thesis differs considerably in both scope and aims from most analyses of innovation. It is important to discuss why the approach taken has been adopted, and to justify its usefulness.

There is no absence of analyses of innovation and associated invention. Individual inventions have been examined, notedly by Jewkes and his co-authors (1); analyses have been made of innovation in selected industries, and this has been related to international trade in these industries (2); the detailed antecedents of individual technological innovations have been traced back in time, both for weapon systems and for civilian products (3); the spread of important new techniques, normally associated with large-scale capital investment, has been analysed (4). Much of this work has been done, either directly or indirectly, to answer specific questions of science policy, and these works have been influential factors in the formulation of science policy.

The questions which may be answered by such approaches are important. Is money aimed at producing inventions (and, by implication at least, innovation) best invested in establishing large research centres, or in encouraging with suitable fiscal measures individual inventors (5)? What is the relationship between the concentration of an industry and its propensity to innovate? Should government finance be concentrated in closely targetted contracts, or in university research? What should the government attitude be towards industries, such as the pharmaceuticals industry, in which successful products enjoy what may appear super-normal profits while overall heavy research expenditure is incurred (6)?

These questions of science policy are weighty and of crucial import-

ance to a series of essentially political decisions that must be made. When there are already such varied analyses of innovation, answering such important questions, it may appear strange to introduce a further type of analysis. The justification lies in the questions which this thesis attempts to answer.

For in addition to the questions of science policy, there are questions on a different scale. These are the queries and problems of the actual innovator within an organisation, the problems of the innovating organisation in gaining acceptance for its new products or processes. Traditional economics treats much of the internal activity of the firm as a black box, about which certain simplifying assumptions are made. It is a feature of technological economics that it is concerned with decision-making within the firm, and with the processes by which this occurs (7). The present treatment of innovation concentrates on the problems of developing new products from the point of view of one actually involved in the innovative process.

The questions raised by such an approach are different from those which are traditionally central to science policy. Yet the questions raised are crucial for the scientist concerned with innovation: how can an invention be recognised? What sort of screen should be used to separate those ideas which are promising from those which are unlikely to succeed? What may be done to avoid waste, either in time devoted to projects which fail, or in projects which are rejected before they are evaluated adequately? What information should be acquired to define the ecology and environment in which the innovation must survive? How can the survival chances of new products be increased? In particular, this thesis is concerned with problems of, and barriers to, innovation, so that the research scientist may at an early stage in a project's life anticipate the direction in,

and problems against, which he may move.

The answers to these questions may be relevant to some questions of science policy. For instance, detailed analysis of the problems encountered with individual innovations may well suggest conclusions which affect the setting up of industrual or government research establishments. But the main usefulness of the approach adopted is that it is aimed at the problems of the practising scientist or technologist, whose considerable knowledge of science and engineering is seldom matched by an understanding of the phenomena of innovation. The aim of this thesis is to analyse innovation, to examine some innovations in detail, and to draw conclusions which may guide those concerned with the movement of projects from research to innovation. The performance of laboratories established to promote innovation has been severely criticised (8); it may be hoped that the performance of at least one such laboratory may be improved if more is known about the innovative process in which they take part.

Necessarily, the different questions raised require different information. The reader expecting answers to certain questions - the relationship between successful and unsuccessful research projects in the pharmaceutical industry, for instance - will be disappointed, since it is not the aim of this thesis to discuss these questions. The approach adopted, limited though it is, is believed to be sufficiently important, and so neglected, to justify ignoring other possible types of analysis.

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1. J. Jewkes, D. Sawers, R. Stillerman, The sources of invention (London 1969). J. Allen, Studies in innovation in the steel and chemical industries (Manchester 1967).

2. G.C. Hufbauer, Synthetic materials and the theory of international trade (London 1966). J.L. Enos, "Invention and innovation in the petroleum refining industry", in Rate and Direction, 299-321. M.J. Peck, Competition in the aluminum industry 1945-1958 (Cambridge Mass. 1961). C. Freeman et al., National Institute Economic Reviews 26, 34, 45.

3. C.W. Sherwin and R.S. Isenson, "Project Hindsight - a defense department study of the utility of research", Science, 156 (23 June 1967), 1571-1577 and Technology in retrospect and critical events in science (Illinois 1968).

4. E. Mansfield, The economics of technological change (New York 1968) and Industrial research and technological innovation (New York 1968). G.S. Maddala and P.T. Knight, "International diffusion of technical change - a case study in the oxygen steelmaking process", Economic J. 77 (September 1967).

5. A.D. Little, Patterns and problems of technical innovation in American industry (Boston 1963).

6. Economics and innovation in the pharmaceutical industry (ed.) G. Teeling-Smith (London 1969).

7. F.R. Bradbury, "Technological Economics: Jubilee Memorial lecture" Chemy. Ind. (October 18, 1969), 1488-1494.

8. Y. Brozen, "Trends in industrial research and development", Journal of Business (July, 1960), 204-217.

Chapter 1

INNOVATION - a literature survey

1. The model adopted:

Despite much discussion, and general agreement on its importance, innovation is a subject defined in a variety of ways. To avoid ambiguity, it is important to define the sense in which innovation is used in the present account:

> "Innovation originates with the recognition that an opportunity exists or that a problem may be resolved. The process of elaboration which produces a practicable and adopted solution to the problem, or continues until the opportunity originally perceived has been grasped, comprises the innovative process".

This definition focuses the area of study considerably. First, by concentrating on the actual process of innovation, it leaves unexamined those factors in the economic environment which are often related to innovation - the relationship between capital investment, the trade cycle, the concentration of an industry and innovation. The studies made here are concerned with the particular pattern of innovation as it has occurred, rather than with the effect of aggregates.

Second, innovation as defined here does not necessarily involve scientific advance at any moment. This is compatible with the recent description of innovation as: "in a general sense ... the technical, industrial and commercial steps which lead to the marketing of new manufacturing equipment or any technical measures to improve methods of production; at the other it might mean the whole sequence of scientific research, market research, invention, development, design, tooling, first

production and marketing of a new product" (1). Despite this, each of the three case studies examined in detail contains a considerable input of science and technology, and most studies of innovation trace a pattern that includes scientific intervention at some point. There are methodological reasons for this. It has been remarked that innovation is probably not a directly observable phenomenon, since in order to observe it, it is necessary to isolate those funds available to finance innovation from total investable funds, an impracticable undertaking (2). Because of this difficulty, that part of innovations whose measurement is most easy is studied, and this leads to study of inputs in general, and of patent statistics in particular. It is therefore important to re-affirm the distinction made by Schumpeter between invention and innovation, and to emphasize that innovation as here defined need not include either new science or new technology (3).

Third, the definition of innovation adopted here, with its emphasis on innovation as a process spread over time rather than as an event, makes innovation much more comparable with other processes for problem recognition and problem solving. Pounds, for instance, has described the way in which managers in an American company define problems. He postulates four types of models - historical, planning, other people's and extra-organisational models - any of which may present the manager with a discernible difference between the existing state of affairs and a desired state suggested by the model. This difference is the trigger which initiates a process of search for, and implementation of, a solution (4). The analogy between general managerial decision-making as described by Pounds

(1) Technological Innovation in Britain (HMSO, London 1968), 1.

(2) E. Ames, 'Research, invention, innovation', American Econ. Rev. '51. (June 1961), 380.

(3) J.A. Schumpeter, Business Cycles (New York 1964), 59-70.

(4) W.F. Pounds. 'The process of problem finding', Ind. Man.Rev. 11 (Fall 1969), 1-19.

and innovation as here defined makes us turn to consider what characterises innovation. What distinguishes innovation from the other problem-recognising and -solving activities of a manager?

1.1 Characteristics of innovation

Typically, an innovation may involve several different organisations. The initial recognition of a difference between a perceived state of affairs and the state which it is believed could occur may be made in various places. Simple examples of where this recognition may occur include the following:-

1. By the end user - e.g. the farmer who uses existing polyethylene sheet to retain moisture and kill weeds.
2. By the manufacturer, or potential manufacturer, of a product - e.g. the manufacturer of polyethylene sheet who persuades a farmer to use them for agriculture.
3. By equipment manufacturers - e.g. the manufacturer of machinery for shrink wrapping polyethylene film.
4. By manufacturers of intermediate products - e.g. introduction of nylon and terylene into the textile industry.
5. By raw material suppliers - e.g. the development of new boilers by the National Coal Board.
6. By suppliers of ideas - e.g. the inventor of cats' eyes, or research associations.

This may be simply represented by figure 1.1, from which it may be seen that the only instance where an innovation may be implemented without involving any need is when the innovation originates with the end user. Thus the farmer who retains moisture and kills weeds by spreading black polyethylene round his crop has to persuade no-one other than himself that this is useful. It may be observed that even the end user often has to persuade others. First, for a need which is not met by any existing product, the end user must set up a chain of innovation: the need for

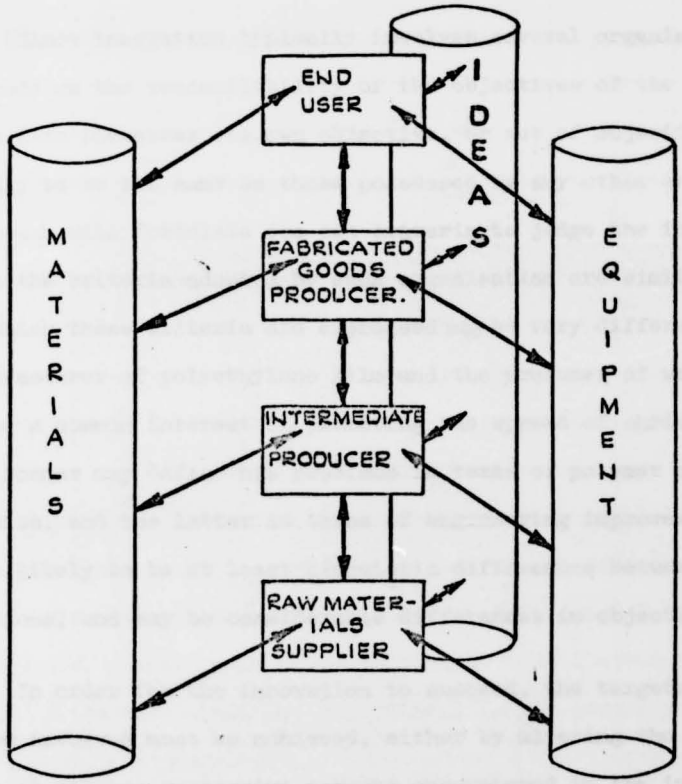
END USER
FABRICATED GOODS PRODUCER.
INTERMEDIATE PRODUCER
RAW MATER-IALS SUPPLIER
MATERIALS
IDEAS
EQUIPMENT

Figure 1.1.

better finishes for aluminium products, first recognised by firms in the aircraft industry which were the end users of aluminium products, involved equipment manufacturers and primary aluminium producers (5). Second, even when the innovation may be completed without any other firm becoming involved, in a large organisation the man recognising the initial opportunity is likely to have to influence others before the innovation can be implemented.

Since innovation typically involves several organisations, its success depends on the reconcilibility of the objectives of the different firms. Each firm possesses its own objective, or set of objectives, which are unlikely to be the same as those possessed by any other organisation involved, and each will formulate its own criteria to judge the innovation. Even when the criteria adopted by each organisation are similar, the language in which these criteria are expressed may be very different. Thus the manufacturer of polyethylene film and the producer of wrapping equipment share a common interest in promoting the spread of shrink-wrapping, yet the former may define his problems in terms of polymer chemistry and physics, and the latter in terms of engineering improvements. There are thus likely to be at least linguistic differences between different organisations, and may be considerable differences in objectives.

In order for the innovation to succeed, the targets of each organisation involved must be achieved, either by altering the initial idea so that it matches successive targets encountered in the innovation chain, or by altering the targets to make the idea suitable. Thus whereas a decision made within a single firm may be viewed as a single cycle of decision and control, an innovation is likely to involve many such cycles.

(5) M.J. Peck, 'Inventions in the post-war American aluminum industry', in The Rate and Direction of Inventive Activity: economic and social factors (Princeton 1962), 285.

The difference is not absolute, however. The behaviour of a firm has been explained as the result of compromise between differing and conflicting objectives, which result in re-adjustment of projects as they progress between departments (6). The innovative process thus represents a more extreme example of the reconciling of objectives which are likely at the very least to be expressed in different terms, and may differ strongly.

2. Innovation: invention and development.

The model which has been adopted here lays emphasis on innovation as a developing process, proceeding in time far beyond the process of invention. Such a model makes analyses of invention alone appear incomplete and it is important to examine in some detail whether studies can be justified that examine invention alone. The justification claimed for studying inventions is two-fold. First, patent data are necessarily public, and so provide good source material; and second it is claimed that invention represents the initial point leading to innovation. This is stated either explicitly, as by Schmookler - "The invention of a new product or process is but the first link in a long, poorly-understood chain of events" - or implicitly, as by Jewkes and his co-authors who open their discussion of invention with the sentence: "Future historians of economic thought will doubtless find it remarkable that so little systematic attention was given in the first half of this century to the causes and consequences of industrial innovation" (7).

(6) R.M. Cyert and J.G. March, A Behavioural Theory of the Firm (London 1963), 99-102.

(7) J.Schmookler, in Rate and Direction, 228; and J.Jewkes, D. Sawers and R. Stillerman, The Sources of Invention (London 1969), 19.

2.1 The study of invention as a separate phenomenon

The justifications advanced for the study of invention alone are open to at least two criticisms. Can invention be meaningfully and appropriately separated from development, investment and manufacture? And is it true that in studying invention one is studying the cause of innovation? The distinction between invention and development is made by Jewkes and his co-authors as one of three presuppositions necessary for their discussion, and they claim the distinction is crucial. Invention is defined as: " ... the confidence that something should work, and the first rough tests that it will, in fact, work"; development as: "... the stage at which known technical methods are applied to a new problem which, in wider or narrower terms, has been defined by the original invention.... the stage at which the task to be performed is more precisely defined, the aim more exactly set, the search more specific, the chances of final success more susceptible to measurement than is true at the stage of invention ... the phase in which commercial considerations can be, and indeed must be, more systematically examined ..." (8).

Yet Jewkes found that the distinction thus described was impossible to observe, and states that his examination of inventions necessarily led him to examine development. Once this is done, however, the conclusions of his study are seen to be very different. Table 1.1 shows the case studies described. Jewkes originally described in detail fifty inventions, of which twenty seven were said to be "individual" inventions against some sixteen which had their origin largely in the research laboratories of manufacturing companies. Seven inventions were not ascribed to either category. Of these seven, all but one (continuous casting of steel) may reasonably be placed as either the work of manufacturing companies, or of government

(8) Jewkes et al., 28-29

research establishments. The balance thus becomes twenty eight "individual" inventions against some twenty two "non-individual" inventions. When the more recent inventions considered by Jewkes are added to the original list, the total number of inventions described rises to sixty, of which thirty three belong to Jewkes' "individual" category, and twenty six to the "non-individual" category, with one remaining uncategorised (9).

Various objections may be advanced against the original list: it appears somewhat chronologically unbalanced, and examination of inventions dating from after 1928 (the midpoint year) shows a predominance of corporate rather than individual inventions; and the selection of inventions studied is suspect (10). These objections apart, the invention which remains uncategorised - electronic digital computers - illustrates the problems of looking at invention alone, for it is impossible either to identify a single inventor, or to disentangle invention from development. And when development is considered as well as invention, Jewkes' emphasis on individual effort becomes less convincing. For example, the hardening of liquid fats was invented by Dr. W. Normann, but "Crosfield's finally discovered the 'know-how' which made the process workable"; air cushion vehicles would have languished but for the development effort financed by the NRDC; continuous hot strip rolling required much capital to transform the invention into an innovation (11). Yet Jewkes claims each as an "individual" invention. Inventions may indeed be "the beginning, without which the other is of no avail", but equally without development the invention may languish. Conclusions based on the study of invention alone may be very different from those based on study of invention and development. The need to commit resources beyond those available to the individual inventor, the commercial ability to establish a business, and the ability to transform an idea to reality are all unexplored in a study of

(9) Jewkes et al. (1958 edition), 263-410; and (1969 edition), 329-356.

(10) C. Freeman, 'Science and economy at the national level' in Problems of Science Policy (OECD Paris 1968), 61-64.

(11) Jewkes et al. (1969 edition), 256,330,242-243.

invention alone. It is clear that the conclusions based on a study of invention may be very different from those based on study of invention and development.

TABLE 1.1: List of case studies described by Jewkes et al.

	Jewkes' category
Automatic Transmission	I
Bakelite	I
Ballpoint Pen	I
Catalytic Cracking of Petroleum	I
'Cellophane'	I
Cinerama*	I
Continuous casting of steel	(I)
Continuous hot strip rolling	C
Cotton Picker	I
Crease resisting fabrics	C
Cyclotron	I
DDT	C
Diesel electric railway traction	C
Electric precipitation*	I
Fluorescent lighting	C
Freon refrigerants*	C
Gyro compass	I
Hardening of liquid fats	I
Helicopter	I
Insulin	I
Jet engine	I
Kodachrome	I
Long-playing record	(C)
Magnetic recording	I
Methyl methacrylate polymers	C
Neoprene	C
Nylon and Revlon	C
Penicillin	I
Polyethylene	C
Power Steering	I
Radar	(C)
Radio	I
Rockets	(C)
Safety Razor	I
Self-winding wrist watch	I
Shell-moulding	(C)
Silicones	C

	Jewkes Category
Stainless steels	(C)
Streptomycin	I
Sulzer loom	I
Synthetic detergents	C
Synthetic light polarizer	I
Television	C
'Terylene' polyester fibre	C
Tetraethyl lead	C
Titanium	I
Transistor	C
Tungsten Carbide	(C)
Xerography	I
Zip fastner	I
Air cushion vehicles	I
Chlordane, Aldrin, Dieldrin	C
Float Glass	C
Moulton Bicycle	I
Oxygen Steel-making	C
Electronic Digital Computers	-
Photo-typesetting	I
Rhesus haemolyfic disease treatment	I
Semi-synthetic penicillins	C
Wankel Engine	I

I = "individual" invention

C = "corporate" invention

brackets indicates that Jewkes did not himself classify the invention.

* = appears in first edition only.

	Jewkes Category
Stainless steels	(C)
Streptomycin	I
Sulzer loom	I
Synthetic detergents	C
Synthetic light polarizer	I
Television	C
'Terylene' polyester fibre	C
Tetraethyl lead	C
Titanium	I
Transistor	C
Tungsten Carbide	(C)
Xerography	I
Zip fastner	I
Air cushion vehicles	I
Chlordane, Aldrin, Dieldrin	C
Float Glass	C
Moulton Bicycle	I
Oxygen Steel-making	C
Electronic Digital Computers	-
Photo-typesetting	I
Rhesus haemolyfic disease treatment	I
Semi-synthetic penicillins	C
Wankel Engine	I

I = "individual" invention

C = "corporate" invention

brackets indicates that Jewkes did not himself classify the invention.

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A second criticism of Jewkes' distinction between invention and development is that it fails to examine any possible interaction between the source of inventions and their eventual chance of success. Yet there is evidence suggesting interaction between the source of a research idea and its chance of success. Carter and Williams concluded from analysis of various innovations that there is not "any simple or uniform percentage of research results that go into development. That varies very largely from firm to firm with the origin of their research or development projects and with the ways in which potential projects are valuated... The less the attention of the research staff to the commercial significance of their projects, the greater the chance that research with great potentialities in industrial application will be excluded, if only because the man who is preoccupied with research as such will not be anxious to father his idea on the development staff" (12). Analysis of research projects within Imperial Chemical Industries showed that the likelihood of success was related to its origins. Table 1.2 summarises these conclusions, showing that the different sources of ideas account for different proportions of the successful and unsuccessful research projects. In addition, Table 1.2 shows an interesting cost relationship, in that ideas stemming from outside ICI tended to cost more to develop than those which originated within ICI.

Table 1.2: Percentage of successful and unsuccessful research projects, by source of idea

Origin	Successes		Failures
	No.	Cost	No.
ICI basic research	5	10	10
Other ICI parts	80	60	70
Outside ICI	15	30	25

(12) C.F. Carter and B.R. Williams, Industry and Technical Progress (London 1957), 58.

In addition to the source of the research idea affecting the chance of success, the type of research project also affected this: research aimed at quality or process improvement had a 70 per cent chance of success, that aimed at novel processes or products 40 per cent, while "omnibus" research projects were reported to be responsible for 10 per cent of all successes, but a "very considerably larger proportion of the company's research expenditure" (13). From this analysis it appears that there may exist considerable interaction between the source of ideas and their chance of success. This contention is supported by analyses done of development projects within an American chemical company's Laboratory. This showed, for instance, that work originating in the Laboratory had twice as high a chance of failure (failure in this context being equated with no increment in sales) as had work originating in customer requests; that no large sales increases resulted from a single project originating in the Laboratory, whereas 20 per cent of those originating in customer requests produced this result; and that 'the magnitude of technical and commercial uncertainty associated with a development project may be related to the project's source' (14).

There are thus two objections to the study of inventions as a separate phenomenon. First, the study of invention alone may suggest very different

(13) Holroyd's analysis depends on his definition of success, which he equates with a decision to adopt a new product or process. One obvious objection can be made. Research may be successful if it reduces an area of doubt: research may for instance respond to the question: "is it worth my adopting this new process?" with the answer "No", which satisfies the research objective. Holroyd, however, would consider this a failure. R. Holroyd, 'Productivity of industrial research with particular reference to research in chemical industry', in Proceedings of the symposium on productivity in research (Institution of Chemical Engineers, London 1964.)

(14) D.L. Meadows, "Estimating accuracy and Project Selection Models in Industrial Research", Industrial Management Review 9 (Spring 1968), 115-116.

conclusions from those suggested by the study of research and development. Second, there is evidence to believe that considerable interaction may exist between invention and development.

2.2 Sources of innovation:

The second question to consider is whether invention is the source of innovation. The definition of innovation adopted, and the six examples of sources of innovation already quoted, show that invention is only one source of innovation, and, conversely, that invention can and indeed often does occur without subsequent innovation. International studies of innovation have confirmed this. Hufbauer has shown that the speed with which a country uses synthetic materials is not related to its ability to discover new synthetic materials, but rather to its adaptibility in imitating what has been invented elsewhere (15). A similar conclusion was reached in an international analysis of the causes of technology gaps, where it was observed that the most clear difference was that between the ability of United States' firms to develop the results of European research into commercial products, and the failure of European firms to develop inventions made elsewhere (16).

Similarly, it is possible to identify industries in which rapid innovation is combined with small amounts of research and development and little claim to invention. The most forth-right statement criticising the implied connexion between research and development and innovation is that of Carter and Williams: "..... it is clearly possible for a firm to be highly progressive without showing much trace of originality. It may simply copy

(15) G.C. Hufbauer, Synthetic Materials and the Theory of International Trade (London 1966), 87.

(16) Gaps in Technology: General Report (OCED Paris 1969), 17

what is done elsewhere: it may be pushed into the stream of advance by its suppliers, or pulled there by its customers. If one looks at an industry of many units, like agriculture, it is nonsense to identify progressiveness with inventiveness. In fact, in agriculture a great many of the new ideas come from outside, from research establishments, machinery suppliers, chemical firms, and so on; the progressive farmer is the one with the wits to select what is appropriate from the stream of ideas which impinge upon him" (17).

A study of innovation made in the United States confirms that innovation may occur without invention. The textile industry, for instance, has shown marked and rapid innovation, with the development of new fibres, finishing techniques and processes, yet is is an industry which has spent on research and development, as a proportion of sales income, approximately one tenth of the average for all manufacturing industry. In 1960, for instance, it spent $35 m., representing 0.25 per cent of sales income, whereas the average proportion of sales income devoted to research and development by United States manufacturing industry was 2.44 per cent. Not only did the textile industry combine rapid innovation with small research expenditure, but detailed study of individual mills showed that high expenditure on research did not lead to profitability higher than the average, and that "those companies which have significantly better performance than the industry average have not made unusual contributions to R. & D.". Of five industries investigated in this study, only the semi-conductor industry was based on research discoveries made within the industry (18).

(17) Carter and Williams, 108.

(18) Patterns and Problems of Technical Innovation in American Industry (A.D. Little, Boston, 1963), 25, 179.

From studies of innovation, it appears that study of invention alone may lead to conclusions which are not applicable to innovation, and that any account of innovation must accept that innovation may be started in many places, and that the progress to innovation may involve different firms and even different industries. The model of innovation proposed at the start of this chapter has been defined to encompass these characteristics. It is now necessary to examine research and development projects, to identify other characteristics of innovation with which an acceptable model of innovation must be compatible.

3. Characteristics of research and development projects

By studying a number of research projects, it is possible to distinguish features which characterise those research projects that result directly in new products or processes, and those which do not. There may be raised the objection that this study represents only one class of innovation, namely that involving invention within a scientific community at an early stage in the innovative process. The objection is a fair one, since it has already been seen that much innovation does not stem from scientific research, and that very much of research will not result in innovation. In justification, two claims may be made for the study. First, one of the features of modern economies is the deliberate attempt to induce innovation, by sponsoring research. This may be seen in the rise of that proportion of the GNP spent on research and development in Great Britain, which has grown from 0.05 per cent in 1900 to 0.25 per cent in 1938, and 2.7 per cent in 1965 (19). Innovation may increasingly result from research, as more effort is devoted to achieving innovation. The second justification for the appropriateness of examining research projects in the way proposed is

(19) A. Hart, Planning for increased research productivity, in Proceedings of the Symposium on Productivity in Research (op.cit., see note 11).

that they are studied not only at their inception, but throughout their development until they have completed the innovative process. The incompleteness implicit in studying invention alone is thus avoided. In short, the study of the conception and development of research projects illuminates characteristics of at least one class of innovation. By such a study, three characteristics may be distinguished.

3.1 Survival of research projects:

The most striking feature of research projects is how few survive. There is a mass of evidence to show that most inventions, whether new processes or products, do not survive to become widely accepted:

(i) Patent statistics suggest that a very large proportion of research ideas that have achieved the initial success of being patented are not in fact used: Jewkes estimates some 95 per cent of patents to be commercially useless. Machlup quotes a German survey which showed some 80 per cent of patents had been allowed to lapse after six years, and more than 96 per cent before their maximum duration of fifteen years; in Britain, as few as 2 per cent survive their full life of sixteen years (20).

(ii) Estimates by those responsible for the management of research also emphasise the low probability of success, when success is defined as a commercial product. Typical estimates include those of Pessemier, who says: "seven out of eight hours devoted to technical product development by scientists and engineers are spent on products that fail at some stage in the process", and of Heinermann: "it takes exploration of about 50 ideas to arrive between 5 and 8 on which bench scale process research should be done, and one which should go into pilot plant with good chances of commercial success" (21).

(20) Jewkes et al., (1958 edition) 106; F. Machlup, 'The Supply of inventors and inventions', in Rate and Direction, 164; and K. Boehm, The British Patent System: I Administration (Cambridge 1967), 81.
Jewkes' judgement of commercial utility must be viewed with caution, since it seems to be based on the belief that an unused patent is commercially useless. However, a patent may be used to protect an inventor, by providing him with a measure of security while he further investigates an area. That it may subsequently be un-used should not be taken as grounds for assuming that it held no value.

(21).

(iii) In particular industries, the chance of success is estimated to be even smaller: in the pharmaceutical industry, for instance, it has been estimated that three thousand compounds must be synthesised, at a cost estimated in 1964 to be about £1 m. for synthesis and screening, before one is proved in clinical trials. In the dyestuffs industry, the discovery of a commercially important colouring agent is thought to emerge from about thirty thousand compounds synthesised (22).

(iv) Surveys in different companies, or groups of companies, show a steep mortality curve for a population of research ideas. In twenty North American companies, the outcome of 540 research ideas were evaluated. Of these, only 92 were of sufficient merit to justify laboratory work, 8 of which went to a development stage. One commercial product survived from the original ideas (23).

3.2 The timescale of research and development.

A second feature of the process from research to innovation is the length of the timescale involved. Analysis of thirty five innovations that occurred in the last three centuries showed that only 15 per cent involved less than 3.5 years between the original invention and the subsequent innovation, and over 40 per cent involved between 3.5 and 8.5 years. The arithmetic mean of 11.0 years (24).

(21) E.A. Pessemier, New Product Decisions (New York 1966), 5; and H. Heinermann, 'How to measure success', Chem. Engr. Progr., 59 (December 1963), 27.

(22) J.R. Vane., in Evaluation of Drug Activities, D.R. Lawrence and A.L. Bacharach (ed.),(London 1964) Vol. 1; and private communication from Mr. A.E. Pink, ICI Grangemouth.

(23) H.M. Corley, 'Successful commercial chemical development', quoted by F.N. Woodward, 'Choosing research projects' in Modern Chemistry in Industry IUPAC/1968, J.G. Gregory (ed.), (London 1968).

(24) J.L. Enos, in Rate and Direction, 306-309.

It has been claimed that the time scale between invention and innovation has declined as modern industry concentrates its effort upon rapid development: the contrast has been made, for instance, between the 112 years required to develop photography with the 5 year development of transistors (25). It might therefore be argued that the extended time-scale of innovation is a feature of diminishing importance. There are strong arguments, however, for rejecting this: the examples cited may be the result of biased selection; necessarily recent discoveries which have been applied must have short delay times, or else they would still be un-applied; lastly, there are considerable ambiguities in the definition of what constitutes the delay between invention and innovation (26). Analysis of five important innovations in the U.S.A. - magnetic ferrites, video tape recording, oral contraceptive pills, the electron microscope, and the techniques of matrix isolation - showed that the average time between conception of the eventual innovation and its first demonstration was nine years. The detailed analysis of critical scientific and technological events which had led up to the innovation might be traced: for magnetic ferrites, a key event was the original conception of Hilpert in 1909 of a "magnetic insulator", yet the eventual innovation became commercially available after 1950 (27).

A further study, based on investigation of weapon systems developed for the United States government, showed that the average time between two generations of weapon systems was 13 years; that despite the very applied nature of the work, between 5 and 10 years often elapsed before an event was used; and that "undirected" science is unfrequently utilised on even

(25) L.R. Hafstad, 'The role of industrial research', Sc.J., 2, (September 1966), 81.

(26) For Discussion of the first two points, see J.Langrish,"Does industry need science?', Sc.J., 5 (December, 1969), 81-83.

(27) Technology in Retrospect and Critical Events in Sciences (TRACES), (Illinois Institute of Technology Research Institute,1968).

a 20 year time-scale (28).

3.3 Target changes during development

A third characteristic of the innovation process from a research project to a finished product is the reinterpretation of the original target that often occurs. There are dramatic examples of the metamorphosis that can occur: a study made of six fighter-plane developments showed that considerable changes in the research target could take place, even when the objective was narrowly defined. Of the six designs investigated, "four out of the six planes ended with different engines, three with different electronic systems. In order to make them satisfactory flying machines, five of the airframes had to be extensively modified; three of the fighters came out of development essentially different airplanes ... three ended up by having quite different operational roles from what was originally planned for them. Only one ... possessed the same technological ingredients and had the same kind of operational role that had been initially planned for it" (29).

Although few inventions are seen to undergo such a transformation while being developed, examination of other innovations suggests that marked changes may occur. The original request made to those who were later to develop radar requested not a means of identifying aircraft, but of disabling them by cutting out their engines; the development of a new type of fastener by Paul Matisse shows a marked change from the first design to the product eventually adopted; two of the three innovations studied in detail later show similar changes (30).

(28) C.W. Sherwin and R.S. Isenson, First Interim Report on Project HINDSIGHT ODDR, Washington DC., 1967.

(29) B.H. Klein, in Rate and Direction, 478-479

(30) T. Burns and G.M. Stalker, The Management of Innovation (London 1968) 37-42. and D.A. Schon, Invention and the Evolution of Ideas (London 1967), 75-91.

4. Models of innovation:

It is now possible to examine different models of innovation to consider whether they are compatible with the three characteristics of the innovative process considered. At once it is possible to see that several are incomplete, in that they offer little explanation for the high mortality rate among research projects, the timespan between invention and innovation, or the changes that occur during a project's life.

(i) Models that emphasise invention:

The first category of model comprises those which emphasise the inventive step. Raisbeck and Old, from analysis of research and development in six weapon systems, identify three necessary conditions for an innovation to occur: an explicitly understood goal, a source of ideas, and resources committed to achieving this goal. Clearly such a model may be helpful in identifying whether new resources, new recognition of objective or new ideas were the trigger which initiated an invention, but equally clearly these conditions tell us nothing about what distinguishes the few successful from the many unsuccessful among all those research projects that started with these three conditions (31).

A similar emphasis is devoted to invention, quite explicitly, by Schmookler, who describes it as a combination of particular state of knowledge and a particular state of industry (32); by Usher, who put forward a perceptual theory of invention (33); and by Jewkes (34). For the reasons outlined earlier, discussion of invention alone is likely to lead to conclusions inapplicable to innovation.

(31) G. Raisbeck and B.S. Old, 'Managing the research environment' in Uncertainty in Research Management, ed. R.M. Hainer (New York 1967) 97-118.

(32) Schmookler, in Rate and Direction, 196.

(33) For a review of Usher's treatment, see V.W.Rutter, 'Usher and Schumpeter on invention, innovation and technological change', Qu.J.Econs., 73, (1959), 596.

(34) Jewkes et al. (1969 edition), 19.

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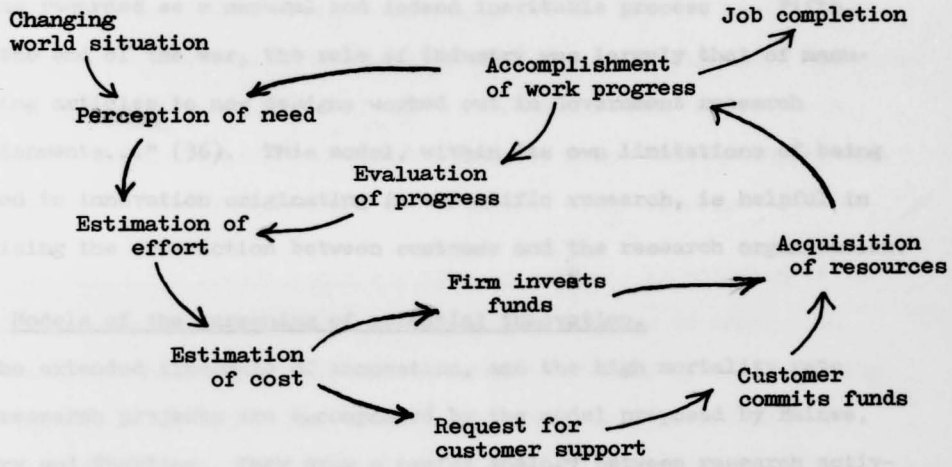
(34) Jewkes et al. (1969 edition), 19.

(ii) Models which include interaction during development:

Of more interest are those models which examine the interaction between different organisations as innovation proceeds. Roberts, for instance, lays great emphasis on the importance of obtaining funds to meet a defined, or at least perceived, need; his model may be shown pictorially as:



Useful though this may be in stressing the economic constraints which affect research and development, the model assumes the perception of need as a determining factor, rather than as a step which requires explanation (35).

A much more explicit account of the interaction between various organisations as the innovative process progresses is put forward by Burns and Stalker. They describe the essential features of technological progress, as exemplified by radar's discovery: "There is first the progress of scientific discovery independent of its practical use. Second, there is direct communication link between user and scientist leading to the definition of (a) a need, and (b) the scientific information relevant to the design

(35) E.B. Roberts, The Dynamics of Research and Development (New York 1964), 5.

of a device which would meet the need. One may note that the user's requirement eventually met was not what was formulated at the outset but one which was arrived at after some positive interaction; the first request was impossible to meet. Third, the main work of technological innovation was accomplished by men who were trained - and saw themselves - as scientists. Fourth, the creations of innovations by a research and development team was regarded as a natural and indeed inevitable process ... Fifth, until the end of the war, the role of industry was largely that of manufacturing articles to new designs worked out in Government research establishments..." (36). This model, within its own limitations of being confined to innovation originating in scientific research, is helpful in emphasising the interaction between customer and the research organisation.

(iii) Models of the screening of potential innovation.

The extended timescale of innovation, and the high mortality rate among research projects are encompassed by the model proposed by Baines, Bradbury and Suckling. They draw a useful analogy between research activities and the well-studied problem of a search strategy. An innovation may occur when the perceived qualities of a new material and the perception of a need are brought together. The bringing together of these two patterns of properties, and their modification, constitutes the invention, and the subsequent survival of the new material whose potential usefulness has been recognised comprises the innovation. Baines and his co-authors discuss this process as the progression of a new material through a series of screens, and discuss the properties and pathology of these screens (37). A screen may be defined as a deliberately erected barrier, whose mesh is so designed to allow to proceed those projects whose profile of properties, or a selected few properties, match those that have been identified as being important.

(36) T. Burns and G.M. Stalker (op.cit. see above note 30), 39.

(37) A. Baines, F.R. Bradbury and C.W. Suckling, Research in the Chemical Industry, (London 1969), 121-129.

The barriers to acceptance of an innovation that are known to exist may thus be simulated. Those research projects which are allowed to pass through screens are those most likely to overcome the barriers to innovation which exist. In one sense, the screens themselves constitute barriers, internally erected to what may be a large proportion of the ideas that are applied to the mesh. In another sense, the screens are attempts to predict the barriers which must be overcome, and the hope is that screens will cheaply or quickly simulate barriers which would be expensive and time-consuming to meet in reality. This model, by emphasising the screening mechanism by which research projects are judged, helps explain why so many are rejected, and the time necessary to overcome these screens.

It is useful to extend their analysis to include, in addition to the deliberately erected screens they consider, the barriers to innovation which exist, and also to examine the effect of different screens existing within different organisations. It is proposed to examine and identify different types of barrier - economic, technological, organisational, personal and perceptual - and to discuss the relationships that can be established between screens and barriers. There is a great attraction in the term "barrier", as an obvious physical analogy to a screen. It might be more accurate, however, to consider the five classes of barrier as five areas, any one of which may present very considerable problems and obstacles, or which may make it more likely that a research idea will succeed. A useful analogy here is with the systems engineering approach to process definition, where a series of problem areas are identified as possibly affecting the final process, and successive approximations are made to each problem area's importance (38). In considering innovation, it is helpful to have a comparable systems approach to the problem areas identified.

(38) F.R. Bradbury, Rose and C.W. Suckling, "Trends in Process Research", Chemy.Brit., 489-499

5.1 Barriers to innovation: economic

In tracing the survival of a new product or process which has been seen to possess useful properties, it is possible to identify different barriers which the new idea must overcome. First, let us consider economic barriers. The first economic barrier is that the organisation undertaking the research is only likely to do this if it believes it to be profitable. The opportunity of new profit, or the threatened loss of existing profit, are thus conditions whose absence presents a barrier. (The latter reason is often a stimulus to research activities: Sayers found that the threat of diesel occasioned research on steam engines, and that competition between radio and submarine cables had a similar encouraging effect on research (39). More recently, competition between nuclear and conventional power stations has stimulated innovation, with the result that power stations have increased markedly in size). A second economic barrier is presented by the purchaser of the new product or process, who must be convinced either that he is gaining the same end results as before at lower cost (e.g. new processes for making existing product at lower cost), or that the extra properties which he acquires with the innovative product sufficiently compensate for any extra cost. The problems of how the consumer perceives these advantages, and how this perception may differ from that of those responsible for research, are considered later. Evidence exists of a third type of economic barrier, comprising the investment decision whether to use the research results. A survey has shown that shortage of funds prevented firms developing all the research and development they desired to; the most common criterion for judging process innovations is an estimate of the cost saving from the new process (40).

(39) R.S. Sayers, 'The springs of technical progress in Britain, 1919-1939', Ec. J., 60, (1950), 276.

(40) Quoted in B.V. Dean, Evaluating, Selecting and Controlling R & D Projects (American Management Association New York, 1968), 50.

It is clear that economic barriers exist in reality, in that products are not purchased for reasons that include the fact that they seem too expensive to the purchaser, and in that research projects that are technically feasible are not used because they do not appear good investments. What is not clear is how explicit is the economic screening of proposed innovation. The first type of barrier is more difficult to screen for, in that it necessitates the research scientist understanding the criteria used by others in the innovation chain, and the identification of who are the others involved may be a difficult task. This problem is one to which we shall return. The second type of economic barrier - whether one should invest in the results of research - should be much easier to screen for, since it involves relatively simple criteria. There is some evidence, however, that this screening may be lacking: a survey carried out in the first half of the 1950's came to the surprising conclusion that "in only thirteen of the 150 firms in the general sample was an explicit financial criterion of this kind (some kind of rate of return) used in judging whether to go ahead with a product or process innovation on which they had done research or development work" (41).

The effects of not explicitly screening for economic barriers may be three. First, projects may be pursued when an economic appraisal would have shown that their chances of commercial success were very small. Second, opportunities may be missed, because researchers in ignorance mistakenly conclude that a target is not worthwhile. Third, the lack of economic targets make it harder to achieve commercial success by concentrating effort on vital factors. It is often stated that a manager's job is not to make the right decisions, but to make his decisions right, and this remark clearly supposes that there is some means of distinguishing between correct

(41) Carter and Williams (op.cit. see above note 10), 84-85 and Investment in Innovation (Oxford 1958) 82-84.

and incorrect decisions. The importance of agreed financial targets was shown by a study of thirteen investment decisions: in three instances, investments with initial returns that were very low or negative were transformed into successful projects through management intervention. Common to all three cases were active management and agreed economic targets, which concentrated management's attention on the discrepancy between objective and achievement (42). In research and development, the lack of economic criteria may have the effect of allowing the researcher's personal drive, or scientific and technological targets, to assume disproportionate importance in the absence of alternative objectives.

5.2 Barriers to innovation: technological:

Two types of technological barrier may be identified. First, a scientific or technological barrier must be overcome: a chemical yield must be increased to a specified percentage, or an electronic component reduced to a certain size. The difficulty of overcoming this barrier may be expected to vary between research projects where the target is defined and the underlying science and technology understood (where it may reasonably be expected that the technological barrier will be overcome), and scouting research, in which a large number of ideas is considered, any one of which may suggest speculative targets. Evidence supporting this comes from:

(i) Holroyd's estimate, based on the experience of one chemical firm, that 70 per cent of the failure of exploratory research, 50 per cent of the failure of improvement research, and 30 per cent of the failure of research on defined targets were due to technical reasons (43).

(42) B.R. Williams and W.P. Scott, Investment Proposals and Decisions (London 1965), 66.

(43) R. Holroyd (op. cit. see above note 11).

(ii) Analysis of an electrical and electronic company's research laboratory projects showed that 16 per cent failed because of unseen technical difficulties, compared with 18 per cent which failed because manpower had been diverted to other projects, and 9 per cent because research objectives had been changed. Analysis in the same laboratory, whose projects were selected with a strong bias towards risk minimisation, showed that delays in completion of research projects were caused much more by management decisions than by technical problems (44).

(iii) Examination of the well-defined target research on weapon acquisition programmes in the USA shows that less than 30 per cent of variance in development time and cost were attributable to "technical difficulties that were both unforseeable and unavoidable" (45).

This type of technological barrier is normally screened for in research and development programmes, whose complex technical and economic targets are often reduced to a single technological objective. This type of objective fits the background experience and background training of most researchers, and accounts of screening in research laboratories show the emphasis placed on achieving scientific goals (46).

A second technological barrier is related to the probability that a discovery made in one organisation will be implemented in, or affect, other organisations, and must therefore either be compatible with, or involve altering, existing techniques and processes. The experience is common:

(44) E. Mansfield, Industrial Research and Technological Innovation (New York, 1968), 59.

(45) F.M. Scherer, in Rate and Direction, 498-500.

(46) See, for example, B.V. Dean, Evaluating, Selecting and Controlling R & D Projects (American Management Association New York 1968), 50.

the development of numerical control machines in the USA led to firms manufacturing machine tools to examine their total manufacturing system, to fully exploit the advantages of numerical control. Such a task is, of course, so basic to the successful use of computers that it has been recognised as requiring a special skill, that of the system analyst, to fulfil it. The task is widespread: the introduction of new equipment for spotting aircraft led to new communication systems; new dyestuffs require new dyeing techniques; new electronic equipment demands new standards of housekeeping. Important although this technological barrier seems (particularly when the model of innovation shown in Figure 1.1 is adopted), there is little evidence of the screening used to predict it. The importance of this will become more apparent when other models are considered defining those factors which affect the chance of success of an innovation.

5.3 Barriers to innovation: organisational:

There has been much discussion of organisational barriers to innovation, often in connexion with the Not invented Here (NIH) concept.

(i) Schon has emphasised that a typical feature of innovation is the need to overcome resistance, and has claimed that a product champion is required to overcome this resistance. A similar explanation of the importance of organisational barriers emerges from analysis of ten successful innovations in the USA, which identified the part played by "couplers", who moved the project from one organisation to another (47).

(ii) Analysis of innovation in the electronics industry in the UK has emphasised the barriers that exist between and within organisations. In one instance, the research department had not only

(47) D.A. Schon, Technology and Change (Oxford, 1967), 115-117. and D. Allinson, "The growth of ideas", Int. Sc. and Techn.(July 1967), 26-28.

become isolated from the rest of the organisation, but had even been separated off by a brick wall - "the only barrier in the plant" (48).

(iii) Examination of a series of innovations within an American engineering firm is based on the importance of the NIH factor, which it is assumed will be present unless specific steps are taken to overcome it (49).

Many discussions of organisational barriers to innovation are couched in terms of human weakness or personal conflict. The models which include the undoubted phenomenon of organisational barriers tend to adopt an eighteenth century belief in an environment whose blemishes are caused by fools or knaves, the assumption seemingly being that a desire for personal success will cause many managers to reject ideas that emanate from other organisations. It seems more realistic to acknowledge that different organisations, and different parts of the same organisation, may have different targets. The model discussed initially, by its emphasis on the number of organisations likely to be involved in an innovation, converts the NIH factor from an example of irrational but much encountered behaviour to an explicable and understandable event.

The recognition that not one, but many, organisations are involved in an innovation; that each organisation may have different motivations; and that even when motives are similar, criteria are likely to diverge provides an explanation of the organisational barriers to innovation. It may be added that when these real difficulties are ignored, and the barriers to innovation are ascribed to personal malevolence, they remain unrecognised, and may grow as the result of lack of attention and because of personal animosity.

(48) Burns and Stalker (op.cit., see above note 30), 185-186.

(49) R.P. Clagget, Receptivity to innovation - overcoming the NIH factor (unpublished M.Sc. thesis, MIT Cambridge 1967).

5.4 Barriers to innovation: personal:

The organisational barriers to innovation which have been described are related to personal barriers, arising from the different backgrounds and targets of different groups. In some organisations studied it has been difficult for those engaged in research to communicate with those responsible for their management. The former, it is suggested, may judge success by scientific criteria, and the desire to extend knowledge, while the latter may adhere to technological criteria, and the desire to produce useful and profitable products. Analysis describing this potential conflict has been made of the Bell Telephone Laboratory, and there is extensive discussion of the resolution, or lack of resolution, of this conflict (50). This type of barrier is easily reconciled with the model adopted.

5.5 Barriers to innovation: perceptual:

Closely allied to both organisational and personal barriers are perceptual barriers. Three types of perceptual barrier may be recognised.

(i) Different groups in the innovation chain may possess different criteria by which an idea is judged. An account of the difficulties experienced by an economist and engineer in discussing a primitive but extremely successful water pump illustrates this. The engineer judged the pump in terms of mechanical efficiency, and of the technical skill required to manufacture it; the economist in terms of comparison between the cost of pump rental against labour charges for traditional water raising activities (51). Such barriers may be seen in different criteria used to judge an innovation, different languages used to express common aims, and different parameters. Sometimes the organisation

(50) See, for instance, R.M. Hower and C.D. Orth, Managers and Scientists (Boston 1963), 138-166.

(51) R.L. Sansom, 'The motor pump: a case study of innovation and development', Oxford Economic Papers (New Series), 21 (March 1969), 118-119.

adopted encourages such differences: an organisation in which there is a project divided between a chemistry team and a physics team is likely to result in the research targets of each team being different.

(ii) Often, the new product is judged by criteria which have been specially designed for an existing product, and this may present difficulties when a replacement product is introduced. Rayon, for instance, was introduced as a 'synthetic silk', and in many cases rejected since it did not approximate to silk. In contrast, each of the recent polymers to replace leather in shoes has been introduced not as a replacement, but as a material to be considered on its own merits, and (at least partly) on its own terms. There are many examples where it is important to ensure that a new product is judged on new terms, since a comparison of the old and the new may suggest the latter is more expensive or less effective, despite other advantages or cost savings in the whole system of which the product is but one part. In extreme cases, the values and criteria of the inventor and the user of the innovation may be completely different: the natives of Yurok first used coins given to them by white traders as extremely flat pebbles with which they played ducks and drakes; other Indians first used flour as a face paint (52).

(iii) A third type of perceptual barrier is the need for a new product to displace an existing one, and to displace the body of beliefs associated with the established product. Often this casts doubt

(52) H.G. Barnett, Innovation (New York 1953), 353.

not only on the existing product, but also on the men who supported it. This type of barrier has been most clearly discussed for scientific theories. Kuhn has suggested that the cause of opposition to the adoption and diffusion of a new theory is to be found in the attitude of those who have to judge it: "the invention of other new theories regularly ... evokes the same response from some of the specialists on whose area of special competence they infringe. For these men the new theory implies a change in the rules governing the prior practice of normal science. Inevitably it reflects on much prior work which they have already achieved" (53). Kuhn discusses the battle a new theory has to displace that already existing. He shows that the chance of an innovation being successful is partly dependent on the strength and position of the paradigm it must dislodge, and that the displacement process may lead to the innovation's being championed by one or more protagonists, who stake their scientific and personal reputation on its success.

The position of this champion is vulnerable, and his scientific reputation is likely to be attacked. In the nineteenth century, for instance, "the observations and discoveries of Jenner, Simpson, Lyell, Pasteur, Darwin, Lister, Helmholtz, Metchinkoff, and scores of lesser contributors were greeted with disdain or incredulity". Helmholtz had difficulty in getting physiologists to pay attention to his ophthalmoscope; Lister's claim that antiseptic practices would prevent wounds suppurating

(53) T.S. Kuhn, The Structure of Scientific Revolutions (Chicago 1962), 6.

was attacked by medical authorities of the stature of Simpson and Morton; the virulent treatment Semmelweis received when he proposed his theory of puerperal fever is believed to have contributed to his death through insanity (54).

6. The relationship between barriers and screens

In this examination of the barriers to innovation, five separate classes of barrier have been indicated - economic, technological, organisational, personal and perceptual - and they have been related to the model of innovation which was adopted. The importance of screens has already been mentioned: they are predictions of the barriers which are believed to exist. To be successful, screens require a definition of the purpose of the research, and an understanding of the general ecology in which the new product must survive. Screens are deliberately erected to simulate some parts of the perceived barriers, by testing particular qualities of the compound or process. The success of screens depends on the foresight with which relevant qualities in the end-product have been predicted, and the accuracy with which the tests carried out provide information about these qualities.

Baines, Bradbury and Suckling have discussed the properties and pathology of screens (55). The properties which may be used to classify a screen are: target definition, width of spectrum, mesh size, quantitative content, degree of abstraction, and sufficiency. Some of these are relatively self-explicatory. Target definition prescribes the target initially: it may be deliberately precise, as in those cases when a particular and clearly differentiated pattern of end effects is required, or it may be much looser, so that unexpected properties may be discovered. Width of spectrum relates to the number of properties tested by any screen: a screen

(54) Barnett, Innovation, 69, 316; and B.J. Stern, Social Factors in Medical Progress (New York 1927), 66-67.

(55) Baines et.al. (op.cit. see note 32), 104-109.

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(55) Baines et.al. (op.cit. see note 32), 104-109.

testing a particular pattern of end effects with precision is unlikely to provide information applicable for many uses. Mesh size relates to the ease with which a compound will pass through a screen, the broad mesh allowing more to pass through. Quantitative content is a measure of the flexibility of the screen to provide information other than simple Go, No-Go decisions. Of particular interest for the model of innovation chosen, with its emphasis on an innovation moving between organisations, are the properties of abstraction and sufficiency, for they help our understanding of how different organisations professing the same aim may adopt different criteria.

6.1 The degree of abstraction

The degree of abstraction of a screen described the relationship between the screen and the eventually desired end effects. Most tests are designed not to measure the precise end effects desired but other qualities which are more easily measured. Sometimes this is more convenient: rather than measure the molecular weight of a polymer directly, it is easier to measure the viscosity of a polymer melt at given conditions. Sometimes, it is necessary: to measure the "creep" of a polymer over its life would be impracticable, so observations are made over a shortened timespan (perhaps under accelerated conditions) and related by theory to the expected eventual distortion.

Abstracted screens are very common and, indeed, all screens are to some extent abstracted: the measurement of both the molecular weight and the creep of a polymer, however the tests are executed, is an example of an abstracted screen, in that the customer in the last resort is interested in neither molecular weight nor creep as such, but in whether it is possible to use the polymer in a certain moulding machine and whether the object so produced will be sufficiently stable to be used in a certain

application. From his own experience and from theoretical analysis, he has related these demands to the scientific parameters which he specifies. Often, the demand specified is entirely abstract: a chemical factory may supply a named chemical to determined standards of purity in complete ignorance of the requirements it has to satisfy other than the abstracted screen.

As the example quoted shows, there are advantages in a screen's possessing a degree of abstraction. First, it allows both the customer and the manufacturer to concentrate on one property of the product, to the exclusion of much redundant information. People drawn from very different industries may communicate by reducing a complex of demands to a few measurable parameters expressed in the lingua franca of science. And second, the abstracting of a research target may allow cheaper research to be done, since the researcher does not need to investigate all the possible phenomena, but can relate them, via theory, to an easily measured observation. The polymer scientist, for instance, does not have to make moulds of every potential plastic he synthesises, but rejects many after measuring their molecular weight. His ability to do so clearly relates to the completeness of, and his confidence in, the theory describing the phenomena under study. A parallel to this may be found in a similar argument put forward to explain technological development in rapidly advancing industries: technologically advanced industries are claimed to be those with a strong scientific base, where "the cost of invention ... is low because the sciences underlying the industry's technology are flourishing" (56).

(56) W.R. MacLaurin, 'Technological progress in some American industries', Am. Ec. Rev., 44 (1954), 178-189.
R.R. Nelson, 'The economics of invention: a survey of the literature', J. of Business, 32 (1959), 108; and 'The simple economics of basic scientific research', J. of Political Economy, 67 (1959), 299-301.

There are also dangers involved in the abstraction of a target, particularly when innovation is considered. An abstracted target may require properties to be tested which are not relevant. As an example, it is possible to cite the early development of fuels for motor cars. In the early days of petroleum refining, the target of a petrol which produced a good performance when used as a fuel for internal combustion engines was abstracted. The target adopted was for straight run gasoline, and branched chain hydrocarbons were shunned. When more was known about motor fuels, the octane rating system was introduced, and it became clear that branched hydrocarbons were preferred. The end target remained the same, but the abstracted target had completely changed (57). It is thus possible for an abstracted target to obfuscate reality and even to lead in the wrong direction. To define the research target properly may require analysis, and perhaps rejection, of the theory which has supported an abstracted target. The connection with perceptual barriers to innovation and with Kuhn's theory of innovation is apparent.

A second danger inherent in the abstraction of screens is that different organisations may abstract different parameters so completely that the component organisations have difficulty in communicating with each other. This is particularly likely when functional teams (based, for instance, on scientific disciplines) are engaged on a project. Alternatively, different organisations may concentrate on abstracted targets to the overall detriment of the total project.

6.2 Sufficiency:

The last property of screens examined by Baines et. al. is sufficiency, which is the degree to which the properties tested in the screen relate to the properties required of the end product. They consider two limitat-

(57) Y. Brozen, 'Invention, innovation and imitation', Am.Ec.Rev., 41 (1951), 244.

ions on sufficiency: that the effect of time cannot be completely simulated, and that no tests can guarantee the results obtained from animal tests will be applicable when humans are involved. These examples of insufficiency are based on the absence of reliable theory to relate long term aging effects to observations made over a shorter period, and on the absence of a theory of biological activity which is reliable enough to "scale up" experiments from other animals to humans.

In addition to these examples of insufficiency, there is a common type of insufficiency which derives from the nature of the innovative process, with the considerable dependence of the originating firm on other organisations to play significant parts. The target as envisaged by the research department initially responsible for a research project is likely to be altered as more becomes known about the other organisations which would be involved in any innovation. Typically, the initial screening of a potential compound may be highly abstracted, evaluating one quality only. Later tests are likely to be less abstracted, approximating to reality more. Indeed, it may be suggested that the initial research screening is but the first example of a continuum of screens that continue from the initial, probably abstracted screen of a research worker to the moment when a product which is widely accepted is sold, subject to quality tests, which are carried out by manufacturer to ensure the product meets specified standards. It is interesting to note that this screen is likely to be even more abstracted and less sufficient than the initial research screen. The continuum of screens is thus likely to be highly abstracted at either end, and most sufficient at some intermediate point. There exists the danger, however, that the expanded and enlarged screen may be insufficient in that it does not test those characteristics of the invention which other organisations are interested in, because of a failure to understand the criteria of other organisations.

The danger of insufficient screening is particularly large for certain types of barrier to innovation. Personal and perceptual barriers, and particular categories of economic and technological barriers ("Does this satisfy the customer's/supplier's set of values?"; "What changes will have to be made in the existing manufacturing system to accept this invention?"), can only be made explicit and be understood by gaining a thorough knowledge of the system into which the invention must fit. The criteria used to judge success are certain to be more complicated and to be more numerous than those adopted at an earlier stage in the innovative process, where a highly abstract screen, normally expressed in scientific terms, is typically found.

7. Factors affecting the acceptance of new ideas

The model of innovation adopted, and the discussion of barriers to innovation and of how screens within a research organisation are related to these barriers, have emphasised the importance of the organisation responsible for the new idea being able to appreciate the criteria and motives of those other organisations which are involved in the innovative process. It is useful therefore to consider what factors are likely to affect the acceptance of new ideas. By considering the innovation not from the viewpoint of the inventor, but from that of the recipient, it is possible to concentrate on the criteria adopted by those accepting inventions. For adequate screening by the inventing organisation, it is important that this should be done.

Two types of model of acceptance of innovation may be distinguished. The first is predominantly economic. It is described in various ways.

(i) Nelson and his co-authors identify three factors which affect the speed with which an invention spreads into use:

(1) the long run advantage of the new product or process over older ones;

(2) the transition costs and frictions, on the one hand, and costs and dangers of maintaining the status quo, on the other; and

(3) the uncertainty about the superiority of the new product, and the ease or difficulty of overcoming these uncertainties.

These factors are suggested to be affected by respectively

(1) the perception of advantages

(2) the need for capital investment and new training; and the existence of inter-organisational co-ordination

(3) the existence of trained receipients and a strong information distribution system; and the ability to carry out "partial experiments" before commitment to an innovation (58).

(ii) Mansfield has traced the diffusion of inventions through large firms in selected industries. The model he adopted was based on the hypothesis that "the probability that a firm will introduce a new technique is an increasing function of the proportion of firms already using it, and the profitability of already doing so, but a decreasing function of the size of the investment required". This model has four determinants: the extent of the economic advantage of the innovation over older methods or products; the extent of the uncertainty associated with using the innovation when it just appears; the extent of the commitment to try out the innovation; and the rate of reduction in the initial uncertainty about the innovation's uncertainty (59).

(58) R.R.Nelson, M.J. Peck and E.D. Kalachek, Technology, Economic Growth and Public Policy (Washington D.C. 1967), 89.

(59) E. Mansfield, 'Technical change and the rate of imitation' Econometrica, 29 (October 1961), 762-763 and The Economics of Technological Change (New York 1968), 119.

These models are both useful in enabling one to predict the chance of invention's succeeding. However, the concentration on economic factors, particularly marked in Mansfield's analysis, confines their usefulness. There are very many inventions which are not measured directly on any economic scale. Any new product, for instance, is likely not to be a simple replacement of an existing good, but to embrace new properties. This is likely to complicate a simple comparison between the old and the new. Some innovations are not in fact measured directly on an economic scale: military products and pharmaceuticals may exemplify this.

In short, concentrating on economic barriers to the acceptance of invention is likely to be most useful in the context in which Mansfield made his analysis, that is the replacement of an existing process by another, both producing the same, or a closely similar product. For other types of invention, a model is required which embraces Mansfield's determinants and also accounts for barriers to innovation other than economic.

Such a model is suggested by Rogers, who identifies five characteristics of a new idea which affect the speed with which it will be accepted:

(1) The relative advantage of the innovation, and the way in which this is perceived.

(2) The compatibility of the new idea with existing values.

(3) The complexity of the idea, and the need for new adjustments in order to accept it.

(4) The divisibility of the new idea, and the way in which it is possible to experiment before complete adoption.

and (5) The ease with which the features of the new idea might be communicated to others (60).

This model is based on analysis mainly of anthropological and socio-

(60) E.M. Rogers, Diffusion of Innovations (New York 1962), 124-135, 305-307.

logical change, and the new products considered are mostly either agricultural or medical. The model, however, seems more widely applicable, and helps an understanding of the spread of new industrial products and processes. For instance, the rather unwieldy listing of 24 characteristics of adoptive firms proposed by Carter and Williams can be reduced to Rogers' five determinants, and is made easier to utilise by so doing (61).

8. Conclusion:

The model chosen has been selected to satisfy three criteria. First it must explain not only the inventive process, but the whole innovative process. Second, it must explain three characteristics of new ideas: that few inventions survive to become innovations, that those which survive normally have a protracted path to follow, and that in following this path they are likely to find their destination modified or changed. The population of newly conceived research projects is characterised by high mortality, slow maturation, and a heavy incidence of mutation. Third, it must recognise that different organisations may be involved in the innovative process. These criteria suggest that many models of innovation are at best only useful when applied to a small part of the innovative process; at worst, they may be severely inappropriate, and hence misleading.

The model that has been adopted has affinities with descriptions of problem-recognition and -solving mechanisms adopted in other managerial situations. It is specifically related to the research environment by its recognition that the innovative process is likely to involve not one, but several, organisations, each of which may possess different (and perhaps differing) objectives and criteria. The model emphasizes the possible conflict between the various research organisations, arising from

(61) Carter and Williams, Industry and Technical Progress, 178-179.

their underlying conflicting objectives. To aid analysis when considering the innovative process, five areas of possible difficulty have been suggested - economic, technological, organisational, personal and perceptual - and the ease or otherwise of screening for these problem areas has been discussed. The model adopted suggests explanations for the central frustration and great attraction of the research scientist engaged in industrial innovation - the knowledge that much of his work will produce no eventual innovation.

This model will now be applied to two situations. The first is the examinaton of three case studies of innovation in the chemical industry - the anaesthetic halothane, the bipridyl herbicides 'Reglone' and 'Gramoxone', and the pigment and dyestuff phthalocyanine. The second is the examination of the activity of a contemporary research laboratory, to assess the usefulness of this model rather than the other model or models used, albeit implicitly, at present. The remainder of this thesis describes these applications, and discusses the changes this testing of the model suggest should be made to it.

Chapter 2

AN INDUSTRIAL INNOVATION : halothane

1. Introduction

The inhalant anaesthetic halothane is now widely used for a great variety of surgical operations. Recent reports confirm its advantages. One remarks that "it has exceptionally valuable properties, for it is potent, non-irritant to the respiratory tract, and can be used in the closed-circuit apparatus in the presence of warm soda-lime"; a second states: "Halothane has now been in clinical service for almost a decade, and its use in modern anaesthetic practice is firmly established. Indeed, it is probably true to say that its introduction represents one of the most important advances in anaesthesia of the century" (1).

So laudatory are these remarks that it might appear surprising that the properties and advantages of halothane were not recognised and accepted soon after the anaesthetic's discovery. Yet analysis of halothane's discovery and introduction to the market shows that there were many barriers to be overcome, not only in initiating successful research, but also in ensuring that the compound, once it had been synthesised and its properties recognised, should be developed.

The successful innovation depended on several different groups of people, each of which had different criteria and motivation, and the differences between these groups accounted for many of the difficulties encountered in halothane's development. An analysis of this innovation must therefore be concerned not only (or even mainly) with its origins, but also

(1) 'Halothane Re-examinded', Brit. Med. J., (1964), II, 325 and G.W. Black, 'A review of the pharmacology of halothane', Brit. J. Anaesth., 37 (1965), 688.

and principally with the elaboration of the original invention into the innovation which has made such a contribution to society.

2. Anaesthetics before halothane:

Before halothane's discovery, the anaesthetist had several inhalant anaesthetics from which to choose. These included chloroform, nitrous oxide, ether, cyclopropane and ethylene. All the available inhalant anaesthetics, however, suffered from at least one of the following disadvantages - explosiveness, toxicity, unfortunate side-effects, or simply undue weakness. Some inhalant anaesthetics combined several defects. The use of chloroform involved risks of damage to the kidney and heart, while the patient was liable to suffer from post-operative nausea.

Nitrous oxide had to be used in 95 per cent concentration, and the duration of operations using nitrous oxide alone was severely limited. Also, muscular relaxation was poor, and the surgeon's task was correspondingly difficult. Even though it was possible to overcome this difficulty by using nitrous oxide in conjunction with barbiturates, there were still difficulties about storing nitrous oxide with its low boiling point ($-89^{\circ}C$). Ether, the anaesthetic in most common use, had a variety of defects; induction was slow, post-operative nausea common; there was the threat of toxicity and it was inflammable. It was not unknown for fires or even explosions to occur in an operating theatre, and the danger of this prevented surgeons from using certain techniques which were possible with an anaesthetic such as nitrous oxide. Other inhalant anaesthetics, like cyclopropane and ethylene, presented similar dangers.

Despite the recognised deficiencies in all inhalant anaesthetics, those in most common use had been known for a considerable time; nitrous oxide had first been used by Beddoes and Watt in 1796, and by Davy in 1800; ether by Morton in 1846, and chloroform by Simpson in 1847 (2). The most

(2) H. McIlwain, Chemotherapy and the central nervous system, (London, 1957), 4.

recently introduced inhalant anaesthetics, such as cyclopropane, were used in only a small proportion of operations. The rate of progress that had been made by inhalant anaesthetics had been so slow as to persuade some anaesthetists that they should be replaced by intravenous anaesthetics, where the new barbiturates were presenting exciting opportunities. Fischer's work in establishing the structure of uric acid in 1822 had led to the introduction of the first barbiturate in 1903, and anaesthetists had been quick to explore the possibilities of using the new drugs.

The combination of small improvement in inhalant anaesthetics with considerable improvement in intravenous anaesthetics had undoubtedly led many anaesthetists, including those who were most skilled, to view intravenous anaesthetics as the growth point for future experimentation. This was expressed in articles which were highly and justly critical of chloroform in particular, and advocated the use of other inhalant anaesthetics, or preferably a combination of nitrous oxide and barbiturates. One such article described chloroform as "almost universally recognised as being too poisonous for the production of surgical anaesthesia in human beings", and concluded that "nitrous oxide, pentothal and cyclopropane, combined with spinal or field blocks where deep relaxation is needed, can cover the whole field of surgery...." (3). In his dismissal of chloroform and, to a lesser extent, ether, the writer was not atypical.

3. The search for new anaesthetics

Although little advance had been made in introducing new inhalant anaesthetics, various search parties had been formed. In 1932, Booth and Bixby in the United States had considered how to manufacture a new non-inflammable anaesthetic, and had concluded that organic fluorine compounds

(3) F.B. Mallinson, 'Modern (non-volatile) anaesthesia', Lancet, (December 11, 1943), 729.

represented the best possibility (4). The title of their paper: 'Fluorine derivatives of chloroform' indicates the train of thought: by replacing one halogen by another, lower boiling point and increased stability might be achieved, but the end result would be a chloroform derivative - presumably, since fluorine was more expensive than chlorine, at greater cost. Since neither of the two compounds tested, $CFHCl_2$ and CF_2ClCH_3, was suitable (both produced convulsions in mice anaesthetised by them), the search party was disbanded. A second, more thorough, search party was formed by Robbins: in 1946, he reported testing forty-two fluoroalkanes as anaesthetics. After tests on mice and in some cases on dogs, Robbins recommended that four of the compounds CF_3CHBr_2, $CF_3CHClCH_2Cl$, $CF_3CHBrCH_3$, and $CHF_2CHClCH_3$, should be further tested (5).

The reasons why this search for a new inhalant anaesthetic failed despite the promise it showed are interesting and illuminating. The compounds which Robbins tested for biological activity were synthesised by W.G. Toland, as part of research for a post graduate thesis. The objective of the work was to explore halogenation methods, particularly new techniques of fluorination and subsequent chlorination and bromination of the materials synthesised. It was as a somewhat incidental addition to the research programme that compounds were submitted to Robbins for testing as anaesthetics, and it is not therefore odd that the satisfactory results obtained by Robbins were not followed up directly. Toland himself ascribes the failure to pursue the potentially interesting anaesthetics to three causes: "(i) We had difficulties establishing analyses of the compounds with three different halogens present, (ii) the emphasis was on halogen-

(4) H.S. Booth and E.M. Bixby, 'Fluorine derivatives of chloroform', Industrial and Engineering Chemistry, 24 (June, 1932), 637.

(5) B.H. Robbins, 'Preliminary studies of the anaesthetic activity of fluorinated hydrocarbons', J. Pharmacol., 86, (1946), 197.

ation chemistry rather than on the synthesis of new anaesthetics, and (iii) our results from Robbins' testing were so slow that my thesis work was completed before the last set of results, which might have inferred the potential value of Halothane, were received" (6). Toland adds that it is likely that Halothane was obtained in the course of their halogenation studies, although it was never identified, since those compounds which were synthesised and identified were closely related to Halothane. (They included, for instance, CF_3CHBr_2, CF_3CH_2Br and CF_3CHCl_2).

The barriers to innovation identified by Toland in his account fall into two categories. First there is a technological barrier, represented by the problem of isolating and identifying different component products. Second, there are the problems in that those responsible for synthesising candidate compounds were neither directly concerned with, nor were they efficiently linked administratively to, those responsible for testing candidate compounds. Robbins' search party, deprived of a suitable flow of candidate compounds for testing, ended.

3.1 The search within ICI for new anaesthetics:

It was as a result of Robbins' paper, however, that a further search party looking for fluorine compounds as inhalant anaesthetics was established. In 1948, the part of ICI with experience in medical products took up the enquiry. This, the Medicinal Chemicals Section of Dyestuffs Division, had already been interested in anaesthetics: in 1934, the first medical product of the division had been cyclopropane, then newly introduced from North America; in 1947, they had started to market the intravenous anaesthetic 'Kemital'. When Robbins' article appeared, it therefore aroused considerable

(6) Private communication from W.G. Toland, March 20, 1969.

interest. Those interested suffered from the same drawback which Robbins had encountered, in that they were unable to synthesise fluorine compounds themselves. To try to obtain fluorine compounds to test with their facilities, they approached the part of ICI experienced in fluorine technology, General Chemicals Division, asking whether that division could provide sample quantities of fluorine compounds, and particularly the four which Robbins had recommended. Each request was refused, on the grounds that fluorine research was already committed to the manufacture of uranium hexafluoride. The search party, which had expressed "interest" in the development of a fluorine anaesthetic, was unable to proceed, and was left dormant.

This barrier to innovation was overcome only when a search party was created, quite independently of previous searches, in the General Chemicals Division of ICI. In 1950, Dr. J. Ferguson became Research Director of the General Chemicals Division, and soon found that he had to make a decision about fluorine research. ICI had started fluorine research in 1933, following the discovery of fluorine refrigerants in the U.S.A. in 1928. The research had been much stimulated by the demand during the war for uranium haxafluorides and fluorlubes: between 1940 and 1943 ICI expenditure of fluorine research increased tenfold, and a further steady increase continued throughout the decade. In 1950, however, there was a dramatic increase in expenditure: expenditure in the first quarter of 1950 was at a rate that was almost three times that of the expenditure in 1949. It was thus necessary to consider the future of fluorine technology, and Ferguson embarked on a review, examining the properties of fluorine and fluorine compounds. The conclusion was that there was: '... only one outstanding general property capable of commercial exploitation. That is the great stability and inertness of certain organic fluorine compounds'. Ferguson

then listed applications where this property was, or could be, useful: refrigerants, heat resisting plastics, heat transfer media, lubricants, transmission fluids, sealing fluids, insulating media, dyestuffs, anaesthetics and fire extinguishers. He also examined the cost of making fluorine, and argued that its high cost should exclude elemental fluorine from being the subject of research. Instead work on fluorine compounds, seeking applications based on inertness, should be pursued. It was this survey of fluorine technology which led to the resumption of the search party for a fluorine anaesthetic.

At this time, Ferguson was unaware of the approaches that had been made to General Chemicals Division in 1948 by the Medicinals Chemical Section of Dyestuffs Division. (Indeed, it is clear from subsequent correspondence that it was not until 1956 that he learnt of these approaches). Ferguson was subsequently to describe the invention of halothane as "merely one example of a successful target research", and he continued to say: "Many others might be mentioned including ... the researches which in 1928 yielded the organofluorine refrigerants" (7). There are, however, important differences, as well as great similarities, between the discovery of halothane and those of the fluorine refrigerants or of Midgley's other great discovery, lead tetraethyl. Fluorine refrigerants and lead tetraethyl were invented in direct response to a demand, in the first case for a non-inflammable and non-toxic refrigerant, in the second for a high performance anti-knock additive for fuels. With fluorine refrigerants in particular the chemical which eventually was used to give the desired effect was tested after many others

(7) J. Ferguson, 'The discovery of the anaesthetic halothane - an example of industrial research', Chem. & Ind., (May 16, 1964), 818.

had been tried or considered (8). With halothane, the initial stimulus for research did not come from a new recognition of social need, but from a combination of analysis of fluorine properties and a recognition of mounting research expenses. Ferguson explicitly states that at the time "the General Chemicals Division had no knowledge of medical matters in general or of anaesthesia in particular, nor whether there was any place at all for a new anaesthetic". An important stimulus to the research project was the substantial commitment made by General Chemicals Division to research in a field of technology not producing hoped-for projects.

The first work in this project was started, at Ferguson's request, by Dr. C.W. Suckling in September 1950. The work represented in some ways a natural extension of Suckling's previous work, since he had been engaged on research on the biological activity of fluorine compounds - albeit labile compounds - in a search for fungicides. His first step was to make a literature survey relating structure to the biological activity of fluorine compounds. This work was soon extended to include discussions with interested and expert parties, which naturally included those who had made the approaches in 1948. It was not until February 1st 1951 that the first sanction was proposed for a research programme which was to include preparing compounds for testing as potential anaesthetics by the Pharmaceuticals Division of ICI (the successor to Dyestuffs Division's Medicinals Section). The sanctioning of this research programme marks the successful constituting of a search party from those who were in a position to synthesise the compounds which might be suitable and from those who recognised the need, and could judge the promise shown by candidate compounds. The

(8) T. Midgley, 'From the periodic table to production', Industrial and Engineering Chemistry, 29 (February 1937), 241.

step which had eluded Robbins in 1946 and Dyestuffs Division of ICI in 1948 was accomplished.

The stimulus which initiated the research was promoted more by scientific motives, than by demand. Ferguson had long had an interest in the mechanism of narcosis - that is, the reversible inhibition of a biological function. In 1939 he had published a paper which showed what a good measure of the narcotic power of a substance was its thermodynamic, rather than its ordinary, concentration. If one considered the volume concentration of different compounds required to obtain anaesthesia, very wide variations were found: nitrous oxide had to be administered in 100 per cent concentration, whereas chloroform required only 0.5 per cent concentration. However, when thermodynamic concentrations were considered, the range of values was much smaller: the relative saturation for anaesthesia for both nitrous oxide and chloroform was 0.01. Whereas volume concentrations might differ by a factor of 200, the extreme values for thermodynamic concentrations differed by a factor of 7. The original paper postulated that, for both vapours and aqueous solutions, the thermodynamic activities or concentrations should be used for comparative studies of the relationship between the chemical constitution of narcotics and their intensity (9). In April, 1950, at a time when he must have been considering the review of fluorine research he was to finish in July, Ferguson read a paper in Paris on the results of tests with grain weevils, which further refined his previous hypothesis. This paper had shown that substitution of a halogen atom for a hydrogen atom in a hydrocarbon molecule did not seriously affect narcotic potency; and some observations on differences between hydrocarbons had been made (10). Although Ferguson was certainly aware of the advantage of his

(9) J. Ferguson, 'The use of chemical potentials as indices of toxicity', Proc. Roy.Soc.B., 127, (1939), 387.

(10) J. Ferguson, Mecanisme de la narcose, (Paris 1951), 25.

treatment of narcosis in clarifying quite complex relationships, his main interest, as displayed in the Paris paper, was in the relationship between chain length and potency.

It fell to Suckling, therefore, to draw explicitly the important conclusion that the property of narcosis was not directly dependent on the chemical constitution of a molecule. The chlorine atoms in chloroform, for instance, did not confer any special narcotic character on the compound, but "merely lowers the vapour pressure of methane to a convenient value for administration". The consequences for Suckling were considerable. To discover suitable narcotics, it was not necessary to analyse chemical characteristics - to try for example to isolate the common properties shared by ether, nitrous oxide, chloroform and cyclopropane. Instead, he recognised that any compound administered at the appropriate relative saturation would possess narcotic properties, provided that this effect were not over-ridden by a more powerful one. Ferguson's treatment allowed a general principle to be applied to what would otherwise have appeared a heterogeneous group of compounds.

In addition, it placed great emphasis in any search for a new anaesthetic upon its inertness. It was already known that many narcotics leave the body unchanged, and it was believed that narcotics act by some physical, rather than chemical, action as whole molecules. With this belief, and also that the thermodynamic concentration gave a good indication of narcotic potency, it was a natural step for someone concerned with a new anaesthetic to conclude that a compound with suitable boiling point (and hence volatility and potency) might be a successful anaesthetic so long as it did not have any harmful physiological effects. The theory of narcosis was laying emphasis on inertness, at the time Suckling and Ferguson were concluding

that: "The fluorine atoms in chemical compounds are very often extremely unreactive ... it can be stated generally that $>CF_2$ and $-CF_3$ groups are exceptionally stable combinations".

Ferguson saw the research for a new anaesthetic at least in part as an opportunity to test his theory of narcosis. After initiating the research programme, he wrote to the manager in charge of it with his hypoethesis about the relationship between chain length and branching in the molecule and potency, with a list of fluorine substituted compounds which he considered worth study. It is characteristic of his interest in thermodynamic concentrations that some years later, after becoming ICI's main research director, he wrote to his successor at General Chemicals Division to correct ambiguities in a report on anaesthetics research which seemed to be irreconcilable with his theory. The long-established interest which Ferguson had in narcosis seems to have been dominant in his choice of a new anaesthetic as the application to which fluorine inertness was to be turned.

It is all the more interesting, therefore, that the treatment which Ferguson developed was not new, although it had long been forgotten. Snow, who was one of the first people to distinguish between different levels of anaesthesia, had remarked on the wide differences in the concentrations of chloroform, ethylene and amylene required to produce the same degree of narcosis, and noted that: "three grains in 100 cubic inches produced the fourth degree of narcoticism, we get 0.035 or 1/28th, as the amount of saturation of the blood in this degree (with ether). Now this is within the smallest fraction of what was found to be saturation of the blood by chloroform, requisite to produce narcoticism to the same degree" (11).

(11) J. Snow, On chloroform and other anaesthetics, (London, 1958), 353-4, 386.

He is also reported to have made explicit the generalisation behind this observation by stating:"We find that the quantity of each substance in the blood in corresponding degrees of narcoticism, bears a certain proportion to what the blood would dissolve - a proportion that is almost exactly the same for all of them" (12). Ferguson's restatement of this observation - quite independent of the original thesis - occurred at a most apposite time.

3.2 Market forecasting:

In the description of the new search for a fluorine - containing anaesthetic, it has been emphasised that demand for a new anaesthetic was not the original stimulus. Even after it was learnt that there were important deficiencies in existing anaesthetics, the commercial consequences of the demand for new anaesthetics does not seem to have been analysed in detail. The initial literature survey stated that no commercial prospects were sufficiently relevant to be mentioned; the subsequent sanction of February 1951 discussed anaesthetics already in use, and claimed that "it is considered that a new anaesthetic having all the desirable properties would largely displace materials used at present", but did not convert this claim into a forecast of likely cash inflow. It is perhaps indicative of the lack of attention paid to the commercial analysis of an anaesthetic's likely success that exactly the same words were used to describe the work's commercial prospects in subsequent sanctions in May 1952 and October 1953. Since General Chemicals Division was undertaking this research in collaboration with the Pharmaceutical Division, who might be more expected to investigate the commercial prospects of a new anaesthetic, this lack of commercial analysis is understandable. There is some evidence which suggests that commercial research was not very much further advanced at Pharmaceuticals Division: at a meeting to consider halothane's properties in June

(12) H. McIlwain, (op.cit. see above note 2), 11.

1954 a spokesman of that division said that: "although there was no prospect of making much money from a new anaesthetic there was no reason why $CF_3.CHClBr$ should not be an economic proposition".

The market forecast of the maximum eventual demand given on that occasion was less than the actual sales achieved in 1960. Within the Pharmaceuticals Division of ICI, which was establishing itself as an independent organisation during the period when this research was occurring, it seems that the market analysis of the new anaesthetic was not particularly detailed. From its origins in 1936, the Pharmaceuticals Division had been concerned to find and produce new drugs, rather than to replicate drugs already in existence. The prospect of a new anaesthetic, and the recognised deficiencies in the existing anaesthetics seem to have been considered sufficient grounds for embarking on a research project. In addition, humanitarian grounds - the worth of human life and of reduction of suffering - were also important in spurring on those most concerned with halothane's development. It is difficult to quantify the importance of such motives, but any account which omitted mention of them would be startlingly incomplete.

Although demand appears to have played a minor part in initiating the research which led to halothane's discovery, it was a necessary condition for the research's continued existence. Suckling soon established contacts with Pharmaceuticals Division; an independent anaesthetist, Dr. T.J.C. McDonald from Aberdeen, made contact with the Research Manager of General Chemicals Division; it is indicative of the concern that existed about inhalant anaesthetics that in 1955 the Medical Research Council established a committee to investigate new non-explosive anaesthetics. The existence of a demand for new anaesthetics was manifest, and its very obviousness, combined with the great utilitarian appeal in discovering a new anaesthetic, may explain the apparent lack of commercial analysis.

3.3 Analysis of the Target

Although the commercial demand for a new anaesthetic received little analysis, the technical requirements which a new anaesthetic would have to satisfy were carefully considered. Suckling consulted Dr. J. Raventós, a pharmacologist in Pharmaceuticals Division, and between them, after discussion with practising anaesthetists, they constructed the target which they hoped to attain. The specifications were severe. The commonly accepted definition of the ideal anaesthetic observed that no less than four people must be satisfied: the surgeon, the anaesthetist, the patient, and the manufacturer, each of whom made different demands upon an anaesthetic. The surgeon required an anaesthetic which was capable of effecting complete muscular relaxtion, was non-explosive, and did not increase capillary bleeding. The anaesthetist expected an anaesthetic to be potent so that a high percentage of oxygen could be administered during anaesthesia, and to take effect with such speed that moment to moment control of anaesthesia was possible. It should be eliminated from the body unchanged, have a high margin of safety, and produce a minimum of functional or organic injury during and following exposure. The patient required a rapid and pleasant induction followed by a recovery which was free from post-operative nausea. The manufacturer, it was claimed, would consider the ideal anaesthetic to be simple and inexpensive to produce, to be purified without difficulty, and to remain unchanged when stored (13). In addition, a further important requirement unspecified in this list was stability over soda lime, used in closed-circuit anaesthetic equipment.

Many of these properties could not be predicted from knowledge of a compound's chemical and physical properties. Absence of post-operative nausea, rapid induction, little mucous secretion, absence of damage to

(13) M.H. Seevers and R.M. Waters, 'Pharmacology of the anaesthetic gases', Physiological Reviews, 18 (1938), 447-448.

the organs of the patient, lack of interference with cardiac regularity, muscular relaxation, and absence of excessive bleeding were desirable properties about which little prediction was possible. In general, the more inert the compound, the lower appeared the chance of chemical interaction with the patient's body. This belief led to a preference for compounds containing $\rangle CF_3$ or $\rangle CF_2$ groups, which Robbins work suggested to be quite innocuous, and to neglect of compounds with CH_2Cl or CH_2Br groups, which Robbins had shown to be frequently highly toxic. Other properties could be defined, and hopefully related to chemical and physical properties of the compound. The target was therefore defined in terms of these more predictable properties:

(i) The anaesthetic should be volatile, so that vapourisation would be simple. Calculation of the likely boiling point of the compounds proposed for synthesis could be made from knowledge of halofluoroparaffins, and this presented little difficulty.

(ii) The anaesthetic should be non-flammable. As has already been mentioned, there were dangers in using both cyclopropane and ether, because of explosion hazards, and this prevented surgeons from using certain desirable techniques, such as cautery. Inflammability might be countered by ensuring that there were few hydrogen atoms present in the molecule, so this property could be used to define the target.

(iii) Stability when passed over soda-lime was a further desirable property. Soda-lime is used in closed-circuit anaesthetic equipment to remove carbon dioxide and moisture from the patient's exhaled breath. Unless the anaesthetic could be shown to be stable when passed over soda-lime it would be excluded from closed-circuit anaesthesia. Since a fluorine compound was expected to be expensive, it was important that it should be able to be administered with closed-circuit equipment, which was more

economic than open-circuit in its consumption of anaesthetic. This could be aimed at by designing compounds which were not likely to eliminate HCl or HBr.

(iv) An anaesthetic of high potency was required, so that it might be administered with large concentration of oxygen. Potency was predictable from Ferguson's theory, so that it could be related to the calculated boiling point, and then more accurately determined when the boiling point was known.

So much was defined from application of Ferguson's principle, and from general chemical knowledge. Close perusal of Robbins' results with 42 alkyl fluorides led Suckling to some hypotheses relating the margin of safety (the ratio of that concentration of an anaesthetic which produced death to that which produces anaesthesia) and the speed of induction and recovery to the physical property of the compounds. It is interesting that at the date, 27th January 1953, on which Suckling reported his analysis of Robbins' results, he had already synthesised the compound $CF_3CHClBr$, which was to become known as halothane or 'Fluothane'.

In addition to defining the research target with precision, Suckling and Raventós decided that in any synthesis of candidate compounds for anaesthetics a high level of purity was necessary. The original test of organic fluorides for non-toxic refrigerants by Midgeley in 1928, which had instigated the interest in non-toxic fluorine compounds, had nearly failed because of phosgene impurities in the dichlorodifluoromethane (14). The difficulties that might arise from impurities in preventing repeatable results being achieved were clear.

(14) T. Midgley, and A.L. Henne, 'Organic fluorides as refrigerants', Industrial and Engineering Chemistry, 22 (May 1930), 542-545.

The screen used by Suckling may be described, by following the analysis suggested by Baines et al., as highly abstract (15). The particular and precise end effects required in an anaesthetic were either deemed to defy correlation with chemical and physical properties (thus no attempt was made to predict speed of induction or the occurrence of post operative nausea), or they were reduced to precise and measurable properties. The screen clearly made no claim to sufficiency: it was possible to predict neither whether the synthesised compounds would be practical anaesthetics, nor whether any compound which was a practical anaesthetic would be more attractive than those which already existed. The contrast between the properties of Suckling's screens, and those used in subsequent testing of the compounds made, will be commented on later.

The definition of the research target, and the relating of the properties that were sought after to chemical and physical properties, allowed compounds to be designed that would certainly approximate to, although not necessarily be identical with, the target. Halothane, $CF_3CHClBr$, was in fact the sixth compound synthesised. Although there was a very large element of luck in hitting the unpredictable pharmacological properties that were desired so soon, the definition of the target was such that the search area was small. In his review of fluorine technology and research in 1950 Ferguson had written: "If chemistry were more advanced, and one were able to design chemical compounds accurately for specific uses, no doubt the fluorine atom would form one of the tools in the armoury of the designer, just like any other atom ... the production of tailor-made chemical compounds is not yet a very advanced technique, though something can be done in this direction". The analysis of desired properties, the explanation of narcosis provided by Ferguson's theory of thermodynamic

(15) A. Baines, F.R. Bradbury, and C.W. Suckling, Research in the Chemical Industry, (London, 1969), 107.

concentrations and the analysis of Robbins' data allowed the ideal that Ferguson had believed impracticable to be realised.

This would not have been possible without the security provided by accurate analytic techniques. The experiences of Midgley and Toland referred to earlier show how inadequate analytic techniques could hamper a research programme. In dealing with these difficulties, Suckling and his colleagues at Widnes were considerably aided by the recent development of new analytical techniques. Vapour phase chromatography enabled rapid testing of compounds, and it was thus possible to check compounds for impurities. This was important not only during the synthesis of candidate compounds, but also during the scale-up of manufacturing facilities, when analysis of the starting materials disclosed impurities. Use of mass spectrometry also confirmed impurities, and later the first use by General Chemicals Division of nuclear mass resonance analysis was for a halothane impurity. By ensuring high purity, Suckling and Raventós were able to have confidence in the experimental results produced by candidate anaesthetics, and Suckling was able to maintain high standards of purity when larger scale of manufacturing started. The developments in analytic technology which occurred in the 1950's greatly facilitated the development of halothane.

3.4 Screening

Within the chemical industry, it is commonly stated that the purchaser buys "effects, rather than chemicals". In no case is this more true than in that of anaesthetics: the definition of the ideal anaesthetic, already referred to, was couched entirely in terms of the end properties desired by different users, and there was no attempt to define the physical properties which an anaesthetic should possess. Indeed, this would be particularly difficult for anaesthetics since there is no agreement about

the mechanism of narcosis. In addition, anaesthesia is a property which can only be measured by testing a compound on a subject and is defined in terms not of the compound conferring anaesthesia, but in terms of the condition of the anaesthetised subject. The various levels of anaesthesia were first defined by Snow in 1847, when he distinguished five; Guedel in 1951 defined the more widely recognised levels of anaesthesia, again in terms of the physical reactions of the patient to stimuli (16).

The screening of potential anaesthetics was, therefore, a difficult test to devise. It was important not to waste the small quantities of compounds that had been synthesised and purified, so the maximum amount of information was to be extracted from each experiment. Raventós decided that his screening tests would examine seven desirable properties: volatility, non-flammability, high potency, high therapeutic index, freedom from liability to cause damage to a vital organ, rapid and quiet induction and recovery, and freedom from severe cardiovascular effects. A first test was designed in which activity, gross safety margin, liability to damage vital organs, and rapid and quiet induction and recovery were tested. In these tests, a known quantity of a compound was volatilised, and used to administer anaesthesia to some 30 mice for a period of an hour; this was then repeated at different anaesthetic concentrations. The symptoms of the mice were observed at one or two-minute intervals, and plotted against time. Surviving mice were observed for a week after the experiment, and any that died were assumed to have suffered damage to a vital organ. This test enabled the therapeutic ratio for safety margin of the anaesthetic to be calculated, with an accuracy of $\pm$ 10 per cent. Such was the success of Suckling's design of compounds, based on an extension of Ferguson's

(16) A.E. Guedel, Inhalation Anaesthesia, (New York, 1951).

analysis, that between half and two-thirds of all compounds submitted for test passed the initial screen.

It is indicative of the close working relationship that existed between Raventós and Suckling that Raventós was sufficiently confident in Suckling's predictions to dispense with any initial screening of compounds to test activity, and was also able to devise a relatively detailed first test, which produced unambiguous results. The geographical separation of synthesis and screening, combined with the fact that those involved belonged to different parts of ICI's large organisation, might have been expected to present a barrier to the successful progress of the research. That it did not was an important contribution to the success of halothane's development, and seems largely due to the mutual respect which Suckling and Raventós soon developed for each other's ability.

Although between a half and two-thirds of the compounds passed the screen in respect of safety margin and potency, this number was reduced by subsequent deaths of mice anaesthetised (so that the compound was rejected as damaging a vital organ) or by occasioning convulsion during anaesthesia. There remained some third of all compounds submitted. After screening on mice, the surviving compounds were tested on rabbits; sign of anaesthesia was noted, and respiration and ECG recorded. To pass this screen, a compound must have a high therapeutic ratio, give a rapid induction, and not occasion severe ECG changes or falls in blood pressure. Many of the compounds which had survived the first screen failed because they seemed liable to cause harmful cardiovascular effects. After screening on dogs (and in some cases before) an extended test of stability of a compound over soda lime was made by Suckling in Widnes, to ensure that he had successfully accomplished his design of supplying stable compounds; this test was subsequently repeated, with live animals in the closed-circuit, at

Pharmaceuticals Division. This test rejected few candidate anaesthetics which had been passed by pharmacological screens.

A third screen for anaesthetics performed by Raventós consisted of repeating the second stage tests on compounds which has been found stable over soda lime, with dogs in place of rabbits. Further tests on the surviving compound, $CF_3CHClBr$, included tests on cats and monkeys, as well as pathological and histological studies on the tissues of a variety of animals anaesthetised with this compound. Tests were also made to guard against chronic toxicity.

The screening tests on candidate compounds successively reduced the number of surviving compounds. It is indicative of the high standards established for screen design that none of the inhalant anaesthetics in common use would have fully satisfied all tests: ether and cyclopropane would have failed on grounds of inflammability; chloroform would be unacceptable because of damage to vital organs, particularly the liver (17).

It is clear that the screen's correct design was a critical step in the successful discovery of halothane. Had the tests been still more stringent, it is possible that a potentially very successful anaesthetic might have been rejected; conversely, had the screen been less demanding, an anaesthetic might have been tested in clinical trials which might have placed a patient's life in hazard. It is illuminating to analyse the successful screen established by Raventós against the list of desirable parameters suggested by Baines et al. These, we may be reminded, are target definition, width of spectrum, mesh size, quantitative content, degree of abstraction, and sufficiency (18).

(17) J. Raventós and A. Spinks, 'Methods of screening volatile anaesthetics', Manchester University Medical School Gazette, 37, (March, 1958), 58-59.

(18) A. Baines, F.R. Bradbury, C.W. Suckling (op cit. see above note 15), 104-107.

It is at once obvious that Raventós' screen was extremely precise in its definition of the target, and in the geometry of the mesh size and shape. The properties of the compounds that were revealed by the screen were those which Raventós had chosen, and it is extremely unlikely that any other properties would be revealed by the screen. Thus the width of the screen's spectrum was narrow. Since the pattern of end effects desired from an anaesthetic was precisely defined, and totally unlike that required by other possible uses of the compounds, the precision and narrowness of the screen were particularly apposite. In some respects, the screen was quantitative, in that it measured the potency of candidate anaesthetics, and established the therapeutic ratio. Similarly, the subsequent experiments on rabbits, dogs, cats and monkeys provided detailed quantified information on the physiological reaction of these animals to halothane anaesthesia: respiratory arrest, and its relation to the concentration of halothane administered, and the occurrence of hypotension, were reported by Raventós (19). It is interesting to note that the screen itself possessed a very small degree of abstraction. Whereas the synthesis of candidate compounds was guided by Ferguson's theory of narcosis, and was highly abstract, the testing of these compounds was empirical. Lastly, the series of screens established by Raventós was as sufficient as any screen for a compound which was eventually to be used on a human could be. Since the human physiological response might be different from that of an animal, a substantial and irreducible degree of insufficiency existed until clinical trials were initiated. However, the testing of halothane on a variety of mammals ensured that the risk of clinical testing was reduced as far as was practicable. The insufficiency of the screens was still further reduced when the safety of halothane in closed-circuit apparatus was guaranteed by tests showing absence of decomposition over soda lime, and stability tests ensured that the compound would not deteriorate

(19) J. Raventós, 'The action of fluothane - a new volatile anaesthetic', Brit. J. Pharmacol., 11, (1956), 394.

in storage. In so far as sufficiency was attainable, the screens of Raventós and Suckling were complete.

The contrast between Suckling's abstract screen, based on Ferguson's treatment of narcosis, and the much more sufficient screens of Raventós, which did not use Ferguson's treatment, is illuminating. It shows the way in which a theory which need not be accepted generally may be of great help to the synthesiser of compounds, while at a later stage this theory must be set aside, and the tests adopted must consequently become much more specific. Thus, in a situation where the relevant parameters are known, it is possible to test the desired end effects by screens which measure chosen parameters. In this way, British Standard tests abstract the required properties of a structure, and test these special features, confident that the results gained will provide an understanding of the total pattern of end effects. In a situation where there is no clear, nor generally recognised, theory to relate certain properties to the desired pattern of end effects, it is not possible to test in this way. Raventós' screen, to carry conviction, had to be based on precise and non-abstract tests, in a way that would have been inappropriate for those of Suckling.

It is also illuminating to see how Suckling and Raventós, who jointly defined the research target they hoped to achieve, used completely different screens to assess the candidate compounds. Indeed Raventós, at least initially, did not accept Ferguson's treatment of narcosis. Despite this there is no evidence of discord between the two. The trials of Raventós supplemented those of Suckling, so the work suggested by one treatment was tested by another. The information needed at each stage, the language in which this information was to be conveyed, and the criteria used to gain

the information, had all changed; the research target remained constant.

4. Clinical Trials:

After the compound $CF_3CHClBr$ had passed the tests of Suckling and Raventós, it was ready for clinical trials, which would introduce it to the anaesthetic profession. The choice made by ICI of anaesthetist who was invited to conduct these trials was Dr. M. Johnstone, of the Crumpsall Hospital. He was an anaesthetist who commanded the respect of Pharmaceuticals Division's Medical Director, and was geographically close to Blackley, where the pharmacological screening was being done. Thus it was possible for Johnstone to satisfy himself that the trials had been thorough, and to prepare himself for the expected results of clinical trials. In particular, Johnstone observed Raventós perform trials with animals, and was able to anticipate the problems which subsequently occurred with his patients. Thus he was prepared for the hypotension that occurred when halothane was administered, since Raventós had shown this to occur with dogs, and Johnstone had seen the extent of it in the trials he watched.

Clinical trials started on 20th January, 1956, and at first proceeded slowly: by 26th January, some 23 cases had involved halothane anaesthesia; by 3rd February, some 70 cases, and by 21st February some 120 cases. The caution shown by Johnstone in his relatively slow early use of halothane can be seen in other ways: for instance, Johnstone opposed the introduction of 0.01 per cent w/w thymol as a stabiliser until it had been confirmed that this did not cause respiratory irritation. Even though Johnstone was not increasing his use of halothane very much initially, the results of his first trials soon convinced him of the anaesthetic's efficacy. After the first 120 cases, he reported to Suckling in conversation that "he was confident that 'Fluothane' would displace other inhalant anaesthetics and

the barbiturate technique he was using". He had been particularly impressed by absence of a shock syndrome in patients anaesthetised with halothane; the patients recovered quickly from anaesthesia, were warm and pink, and suffered less post-operative discomfort ascribable to the anaesthetic than was normal. Johnstone's great care not to risk his patients' health was accompanied by an active concern to improve their treatment, and his great caution in using halothane was soon allied with a recognition of its qualities.

At the same time as Johnstone's trials, the MRC Sub-committee on non-explosive agents also began tests on halothane. Its chairman, Professor J.H. Burn, had carried out pharmacological tests on halothane at Oxford, and wished the subsequent clinical trials to be made by members of the MRC Sub-committee. It was subsequently agreed that trials should simultaneously be made by Johnstone and members of the sub-committee, as well as taking place in North and Central America.

5. Barriers to diffusion:

At the point where Johnstone reported success in the clinical trials, the candidate anaesthetic had passed the successive screens established within the research and development phase. Yet to prove of use to the medical profession, and to emerge as a successful commercial venture halothane still had to gain acceptance. The screening process has been described as two stages: "first, assessment of technical promise and potential market becomes more realistic and tough minded as the project proceeds along the R. &. D. path from embryonic design concept through development to the decision to introduce it to the market. Second, if it is brought to the market, there is the period of trial use by both producers and potential consumers" (20). Halothane had reached, with the testing by Johnstone

(20) R.R. Nelson, M.J.Peck and K.E.D. Kalachek, Technology, economic growth and public policy, (Washington, 1967), 89.

and the MRC representatives, this second stage.

It is illuminating to analyse the debate which occurred when halothane was put on trial, and the difficulties it encountered in gaining acceptance, in the light of five categories suggested by Rogers (21).

These are, we may be reminded,

(1) The relative advantage of the innovation, and the way in which this is perceived.

(2) The compatibility of the new idea with existing values.

(3) The complexity of the idea, and the need for new adjustments in order to accept it.

(4) The divisibility of the new idea, and the way in which it was possible to experiment with it before complete adoption.

and (5) The ease with which the features of the new idea might be communicated to others.

5.1 Relative advantage:

The discussion which brought halothane to the forefront of anaesthetists' attention was concerned with the risk of explosions, which existed whenever ether or cyclopropane were used. The Ministry of Health had appointed a Working Party on Anaesthetic Explosions in 1953, which in 1956 reported on the danger of explosions. Between mid-1947 and mid-1954, there had been reported some 36 explosions; each year anaesthetics had been used in some 2.75 million cases, of which some 0.86 million cases had involved explosive anaesthetics (22). Yet in this period, only three people had died as a result of anaesthetic explosions; contemporary comment on the report tended to dismiss the danger: "the explosion risk, particularly associated with loss of life, has probably been greatly overemphasised" (23). This conclusion seems

(21) E.M. Rogers, Diffusion of Innovations, (New York, 1962).

(22) Report of Working Party on Anaesthetic Explosions, Ministry of Health, HMSO, (London, 1956).

(23) Editorial, Brit. Med. J., ii (1956), 1225.

particularly justified when one compares the small number of reported cases of anaesthetic explosions, and the small number of fatalities, with an analysis of the first thousand deaths since 1949 under anaesthesia, which showed that inhaled vomit was the single most common cause of death, and also revealed "the frequency with which the intravenous anaesthetics cause death" (24).

Despite what might appear a relatively small need to solve the problems associated with anaesthetic explosions, steps had been taken to overcome these dangers. The MRC in January 1955 had appointed a sub-committee to investigate non-explosive anaesthetics. This committee not only investigated compounds submitted to it by various organisations, but also one of its members, Professor Stacey of Birmingham University, synthesised chemical compounds for testing. It was this committee which, after Johnstone, performed the early clinical trials on halothane. Thus halothane was introduced at a time when the risk associated with anaesthetics' explosiveness was at the front of anaesthetists' minds and was first tested by a government organisation whose main interest was in finding non-explosive anaesthetics.

From contemporary accounts it is possible to see the importance of this. The first comment on a report of clinical trials of halothane started by mentioning the need for non-explosive anaesthetics, and contrasted fluothane and fluoromar (25). The title of a paper by Oxford anaesthetists is another indication of this: "A non-explosive volatile anaesthetic agent", and shows the relative importance of non-explosiveness in attracting attention (26). An early (and unfavourable) review of clinical trials began:

(24)Editorial, Brit. Med. J., ii (1956), 868.

(25)Editorial, Brit. Med. J., ii (1956), 987.

(26) R. Bryce-Smith and H.D. O'Brien, 'Fluothane: a non-explosive volatile anaesthetic agent', Brit. Med. J., ii (1956) 969.

"Our interest in fluothane was first aroused on account of its non-combustibility ... " (27), and the authors were undoubtedly speaking for many when they said this.

Yet the most striking features of halothane as reported by Johnstone were not connected with its non-explosive nature, but rather that "the shock syndrome has been completely absent in all cases", that "smooth and rapidly reversible anaesthesia has been maintained in all cases", and that there had been "a complete absence of nausea, vomiting and retching during recovery in over 90 per cent of the patients" (28). This claim was particularly important to an anaesthetist whose prime concern was to protect the patient undergoing an operation from the severe effects of surgical treatment. There were, however, difficulties in advancing this claim, since there was dispute as to the nature of shock. In comparison with the clearly measurable and irrefutable claim to non-explosiveness, any claim about absence of shock syndrome was much more difficult to test, or to reach agreement on. The advantage which had so impressed Johnstone after his initial clinical trials was difficult to record, and so in the first announcements of halothane's properties was not emphasised.

It is interesting to observe that the publicity leaflets issued by ICI to introduce halothane listed six advantages: suppressed secretion, vasodilation, lability of the blood pressure, maintenance of anaesthesia without bronchial irritation, prompt recovery of consciousness, and, last to be mentioned, non-flammability and non-explosiveness. Only in the German publication was the non-explosiveness stressed. The advantage of non-flammability and non-explosiveness, which attracted much attention to halothane, does not seem to have been the main advantage perceived by anaesthetists who tested the anaesthetic. The ease of control, healthy

(27) H.R.Griffith, 'Fluothane - a modern substitute for chloroform', Anaesth. and Analg., 37 (1958), 316.

(28) M. Johnstone, 'The human cardiovascular response to fluothane anaesthesia', Brit. J. Anaesth., 28, (1956), 392.

condition of the patient, and his pleasant and rapid induction and recovery appealed more. Non-flammability and non-explosiveness did more, however, than merely to interest anaesthetists in an anaesthetic whose pharmacological properties were shown by subsequent testing to be excellent. To the surgeon, a non-explosive volatile anaesthetic enabled him to use techniques which were impossible with other volatile agents. Any opposition of surgeons, who might have hindered halothane's adoption, was overcome by the advantage it offered to them.

5.2 Compatibility with existing values

The position of intravenous and inhalation anaesthetics has already been discussed, and the disfavour with which chloroform was held (particularly by the more recently qualified anaesthetists) has been emphasised. The most important advance in anaesthesia in the decade before halothane was introduced was generally recognised to be the replacement of chloroform by the relaxant drugs, particularly curare, which had been introduced into the United Kingdom by Professor T.C.L. Gray of Liverpool. The introduction of an inhalation anaesthetic which could be used for inducing and maintaining anaesthesia thus represented a sharp break in the development of anaesthetics, in that it reverted to an older tradition and philosophy, much of which had been rejected by anaesthetists.

In particular, fluothane suffered on its introduction by a very explicit comparison with chloroform, probably the most discredited of the existing inhalation anaesthetics. The initial grounds for this comparison were summed up in comment on the report of MRC trials on halothane: "Its (halothane's) potency is similar to that of chloroform and some of the side-effects are such that many clinicians will recognise a surprising similarity between these two drugs" (29). The report itself had specif-

(29) 'Report on halothane', Brit. Med. J., ii (1957), 514.

ically compared halothane and chloroform, in connexion with induction characteristics (30). The comparison was even more explicit elsewhere in an article entitled: 'Fluothane - a modern substitute for chloroform': "The chemical and physical resemblance between chloroform and fluothane is so striking that it seems useful to review the role of chloroform in anaesthesiology and to decide whether fluothane has any advantages over this long-established agent ... The primary cardiac and circulatory effects of fluothane seems to us to be similar to those of chloroform" (31).

Chemical similarities between chloroform and halothane - less obvious, it might be observed, to the chemist than to the anaesthetist - were followed by claims that both possessed similar properties. The initial comparison was thus based on the facts that both were halogenated hydrocarbons, and that both sensitised the heart. This was followed by a more explicit claim, comparing liver damage arising from anaesthesia with chloroform and with halothane. In 1958, reports began to appear of liver damage which were claimed to be connected with the use of halothane. From the early reports, it is clear that the incidence of liver damage after halothane anaesthesia was remarked upon largely because of the analogy between halothane and what one report called "its close relative chloroform" (32). A further review of halothane anaesthesia mentioned: "... anaesthetists who recognise it as a halogenated hydrocarbon like chloroform, carbon tetrachloride and tribromoethanol", and compared liver damage after halothane and chloroform anaesthesia (33). Extensive analysis of the dangers of damage to the liver after halothane anaesthesia subsequently showed that halothane was associated with no greater incidence of liver damage (1 in 4895 cases)

(30) T.H.S. Burns, et.al, Brit. Med.J., ii (1957), 483.
(31) H.R. Griffith et al., 'Fluothane - a modern substitute for chloroform', Anaesth. and Analg., 37 , (1958), 316.

(32) A.L. Deacon, 'Liver damage after halothane', Brit. Med.J., ii (1963), 56.

(33) Editorial, Brit. Med.J., i (1963), 494.

than other anaesthetic agents tested (1 in 4605), and that it was certainly not comparable with chloroform in this respect (34). The anxiety with which reports of liver damage following halothane anaesthesia were first greeted seems explicable more in terms of the comparison with chloroform than as a result of the actual incidence of liver damage.

More generally, the analogy drawn between halothane and chloroform by many anaesthetists undoubtedly hindered halothane's introduction. What was viewed by those responsible for its discovery as a startling new discovery - "a drug totally different from all other anaesthetics" - was compared by anaesthetists with inhalation anaesthetics, particularly chloroform, deemed to be "almost universally recognised as being too poisonous for the production of surgical anaesthesia in human beings". The success of halothane depended to no small extent on breaking the association of ideas which past experience had established in anaesthetists' minds. The need to disassociate halothane from chloroform will reoccur in the discussion on the communicability of the invention.

5.3 The complexity of the idea

High on the list of halothane's special qualities was its high potency: whereas ether had to be administered in over ten per cent concentration, halothane was effective in the range of one to four per cent. This was one of the targets which Suckling and Raventós had defined, and subsequently achieved. It carried with it, however, complexity of administration which had not been fully appreciated. Since only small concentrations of the anaesthetic were required, small absolute changes in the percentage delivered to the patient had more effect than would the same increase in percentage delivered of ether and chloroform. Thus whereas accurate control over the

(34) Editorial, Brit. Med. J., ii (1964), 325.

concentration of anaesthetic delivered had not proved so important with earlier inhalation anaesthetics, with halothane it quickly became apparent that this was required. The anaesthetist using halothane had therefore to adopt or devise new methods of precise control. Although simple Boyles' apparatus was used in the first Manchester trials, it soon became apparent that its calibration and control were not sufficiently precise for halothane: "these extremely wide variations... were of such an order to make this apparatus ... unsatisfactory if not unsafe for the administration of fluothane" (35). To overcome this, a special anaesthetic apparatus was designed, known as the 'Fluotec', which administered (from the Mark 1 machine) concentrations of halothane between 1 and 3 per cent. This proved unsuitable for inducing anaesthesia, and a Mark 2 Fluotec was introduced, which was effective over the range 1 to 10 per cent. Both these machines were fitted with automatic thermostatic control, and delivered accurately to within 0.1 per cent concentration. The introduction of these machines, however, increased the difficulty which an anaesthetist might have in adopting halothane, since it emphasised that a new technique of administration was required.

Not only was it necessary to purchase machines of a new complexity, or to have new calibrations fitted to existing apparatus (both of which were subsequently done freely for halothane users by ICI), but it was also necessary to compel anaesthetists to change their technique. Traditionally, anaesthesia has been defined in terms of the reaction of the anaesthetised patient, and anaesthetists used these reactions as the criteria on which to judge whether to modify their anaesthetic treatment. With halothane, it was in addition necessary to pay detailed attention to the percentage of halothane administered. This principle met with opposition, best summed

(35) H.J. Brennan, 'A vaporizer for fluothane', Brit. J. Anaesth., 29 (1957), 332.

up by an Ottawa anaesthetist who wrote " ... mathematics, however essential preoperatively, has little place in the operating-room... I am afraid of halothane vaporizers delivering percentages as indicated on a gauge..." (36). The alternative, however, was possibly more complex, for the Boyle vaporizer could be affected by many factors, as Johnstone admitted:" ... its control system did not facilitate the teaching of the method and undergraduates found it confusing, particularly as the dose of halothane was influenced by four variables - the positions of the lever and plunger, oxygen flow rate, and the temperature of the halothane liquid" (37). The administration of halothane therefore occasioned the design of new machinery, and caused anaesthetists to adopt a new technique.

The need for precise control over the anaesthetics concentration was not the only cause of this. Halothane, compared with other inhalation anaesthetics, was expensive, and it was obviously wasteful to use it in an open-circuit, particularly as it was known that it did not decompose, and therefore could be used in closed-circuit apparatus. An account of halothane use indicates the sequence of changes which were brought to a hospital whose anaesthetist decided to adopt halothane. In the North Down Group of Hospitals, halothane was first used in July 1957 (following Johnstone's article) with N_2O and O_2, but this proved so wasteful of halothane that a semi-closed circuit was soon adopted. "The only difficulty we encountered was an economic one. Halothane is expensive, and we soon found consumption of it was greater than could be justified" and this required adopting a closed-circuit technique (38). Thus in just over a year, an anaesthetist had changed his technique of administration twice. Some anaesthetists had realised the need from their first receiving halothane: Dr. H.R. Marrett wrote that he realised that the price of £10.5.0d. for 250 ml. made closed-circuit administration necessary from the start, and it was his

(36) H.T. Kay, Lancet, ii (1957), 385.
(37) M. Johnstone, 'Halothane-oxygen: a universal anaesthetic', Brit.J. Anaesth., 33 (1961), 29.

(38) T.A. Brown and M.A. Woods, 'Halothane ("Fluothane") in a country hospital', Brit.J. Anaesth., 30 (1958) 333.

description of its closed-circuit administration which guided the Irish anaesthetists.

A further complexity associated with halothane administration was that wet halothane attacked certain materials used in normal anaesthetic apparatus: aluminium, brass, lead, tin, cork agglomerates, some leathers and rubbers, and plasticised polyvinylchloride were all found to be unsuitable for contact with halothane. Thus anaesthetists who adopted halothane had to cope with washers, gaskets and other components which deteriorated, and the need for special spare parts. Although the 'Fluotec' apparatus, being specially designed for halothane, was not attacked, the problem presented anaesthetists with a further complexity when considering whether to introduce halothane.

5.4 Divisibility and communicability

From the discussion of problems associated with the early administration of halothane, it is clear that it was not a simple matter to experiment with halothane anaesthesia. This was certainly the impression given by early reports on clinical trials, which tended to emphasise the need for highly skilled anaesthetists for safe control of the potent drug. This might have discouraged anaesthetists from experimenting for themselves, as might the insistence in all reports for a precise control of the amount administered. In fact, there is some evidence that these apparent complexities did not deter anaesthetists from experimenting.

Particularly striking among the earlier reports of clinical trials is the part played by anaesthetists in non-teaching hospitals: Marrett at Coventry, who pioneered the closed-circuit apparatus; Pope at Crewe with reports on general surgery among elderly patients; Robertshaw of West Manahcester for thoracic surgery; Raines in North Manchester for

paediatric cases, and Johnstone at Crumpsall Hospital in Manchester (39). Johnstone himself believed that the most important task was to persuade anaesthetists to experiment with halothane, and that, once an anaesthetist had experimented, he would be convinced of halothane's value. That so many anaesthetists in non-teaching hospitals could be persuaded of halothane's worthwhileness shows experiment was possible. Indeed, it suggests that the opposition which was shown to halothane in some important centres of anaesthesiology may have been based more on the connexion with other halogenated hydrocarbons than on the actual results of trials.

To persuade anaesthetists of halothane's claim to at least a trial, it was necessary to communicate to them its special features. Its non-explosive nature was, as has been seen, the most immediate opportunity of doing this, but to be effective halothane's supporters had to overcome certain barriers. It was necessary to show that halothane was considerably better than other techniques which allowed the use of non-explosive agents, so that the considerable cost of halothane could be justified. This was particularly difficult when comparison was made with chloroform: the question of why halothane should be used when chloroform cost four shillings a bottle was asked by those who believed the two agents to be comparable, and could be answered only by refuting the comparison. Even after this comparison had been refuted, the economic barrier to halothane's acceptance persisted: some anaesthetists believed that halothane should be used for inducing anaesthesia, which could then be maintained (at smaller cost) with trichloroethylene; some senior anaesthetists refused to allow halothane into their department at all, on grounds of cost; a 1962 review of halothane admitted its advantages, but made the proviso "... that there are many

(39) M. Johnstone, 'The development of halothane: the clinical trials', Manchester Univ. Med. School Gaz., 37 (1958), 60.

occasions when cheaper agents will serve equally well" (40).

It is interesting to note that some anaesthetists immediately rejected the relevance of the high cost of halothane, claiming that the total cost of an operation was such that the cost of the anaesthetic agent involved was too small to influence their choice. This had been the belief of Raventós and Suckling when they drew up their list of targets for anaesthetic research, for they specifically rejected any cost constraint, arguing that the high total cost of an operation, and the importance of any advance in anaesthesia, would justify a new anaesthetic agent, irrespective of its cost.

Subsequent analysis of the cost of using halothane shows that the actual cost is quite small. Using an open-circuit system with halothane for a hundred operations, the anaesthetist reporting his analysis calculated that the cost of all agents used (including relaxants, other anaesthetic agents and soda lime) was $4.14 per operation, and only $2.35 per hour of anaesthetic treatment (41). This was obviously small in comparison with the large labour costs for surgeon, anaesthetist and nurses. However, within this total expenditure on anaesthetic agents, halothane costs comprised over 80 per cent, and represented a large and identifiable item. The cost of halothane may therefore have appeared daunting to those who did not appreciate the benefits its use brought. Certainly, to those who compared chloroform and halothane its high cost represented a considerable disincentive.

6. Discussion

Historical analysis of halothane's development illuminates the inno-

(40) 'Halothane', Brit. J. Anaesth., 34 (1962) 1.

(41) S.C. Cullen, 'Cost of halothane anaesthesia in low flow systems', Anaesthesiology, 21 (1960) 324.

vative process. The innovation was extended in time, from halothane's first synthesis in 1952 to its adoption in the years following clinical trials in 1956. It is even possible, without much distortion, to trace halothane's invention back to Robbins' work in 1946, and to Ferguson's paper in 1939, and to extend its adoption to the present time. Analysis of the events within the shortened timespan displays a number of barriers which impeded the innovation, and the absence of some barriers which might reasonably have been expected to exist.

6.1 Economic barriers

Particularly noticeable is the absence of economic barriers within ICI. Largely this can be ascribed to the small amount at risk in the early stages of the project's life and to the fact that when large investments had to be made the risk had substantially diminished. The early sanctions required for authorising work on candidate anaesthetic compounds comprised little more than the financing of Suckling's time, with appropriate supporting staff. Sizeable amounts of halothane were not prepared until tests on mice and rabbits had been successful, and testing over soda-lime had shown no decomposition. The first large order, for 55 lbs., at the end of 1955, was sanctioned after impurities had been controlled, and halothane's stability in storage and non-flammability had been proved. It was not until after the success of the first clinical trials that expenditure sanctioned in General Chemicals Division increased sharply, as first 150 lbs., and then 5000 lbs., were ordered.

If the amount sanctioned in 1950 is taken as an index of 100, in each year between 1951 and 1954 sanctions were equivalent to 250; in 1955 sanctions were 650, and in 1956 200,000! Actual expenditure followed a similar, if less dramatic pattern: with 1951 expenditure taken as an

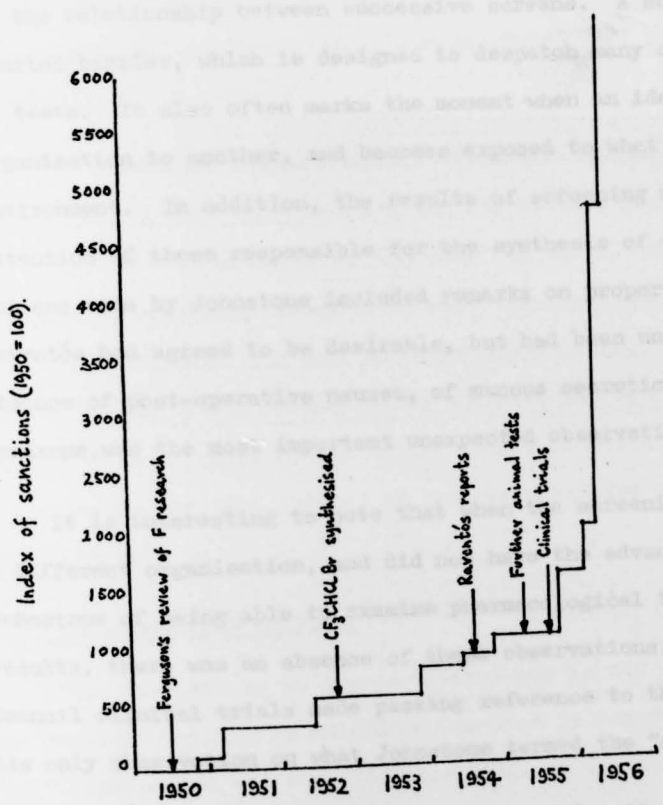
index of 100, successive years were:

1952 - 105
1953 - 164
1954 - 47
1955 - 395
1956 - 5450

In addition, it is significant that in the years between 1951 and 1955, when General Chemicals Division was supporting halothane research, it never comprised more than 0.7 per cent of the division's research budget, and in 1954 was as low as 0.2 per cent. When, in 1956, the expenditure rose so sharply, the risk incurred by General Chemicals was reduced by its selling halothane to Pharmaceuticals. Thus when the expenditure at risk increased it was born by the part of ICI which was throughout more enthusiastically committed to the project.

This may be seen in Figure 2.1, which shows the increase in expenditure sanctioned at Widnes and relates this to the information which had come available about candidate anaesthetics. From this can be seen that there was no need to commit many resources until much of the uncertainty associated with the candidate compound had been removed: sanctioned expenditure did not markedly increase until the end of 1955, on the eve of clinical trials; no decision on capital was necessary until May 1956, when successful clinical trials had been conducted for four months. Thus the initial interest taken by Ferguson in anaesthesia, supported by the enthusiasm of those working on the project, was sufficient to maintain the research programme until the case for further resources was apparent. An important factor allowing this to occur was the availability of plant which could be used for halothane synthesis. This, and the ability to make halothane in glass equipment specially but cheaply erected, ensured that there was no economic barrier to halothane's development within ICI.

Figure 2.1: Sanctions for Widnes research on anaesthetics.



6.2 Screening

The profile of expenditure shown in Figure 2.1 emphasises the importance of designed screens which reduce the number of candidate compounds or ideas as soon as is practicable. The characteristics of screens, and the interfaces between those responsible for synthesis and those undertaking the testing of synthesised compounds, are critical factors in determining the survival of a project, and (equally important) the early death of those projects which deserve to perish. The characteristics and pathology of screens have already been discussed (42), but as important is the relationship between successive screens. A screen is a deliberately erected barrier, which is designed to despatch many of the candidates which it tests. It also often marks the moment when an idea moves from one organisation to another, and becomes exposed to what may be a hostile environment. In addition, the results of screening may often redirect the attention of those responsible for the synthesis of compounds: the observations made by Johnstone included remarks on properties which Suckling and Raventós had agreed to be desirable, but had been unable to predict. Absence of post-operative nausea, of mucous secretions and of the shock syndrome was the most important unexpected observation.

It is interesting to note that when the screening party belonged to a different organisation, and did not have the advantages possessed by Johnstone of being able to examine pharmacological trials with detailed results, there was an absence of these observations. The Medical Research Council clinical trials made passing reference to the absence of secretion; its only observation on what Johnstone termed the "absence of shock

(42) A. Baines et al., (see above, note 15), 107.

syndrome" was to remark on the skin's remaining "pink, warm and dry"; it specifically observed that vomiting "was ...not as rare as preliminary reports have suggested", though Johnstone pointed out in reply that the "report does not make adequately clear whether the figures relate to fluothane anaesthesia or to opiate-fluothane anaesthesia" (43). Certainly the conclusions reached by those responsible for each screen were very different. Whereas Johnstone commented on four favourable features which distinguished halothane, the MRC trials stressed the incompleteness of their experiments, and the need for exercising care. The combination of deliberately erected barrier with the change of organisation between synthesiser and screener seems to have overwhelmed the possible advantages possessed by the compound.

The duties of a screen are to illuminate disadvantages as well as advantages, and both Johnstone's and the Medical Research Council's screens did this; the sensitivity of the heart to adrenaline and the hypotension produced by halothane anaesthesia were remarked upon, and both screens emphasised the need for more accurate vapourisers. The difference in emphasis between two screens, both administered by men of the highest competence, does not seem to lie in the design of screen, but rather in the organisation gap that existed in one case, and the close collaboration in the other.

6.3 Organisational barriers

This emphasis on an organisational gap is all the more striking when the earliest barrier to halothane research is considered. Both Robbins' early examination and the 1948 approaches to General Chemicals Division it inspired were defeated by the refusal of those with the command of the relevant science and technology to commit them to a recognised need. This

(43) T.H. Burns et al., (op cit., see above note 30), 483, and M. Johnstone, 'Fluothane', Brit. Med. J., ii (1957), 641.

organisational barrier was breached more easily by the decision to acquire knowledge about the market; even without consulting Raventós, Suckling was able to examine available literature to confirm the suitability of the target Ferguson had suggested.

The barrier between those who recognised the need and those who were in a position to satisfy it certainly hindered halothane's initial research, but it is worth observing that the barrier was lowered in that both sets of people belonged to the same company. Criticisms of large scale industrial research are well known (44), but the synergistic advantages of the large organisation are less often recognised. It is interesting that the only other organisation in the U.K. able to combine knowledge of fluorine chemistry with facilities for pharmacological testing was established by the Medical Research Council, using the resources of Birmingham University and London teaching hospitals. Even this combination lacked the deep knowledge of fluorine technology possessed within General Chemicals Division.

In examining the organisational barriers to halothane's development, it is interesting to see how few were the organisations involved, and how few the men who worked on research. In General Chemicals Division of ICI the prime responsibility fell to Suckling; in Pharmaceuticals Division the testing of the compounds synthesised by Suckling was performed by Raventós and Spinks; at Manchester clinical trials were made by Johnstone. The enthusiasm of all these men provided much of the impetus to maintain the research programme, while their mutual respect prevented organisational differences from hindering their progress. The division of skills between divisions necessitated there being three separate organisations involved. It is interesting to note that when other problems arose, they were dealt with by the same divisions and even by the same men. For example, when anaesthetists using halothane discovered corrosion problems, General

(44) J. Jewkes, D. Sawers and R. Stillerman, The Sources of Invention (London, 1960), 167-178.

Chemicals Division started a small research programme to discover suitable materials of construction, and Suckling himself performed much of the technical service work for anaesthetists. Suckling, Raventós, Spinks and Johnstone published papers which showed the thoroughness and high scientific quality of the work on synthesis and screening. The continued involvement of these men ensured that those organisational barriers which existed were overcome.

Organisational barriers are often treated as the result of irrational responses to new ideas. These barriers to innovation assume greater justification if it is recognised that different parts of the same organisation may have different objectives. The Medicinals Section of Dyestuffs Division, for example, was at least in part concerned with establishing itself amid the ranks of those who were respected by the medical and pharmaceutical professions, and in ensuring its transition into a separate ICI Division. The absence of detailed analysis of the expected return from anaesthetic research seems to indicate that high profitability was not a necessary condition for undertaking a project. In General Chemicals Division, however, there was no such urge to gain recognition, and different motives were required to justify a research project. Similarly, conflict of interests was to be expected to some extent between those required to experiment with a new anaesthetic, and those supplying it.

6.4 Perceptual barriers

Less obvious are the different paradigms adopted by those in different parts of the organisation. The initial stimulus for halothane research within General Chemicals Division came from Ferguson's treatment of narcosis, and this theory guided the initial selection of candidate compounds - with conspicuous success. Although Suckling based his synthesis on a belief in the thermodynamic concentration of a compound providing an index of its

likely success as an anaesthetic, this belief was not initially shared by Raventós, who, in company with most anaesthetists, was sceptical whether the complex patterns of anaesthesia might be explained by use of one physical index. While this difference in paradigm had no deleterious effects on the relationship between Suckling and Raventós, that which occurred between those who had been concerned with the internal synthesis and screening of the anaesthetic and other anaesthetists had longer reaching and more harmful results. Anaesthetists who tried to reduce the complex pattern of end effects produced by halothane to a simpler form used chloroform as their analogy, and thus associated the new drug with one which was both outdated and commanded little respect. The anaesthetic viewed by Suckling, Raventós and Johnstone as new and exciting was seen by many as an expensive replacement for a cheap drug that was already rejected.

Kuhn has analysed the success of ideas in displacing other scientific concepts, and has agreed that the success of an idea depends often on its re-adjusting the criteria by which it is judged (45). A similar process occurred in halothane's development. When viewed as a completely new anaesthetic, for which new techniques and instruments must be devised, it proved successful. When it was treated as a chloroform analogue, entirely different results were obtained. The clearest statement of the second belief was contained in the result of a 'blind study' investigation of halothane and chloroform, when the anaesthetist was not aware of whether he was using halothane or chloroform. This concluded: " ... it was found it was not possible to identify the agent solely by means of its clinical effect. The changes in blood pressure, in pulse rate, respiration and complications during anaesthesia were similar to the two groups of patients. We believe halothane bears a strong clinical resemblence to chloroform (46).

(45) T.S.Kuhn, The Structure of Scientific Revolutions, (Chicago, 1962), 6.

(46) B.J. Bamforth, et al., 'A clinical comparison of chloroform and halothane by a blind study technique', Anaesthesthiology, 21 (1960), 273

The paradigm - the belief that halothane should be treated like chloroform - was self-justifying, in that when halothane was treated like chloroform, it was found to give comparable results. The paradigm was not only an idea, but carried with it a series of physical tests, which translated the idea into practicalities. The success of halothane depended on escaping from these tests, by escaping from the comparison with chloroform.

6.5 Technological barriers

The barrier to Robbins' original research had not only been organisational. Toland's account shows that an important obstacle to Robbins' progress was the doubts that existed on the chemical purity of samples. Advances in analytic techniques, already mentioned, overcame this obstacle. At the same time, Ferguson's treatment of narcosis simplified the choice of suitable compounds. The subsequent refining of Ferguson's treatment by Suckling, who accounts for much of the variation left unexplained by incorporating the effect of activity coefficient, further reduced the technological uncertainty. The technological barrier to halothane had become small enough for a determined attack to succeed.

Chapter 3

THE DISCOVERY AND DEVELOPMENT OF NEW HERBICIDES

1. Introduction:

The discovery and development of the bipyridyl herbicides diquat ('Reglone') and paraquat ('Gramoxone') further illustrate the barriers that exist between a scientific discovery and a commercially successful product. Both these herbicides possess a mode of action which differs from that of other herbicides, as well as a pattern of end effects which is quite unlike that possessed by recently developed herbicides . The recognition of the potential usefulness of these properties, and the subsequent persuasion of others of their worth, comprised problems just as complex as any posed by chemical or manufacturing constraints.

To understand the problems with which those developing bipyridyl herbicides had to contend it is necessary to understand some of the characteristics of weed control. Destruction of unwanted vegetation has always been an important task for cultivators, and mechanical, biological and- most recently - chemical methods have been used to achieve this. In all methods, the objective is to remove, or to prevent the growth of, unwanted vegetation, preferrably without harming the intended crop. Mechanical means typically include ploughing, where the destruction of weeds is achieved while the crop is not yet sown, and inter-row weeding or hoeing, where the crop is left by physically discriminating between it and the weed. Biological control may be accomplished by encouraging animals or insects to flourish which selectively devour weeds, leaving the crop. Chemical control is often more complex, and may depend on a combination of chemicals, each of which contributes its particular effect to the aggregate pattern. Chemical destruction of the unwanted growth without damage to the preferred crop may occur by various means:

it may be biochemically induced, in that the herbicide affects one plant but not another; it may be achieved by timing the application of the herbicide to occur when one plant has developed and is vulnerable, while another has not emerged from the ground, and is thus protected by ensuring that the chemical contacts only those plants whose destruction is desired.

1.1 Development of new herbicides:

In general, it may be said that the evolution of chemical weed control has been marked by the development of compounds whose end effects are distinctive and selective. Selectivity is used to describe the ability to apply a chemical to a mixture of vegetation in such a way that certain unwanted plants are killed without harming the preferred crop. It has long been known that a form of chemical control could be achieved by spreading salt or industrial waste on ground to prevent all growth. The development of modern herbicides, however, may be traced back to the discovery by Bonnet in 1869 that Bourdeaux mixture applied to vines to cure downy mildew also blackened the leaves of yellow Charlock growing in the vineyard. Subsequent herbicides, however, tended not to display a comparable selective activity. Thus the use of sodium arsenite, first reported by Bolley in 1901, was mainly found in maintaining rights of way and firebreaks, and on other applications where a total kill of vegetation was required. Sodium chlorate was used similarly. Sulphuric acid was also used widely, with a degree of selectivity based on the different wetability of different leaf structures. It was not until 1932 that the first organic chemical, 2-methyl - 4, 6-dinitrophenol (DNOC), was introduced (1). The relatively minor contribution of chemical compounds to weed control may be judged from the fact that a 1946 edition of a standard text book of some size on crop protection devoted

(1) R.C.Brian, 'The classification of herbicides and types of toxicity' in L.J. Audus (ed.), The Physiology and Biochemistry of Herbicides (London 1964), 1,11,432.

only five pages to chemical weed control, two of these pages being devoted to uses of sulphuric acid (2).

1.2 Discovery of the hormone weedkillers:

The importance of chemical weed control grew rapidly following the discovery of the hormone weedkillers, and their release in 1946-47. The hormone weedkillers, 2, 4-D (2,4 - dichlorophenoxy - acetic acid) and MCPA (2 - methyl - 4 - chlorophenoxyacetic acid) possessed an impressive range of properties, and could be used in a variety of ways. As contact weedkillers applied to plant foliage they acted on perennial weeds to kill them; applied to the soil, either before or after a crop had emerged from the ground, they were absorbed by weed roots. They were selective against many broad-leafed weeds in cereals, and potent enough to be used in low volume. This meant both that cheap application methods were possible, and that a small amount of what was anyway a relatively cheap chemical could be used. Costs for toxicant of about $1.00 per acre treated were possible. The mode of action of the hormone weedkillers is manifested through an altering of growth rates, and herbicidal activity of these hormones is often related to stimulation or inhibition of growth. Although the actual toxicity of hormone weedkillers is believed to involve further mechanisms, their testing is normally performed by observing how they influence and change plant growth. To facilitate experiments, this is normally done on shoots of young plants, whose response to a hormone weedkiller can be rapidly seen. The control of growth rates gives them the name of "hormone" weedkillers. Analogy is often made with the natural plant substances - auxins - which control plant growth and the hormone weedkillers' action is called "auxin"-like (3).

(2) C.J. Lewis, 'Contribution of herbicides to food production in the next three decades', Chemy. Ind. (29 June 1968), 860.

(3) A.S.Crafts, "The Chemistry and Mode of Action of Herbicides" in R.L. Metcalf (ed.), Advances in Pest Control Research, Vol.1 (New York, 1957), 40, 48.

The discovery of MCPA was not only important in the development of chemicals possessing special and effects, but also marked the first major discovery of a new herbicide by Plant Protection Ltd., at Jealotts Hill. Plant Protection Ltd., had been established as the sales outlet for ICI's products to the horticultural industry, with Jealotts Hill as its testing station where compounds submitted by other parts of ICI might be tested for biological activity. Studies of the effect of growth substances on plants was started there in 1936, and in 1940 it was discovered that ∝-naphthylacetic acid applied at a rate of 25 lb/acre to oats infested with yellow charlock killed the weed while leaving the oats only slightly harmed. Further experiments led to the discovery in 1941 of 4-chloro - 2 - methylphenoxyacetic acid which was over fifty times as active as ∝-naphthylacetic acid. Its activity was so great that weeds could be eradicated from cereal crops without any harm to the cereal, and this could be achieved whether the chemical was absorbed through the root or the leaf of the plants (4). The discovery and development of MCPA, as the compound came to be known, owed much to the systematic way a promising compound was followed up. After the recognition of the activity of ∝-naphthylacetic acid, another thirty-two compounds (including both MCPA and 2, 4-D) were synthesized and tested. The combination of synthetic chemists preparing analogues of ∝-naphthylacetic acid and other related compounds with the testing facilities at Jealotts Hill comprised a powerful weapon with which to attack the target of a selective herbicide with high activity. The strength of the combined knowledge of synthetic chemistry and biological activity contained within ICI was to prove still more important in the subsequent development of the dipyridyl herbicides.

(4) R.E. Slade, W.G. Templeman and W.A. Sexton, 'Plant Growth Substances as Selective Weedkillers', Nature, No. 3939 (London 1945), 497-498.

MCPA and 2, 4-D ushered in a new era in chemical weed control, with rapid and considerable increases in the amount of land treated in this way. The area treated with herbicides in the United States, for instance, grew from 33.5 million acres in 1952 to 85 million acres in 1965 (5). This was not entirely due to hormone weedkillers however. Important herbicides discovered since the hormone weedkillers included triazine weedkillers, which possessed markedly different effects on different plant species when applied at low rates, combined with long term non-selective activity when applied at higher rates; and the substituted ureas, which also combine selective activity when applied at low rates, with long term soil sterilisation effect, including activity against annual and perennial grasses, when applied at higher rates. In addition to chemicals of quite general use, there had also been developed a number of weedkillers of specific use for particular applications: for example, to clear celery beds, N-(3, 4-dichlorophenyl) - 2 - methyl pentanamide was known to be effective, and for clearing strawberry beds, N, N - dimethyl -α,α-diphenylacetamide was preferred. Depending on the time of year, and the weed, the farmer could choose any one of four chemicals for his strawberry bed (6). Yet further variety was possible through the mixing of chemicals where the precise advantages of one chemical might be combined with those of another, to widen the range of plants affected or the timescale during which plants were affected, or to promote synergistic effects.

2. Research targets within Plant Protection Ltd:

Within Plant Protection Ltd., the relative importance attached to the hormone weedkillers may be assessed in two ways. First, estimates of future demand for crop protection chemicals displayed the importance attached to

(5) C.J. Lewis (op. cit., see above note 2), 860.

(6) A.S. Crafts and W.W. Robbins, Weed Control (New York 1962), 546-547.

MCPA and 2, 4 - D. A major investigation of world demand for crop protection chemicals estimated that a replacement, or improved form, of hormone weedkiller comprised 53 per cent of the market for herbicides, and 14 per cent of the total market for all crop protection chemicals. This market was estimated to be six times as great as the next largest market for a herbicide (7). This estimate shows the importance attached to discovering a chemical with the properties of hormone weedkillers - that is, a herbicide possessing selective activity, which could be applied either to foliage or to the soil. A more direct indication of the importance given to achieving these properties may be found in the actual screening tests used to assess the activity of candidate compounds. In 1950, initial greenhouse screening took the form of agar tests designed to measure a compound's activity on wheat, mustard, marigold and linseed. If this test showed activity, the screen was then broadened by including further plants. When these tests were reorganised in the last quarter of 1950, still further emphasis was placed on screens designed to test compounds whose activity was comparable with hormone weedkillers: cell elongation and cell division tests were designed in this way, and root tests on five classes of plants ensured that selectivity, if it existed, was recognised. Further changes that were made in the screening procedure resulted in the tests including in 1953 the oat coleoptile cell elongation test, box tests on various plants, both pre- and post- emergence, and field tests on compounds deemed suitable. These screens were designed to show any herbicidal activity, but in particular to measure the auxin-like reaction found with 2, 4 - D and MCPA, to assess the likely selectivity of the compound under test, and to ascertain whether it possessed pre-emergent activity.

(7) G. Edmund Jones. PPL Report No. MS/14 (September 1958).

The importance of selectivity may be seen not only in Plant Protection's market forecasts and testing, but also in contemporary accounts of developments in herbicides. Writing in 1957 of recently developed herbicides, Crafts claimed that "they represent greater and greater complexity of molecular configuration. This may evidence two possible trends: (i) a search for, and development of greater selectivity, or (ii) a tendency to put out compounds of unique chemical composition that can be patented. If selectivity is the objective of the tremendous efforts being expended by industry, it is commendable because we need herbicides to fit into many niches not filled at the present time. Less expensive and less harmful pre-emergence chemicals are needed in corn and sorghum crops. More selective materials are required for use in soybeans, field beans and snap beans. A general pre-emergence spray for control of both broad-leaved weeds and grasses is needed for cotton. And highly selective materials are desirable in sugar beets, tomatoes, and a host of vegetable crops". (8).

3. The recognition of a new herbicide:

It was in this framework of seeking after selective herbicidal properties and in an organisation whose professed objectives and actual testing facilities stressed the importance of chemicals possessing these properties, that the bipyridyl herbicides were discovered. The observation which led to research activity was made at Jealotts Hill in 1947, when, in the course of trials establishing the effectiveness of a compound formulated with a wetter, it was noticed that the wetter itself possessed herbicidal activity. The knowledge that many surface active agents

(8) A. S. Crafts (op. cit., see above note 3), 74.

possessed phytotoxicity when administered in sufficiently large doses was reinforced by the observation that one such compound, dodecyltrimethyl ammonium bromide, was active in the field. Examination of surfactants followed, the belief being that the detergent scoured the wax from the plant leaves, producing a characteristic scorch. This led to the conclusion that "quaternary ammonium salts having one long and three short carbon chains attached to the nitrogen atom were more active than other types, e.g. long chain sulphonic acids" (9). Typical application rates were some 15 lb/acre in greenhouse tests, estimated to be equivalent to about 60 lb/acre in the field. The 1947 observation of dodecyltrimethyl ammonium bromide was repeated when the compound was resubmitted in February 1954, and efforts were made to find other suitable quaternary ammonium salts. This involved not only the synthesis of compounds which held promise, but also the testing of existing compounds which had been made for some other purpose, and which seemed likely to possess herbicidal properties. In the third quarter of 1954, for instance, some 160 compounds were screened at Jealotts Hill, including as well as compounds specially synthesized such by-product materials as unwanted process oil from the methyl methacrylate skimming tank (which did not prove to be useful). An idea of the interest in different compounds may be gained from examining the six categories of compounds undergoing screening at Jealotts Hill in 1954. These comprised compounds specially synthesized at Blackley, by the Dyestuffs Division of ICI, aspirin derivatives, benzy thiocyanates, benzoic acids, derivatives of CMU (3 - (p - chlorophenyl) - 1, 1-dimethylurea), and quaternary ammonium salts.

In 1954, the impact began to be felt of the 1953 decision to modify the testing procedures by replacing agar tests with box tests, in which

(9) W.R. Boon, 'Diquat Introduction to symposium, 27 May 1960', unpublished.

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(9) W.R. Boon, 'Diquat Introduction to symposium, 27 May 1960', unpublished.

small steel boxes with established plants and seeds were sprayed. In particular the number of compounds screened at Jealotts Hill increased markedly. Whereas in 1951 the average number of compounds tested was between 40 and 50 each quarter, this rose rapidly in 1953, and by 1954 the number tested each quarter was close to 170 (10). The availability of resources for carrying out screening placed pressure on those responsible for providing compounds for test. The synthetic chemists were occupied in a planned programme of synthesizing aspirin and CMU derivatives, and less-planned programmes were enlarged as was possible. The effect on the programme investigating quaternary ammonium salts can be clearly recognised. Not only were compounds related to the original lead of dodecyltrimethyl ammonium bromide synthesized, but any related compounds already in existence were used as candidates for screening. In late spring and summer of 1954, the specimen collection of chemicals of Dyestuffs Division in Blackley was examined for quaternary ammonium salts, and suitable compounds were set aside for testing at Jealotts Hill.

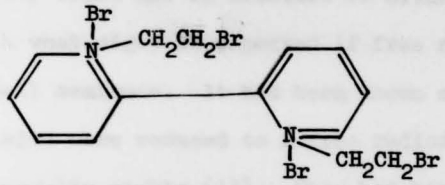
Thus whereas in the last quarter of 1954 25 quaternary ammonium salts were screened at Jealotts Hill, of which 11 proved of interest, in the first quarter of 1955 some 50 quaternary ammonium salts were tested. The report on the biological testing of these mentioned "a dipyridyl and a number of dodecyl quaternary ammonium hydroxides were of particular interest" (11). The dipyridyl had been selected from the Dyestuffs Specimen collection in October 1954, and was tested at Jealotts Hill in February 1955, as specimen K.8483. It was recognised as being very active when applied at 10 lb/acre, and steps were immediately taken to investigate it further,

(10) In the second and third quarters of 1950, the number of compounds tested was 38 and 21 respectively; in the same quarters of 1951 it became 36 and 54 respectively; by the fourth quarter of 1953 it had reached 105. In 1954, the number of compounds tested each quarter again rose, comprising 138, 180, 160 and 195 for the four quarters (Jealotts Hill Reports, 1950-1954).

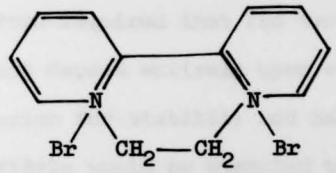
(11) Jealotts Hill Report for quarter ending 31 March, 1955.

both from the approach of the synthetic chemist, and from that of the biologist.

First, the compound was re-analysed. Originally, it had been synthesized in December 1950 by R.J. Fielden of Dyestuffs Division (in the course of work not intentionally associated with synthesizing biologically active compounds), who had assigned it the structural formula



This was reinvestigated, and found to be in error. Analysis showed the constitution to be N, N′ -ethylene - 2, 2′-dipryidiniumdibromide



The next steps taken by the Blackley synthetic chemists were to modify Fielden's method of preparing the compound (originally, in two preparations each lasting 8 hours, Fielden had synthesized just over 18 grams) so as to prepare 150 grams for testing on further screens, and to prepare or collect other quaternary salts closely related to K.8483. In March, April and May the Blackley chemists provided nine close analogues to K.8483, including the compound K.8606 that was to be the precursor of the 4, 4′ - dipyridyl, paraquat (12). These enabled further tests on biological activity to be made on these compounds, and a theory to be established relating activity to chemical structure.

(12) R. J. Fielden, Laboratory Notebook 5431, 78 and letter from R.L. Jones to W.G. Templeman, 24 June 1955.

3.1 Establishment of activity-structure relationship:

To relate the activity of the compounds to their structural formulae, it was necessary both to study the physical chemistry of dipyridyls and to observe the nature of their herbicidal activity. It was observed quite soon that those bipyridylium salts that possessed activity were distinguished by extremely rapidly affecting the plant, in a way that suggested that the activity could not be ascribed to metabolic disturbance, but was compatible with what might be expected if free radicals were produced and ruptured the cell membrane. It had been known since 1933 that 4, 4' - bipyridylium salts were reduced to a free radical, and that this free radical was unusually stable (13). This had been attributed to resonance in the radical, and it had been observed that this stability depended essentially on the delocalisation of the odd electron over the whole molecule, which in turn required that the two rings should be co-planar. This stability does not depend entirely upon co-planarity: were co-planarity a sufficient criterion for stability and hence for herbicidal activity, 2, 3' - and 3, 3' -dipyridyls would be expected to be active. In fact, they were not, and it was necessary to assume that a second condition for free radical stability was that the two nitrogen atoms should occupy suitable positions, these excluding any molecules with nitrogen atoms in the meta - position. By analogy with 4, 4' - bipyridyl, it was possible to guess that 2, 2' - would behave as a free radical producer, and also that 2, 4' would be less active than either 2, 2' or 4, 4', because of steric hinderance preventing co-planarity (14). This fitted the observed facts that when the nitrogen atoms in the ortho - positions had unlinked substituent groups, herbicidal activity disappeared, and helped explain why herbicidal activity lessened as the chain length between quaternary ammonium groups increased, for while

(13) L. Michaelis and E.S. Hill, 'The Viologen Indicators', The Journal of General Physiology, 16 (1933), 859-873.

(14) R.F. Homer, G.C. Mees, and T.E. Tomlinson, 'Mode of action of dipyridyl quaternary salts as herbicides', J. of Scientific Food Agriculture, 11 (June 1960), 309-315.

two carbon atoms could be accommodated without loss of the structure's planarity, further increase in chain length caused twisting.

This posited explanation of the bipyridyl activity concentrated attention on the general ability of a compound to be reduced, and the relationship between free radical formation and phytotoxicity. Generally, it was found that bipyridylium quaternary salts that were not reducible, such as the 2, 3' and 3, 3' isomers, were not biologically active. This correlation was examined further, by relating biological activity with the ease of reduction measured by ascertaining the redox potential. Work to assess this theory was reported in progress in March 1957, and in September the redox properties of 42 compounds had been measured, including those of 27 derivatives of 4, 4' - dipyridyl and 8 of 2, 2' - dipyridyl. A relationship was discovered between the ease of reduction and the herbicidal activity: diquat, as K.8483 became known, had a redox potential of -349 mV, and was highly and rapidly active; paraquat had a redox potential of -446 mV, and was highly active but slower acting; but salts with redox potential less (i.e. more negative) than -500 mV were not all rapid in action, and might possess no activity at all. Further calculations were made, to test the belief that free radicals were responsible for the compounds' phototoxicity. A reduction potential of -380 mV was assumed for a plant, and the free radical concentration in the plant was calculated for a chemical dose that just failed to kill it. Whereas the chemical dose differed between compounds by a factor of several hundred, the free radical concentration differed by only a factor of three. By this work, which was reported in 1960, a theory was established which enabled the action of dipyridyl herbicides to be predicted more accurately (15).

(15) R.F. Homer et al. (op. cit., see above note 14) and R.C. Brian, 'Electrons and the mode of action of certain herbicides', Chemy. Ind. (November 27, 1965), 1959.

Thus the first screen which had operated in the minds of chemists responsible for providing compounds for biological testing had been successively refined, first from the general class of quaternary ammonium salts to dipyridyls in particular, and then within this restricted category to those compounds which possessed particular measurable physical properties. Through this refinement and abstraction of the conceptual screen, chemists were able to concentrate on the compounds that had been chosen - diquat and paraquat - with some confidence that they were not neglecting other, possibly more attractive, compounds.

In July, 1958, Homer was able to report that "no compound more herbicidally active than K.8483 has been found, and from a consideration of the steric requirements necessary to give a molecule reducible in one-electron steps via a free radical, it would appear that little further exploration in this field is possible" (16).

It is interesting to contrast the development of this abstract screen with the development of that used by Suckling in the synthesis of the anaesthetic halothane, where the theory was well formulated before any compound was synthesized. In the development of the theory behind the bipyridyl herbicides, the measurement of free radical concentration has a striking similarity with that of thermodynamic concentration advanced by Ferguson for anaesthetics. Whereas halothane was a compound synthesized and tested early in the research programme, diquat was a compound submitted much later to screening for biological activity. In both cases, the theory behind the particular pattern of end effects desired was refined: for the anaesthetic, the coefficient of activity of compounds was introduced;

(16) ARA Report 1172 (July 1958).

for the herbicides, the original theory of detergent-like scouring of wax from the leaves was much changed to recognise the importance of free radical concentration. In both cases, the theoretical screen provided a means of using known physical chemical measuring techniques to approximate to end effects which could only be measured with greater complexity and at higher cost. By developing an acceptable and trustworthy abstracted screen, the synthetic chemists had established for themselves an impressive contact with the body of scientific knowledge that had previously been established.

In this context, it is important that both screens were necessary but not sufficient: an anaesthetic compound might have about the correct thermodynamic concentration yet prove unacceptable because it caused unwanted side effects; and a compound with the correct planarity of structure and with approximately the desired redox potential might possess no herbicidal properties. In both these cases, the explanation is believed to be found in physiological factors in the human body or the plant cells, and reflects upon the partial nature of the theories describing narcosis or phytotoxicity.

3.2 Analysis:

Parallel with the synthetic work to examine candidate compounds and to evolve a theory relating biological activity with chemical properties, analytic methods for examining bipyridyl herbicide residues were being devised and refined. By the end of the first quarter of 1957, a method had been evolved, involving hydrolysis of starch followed by absorption of diquat on cation-exchange resin. This produced results accurate to 1 p.p.m in potatoes, and 5 p.p.m. in wheat. By March 1959, these results

had been improved to be accurate within 0.01 p.p.m., and in February 1960 it was possible to determine diquat in potatoes with a sensitivity of 0.005 p.p.m. These analytic techniques showed extremely low residue levels were obtained: in potatoes sprayed with diquat at 1 lb/acre and at 4 lb/acre, residues were between 0.025 p.p.m. and 0.525 p.p.m. There was no difference between the peel and body of the potato, and boiling allowed them to lose about a third of the diquat residue (17). This concentration on residues in potatoes indicates the most clearly defined target envisaged for diquat in the period 1957-1960.

3.3 Field Trials:

From biological screening and subsequent field trials in 1955 and 1956, various applications for diquat had been examined. Initial trials were reported in June 1956, showing satisfactory results against potato haulm, various results on cereals with some variation in the reaction of different species, the eradication of weeds like yellow and white charlock, but destruction of the foliage only of perennial weeds. Trials also showed that contact with the soil rendered diquat inactive (18). Contemporary belief in diquat's biological activity may be further assessed by examining the claims made in the patent covering manufacture and use, whose complete specification was filed on June 1, 1956. This states that complete kill of wheat, mustard, marigold, sugar beet, red clover and cleavers had been achieved when one part of the salt was mixed with 100 parts water and applied at 20 gallons/acre. An 0.0625 per cent solution applied at the same rate killed broad leaved weeds with negligible damage to wheat, oats and barley; at 0.5 per cent, the solution was effective against potato haulm and provided complete control of annual weeds, but killed only the shoots of perennial weeds (19). In 1957, the results of two years' trials with

(17) PPL Report PP/E/37 (February 1960).

(18) Jealotts Hill Report for quarter ending 30 June 1956.

(19) B.P. 785,732.

diquat were internally reported: its mode of action as a contact weed-killer and its inactivation by the soil were described; its control over various annual weeds was examined; in cereals, the yield of barley, wheat and oats had been lowered unless the herbicide was applied at the 2-3 leaf stage, when only barley was affected; against potato haulm, the results seemed better than any achievable with sulphuric acid or sodium arsenite (20).

From these field tests, it is possible to understand the properties that were being looked for: a measure of selectivity was sought, particularly for control of weeds in cereals; control of various other weeds, both perennial and annual was desired; potato haulm was investigated because diquat seemed particularly suitable; desiccation of cotton and clover was also examined. The importance of establishing selective characteristics can be seen from the internal report for the last quarter of 1958, which referred to sorting tests aimed at "altering the selectivity of the chemical". The current thinking was summed up in the first external report on diquat, published in Nature; "clearly, 1:1' - ethylene - 2:2' -dipyridylium dibromide is a very potent, translocatable, rapid-acting, non-persistent, post-emergence herbicide. Potential outlets seem to lie mainly in the field of potato haulm destruction, crop dessication and non-selective weed-killing, though it may find some application as a selective weed-killer in cereals. More research is needed before the full potential of this new herbicide can be defined" (21).

The significance of these conclusions may be judged by comparing them with the 1958 survey made by Plant Protection Ltd., of the potential world market for crop protection products. This showed that the applications singled out in the Nature report comprised a relatively small market. The demand for compounds had been estimated at two price levels for each

(20) Jealotts Hill Report for quarter ending 30 June 1957.

(21) R.C. Brian, R.F. Homer, J. Stubbs and R.L. Jones, 'A new herbicide', Nature 181 (London 1958), 446-447.

application. At the higher price, the potential market for chemicals to destroy potato haulm and to desiccate crops was estimated to be approximately £1.25 million; and at the lower price level £1.75 million. Should the compound show sufficient selectivity to be used against wild oats in wheat in North America a market of £0.8 to £2.5 million, depending on price, might be possible. However, the prices for all these applications were extremely low: the estimate for potato haulm, for example, was based on a high price of £1 - 1.25/acre, and on a low price of £0.75/acre (22). It was reported that excellent destruction of potato haulm required between 1 and 2 lbs of diquat per acre, and the estimated maximum price for this application that could be calculated was therefore between £0.375 and £1.25 per lb of diquat. The estimated maximum price of diquat for desiccant usages may similarly be calculated as between £0.125 and £1. 0 per lb.

In addition to these applications which were being investigated, other uses were being actively considered. In the summer of 1957, Dr. W.R. Boon, the research director of Plant Protection Limited, made an extended visit to North America. Although he paid relatively little attention to herbicides, since a colleague was also in the United States to do this, he recommended early trials for K.8483, to ensure meaningful American results. Particular uses he recommended investigating included weed control in cotton and maize, control of weeds in small grains, particularly those resistant to hormone weedkillers, industrial applications, for desiccation, and to reduce tillage and soil erosion in the Western States. In 1957, field trials had included diquat (then known as FB2) for killing woody plants; rapid defoliation was followed by rapid regrowth, and the conclusion on perennial weeds was quite explicit: "little difference between FB2 treated plots and

(22) G. Edmund Jones (op.cit., see above note 7).

controls was visible. It was just possible to see that FB2 plots had been sprayed". In 1958, more extended trials occurred, testing diquat for four main applications:desiccation and defoliation, potato haulm, weed control and acquatic weed control. The results were encouraging for desiccant uses, and for potato haulm, but weed control showed that initial knockdown was followed by regrowth. One trialist reported that although it was an outstandingly successful contact weedkiller, it was unlikely to be commercially successful, since it possessed no residual properties. The prices which successful application might accept remained quite low: as a desiccant in corn,a price of as high as $10 per lb. of diquat seemed possible, but other applications would be attractive only at a price of about $5 per lb (23).

3.4 Pricing

The importance of price was recognised in all reviews of future demand. In July 1959, the estimated sales of diquat was given for proven applications, applications that were nearly proven, and for speculative outlets at consumer price that ranged from 10/- to 40/- per lb. At the lowest price level, sales of over 350 tons a year in three years' time were forecast for markets where diquat was almost technically proven: at the highest price level, this was only 10 tons a year. It was thus recognised that the sales of diquat heavily depended on the costs of production, and effort was concentrated on examining possible routes for manufacture.

It is interesting to note that contemporary estimates of likely costs of dipyridyls, although they varied considerably, were between one and two

(23) W.R. BOON, Report ARA 1120 (September 1957); R.H. Hirst and D.L. Martin, Report F/XC/2 (January 1959); and T.C. Breese, Report F/OX/109 (February 1959). There is potential confusion over nomenclature: the compound used was known successively as Specimen Collection No. 12,838 at Blackley, as trial compound K.8483 at Jealotts Hill, and as FB2 for American trials. In June 1959 the British Weed Control Council approved the name diquat which was used until the decision was made in January 1960 to apply for the trade name 'Reglone'. Paraquat had similar changes of name. Originally submitted to Jealotts Hill as compound K.8606, it was subsequently known as R9910 or PP910 before the title of 'paraquat' appears in the Development Committee minutes of November 1960. The name 'Gramoxone' was agreed on later.

order of magnitude higher than the estimated maximum price possible for applications that could be foreseen. These conclusions might have been viewed as enough to end research in this area, since the gap between maximum price and minimum cost was so large. In fact, the effect of this gap's being identified was to concentrate attention on closing it. There seems to have been several reasons for this. First, the synthetic chemists at Blackley who transferred to Jealotts Hill in the late summer of 1955 had experienced the dramatic fall in price undergone by hexamethylene diamine as it was transformed from being a speciality chemical produced in small quantities to a major intermediate for nylon production, manufactured on a very large scale. Dr. Boon, Research Director at Jealotts Hill, claims that the discrepancy between price and first cost estimates was not a tremendous worry, for he was confident that the estimate of cost would fall when large scale production was achieved. Second, the gap between the desired and the achieved cost was so clearly identified that it acted as a challenge to the ingenuity and scientific skills of chemists. A class of compounds hitherto best known as viologen indicators, used in minute quantities, was desired on a large scale at low cost. The molecule required, scale of production and price were all defined, and the chemist was working towards a very clearly recognised goal.

3.5 ICI effort to devise manufacturing routes:

It is perhaps predictable that this challanege should be taken up, but the breadth of response to it could not be foreseen, for several parts of ICI became involved, each contributing its own expertise. At Jealotts Hill itself, experiments were made to gain information about possible routes to K.8483, and to prepare isomers and analogues for further elucidation of the mechanism. Thus in 1956 work took place to synthesize 2, 4' - dipyridyl;

by February 1957, some 30 quaternary salts of dipyridyls had been synthesized (24). During March, after the relationship between molecular structure and biological activity had been postulated and it had become clearer that K.8483 was likely to be among the most effective compounds, attempts were made to synthesize K.8483 by new economic routes: one reaction was based on pyrolisis of pyridine N-oxide; another involved seven stages, and produced "minute quantities of an inactive compound"; a successful four-stage route to 2, 2' - dipyridyl was devised; and other routes were investigated, including one based on ferric chloride and pyridine.

This work was taken up in other parts of ICI, so that by June 1957 work to find a method suitable for the manufacture of K.8483 was proceeding actively at Dyes, Billingham and Jealotts Hill. Earlier a joint meeting had been held and a list of possible routes prepared. The work at each of these centres was concentrated on different approaches. At Dyestuffs Division, where K.8483 had first been synthesized, and where equipment existed for small scale manufacture of organic chemicals, the original synthesis devised by Fielden was modified for larger quantities. The new route was based on o - phenanthroline, which was oxidised before decarboxylation to 2, 2' - dipyridyl. Using this route, by December 1956 some 50 lbs had been made, and by March 1957 87 lbs had been manufactured. The cost of this route was prohibitively high for all but trial quantities, since the starting material was quite expensive, and three stages with quite small overall yield were required. At Billingham, in the part of ICI with most experience in large scale production of organic chemicals, work was done to investigate the technology of a route suggested in early work at Jealotts Hill, based on the reaction between ferric chloride and pyridine. These when reacted together at high temperature give yields of predominantly 2, 2'dipyridyl, with a mixture of other products, including some tripyridyl.

(24) ARA Report 1087 (February 1957).

This work was started in the autumn of 1957, and continued throughout 1958. Work was aimed in particular at raising the yield of 2, 2' -dipyridyl and in overcoming extremely severe corrosion problems. These corrosion problems remained, and the expected cost of K.8483 from this process, with pyridine costed at £515/ton, for a plant producing 300 tons of 2, 2' - dipyridyl annually, was over £1,300 per ton. This price was considered too high by Plant Protection, and Boon subsequently reported in November 1959 that Dyestuffs Division had decided that they would not be able to make plant available to use this route (25).

In November 1959, at the same time as reporting that the ferric chloride route did not seem very promising, Boon reported that a route to 2, 2' dipyridyl based on pyridine using a specially prepared Raney nickel catalyst appeared promising, and that ICI (Australia and New Zealand) had done some work that could provide the basis for a manufacturing route. Dyestuffs Division was investigating, and a route for manufacture in 1960 seemed possible. By 28 January 1960, Dyestuffs Division had reported that they should be able to make dipyridyl at a rate equivalent to 1 ton of diquat per week by the end of February, and 5 tons of diquat per week by the end of May. In March, it was reported that Dyestuffs Division hoped to make 45 tons of diquat in August and September, and on 30 June it was reported that the Huddersfield plant had started operation the previous day (26).

The variety of response to the challenge of devising an economic manufacturing route is somewhat surprising if one considers that different divisions of ICI were involved, each of which was geographically remote and administratively distinct from Plant Protection. In part, these barriers were overcome through the active efforts of Boon, who was acutely conscious of the fact that a compound with useful properties required only a manufact-

(25) Jealotts Hill Reports 1957-1958; A.H. Jubb, '2, 2' - dipyridyl' HOC Report (1959); and Development Committee Minutes July 31 and November 30, 1959.

(26) Development Committee Minutes, November 30, 1959 and June 30, 1960.

uring route. With diquat, as with paraquat later, Boon repeatedly pressed his colleagues in manufacturing divisions to carry out work to make this possible. By June 1957, he was successful to the extent that work was taking place in Dyestuffs Division at Blackley and Heavy Organic Chemicals Division at Teesside; by July 1959, General Chemicals Division at Widnes was also involved, and in November 1959 I.C.I.A.N.Z. in Australia contributed a route.

The reaction of divisions to Boon's enthusiasm was helpful, and a contributing reason was the contact that already exi[illegible] between these ICI divisions and Plant Protection. Dyestuffs, Heavy Organic Chemicals and General Chemicals Divisions were all accustomed to providing compounds for test at Jealotts Hill, and representatives of these Divisions made frequent trips to Jealotts Hill to discuss the progress of candidate compounds. Visitors from Blackley were particularly frequent when chemists there were responsible for synthesizing candidate compounds; Boon, for instance, while at Blackley spent more than a week in all at Jealotts Hill in each of 1954 and 1955 (27). In addition, Boon had the advantage of having worked at Blackley alongside his colleagues whom he was now persuading to undertake research on his behalf. The geographical and administrative barriers which might easily have impeded diquat's successful development were overcome, and a great deal of the responsibility for achieving this is attributable to Boon's championship of the project. The role of product champion described by Schon was filled, in the development of bipyridyl herbicides, by Boon (28).

At the point in 1960 when manufacture of diquat became possible, important developments were being made in the knowledge of applications of diquat and derived compounds. In July, 1959, sales outlets believed

(27) Jealotts Hill Reports, 1953-1955.

(28) D.A. Schon, Invention and the Evolution of Ideas (London, 1953).

"almost technically proven" comprised potato haulm destruction in the U.K., and cotton and seed crop desiccation in the U.S.A., and the total market after three years' sales was estimated to be about 370 tons, at the lowest price considered. By March 1960, sales to technically proven applications were estimated to comprise 990 tons in the third year of marketing, while anticipated outlets were estimated to comprise a further 1030 tons. The major new applications were for firebreak desiccation in Australia, and for weed control in Malayan rubber. In November 1960, the sales potential had again been revised, and sales in 1965 were estimated to comprise 1200 to 1400 tons, of which a third was attributable to potato haulm destruction (29). However, at the same time that these fluctuating estimates were being made, information was becoming available about a second bipyridyl herbicide, which had many attributes in common with diquat, but possessed sufficient distinctive features to make it extremely interesting on its own account.

4. Recognition of paraquat:

In the second quarter of 1958 field trials with diquat had been rounded off in the U.K., and a further series of tests were performed on another bipyridylium herbicide, known as K.8606. This had originally been submitted to Jealotts Hill from Blackley on April 25, 1955, when its activity had been observed to be slightly less than that of diquat. In the third quarter of 1958, it was retested, and seen to be "more effective in controlling grasses than K.8483, but less effective against red clover and several broadleaved weeds...." In June 1959, it was reported that 10.9 lb of K.8606 (1,1' - dimethyl - 4,4' - dipyridylium diiodide) had been despatched to Malaya, where trials were taking place with diquat, which

(29) Development Committee Minutes, July 31, 1959 and March 3 and November 3, 1960.

was expected to have a market of some 500 tons annually for control of weed. Preliminary results indicated that K.8606 "gives a better and much more persistent weed control and is comparable at 1 lb/acre with 8 lbs of dalapon or 20 lbs of chlorate for at least six weeks. A preliminary trial ... comparing K.8606 with diquat ... shows that K.8606 is superior" (30).

It thus occurred that, at the time it had been proved possible to manufacture diquat, a new herbicide was recognised, with apparent important advantages. As had been the case for diquat, it was not able to be manufactured economically; unlike diquat, there was not such a strong patent position.

4.1 Manufacturing routes for paraquat:

In 1959, considerable effort was devoted to developing Plant Protection's understanding of the new compound. Field trials were initiated in the U.K., as well as in Malaya, and work was performed at Jealotts Hill on routes to 4, 4' - dipyridyl, originally investigating the reaction between pyridine, zinc and acetic anhydride, with the purpose of making quantities of 4,4' - dipyridyl for quaternisation for trial purposes. More speculative work on reactions involving sodium and pyridine and the reaction between pyridine-N-oxide and ammonia. The route from sodium and pyridine had been reported in 1924, but had the same disadvantage that the reaction was highly inflammable, involving a pyrophoric mixture of sodium, pyridine and oxygen (31). Boon was aware of work occurring in General

(30) Jealotts Hill Report for quarter ending June 30, 1959.

(31) C.R. Smith, 'Dipyridyls from pyridine', in J.Am.Chem. Soc., 46, 2 (February 1924), 414-419. It is interesting to note that Smith was a chemist engaged on synthesising compounds for the United States Dept. of Agriculture, in the Insecticide and Fungicide Laboratory. Smith records that he tested γ, γ, - dipyridyl, and found an impure mixture to be toxic, while a purified sample displayed no toxicity.

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Chemical Division of ICI on sonically dispersed sodium, and he asked C.G. Harris, the General Chemicals Research Director, whether he would investigate whether the finely dispersed sodium might be used, with the prospect of diminished fire risk. In November 1959, Boon reported that General Chemicals Division was investigating a process for R9910 (32).

The research thus started in General Chemicals Division developed rapidly. In December, 1959, two possible routes to the 4,4'- dipyridyl were envisaged, based on the reactions between pyridine, acetic anhydride and zinc and between pyridine, acetic anhydride and sodium, with oxidation of the products to yield dipryidyl. Throughout 1960, work continued to investigate the conditions under which the sodium reaction proceeded. By June 1960, it had been shown that the reaction gave yields greater than those obtained from zinc, and that it could be controlled using finely dispersed sodium. It had also become evident that ultrasonic dispersion of sodium would prove too expensive, particularly when scaled up, and efforts then centred on mechanical means of dispersion.

In December, 1960 it was reported that research was continuing on three levels concurrently: laboratory experiment, semi-technical scale experiment and design work for a 50 ton per year pilot plant. The process to be used in the pilot plant was only known in outline: sodium was mechanically dispersed in a solvent, was then reacted with pyridine, oxidised, and then had the solvent and dipyridyls removed by filtration and distillation. Although it had low efficiency overall, the process had the great appeal of being workable, and would produce sufficient quantity for the trials which Plant Protection required. Initially, it had been proposed to make 100 lb of 4,4'-dipyridyl ion for 1960 field trials on a Widnes

(32) Development Committee Minutes, November 30, 1959.

semi-technical plant (33). Although this demand was eventually met from Blackley, the larger amounts required for extended field trials could only be supplied from a larger plant, and this was the first objective of General Chemicals Division's research, and the stimulus for the extreme urgency with which this objective was pursued. The justification for this effort can be seen by examining the importance of field trials.

4.2 Market Development:

Work on economic routes for synthesising the 4,4'-dipyridyl salts was justified by the applications that were simultaneously being developed. The actual market first indicated, the suppression of weeds in Malayan rubber holdings, was not particularly large. The 1958 survey of world markets for crop protection products, for example, had estimated it at £600,000 (34). More interesting than this market alone was the property that the trials had shown to be possessed by paraquat, of control of grass weeds. This presented opportunities which were imaginatively developed. Perhaps the most simple application was to extend the number of places where paraquat could be used against grassy weeds. Jeater on his way to Malaya had stopped in Ceylon, to consider the problems of aquatic weeds there, and he also examined what outlets for chemical weed control were provided by the tea estates. For the principal problem - control of weeds in ravines bordering tea estates - he recommended in a report written after his experience with paraquat in Malaya that trials with paraquat should be made. It was subsequently decided that this should be done providing that an economic manufacturing route seemed possible (35). It was also decided

(33) General Chemicals Quarterly Research Report, December 31, 1960.

(34) G. Edmund Jones (op. cit., see above note 7).

(35) PPL Reports PP/E/19 and PP/E/18.

that Jeater should return to Malaya for two months in 1960, and for the whole of 1961, to develop more fully the uses of paraquat there. The Malayan market, though not on a very large scale itself, was invaluable in that it provided an application which was sizable and justified development effort into other more speculative applications. In November 1960, the first market forecast for paraquat was quantified for tropical crops alone. When, in February 1961, a more detailed market forecast was produced, it was estimated that tropical crops would account for 65 per cent of the 1962 paraquat sales, 55 per cent of sales in 1965, and 35 per cent of 1967 sales. The importance of the Malayan outlet for paraquat, particularly in the first stages of development and decliningly so later, can be seen from these estimates (36).

While Jeater was establishing the conditions for using paraquat in Malaya, more speculative outlets were being developed in the U.K. The November 1960 market forecast specified pasture renovation, total weeding, chemical mowing and chemical hoeing as potential outlets, and stated that paraquat seemed very promising for pasture renovation. At the same time, applications were being investigated that utilised the greater activity of paraquat against grasses, or where increased activity seemed possible. In 1959, experiments were made against bracken, using a paraquat-dalapon mixture; in 1960 experiments tested the efficiency of paraquat for removing grass at the base of apple trees; and in 1961 paraquat and diquat were both tested for use in daffodil beds. These tests were complementary to those which had been performed with diquat, which by 1961 had been tested for weed control in sugar beet, bulbs, potatoes, lettuce, parsnip, carrot, turnip, cabbage, raddish, onion and other vegetables (37).

(36) Development Committee Minutes, February 2, 1961.

(37) PPL Report PP/E/119 (September 1961).

A further use of diquat had been considered, which used the non-residual properties of the herbicide. A pasture which had become run down was treated with diquat to destroy the invading weeds, and then reseeded with grass. This technique had been tested in Australia, where it was useful in pastures on which weeds had very severly encroached. It was not, however,so useful against grassland with only small weed infestation, since diquat was predominantly active against broad-leaved weeds, and the pasture would still be predominantly grassy. The activity of paraquat against grasses suggested that pasture renovation could occur using this herbicide before the weed encroachment grew too severe (38).

4.2 Ploughless farming:

The use of paraquat for pasture renovation, allied with its other envisaged uses of chemical hoeing and chemical mowing, suggested a further question to Dr. Boon: why plough at all, when paraquat could be used to destroy weeds. The prospect thus opened was immense, no less than the possibility of displacing one of the central activities of farmers. The bipyridyl herbicides offered the opportunity not of replacing other herbicides, but of displacing a mechanical technique hitherto essential for large scale farming. The opportunity was subsequently described: " it could be that the introduction of the two new herbicides will bring about as big a revolution in agriculture as the steam engine did in manufacturing industry" (39).

The question and its consequences, seemed revolutionary. There was, in fact, a considerable body of previous work which supported the inquiry.

(38) M.A.Ross, 'And now paraquat....' J. of Agric., South Australia (February 1963), 258-260.

(39) W.R. Boon, 'Diquat and paraquat - new agricultural tools', Chemy. Ind. (May 9, 1965), 787.

In 1944 Russell reported experiments at the Rothainsted Experimental Station which had been started nearly twenty years previously: he started by observing that a hundred years ago the farmer had no alternative to ploughing when he wished to loosen the topsoil, but that the situation had changed, "there is no reason to assume that this implement, which was designed in the era of wood and steel, to be drawn by an eight ox team, should have any fundamental importance today". Trials on sub-surface tillage and on a process of maintaining a crop on the land, and working all organic material into the top 2 or 3 inches, had been made, and the effect of hoeing and depth of ploughing had been examined. The conclusion drawn was that ploughing and other techniques were more important in destroying weeds than they were in forming a correct tilth (40). For those developing paraquat, the further conclusion could be drawn that were it possible to remove weeds chemically, the plough might be displaced. The experiments performed by Russell had been continued elsewhere. At Bridget's Experimental Husbandry Farm trials had been started in 1956 to investigate ploughing at depths of 12, 8 and 4 inches, and to compare this with no ploughing; the crops under cultivation were a grass/clover ley, winter and spring wheat, spring barley and potatoes. The results of the trials, reported in 1963, were impressive, since only two crops, winter wheat and spring barley, gave lower yields in the "no plough" trials. The report of the trial contained the concluding statement: "The question of 'At what depth must I plough?' may be changed to simply 'Must I plough?'" (41).

Although the question as posed was quite general in its application to different farming techniques, most studies had been made on areas where there were physical barriers to ploughing, either because the land was too

(40) E.W.Russell, 'What are the minimum cultivations necessary for high farming?', Proceedings of the Institution of British Agricultural Engineers, 3 (February 1944), 100.

(41) Bridget's Experimental Husbandry Farm: Annual Report, No 4 (1963), 6-8.

rough, or because of the threat of erosion. Work had been done on chemical fallow in the Southern states of America, and in the eastern half of the United States where it was estimated that there were some 50 million acres inaccessible to the plough which would be dramatically improved by tillage. Experiments with herbicides had been made since 1949, when sodium TCA had been tried; subsequent chemicals had included dalapon, amitrol and cacodylic acid. The experimenter observed that "as this is an entirely different use for an herbicide, finding the right chemical has been slow. One is needed to quickly and completely kill all vegetation without leaving a residue in the soil which will affect new seedlings" (42). A similar conclusion had been drawn by New Zealand agricultural experts. In a country where only a third of farming land could be developed mechanically (other than through aerial applications) a selective grass killer was needed so that aerial overseeding could be used, with competition from other plants overcome by chemical treatment. It was stated that "possibly the biggest limiting factor is the need for a chemical (or chemicals) that has no residual effect in the soil and would not be affected by adverse climatic conditions" (43). In Britain, similar work had concentrated on sward renewal for hill pastures using, for instance, dalapon. Reports on experiments testing this technique had been made at the 1960 British Weed Control Conference (44).

The first trials undertaken by Plant Protection on paraquat as a means of avoiding ploughing were designed to test whether hill pastures might be renewed using paraquat. Trials were carried out in North Wales on rough hill pastures which were treated with paraquat and then seeded with grass

(42) A.F.Wiese, J.J. Bond and T.J. Army, 'Chemical Fallow in the Southern Great Plains', Weeds, 8 (1960), 32 and M.A. Sprague,'Pasture Renovation with Herbicides', Farm Chemicals (June 1959), 44-45.

(43) L.J. Matthews, 'Chemical Ploughing in New Zealand', Span 3 No. 4 (1960), 160-163.

(44) C.E. Davies et al, 'Hill Pasture Improvement with Dalapon', Proceedings of 5th British Weed Control Conference (1960)

and clover. It was discovered that this reseeding was successful, and that the reconstituted pasture could support lambs. This trial, as the authors of the report on it recognised, represented relatively simple development of earlier experiments using residual herbicides. The special non-residual features of paraquat were such that the trials were greatly extended. In 1963, the report on pasture renewal claimed "paraquat has been used successfully to replace ploughing in renewing permanent pastures," and the phraseology is indicative of the ambitions which had been realised by the successful trials (45).

The same ambitions may be seen in two articles which appeared in Nature with the titles "Destruction of pastures by paraquat as a substitute for ploughing" and "Crops grown using paraquat as a substitute for ploughing", and in the more generalised title "The use of paraquat as an alternative to ploughing" (46). The last of these papers reported the results of trials in progress at Jealotts Hill where winter wheat was grown by two methods: spraying with paraquat was followed by direct drilling into stubble, and this technique was compared with conventional cultivation by ploughing. These experiments were completed in 1964, and showed that the result of three years direct drilling of winter wheat into stubble sprayed with paraquat was a yield not significantly different from that obtained from conventional cultivation. The possibility of using paraquat and then direct drilling, in place of ploughing, was thus reported.

The market opened by the possibility of a chemical alternative to ploughing was immense, and it is not surprising that increasingly attention was devoted to paraquat. Initial efforts were made to interest and gain the

(45) PPL Report PP/E/197.

(46) A.E.M. Hood, H.R. Jameson and R. Cotterell, 'Destruction of pastures by paraquat as a substitute for ploughing', Nature, 197 (London 1963), 748; and 'Crops grown using paraquat as a substitute for ploughing', Nature 201 (London 1964) 1070-1072; and A.E.M. Hood, D.G. Sharp, D.W. Hall and R. Cotterell. 'The use of paraquat as an alternative to ploughing,' Proceedings 7th British Weed Control Conference (1964), 907-912.

support of advisory institutions. In May and October 1962 Boon announced the results of discussions with the directors of the Grassland Institute and the National Agricultural Advisory Service. Within Plant Protection, a special paraquat working party was set up in 1962, to consider how best to develop the herbicide. Most clearly, the importance of the decision to develop paraquat can be recognised in the research and development expenditure associated with the bipyridyls. The total research and development expenditure of Plant Protection Ltd., rose relatively little between 1960 and 1964, and in 1964 was less than 30 per cent higher than the comparable expenditure in 1960. Within this total, the proportion devoted to bipyridyls rose markedly: in 1960, and in 1961, research and development on the bipyridyls comprised less than 10 per cent of the total research and development expenditure; in 1963 and subsequent years, it comprised over 25 per cent of a total that began to rise sharply. Whereas the increase in total research and development expenditure rose by less than 30 per cent between 1960 and 1964, between 1964 and 1965 it rose by just under 70 per cent, and between 1964 and 1969 by 290 per cent. By far the greater part of this increase was due to paraquat, for only in 1960 was the expenditure on diquat greater than on paraquat, and in later years the difference between expenditures on each herbicide became considerable. Table 3.1 shows the perecentage of the total research and development budget devoted to each of diquat and paraquat, and an index of the growth in the total expenditure.

Table 3.1: Index of Plant Protection R. & D. expenditure

	Total Research & Development Expenditure 1960 = 100	Percentage spent on Diquat	Paraquat
1960	100	8.6	1.1
1961	109	2.7	6.8
1962	103	10.3	17.4
1963	n.a.	n.a.	n.a.
1964	128	3.4	27.5
1965	217	5.4	24.6
1966	272	1.7	38.5
1967	372	1.8	27.9
1968	384	1.5	29.4

Source: see note (47).

The growth in total research and development expenditure, and still more the very marked rise in the proportion of this total accounted for by the paraquat and (to a lesser extent) diquat programmes, show the effect of more extended field trials. They are also a mark of the importance of assessing the chemicals' activities in the fields. It is thus clear that the availability of paraquat for trial purposes enabled new applications of great importance to be developed. It is also interesting to trace back the effect of more complete market information on the research and development into processes for manufacturing paraquat.

4.4 Research and Development Expenditure at Widnes:

The first sanction for research on a process for 4,4'-dipyridyl had been made at Widnes in November 1959, when expenditure was sanctioned for three months' laboratory work. The information on the commercial prospects

(47) Development Committee Minutes, 1959-1967.

available at the time was stated to be that the unique property of deactivation on contact with the soil was attractive. The second sanction, agreed on April 18th, 1960, was for a larger amount of work, "to provide information for the design of a plant for its (paraquat's) manufacture". By April, it had therefore been decided that the prospects for paraquat could be probed in sufficient detail only by more extended market tests. At the time, the market informaton on paraquat was small. The sanction justified it in the following terms: "PPL estimate that there is a world market of at least 1000 tons per year of R9910 which may grow to 2000-3000 tons per year. Similar figures are quoted for FB 2 prospects". When this sanction was extended in December, 1960, the commercial prospects had been refined only to the extent that the main immediate market had been firmly identified as Malayan rubber plantations, which was expected to consume several hundred tons "within a few years", while the possibility of using paraquat in pasture renovation and as a substitute for ploughing was also mentioned. This information also justified the starting of a research programme into routes to pyridine, as it became evident that successful development of diquat and paraquat was likely to strain the available supplies of pyridine. No additional information had become available when the sanction on research into a process for 4,4' -dipyridyl was again extended in March 1961. This sanction more than doubled the cash available for the research programme. Similarly, no additional information on the market for paraquat had become available when in June 1961 sanction was granted for pressing ahead with the research on synthesizing pyridine, by taking the process to a semi-technical plant. In none of these sanctions was a price-demand relationship established, the assumption being in all cases that successful process development would reduce the cost to a level at which paraquat would be competitive with existing herbicides (48).

(48) General Chemical Division Sanctions, G/EXP/R.2610, R.2628, R.2628A, R.2628B, R.2648 and R.2666.

In August 1961, the first market forecast was completed and available in General Chemicals Division, that related demand to price. This showed a market of considerable size, at a price which was not too far removed from that which was deemed possible. The market envisaged was far beyond the capacity of the 50 ton per year pilot plant, and work was continued to obtain sufficient knowledge for a larger plant to be built. In 1960, experiments had been done to test the effectiveness of paraquat as a desiccant for cotton in the U.S.A., and the favourable reports of the effectiveness of paraquat in Malaya were being further tested by more trials. The greater quantities coming available in 1961 from the pilot plant enabled these trials to take place.

The results of these trials was to establish those markets where paraquat could compete. Trials using paraquat manufactured on the pilot plant tested the efficiency of paraquat when applied to weeds among daffodils, weeds in orchards, weeds in Malayan rubber estates, against wild oats and bracken, and when used for pasture renovation (49). The conclusions drawn from these trials were not unanimously favourable, as may be seen from successive forecasts made in August 1961, February 1962 and March 1962. If the expected demand for each year is represented by an index of 100 in the first forecast, those for subsequent forecasts are as indicated in Table 3.2.

Table 3.2

Forecasts of Paraquat Sales

	August 1961	January 1962	March 1962
1962	100	62	42
1963	100	79	63
1964	100	77	50
1965	100	82	55
1966	100	79	67

Source: see note (50)

(49) PPL Reports PP/E/114, PP/E/85, PP/E/146, PP/E/158, PP/E/149, PP/E/141 and PP/E/204.

(50) General Chemical Division Report DN 1939.

The price at which these sales were hopefully to be realised had also altered, by varying amounts, averaging a rise of about 7 per cent. Despite the reduction in many of the short term forecasts, the overall prospects for paraquat remained good. The uncertainty which had cloaked the early market estimates had been markedly reduced - even if some of the market estimates had simultaneously suffered reduction.

It is worth emphasizing that the usefulness of the pioneer plant which was operated in 1961 was not principally that it supplied new information about the technology of producing paraquat, but rather that it allowed the major uncertainty - that affecting the market forecast - to be reduced. To achieve this end, the opportunity of waiting until a more suitable process, capable of further development, became available was deliberately foresworn, so that information on demand would be obtained as soon as possible. To erect such a plant required a different approach from that adopted for building a semi-technical plant to prove the technology - Dr. F.R. Bradbury, the project leader for paraquat research at General Chemicals Division, speaks of "distorting the science" so as to be able to produce quickly a workable process. The criteria for success of the plant had also to be clearly defined. The decision to build a second paraquat plant, using a process based on the reaction between pyridine and magnesium rather than that between pyridine and sodium, was made by the General Chemicals Division Board in December 1961. Yet at this time the pioneer plant had been operating for less than nine months, at flow rates lower than those expected, and with costs considerably higher than budgetted. The importance and usefulness of pilot plants have been discussed under various categories (51). It is important to recognise that some of the aims in building a pilot plant may be incompatible or conflicting. The success of paraquat development was the identification of

(51) A. Baines, F.R. Bradbury and C.W. Suckling, Research in the chemical industry (London 1969), 223-225.

demand factors as the major uncertainty, and the construction of a pioneer plant to reduce this uncertainty was achieved at the cost of leaving much of the technological uncertainty unresolved.

At the same time that the pioneer plant was being built and operated, research was continuing in the laboratory on other routes to 4,4' -dipyridyl. In June 1961, the possibility of using a process based on magnesium rather than sodium was reported, and by December a process had been outlined in sufficient detail for the likely capital costs to be calculated and approved, and sanction given for a plant several times larger than the existing pioneer plant to be built by the end of 1962. Simultaneous with this work on the magnesium process, laboratory work was being carried out on further exploratory routes to the bipyridyl, and in September 1962 it was reported that a route based on reduction of sodium in liquid ammonia with pyridine and solvent followed by air oxidation seemed still more promising for the large scale plant envisaged as the "third generation" of producing plant. By September 1963, the liquid ammonia, or low temperature sodium (L.T.S.) route had been taken to a semi-technical scale plant, and the magnesium route had become the second production plant. In developing these routes, semi-technical plants had been built not to further probe the market, but to gain more information about the technological feasibility of the processes being investigated, and to ensure that the products of these processes were as powerful biologically as that of the original sodium route (52).

The worthwhileness of reducing the technological uncertainty had previously been established by the market information "purchased" by operating the pioneer plant. It is possible to trace the way that this information was used. The first market forecast, in August 1961, was followed

(52) General Chemicals Division Quarterley Research Reports, 1960-1962.

by sanctioning of research expenditure which increased the total sanctions for paraquat research nearly six-fold. Following the March 1962 market forecast, the sanctions rose again. If the amount sanctioned in January 1961 is taken as an index of 100, the subsequent rises may be plotted, as in table 3.3.

Table 3.3: Index of R. &. D. sanctions for paraquat at Widnes

January 1961	July 1961	March 1962	January 1964
100	250	1450	2660

The additional market information that became available at the end of 1961 and the start of 1962 was used to justify further research, aimed at reducing both the market and technological uncertainty. If it is assumed that the pioneer plant at Gaskell-Marsh was designed to reduce the commercial uncertainty - and it has been seen that it was successful only when judged against such a target - by August 1961, 55 per cent of the sanctioned expenditure had been authorised to discover essentially market, rather than technological, information. By April 1962, the proportion which is attributable to reduction of commercial uncertainty had sunk to less than 45 per cent, and was progressively to dwindle as more effort was devoted to reducing the technological uncertainty. It is striking that the expenditure sanctioned for dipyridyl research in July 1961 was just under a tenth of the total authorised by January 1964, yet by March 1962, after progressive market forecasts had refined the commercial prospects, had reached over a half of the 1964 total. The commitment of resources to reducing technological uncertainty was dependent on having reduced the commercial uncertainty. The fastest rate of increase in sanctioning occurred only after the risk of failure had been reduced.

5. Development of applications for paraquat

General Chemicals' decision to commit more resources to developing routes for paraquat manufacture enabled Plant Protection to increase its efforts to develop paraquat. It would be an immense task to document in detail the reasons for paraquat's adoption by farmers throughout the world, for each application depended on the particular local conditions. Soil conditions, climate, competition from other herbicides, crop, terrain, farming practices and a great variety of other factors were all of influence in persuading farmers whether to use paraquat. Broadly, however, the various applications of paraquat may be categorised, following Calderbank (53), into:

(i) Weed control in tree and bush crop

(ii) Weed control in arable row crops

(iii) Precrop and postcrop emergence weed control

(iv) Direct drilling into uncultivated land

(v) Pasture renewal

(vi) Selective weed control

(vii) Aquatic weed control

It is helpful to consider the advantage offered by paraquat in each of these applications, and to compare the opportunity for innovation perceived by the farmer or horticulturist with the opportunity offered to those responsible for the research and development within plant protection. At the same time, the way in which farmers' perceptions were being changed by those responsible for offering advice and framing legislation must be examined. It is interesting also to examine the seven applications of paraquat against the criteria recommended by Rogers as helping understanding

(53) A. Calderbank, 'The Bipyridylium Herbicides,' Advances in Pest Control, 8 (1968), 127-235.

of an innovation; these, we may be reminded, are relative advantage, compatibility, complexity, divisibility and communicability (54).

5.1 Weed control in tree and bush crop

It has already been seen that the first market envisaged for paraquat as a result of field trials was suppression of weeds in rubber estates. This was the first specific market in the general category of weed control amid tree or bush crop. The advantages offered to the farmer or estate manager were considerable. There was the obvious advantage of avoiding weeding, which, as well as being time consuming and labour intensive, had the danger that the roots of the preferred crop might be disturbed. These advantages were realised quickly, and further advantages could become apparent subsequently, including better moisture conservation and reduced incidence of damage to the bark of trees. To experiment with the technique, the farmer had to make little alteration to his standard practices: spraying could occur when it fitted into his work pattern, and required little new equipment or skills. The danger that paraquat might be sprayed inaccurately was less pressing in this than in many other applications, since the woody bark of trees tended to be impervious to paraquat. To ensure precise control over spray, Plant Protection developed a small sprayer which guarded the tree. The cost of this spray, the Arbogard, was relatively small, and it was, in any case, only needed to protect the leaves of small saplings. The benefits of using paraquat in this application were thus quickly discernible, and could be achieved with little alteration to the farmer's normal practices, and with little initial investment in an unknown technique.

The disadvantage of paraquat remained, that its lack of residual activity necessitated repeated applications. This could be overcome in various ways,

(54) E.M. Rogers, Diffusion of Innovations, (New York 1962), 124-133.

either by using mixtures of paraquat with residual herbicides, or by split applications of first a residual and then paraquat herbicide. The latter technique represents an increase in the complexity to the farmer of using paraquat, and so to some extent detracts from its appeal.

5.2 Weed control in arable row crops

Similar advantages existed for weed control in arable row crops as occurred in tree and bush crops. Weed control, without weeding and with no danger of damage to roots, was attractive to farmers, and was compatible with their existing techniques of cultivation. The danger of mis-locating the herbicide was greater, however, since the crops grown were liable to be harmed by accidental contact with paraquat in a way which trees and shrubs were not. Selectivity between plants was to be achieved by physical location of the spray since it was not possible in many applications to use any chemical selectivity. Sprays used for conventional herbicides did not possess the required accuracy, and it was therefore necessary for the farmer to acquire, and for Plant Protection to design, special applicators. Plant Protection designed low pressure applicators which could be drawn between rows of crops, with shields to ensure that the spray was confined to the area in which weeds were to be controlled. A special electrically driven oscillator was designed to produce a pattern of drops which were not liable to drifting. The farmer who wished to use paraquat for inter-row weed control had thus to acquire special equipment, which made the innovation slightly more complex, and less easy to experiment with. The cost of the three applicators developed for this was still relatively cheap, and the need for new machinery is unlikely to have deterred many farmers. As with weed control in tree and bush crops, the rapid action of paraquat lent itself to easy demonstration.

5.2 Precrop and postcrop emergence weed control

For weed control pre- and post-crop emergence, paraquat had applications where an easily recognised advantage existed. In the UK, for instance, paraquat could be used to kill weeds in grassy stubble before ploughing. Application of paraquat was simple, requiring no extra equipment, and resulted in considerably easier ploughing. Nor did it require precise timing, as some postemergence weed control applications needed. It is not surprising therefore that paraquat should be appreciated by farmers as a useful adjunct to ploughing. This application, however, was far removed from, and in some ways inimical to, that envisaged by some who were concerned with paraquat's development, who saw in paraquat the instrument to avoid the need for ploughing at all.

5.4 Direct drilling

The developments of paraquat had been greeted with much enthusiasm by those who saw in it the opportunity to reduce the number of mechanical cultivations, and perhaps to proceed to the point where it was no longer necessary to plough at all. The advantage to the farmer was more difficult to assess accurately, and certainly could only be achieved by considerably altering his agricultural and organisational techniques, before the full benefits of adopting paraquat could be perceived. Direct drilling following paraquat weed killing offered advantages that were clearly discernible in specific circumstances: the danger of soil erosion was reduced; cattle ran less risk of poaching the ground after direct drilling of kale; the direct drilling could be accomplished rather earlier than ploughing.

The main advantage for the farmer, however, was that application of paraquat followed by direct drilling enabled him to reduce the man-hours required at peak times on the farm, and thus save labour. This advantage

would only become evident if the labour saving with paraquat was sufficient to reduce the total labour force by one man (or possibly to reduce the use of hired labour during peak periods). It would be possible only if suitable conditions existed: these included suitable soil conditions, a weed susceptible to paraquat, efficient drilling techniques, and application of adequate amounts of fertiliser. The relationship between the use of paraquat in direct drilling and farm profitability was neither simply discernible, nor independent of other organisational changes. Both relative advantage and compatibility suggest that the farmer might be less enthusiastic to develop direct drilling than other applications of paraquat.

Since a prerequisite for successful use of paraquat in direct drilling was a suitable method of introducing the seed into the soil, the farmer had to acquire drills capable of doing this. Normal seed drills became clogged with surface trash, or failed to penetrate evenly into the ground, or left the slit into which the seed was injected open, with subsequent attack by slug or bird. Plant Protection designed a drill, the Fernhurst Triple Disc Drill, for sowing seeds into uncultivated soils. To overcome the disadvantages of normal drills, special features had to be incorporated into the drill. Triple disc coulters were required to prevent trash build-up in the drill; special long springs were required to cope with uneven surfaces; hydraulic control varied the pressure to ensure even penetration of the soil irrespective of ground conditions. The final machine developed by Plant Protection for use in the trials weighed 26 cwt., and obviously represented a considerable investment for any farmer (55). The need for a special drill for direct drilling following paraquat spraying reduced the ease with which a farmer might experiment with this technique.

(55) Fernhurst Triple Disc Drill, Plant Protection Leaflet (1968).

5.5 Pasture renewal

The use of paraquat in pasture renewal was dramatically demonstrated at an early stage, when in 1962 a Welsh hillside plot was treated with paraquat and reseeded. Lambs were reared on this plot, and showed a live weight gain over ten times as large as those raised free on the hillside (56). Subsequent trials extended the use to pasture renovation in lowland pastures. Striking though the demonstration proved, it provided not very much information to the farmer who had alternative means of improving marginal lands through, for instance, liming or draining. In some countries, however, paraquat allowed territories that were not able to be cultivated mechanically to be brought under control. In Australia and New Zealand, paraquat appeared to offer a relative advantage (57). It was soon observed, however, that the advantages occurring from using paraquat were dependent on the techniques of farming used. In particular, it was claimed that it was necessary to have grazed the pasture thoroughly before oversowing with the aid of paraquat (58). Use of paraquat therefore involved the farmer in various other alterations to his normal practices. Low application rates could only be achieved by those who had close and controlled grazing.

5.6 Selective weed control

Paraquat can be used selectively in applications where this selectivity owes its origins to causes other than physical location of the herbicide. The advantage to the farmer of a single spraying of a crop, without the need for careful location of the herbicide, is apparent. Paraquat can be used against certain weeds with some selectivity, but against others, such as

(56) W.R. Boon (op. cit., see above note 39), 788.

(57) M.A. Ross, 'And Now Paraquat ..., 'J. of Agriculture, South Australia (February, 1963), 258-260.

(58) M.A. Ross and P.C. Cocks, "Grazing is vital in pasture over sowing," J. of Agriculture, South Australia (April 1964) 288-291.

grassy weeds amid lucerne, selectivity could only be achieved by careful application of the herbicide at a time when the preferred crop was dormant. Success therefore depended on careful timing of application. The advantage to the farmer of using paraquat for selective weed control was thus not very clearly discernible, particularly when other herbicides were available which were chemically selective. The advantage was further reduced by complexity of administration.

5.7 Aquatic weed control

The advantages conferred by using paraquat for aquatic weed control include rapid action, and the possibility of using water treated in this way for irrigation 48 hours after treatment, without danger of damaging the crops irrigated. Low toxicity to fish, a further property of paraquat, would represent an advantage to those concerned with preservation of wild life. The ease of spraying, lack of special times at which application was necessary, and general ability to kill all green plants allowed paraquat to be demonstrated easily to farmers, and for them to conduct their own experiments with it without disturbing their normal routine, or making a large initial experiment.

6. Factors affecting farmer's perception of the advantages of using paraquat

In examining the relative advantage from using paraquat perceived by the farmer, it has been clear that different applications required very different properties. A further difference between applications is the extent to which the farmers in each case were affected by other influences, which helped to alter their criteria in such a way as to make paraquat more or less suitable.

The clearest influence on farmers was that of advisory or legislative bodies which permitted or forbad the use of paraquat and competitive products

for specific purposes. This was particularly important in the development of paraquat's first application, to control weeds in Malayan rubber estates, for the herbicide traditionally used,sodium arsenite, was threatened with banning because of its danger to animals. The Malayan estate manager thus had an incentive to use paraquat even though it lacked residual activity, a property which would otherwise have been demanded. The importance of this legislation may be compared with a similar decision made in 1959 by the Association of British Manufacturers of Agricultural Chemicals (ABMAC) to abandon sodium arsenite for use against potato haulm. For both diquat and paraquat the decision to invest in a manufacturing plant was based on market forecasts which relied heavily on the demand established by abandoning sodium arsenite. In paraquat's case, the impact of legislation was still more important, for it was the Malayan trip made by Jeater in 1959 that reopened interest in paraquat, and justified subsequent research. For both paraquat and diquat, prohibition of an existing herbicide, or the threat of prohibition allowed the new product a clear market, without the problem of displacing a rival.

The spread of both diquat and paraquat was affected by legislation in different countries requiring registration of agricultural chemicals. In Israel, for instance, paraquat could be registered for general weed killing only, for non-crop usage; in Belgium and Italy, aquatic weed control was a use particularly specified, whereas in Sweden all uses except aquatics were permitted. The requirements demanded in the trials by the various registration authorities differed, as the apparently conflicting results might suggest. The properties demanded by the registration authorities were very different from those of farmers, and concentrated largely on the need for careful control of residues and of any harmful side-effects from paraquat.

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A further influential factor in paraquat's development was the attitude adopted by those responsible for advising farmers on the use of new agricultural techniques. Although Boon had discussed with the Director of the British National Agricultural Advisory Service (NAAS) the use of paraquat for pasture renovation, the reaction of at least some NAAS advisers was not particularly favourable. In part this may be ascribed to the fact that many NAAS officers had come to look upon themselves as advisers in farm management rather than as agronomists advising on special problems in isolation. Consequently, a number was reluctant to recommend reseeding of difficult underproductive pastures (59). This attitude clearly differed from country to country. In Australia and New Zealand, enthusiastic development work was done by members of their Farm Advisory Services. A further factor influencing the rate of adoption of paraquat was the framing and interpretation of existing regulations governing grants. In Britain, for instance, the Ministry of Agriculture, Fisheries and Food awarded a grant of £5 per acre for any grass field over three years old which was ploughed and put into a new crop. Applications for this grant made by farmers who had used a paraquat and direct drilling technique in place of ploughing were rejected by the Ministry, at least initially (60).

The willingness of farmers to experiment with paraquat depended in some applications on the availability of suitable equipment. For inter-row weed control, machinery had to be developed with accurate spray control. For direct drilling a suitable drill had to be designed, and for application amid trees an applicator yielding adequate protection was required. All this machinery was designed at Plant Protection, where a machinery section was specially commissioned for this purpose. Its aims were quite simply to ensure that the development of applications for paraquat was not held back by lack of suitable equipment.

(59) Development Committee Minutes, May 31, 1962 and May 5, 1964.

(60) Development Committee Minutes, January 26, 1965.

7. Criteria of acceptance

From examining the development of paraquat, it has become clear that its success depended on its advantages being recognised not by one, but by many, protagonists. It is possible to enumerate these, and to examine the criteria which they used to judge the innovation. Table 3.4 shows in a simplified form the protagonist, the action they took and the criteria which they used to judge their success or failure.

It is at once clear that the criteria used to judge the usefulness of the bipyridyls differed radically according to the protagonist involved. To the Blackley chemist responsible for submitting K8483 and K8606 for test the criterion was simple, and completely chemical: was the compound in the Dyestuffs specimen collection a quaternary ammonium salt? To the biologist concerned with testing the submitted compound the criterion was as simple, but completely biological: did the compound exhibit biological activity? Other protagonists had more complex criteria. The chemists devising routes which could be used to manufacture the bipyridyls had to judge success against more complicated standards: the process must be chemically and technologically feasible; it must produce a chemical which was biologically as active as those tested in earlier trials; the process must be economically justified. The actual tests used to assess whether these standards had been met involved chemistry, engineering, biology and economics, with each discipline contributing to the end decision. Other protagonists, such as the registration authorities, had standards which were different yet again. The innovation, that is the successful development of the bipyridyls to the point where they were commercially successful, depended on each of these criteria being adequately met.

It is worth observing that not all these criteria were easily compatible. The machinery development department at Jealotts Hill, for instance,

wished to see the applicators it had developed produced by a wide range of manufacturers so that everything possible was done to promote paraquat sales. Any individual machinery manufacturer, however, was concerned with his profit, and not necessarily with making application machinery freely available. Similarly, use of paraquat as a herbicide before ploughing (stubble cleaning) made ploughing easier, and hence the task of those promoting ploughless farming more difficult.

Many potential conflicts were averted because of organisational liaison. Thus Boon was able to persuade colleagues in other ICI Divisions to undertake work on routes to the bipyridyls, without any of the conflict between supplier and buyer which might have occurred. General Chemicals Division of ICI was particularly active in its pursuit of a route to 4,4' - bipyridyl, and this must be ascribed not only to the activity of those in charge of the research, but also to the willingness of those sanctioning research and new plant to support the subsidiary company, Plant Protection Ltd. The work performed to analyse the toxicology of the bipyridyls was done at ICI's Industrial Hygiene Research Laboratory; the development of machinery was achieved within Plant Protection itself.

In all these examples, organisational rather than commercial justifications for undertaking work were prominent.

8. Discussion

The discovery and development of the bipyridyls, documented in the previous pages, were widely spread in time: the innovation may be traced back to the first testing of K.8483 in 1954; it is continuing today. Yet such a tracing of events, useful though it is as an illustration of the extended time period covered by the innovation, may be misleading if it suggests that the innovation may be attributed to any one invention. For

the initial recognition of useful properties would have been fruitless had subsequent effort not been devoted to investigating the observation. Without subsequent invention of new processes to manufacture diquat and paraquat, without the development of new machinery to apply the herbicides, and without the discovery of new markets for compounds with unique and unusual properties, the recognition would have been in vain. At this stage in the discussion, two points may be advanced. First, the complex interplay of events comprising the innovation suggests strongly that any division of the innovation into invention and subsequent development is difficult to achieve, and would be misleading were it accomplished. Much more illuminating is an account of innovation which emphasizes the number, and different types, of protagonists involved, and the various criteria by which they judged the project, or that part of it with which they were concerned. A second point which may be raised may be framed as a question: 'Why was so much effort devoted to supporting the first recognition?'. One answer to such a question may be sought in the personalities of those involved:'things happen because people make them happen' is one answer. But it may be argued that this answer merely draws attention to the question of why people determined to achieve a certain goal. In the bipyridyls' development, the confidence of Boon and his colleagues in the eventual success of the compounds discovered may indeed have been the most significant contribution to their success, since it justified, as it also occasioned, the intense effort devoted to solving the many problems. It is as important, however, to observe that this confidence was based on long experience of the herbicide business. It is hard to imagine that the bipyridyls, even had their herbicidal activity been observed, would have been developed in an organisation which knew less about the business area. The discoverer would then have been in no position to know the true value of what had been discovered, or to appreciate the

tests that should be used to assess the discovery. The original discovery of paraquat may in part be described as "accidental", and to the extent that biochemical activity was first observed in the course of a control experiment to test whether a detergent possessed biological activity there is some truth in this claim. The claim palls in significance with the importance of the organisation within which the chance observation was made. The knowledge of the market for herbicides, present and future, actual and potential, enabled the testers to rapidly assess the opportunity, and to be confident in their decision. The interplay between recognition and development, the need for not one but several inventions, and the involvement of many protagonists all reduce the importance of "accident", and increase that of being in a position to recognise opportunity.

Table 3.4

Those involved in bipyridyls discovery and development

Protagonist	Action	Criteria
Blackley chemist	Pick K8483 for test	Quaternary ammonium salt
PPL (i) biologist	Recognise activity	Action on test plants
(ii) chemist	Attempts to synthesize K8483	Reasonable yield; prospects of cost reduction
(iii) chemist	Devise analytic methods	Accuracy better than 1 ppm
(iv) chemist	Formulate K8483	Good storage; easy and successful use
(v) biologist	Test K8483 in the field	Action on test plants under differerent conditions; cost
Dyestuffs) H.O.C.) chemists G.C.)	Devise workable route	Chemically feasible, technologically achievable; economically attractive
Dyestuffs Board	Sanction capital investment	Profitable investment
G.C. Board	Sanction capital investment	Profitable investment; help subsidiary company
PPL (i) salesmen	Market 'Reglone' and 'Gramoxone'	Profit; bring about 'ploughless farming'?
(ii) engineers	Design application machinery	Aid to sales of bipyridyls

Registration authorities	(i) allow bipyridyls for specific uses (ii) prohibit competitive products	Toxicology of residues; safety to users; safety to consumers; safety to environment; biological efficiency of product
Machinery manufacturers	Manufacture application machinery under licence	Profit from sales of machinery
Farmers	Buy or refuse to buy bipyridyls	Efficiency, advantage, ease to experiment, compatibility
Advisers	Advise for or against bipyridyls	Farm management; agronomy

Chapter 4

The phthalocyanine pigments - their discovery and development

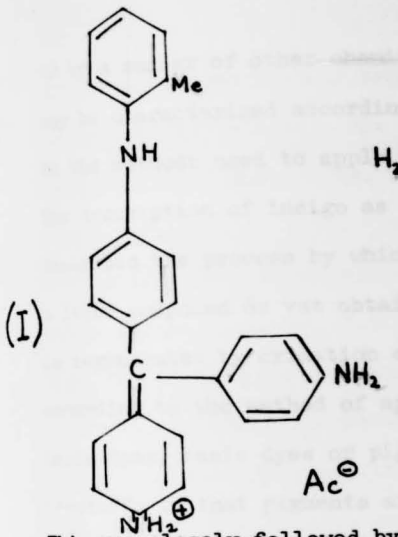
1. Introduction

To understand the significance of the phthalocyanine pigments, which were introduced into commercial use in 1935, it is important to know something of the background, history and technology of colouring agents. The paragraphs which follow set out to provide such information, and may conveniently be avoided by the reader with a knowledge of dyes and pigments, who could with advantage move to the section describing the discovery of phthalocyanine.

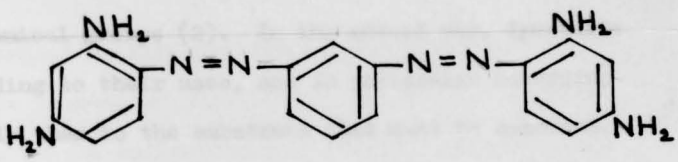
1.1 Early synthetic dyes

It has always been one of man's desires to colour materials, and natural colouring agents have long been used. Today, however, very few natural dyes are of any significance, and the overwhelming majority are derived by known chemical steps from raw materials, principally those obtained from coal tar.

Traditionally, the synthetic dye industry is traced back to the historic action of W.H. Perkin, who not only in 1856, synthesised a purple substance by the treatment of aniline with sulphuric acid and potassium dichromate, but also the next year established a factory for its manufacture. This was followed by sustained creative effort, during which many new dyes were discovered both in Britain and, more particularly, in Germany. Between 1856 and 1914, there were three main lines of development. First was the discovery of dyes based on triphenylmethane, of which Violet Imperial, discovered in 1860, is an example (I).

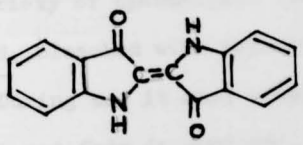


(I)



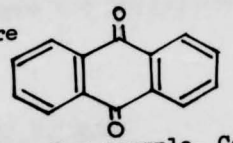
(II)

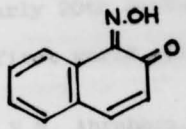
This was closely followed by the azo dyes, in which category falls the dyestuff known as 'Bismarck Brown', invented in 1863, whose structure is also shown (II). Third came the development of the so-called vat dyes, which was inaugurated by the discovery of synthetic indigo (III) in 1897 (1).



(III)

1.2 Classification of dyes, and the properties required

The previous examples show the ways by which dyes may be classified: that is, according to their chemical structure, or to their method of application. In the former way, dyes may be characterised as anthraquinone (containing the anthraquinone structure 

or one related to it), nitroso (such as, for example, Colour Index Mordant Green 4 1005) 

(1) P.D. Welham, 'The Early History of the Synthetic Dye Industry; The Chemical History', J. of the Society of Dyers and Colourists, 79, (1963), 98-105.

or by a number of other chemical groups (2). In the second way, dyestuffs may be characterised according to their uses, and in particular according to the methods used to apply them to the substrate that must be coloured. The description of indigo as a vat dye is an example of this convention, and described the process by which the dye is applied from an aqueous medium as a leuco compound or vat obtained by reduction of the original dye; the dye is regenerated by oxidation of the vat (3). Dyes may also be characterised according to the method of application into, for example, reactive dyes, basic dyes, basic dyes or pigments. This last category differs from other dyestuffs in that pigments are normally inert, stable coloured substances, insoluble in water, which are incorporated into an article during manufacture, either dispersed throughout it, or spread on its surface as a paint.

In general, a dyestuff is required to colour an article which may then be subjected to a variety of operations. During textile manufacture, a fibre may be washed, boiled, bleached with hypochlorite, or milled in acid or alkaline conditions. During use it must withstand washing, and the effects of perspiration; it must not fade in sunlight, and should not stain. Tests are designed to measure how effectively a dyestuff withstands these conditions. The effectiveness, as may be expected, differs between different classes of dyestuffs: triphenyl methane derivatives, for instance, combine brilliant shades with great susceptibility to light; sulphur dyes are distinguished by their wash fastness for cotton; vat dyes are recognised by clear bright shades (4).

1.3 The early 20th century development of dyes

In Britain, the early 20th century development of dyestuffs lagged behind that in Germany. The first world war, when German supplies were no longer

(2) See, for example, E.N. Abrahart, Dyes and their intermediates, (Oxford, 1968), 15-21.

(3) See, again, note 2, 34-39.

(4) C.J.T. Cronshaw, 'In quest of colour', Chemy. Ind. (1935), 547-552.

available, showed how far behind Britain had fallen, and stimulated a renewed British effort. The success of this effort, and the developments in dyestuffs in the 1920's, may be understood from an official government report published in 1930: "During recent years five outstanding developments in dyestuffs have taken place, namely, Naphthol Ice colours, Caledon Jade Green, Duranol colours, Indigosol products, and Soledon colours, and of these three are British discoveries covered by British patents" (5). The five dyestuffs mentioned are worth attention, since by considering them it is possible to discern where the greatest contemporary advances in dyestuffs were seen in 1930 to have occurred. Table 4.1 sets out some details of these dyestuffs.

Table 4.1 : Important dyestuffs developed in the 1920's

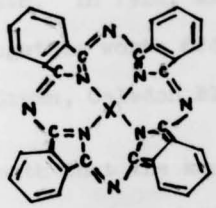
Dyestuff name	Chemical category	Application	Inventor
Naphthol Ice	Azo	Azo	Winther, Lasha and Zitscher in 1912.
Caledon Jade Green	Anthra-quinone	Vat	Davies, Fraser-Thompson & Thomas of Scottish Dyes in 1920.
Duranol	Anthr-quinone	Disperse	Baddiley & Shepherdson in 1923
Indigosol	Indigold	Vat	Bader & Sunder in 1921.
Soledon	Anthra-quinone	Vat	Scottish Dyes chemists

The three British developments were distinguished in different ways: Caledon Jade Green by great brilliance of shade and general fastness; Duranol by good light fastness for acetate fibres; Soledon by good light fastness for wool. Two of the three were vat dyes. The significance of these successes on the shaping of subsequent research targets will become clear when the discovery of phthalocyanine is examined.

(5) Report of the Dyestuffs Industry Development Committee to the Board of Trade, August, 1930.

2. Phthalocyanine

Phthalocyanine pigments have two claims to a position of importance among colouring agents. The first is that to the user of colouring agents, they represented an important advance on any available before their introduction in 1935. They are exceptionally fast to heat and to light, absolutely resistant to aqueous alkalis and acids, insoluble in most solvents, and possess high tinctorial value and brilliance of shade. They have found a multitude of uses: printing inks, artist colours, paints, lacquers, enamels, coated textiles, paper, linoleum and plastics have all been coloured with phthalocyanine pigments. Various types of phthalocyanine are used. The basic structure is now known to be:



X = metal atom.

Where the metal atom is copper, the phthalocyanine thus formed is particularly valuable, since it is close to an ideal blue, absorbing almost completely the red and yellow parts of the spectrum, and reflecting blue and green bands only. This property makes copper phthalocyanine particularly suited for the provision of blue for three-tone printing.

The second claim of the phthalocyanines is on the student of invention, for their discovery is often quoted as a prime example of the invention which occurs as a result of happy coincidence between chance event and acute observation, perhaps only matched by the accidental discovery of mauve by Perkin in 1856. It is therefore valuable to examine the early history of this industrially important chemical, remote in time though this may appear, to see

to what extent a chance event was responsible for the advent of a new colouring agent, and to examine the other factors which contributed to its development.

2.1 The discovery of phthalocyanine

The discovery of phthalocyanine which led to the elucidation of structure and to the development of colouring agents was made, in 1928, at the Grangemouth works of what is now the Dyestuffs Division of Imperial Chemical Industries Ltd. At the time, the works was the principal manufacturing site of Scottish Dyes Ltd., a company which had been formed to supply dyestuffs to its parent textile company, after the first world war had cut off German sources of dyes. The dyestuffs were manufactured at Carlisle (the original site), and at Grangemouth. In 1924, all dyestuffs and intermediates made at these two sites were together worth £24,000, and the principal products included Caledon Jade Green, Caledon Blue R.C., and phthalic anhydride (6).

It was at Grangemouth that the key discovery of phthalocyanine was made. Among the products manufactured at Grangemouth was phthalimide, and it was noticed that this contained impurities, which are said to have caused complaints from the Blackley dyestuffs works to which the phthalimide was supplied. The reason for these impurities was investigated.

The investigation followed a simple course. It had been observed that the impurities - the phthalimide was described as "of inferior quality and dark and green in colour" - occurred when there was rust in the pots. A series of experiments using rusted and cleaned pots was made, and the decision based on the report was quite straight forward: "Phthalimide ... is to be manufactured in enamelled pans", thus avoiding the danger of rusting (7).

(6) S.W. Dunworth, 'Early Years of Scottish Dyes at Carlisle and Grangemouth' private communication.

(7) P.F. Bangham, Dyestuffs Division Report R.1.1367, (1928).

The background to the investigation is clear from the first report made by S.W. Dunworth, the works analyst. This is worth quoting in some detail:

"The manufacture of phthalimide is carried out by passing ammonia gas from cylinders of anhydrous ammonia into molten phthalic anhydride. The reaction was carried out in an iron vessel which was not enamelled. It was found that several batches were contaminated with small quantities (up to 1%) of a greenish black impurity. The presence of this was attributed to the presence of impurity in the phthalic anhydride. This supposition proved to be very unlikely and further investigation of the process made it appear that the most probable cause of the formation of the green impurity was the presence of metallic iron in contact with the reaction mixture. There were also indications that the amount of green impurity was increased when the melt was stirred so that air had free access..." (8).

The conclusion drawn by Dunworth from his analysis of the impurity did much more, however, than to suggest how the reaction could be controlled to avoid forming it. Instead, Dunworth concluded:

"The blue* product found as an impurity in phthalimide made in an unenamelled iron pan is a new vat dyestuff containing about 12% of iron and 17% of nitrogen. The iron appears to be an essential constituent of the dyestuff. An empirical formula such as

$$Fe(C_7H_4N.CO.NH)_3 \qquad \begin{matrix}(Fe\ 11.4\%)\\(N\ 17.1\%)\end{matrix}$$

might represent this substance" (9).

Also in May 1928 (the application date is May 16), a patent was filed in the names of Dunworth's colleagues A.G. Dandridge, H.A.E. Drescher, and

(8) S.W. Dunworth, 'The investigation of a blue product obtained in the manufacture of phthalimide', May 1928.

(9) S.W. Dunworth, (see above, note 8).

* An indication of its shade can be gained from the fact that Dunworth had originally written "green", which he then crossed out and substituted "blue".

J. Thomas relating to "Improvements in and relating to the manufacture and use of colouring materials" in which it was claimed that" ... we have found what is apparently a new class of dyestuffs can be prepared by passing ammonia into phthalic anhydride in the presence of a suitable metal..." (10). The patent, and Dunworth's reported analysis, mark the point where what was seen as an impurity began the transformation to a colouring agent. The discovery, as described, seems a simple example of chance invention.

It is worth pausing, however, to consider whether this chance observation might have been made before, and if so why the invention was not made earlier. It is known that the observation of what is now known to be a phthalocyanine had been made before . In 1907, Braun and Tcherniac reported that molten o-cyanobenzamide contained small quantities of a substance of dark blue colour, which proved insoluble in alcohol (11). In 1927, de Diesbach and von der Weid had published reports of experiments which had resulted in the formation of a blue compound. In the first of these, o-dibromobenzene, copper cyanide and pyridine were heated together to yield an indigo blue product, insoluble in ether and stable to heat. A second experiment, involving the heating of phthalonitrile, copper bromine and pyridine at reflux temperature, yielded the same substance, to which de Diesbach and von der Weid ascribed the formula $C_{26}H_{18}N_6Cu$. Their account ends with the statement, "Retenus par d'autres travaux, nous serions heureux si des collègues plus specialisés dans l'étude des sels complexes voulaient bien eclaircir la constitution et les causes de la stabilité de ces nouveaux produits" (12).

In addition to these two reports which appeared before the work of Dunworth and Drescher (but of which the Grangemouth workers had no knowledge),

(10) B.P. 322,169.

(11) A. Braun and J. Tcherniac, 'Uber die Producte der Einwirkung von Acetanhydrid auf Phthalamid', Chemische Berichte, 40, (1907), 2709-14.

(12) H. de Diesbach and E. von der Weid, 'Quelques sels complexes des o-dinitriles avec le cuivre et la pyridine', Helv.Chem.Act., 10 (1927), 886-888.

there are other accounts, subsequently published, which suggest that phthalocyanines had been formed before. The announcement of the phthalocyanine pigments' commercial production in 1935, for instance, was the occasion for a report of the accidental discovery, in Manchester University in 1907, of the nickel member of the phthalocyanine group. The author of the report, H.H. Gray, was preparing indigo from phthalic acid when his nickel spatula dropped into the flask. At the end of the experiment, the spatula was found to be covered in a dark blue substance, which "a few experiments showed ... was insoluble in all the usual solvents", and the work was stopped (13). There must have been many opportunities for observing phthalocyanine, for it can be easily formed by merely heating phthalonitrile in a glass tube, and phthalonitrile had been known to and used by chemists since 1890. It has even been claimed that phthalocyanine's "right to exist is almost declamatory!" (14).

It is important therefore to examine the circumstances which were different in the recognition of the blue compound at Grangemouth, and distinguished the successful innovation from the observations made previously, which proved sterile.

There were two features which distinguished the recognition by Scottish Dyes of the significance of phthalocyanine. First, the observation was made within a dyestuffs works, where the importance of a new colouring agent was well known. This circumstance at once distinguishes the observation made at Grangemouth from those made by Tcherniac and Braun and by de Diesbach and von der Weid, all of whom were not particularly concerned with dyestuffs. It does not however distinguish the discovery from that made by Gray in 1907, for he was working in a laboratory concerned with dyestuffs, and considered explicitly whether the product of his experimental accident could be the

(13) H.H. Gray, correspondence, Chemy. Ind., (1935), 469.

(14) C.J.T. Cronshaw, 'Phthalocyanines', Endeavour, 1 (1942), 79.

basis for a new blue dyestuff. To explain why Gray failed, it is necessary to consider the second distinguishing feature which characterised the Grangemouth discovery. This is the analysis of the phthalocyanine. The analysis made by Dunworth, which he reported in May 1928, went beyond Gray's report that phthalocyanine was insoluble in most solvents. And in one important respect Dunworth went further than de Diesbach and von der Weid, for in addition to discovering the empirical formula, he ascertained that phthalocyanine could be used as a vat dyestuff, with soap fastness. The patent filed by Dunworth's colleagues Dandridge, Drescher and Thomas gave examples of the iron, copper and nickel phthalocyanines, which shows that the initial observation had been investigated more thoroughly than had been done by earlier observers. In June 1929, Drescher published as an appendix to Dunworth's analysis of the impurity a report on ways of synthesising the product in some quantity. The route eventually adopted was based on passing ammonia through phthalic anhydride or phthalimide in the presence of a sufficiently active metal or metallic salt. Various dibasic acids, including succinimide, were tried, but only phthalimide yielded the blue-green product; of the metals tried - iron, zinc and copper - only iron gave an appreciable yield; of the various bases tried, ammonia was the only one to work well, though aniline also gave a small yield. In all, Drescher experimented with some 27 possible processes, and with those that yielded the impurity he tested the product as a dyestuff with cotton, rayon and wool (15).

The combination of recognition of the possible use for a new pigment, and of the analysis and investigation started by Dunworth and Drescher, meant that the chance observation previously made became the starting point of an innovation.

(15) H.A.E.Drescher, Dyestuffs Division Report, B.1879, (1929).

2.2 The organisation in which phthalocyanine was developed

Dunworth's analysis did not go any further than that performed by the Swiss workers. Clearly, his identification of the usefulness of the compound was crucial, but his work still left the actual structure of the molecule unelucidated. The elucidation of the structure was to be performed elsewhere.

To understand how this came about, it is necessary to appreciate the organisation within which the discovery was made. Scottish Dyes, which employed Drescher and Dunworth, became part of British Dyestuffs Corporation soon after the initial discovery at Grangemouth of the phthalocyanine. In 1926, British Dyestuffs Corporation had been one of the four founding firms which merged to form Imperial Chemical Industries. The discovery made at Grangemouth was thus developed by a larger organisation than that in which the first observation was made.

The invention might have been lost within the larger organisation of the British Dyestuffs Corporation (soon to be known as the Dyestuffs Division of ICI) had there not been an appropriate institution or group to receive it. Such a group existed in the Dyestuffs Group Research Committee.

This body had its first meeting on May 14, 1929. It comprised various representatives of ICI Dyestuffs Division, and was chaired by the chairman of Dyestuffs Division, C.J.T. Cronshaw. This Committee included, in addition to various Dyestuffs Division employees, Professor J.F. Thorpe, Professor of Organic Science at the Royal College of Science, and Professor R. Robinson and Professor I.M. Heilbron, both Professors of Organic Chemistry at Liverpool University. The purpose of the Committee, which met monthly, was to ensure that Dyestuffs Division benefitted from advances in academic chemistry, and to maintain contact between universities and industry for their mutual benefit.

At the first meeting of the Committee, Cronshaw listed the problems encountered by Dyestuffs Divisions: the azo section had physical problems, and needed components for blue dyes; the aniline section was characterised by empirical manufacture with low yields; anthraquinone and vat dyes lacked a good red, and some dark shades (16).

The Committee did much more, however, than concern itself with existing problems and its importance within Dyestuffs Division may be inferred from the fact that Cronshaw though sufficiently highly of it to act as its chairman. The Committee's justification was stated at a later meeting by Cronshaw, speaking as both Committee and Dyestuffs Division chairman, when he said: "it was intended to pin our faith in future to the exploitation of our own inventions and discoveries, and only to imitate competition products when commercial consideration made it imperative" (17). The Grangemouth discovery was thus received within a sympathetic and even enthusiastic environment (18).

It might have proved difficult to effect the transfer from Scottish Dyes to Dyestuffs Division, and to translate the invention from Grangemouth to Blackley, the organisational and research centre of Dyestuffs Division, had it not been for the personal interest in phthalocyanine shown by Dr. J. Thomas, the Managing Director of Scottish Dyes. Thomas was an able chemist, who combined his post as Managing Director of Scottish Dyes with continued interest in science.

(16) Minutes of Discussion, Dyestuffs Group Research Committee (DGRC), 14th May, 1929.

(17) DGRC Minutes, 14th May, 1929.

(18) DGRC Minutes, 1st October, 1929.

It is indicative of the enquiring atmosphere of the Dyestuffs Group Research Committee that it was at one of their meetings that Dr. Michels of Amsterdam University gave an account of his work on high pressure physical chemistry, and the practical bearing of this on industrial chemistry was discussed. Among those present was M.W. Perrin, who just under two years later was to be prominent among those responsible for the polymerisation of ethylene.

This may be inferred from the fact that his name appears on the first patent, with those of Drescher and Dandridge, and also from his academic record: he, alone among the men responsible for the early development of phthalocyanine, possessed a second degree. He had earlier been one of the discoverers of Caledon Jade Green, as an anthraquinone vat dyestuff.

Thomas moved from Grangemouth to Blackley in 1929, and by so moving, ensured that the invention in whose birth he had participated would be nurtured in the new environment of Blackley. Thomas drew Cronshaw's attention to the Grangemouth discovery by sending him a copy of Drescher's report on synthetic routes. At the first meeting of the Dyestuffs Group Research Committee, Thomas drew its attention "to a blue pigment which he had obtained by heating phthalic anhydride with ammonia (or ammonium sulphide) and iron", and it was agreed that Professor Thorpe would investigate its constitution. Within the committee, Thomas maintained his interest: at the fourth meeting, Thorpe and Thomas were made jointly responsible for ensuring that the provisional patent application was as wide as possible (19). There is evidence showing Thomas's continued interest: a chemist who was involved in the development work to transform the discovery into a colouring agent with suitable physical properties recalls that he was first introduced to the phthalocyanines when Drs. Cronshaw and Thomas brought samples to the laboratory in which he was working (20). Thomas also ranked, with Thorpe and Linstead, among the inventors of the second route to phthalocyanine compounds, via o-cyanobenzamide. Thomas's championship of the invention was particularly important since it maintained the impetus that had been started at Grangemouth, but which might have ended with the death of Drescher, who was killed in a motor cycle accident on August 12, 1929.

(19) DGRC Minutes, 1st October, 1929.

(20) A.C. Stewart, private communication.

Drescher performed much of the early work investigating phthalocyanine, particularly routes for its synthesis. He had a reputation as a most able chemist, with numerous patents on anthroquinone topics to his name. His death removed an active research worker, whose enthusiasm might have been expected to ensure that the project received attention.

2.3 Initial development of phthalocyanine

The continued survival of the invention made at Grangemouth thus depended on the combination of a sympathetic organisation, and the committed support of a senior member of that organisation. The importance of these factors become apparent when the problems encountered in phthalocyanine's initial development are considered.

The initial problem was associated with the identification of pthalocyanine as a vat dyestuff. At Grangemouth, the invention had been described, and treated, as a vat dyestuff. Dunworth, for instance, tested it only by vatting. The patent claims: "The dyestuff ... forms a practically colourless vat. When cotton or other fibres are impregnated with this solution and subsequently exposed to the air, they are dyed blue shades of good fastness". Thomas's first report of the discovery to the Dyestuffs Group Research Committee included the phrase: "The pigment contains iron, and behaves exactly like a vat dye" (21). Such an emphasis on vat dyestuffs is in no way surprising, when one considers the developments which had previously occurred in the dyestuffs industry, and is even more understandable when one considers that the two previous discoveries made at Scottish Dyes were both vat dyestuffs.

The result of this identification of phthalocyanine as a vat dyestuff may be traced through various meetings of the Dyestuffs Group Research

(21) B.P. 322,169; DGRC Minutes 14th May, 1929.

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(21) B.P. 322,169; DGRC Minutes 14th May, 1929.

Committee. At the fifth meeting, in November 1929, it was reported that: "It is difficult to obtain a good yield of the iron compound from phthalimide, and the product is not homogeneous. Only 11 per cent of it has vatting properties". At the next meeting, in December, it was reported that a vat dye was in fact obtainable; in February 1930, it was reported that the yield of the dye on reoxidation with air was unsatisfactory, and in March it was decided that since the vat dyestuff was too sensitive and fugitive for practical purposes, attention should now concentrate on the pigment, which could quite easily be purified (22). Between May 1929, when the phthalocyanine was first discussed in the Dyestuffs Group Research Committee, and March 1930 the target for the discovery thus changed from being a vat dyestuff, to being a pigment. The problems presented by this change were considerable: a pigment could be used to colour a manmade fibre like rayon (the only synthetic fibre of any importance then in existence) simply by incorporating it in the viscose bath before extrusion through spinnerets, but it could not be used to colour natural fibres by conventional dyeing methods. For a substance like the phthalocyanines, completely insoluble in water, the problem was formidable.

In addition to the problems presented by the change from a dyestuff to a pigment, there remained other problems. The structure of the compound had to be elucidated; manufacturing routes had to be devised, to investigate other methods of making the compound and others closely related to it. The compound obtained by various manufacturing routes had to be transformed into suitable physical form for use as a colouring agent; the colouring of different substrates had to be investigated. Each of these problems was complex, and their solution demanded contributions from a range of individuals and institutions.

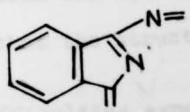
(22) DGRC Minutes 12th November, 1929; 10 December, 1929; 2 February, 1930; and 11th March, 1930.

Two observations may be made: first, the chance discovery so alertly pursued at Grangemouth might well have foundered without the strength of the support it received from Blackley, particularly when it was discovered that its uses were restricted to those as a pigment; second, the way in which these inter-related problems were tackled was to have a marked influence on the speed with which the invention was transformed into a commercial product.

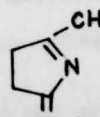
3. Analysis of phthalocyanine

The first problem to be tackled was the elucidation of phthalocyanine's structure, and this was to show both the magnitude of the problems that remained after the initial invention, and also the consequence of subordinating work on other problems to this aim. At the request of the Dyestuffs Group Research Committee, Professor Thorpe undertook to study the compound's structure, and this work was soon taken on by R.P. Linstead at Imperial College, "as it appeared that the substance might prove of academic interest" (23). Linstead and Thorpe reported their findings to the Committee either verbally or in writing, and the Committee played an active part in discussing their conclusions.

The announcement to the outside world of the new pigment was made by Linstead at the 1933 meeting of the British Association. Linstead, who had given the pigment the name "phthalocyanine", showed that its fundamental unit (I) resembeled that of porphyrin (II), the basis for the naturally occurring pigments of the chlorophyll and haemin group (24).



(I)



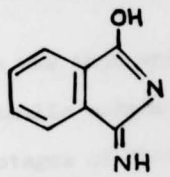
(II)

(23) R.P. Linstead, 'Phthalocyanines. Part I. A new type of synthetic colouring matters', J.Chem.Soc., (1934) 1016 and DGRC Minutes 8th May 1931.

(24) R.P. Linstead, 'The phthalocyanines: a new class of synthetic colours', Report of British Association for the Advancement of Science (1933), 465-466.

The actual analytic techniques used, and the detailed evidence to support the final deduction of the structure of phthalocyanine, were published in 1933 in a series of papers by Linstead and his co-workers, A.R. Lowe and C.E. Dent, and their analysis based on organic chemistry was confirmed the next year by J.M. Robertson's X-ray study of both the metal-free phthalocyanine and three metal derivatives (25).

The time that elapsed between the work being undertaken by Linstead and his co-workers, two research students, and his final elucidation of the structure may be explained by the difficulty of his task. The great stability and resistance to solvents displayed by phthalocyanines made them difficult to characterise. They could not be crystallised from the usual media nor sublimed in high vacuo. Nor was it possible to determine their homogeneity by ascertaining melting points, since they only decomposed without melting at a dull red heat. Difficulties in obtaining pure samples led to the belief that the basic unit of phthalocyanine contained oxygen. In May 1930 Linstead suggested with some conviction that the basic unit was:



which linked up by a condensation reaction to form chains and rings. In June 1931, the basic structure of the manganese compound was "confirmed" as R_6OMg, where R = $C_8H_4N_2$; in February 1932, Linstead still believed that the oxygen atom was an essential part of the structure (26). It was not until 1933 that the structure was successfully identified.

The difficulties experienced by Linstead and his colleagues show the very considerable problems encountered by those wishing to elucidate

(25) R.P. Linstead et al., 'Phthalocyanines, Parts 1-6', J. Chem. Soc., (1934), 1016, 1017, 1022, 1027, 1031, 1033 and J.M. Robertson, 'An X-ray study of the structure of phthalocyanines', J.Chem.Soc., (1935), 615.

(26) DGRC Minutes 8th April, 1930 and 4th July, 1930.

phthalocyanine's structure. It took the concentrated effor of Linstead, aided by at least two research students, from 1930 to 1933 to examine the structure of phthalocyanine and to deduce its composition. Confirmation of the structure required X-ray crystallography. When this is considered, it is not surprising that the earlier discoverers of phthalocyanine should have been unable to identify it analytically. The successful innovation would have been held back without the technical expertise required for phthalocyanine's identification, just as de Diesbach and von der Weid had been unable to advance in 1927.

3.1 Interaction between analysis and the devising of manufacturing routes:

In the course of deducing phthalocyanine's structure, Linstead and his colleagues had to produce quantities of phthalocyanine. It was natural, therefore, for them to consider and devise new ways of synthesising phthalocyanine compounds. The devising of these routes, and some of the implications, may be traced from the patents which were obtained to describe them. These are summarised in Table 4.2, and shown in Figure 4.1.

The first route was that which led to the original discovery: ammonia was reacted with phthalic anhydride or phthalimide in the presence of a metal. The disadvantages of this route were apparent. It involved the reaction between a molten substance, the solid metal, and a gas (ammonia), and control to give a good yield was difficult. In November 1929 Thorpe reported that a new route had been devised, using o-cyanobenzamide, which when heated with a suitable metal yielded the metal phthalocyanine.

The consequences of the change in manufacturing route, although not fully appreciated at the time, were considerable. The original route had produced three kinds of phthalocyanine, the iron, nickel and copper compounds. The patent specification gave an analysis of the copper phthalocyanine, showing that it contained 10.27 per cent copper, and an example of the use of copper phthalocyanine as a blue dyestuff was also cited (27).

(27) B.P. 322,169.

The next patent, describing the production of phthalocyanine compounds by a route based on o-cyanobenzamide, was filed by Thorpe, Linstead and Thomas in 1931. The phthalocyanine compounds considered had altered. The metals that were mentioned as being particularly suitable for the production of phthalocyanine were iron, magnesium, nickel, cobalt, lead and antimony. Copper was mentioned only as one of a group comprising magnesium, copper, cerium, tin, lead, antimony, bismuth, chromium, molybdenum, tungsten, manganese, iron, cobalt and nickel. Magnesium was claimed to be particularly interesting, since it lost the magnesium on treatment, with a strong acid to give the metal-free phthalocyanine (28). A further patent, almost exactly comtemporaneous with that describing the process based on o-cyanobenzamide, extended the original patent to cover magnesium and antimony. Both these were of interest as they would yield the metal-free compound (29). Thus the work conducted in 1930 and 1931 drew attention away from the copper compound which had been the subject of earlier workers' attention, and which was eventually to prove the basis of a new colouring agent of great industrial importance.

The following-up of the manufacturing route to phthalocyanine compounds from o-cyanobenzamide resulted in little attention being paid to the copper compounds. In January 1931 it was reported that good yields were gained with iron, nickel and magnesium and their oxides, while poor yields were obtained from copper and copper compounds. In February, 1931, Linstead reported that the most useful metals to be used in the process based on o-cyanobenzamide were iron, nickel, cobalt, magnesium and antimony (30). These were the basis for the metals mentioned in the subsequent patent.

(28) B.P. 389,842.

(29) B.P. 390,149.

(30) DGRC Minutes, 13 February, 1931.

The concentration on those metals which produced phthalocyanine compounds most readily with o-cyanobenzamide continued in 1932. In February,1932, Linstead considered the intermediate phthalonitrile but it appears that this was temporarily abandoned "when it gave no pigments with the reagents (Mg, MgO, Fe, etc.) which gave an immediate reaction with cyanobenzamide" (31). It is perhaps surprising that Linstead's consideration of phthalonitrile did not lead him to consider the work of de Diesbach and von der Weid, reported in the British chemical journals in 1928, which showed among other experiments that phthalonitrile and pyridine, when heated with copper cyanide, would yield a blue product which may now be identified as a phthalocyanine. It is clear that Professor Heilbron and Dr. Irving drew Linstead's attention to the de Diesbach reference in September 1932 through the Dyestuffs Group Research Committee, and it was only later in 1932 that Linstead returned to investigate phthalonitrile (32).

The attention paid to de Diesbach and von der Weid's paper had the important effect of renewing interest in the copper phthalocyanine. Whereas phthalocyanines produced via o-cyanobenzamide were best made with magnesium the route via phthalonitrile favoured copper phthalocyanine. The patent covering the process (application date November 16, 1932) initially raised the copper phthalocyanine to a position of importance; the complete specification stressed the copper compound, and stated that: " a particularly satisfactory pigment is that obtainable from phthalonitrile and copper (33).

It thus took until November 1932 for the ICI workers to reinvestigate the copper phthalocyanine, even though it was one which Drescher had synthesised early in 1928, and which, it may now be seen, was that synthesised by de Diesbach and von der Weid in 1927.

(31) R.P. Linstead, Dyestuffs Division Report X.204 (1932).

(32) R.P. Linstead and A.R. Lowe, Dyestuffs Division Report X.261 (1932).

(33) B.P. 410,814.

There seems some doubt in the minds of Linstead and his co-workers on the significance of the earlier disclosure of de Diesbach. Linstead and Lowe in the published work on the phthalonitrile route refer only to de Diesbach's report of the reaction based on o-dibromobenzene, and in March 1934 in an ICI meeting it was minuted, apparently in ignorance of the fact that the full experiments performed by de Diesbach included a synthesis involving phthalonitrile, that "Heilbron and Irving drew the inference that phthalonitrile was convertible into phthalocyanine" (34). By the time the full patent was published in May 1934 the situation had been clarified, for the full patent refers to all the experimental work of de Diesbach and von der Weid, and limits the patent claim to avoid any conflict with their route based on phthalonitrile, cuprous bromide and pyridine.

The length of time for the full report of de Diesbach and von der Weid's work to be appreciated is itself indicative of the absence of concentrated effort on the copper phthalocyanine. Throughout it appears that the choice of phthalocyanine compound to investigate was dictated mainly by the synthetic preparation chosen, rather than the desire for specific compounds leading to the choice of synthetic preparation most favouring the chosen compound. The result of this was to detract attention from the copper phthalocyanine, whose properties were the most suited for the use of compound as a pigment, and whose properties had been noted, in many ways accurately, by Dunworth and Drescher in 1928.

It is not altogether clear when attention became concentrated on the copper phthalocyanine. As late as June 1934, Linstead, reporting to the D.G.R.C., concluded that the metal phthalocyanines to be considered in detail should be those containing sodium, magnesium, beryllium, copper, iron or nickel. Copper, while included, was not given any prominence.

(34) W.A. Silvester, Dyestuffs Division Report H. 1427 (1935).

Others, within ICI, however, seem to have identified the importance of the copper compound some time before this. A research programme started in March 1933 to make phthalocyanine from phthalonitrile named only one metal phthalocyanine, that being the copper compound. By December 1934 attention had been concentrated sufficiently on the copper compound to justify a crash programme to produce phthalonitrile. A report was published on January 10, 1935, even though all parameters had not been investigated, because "phthalonitrile in bulk was required for experimental trials in the manufacture of Monolite Fast Blue B (copper phthalocyanine)". The decision to manufacture and sell copper phthalocyanine was made on June 4, 1935 (35).

Elsewhere, others had also recognised the attractiveness of copper phthalocyanine. The German chemical firm, I.G. Farben, who produced copper phthalocyanine not significantly (if at all) later than I.C.I., started work on the copper phthalocyanine in the last quarter of 1933. The unusual properties of the copper compound - its great stability, and resistance to heat, acid and alkali - and the structure of the phthalocyanines had been disclosed by Linstead, and quite widely reported in the chemical press in September 1933. It does not seem unreasonable to surmise that German workers recognised the significance of de Diesbach and von der Weid's earlier disclosure. The phthalocyanine structure and formula had already been disclosed in the 1932 patent, and could be compared without difficulty with de Diesbach and von der Weid's work. I.G. Farben was in a position to recognise that a compound with exciting properties, patented by an international rival, could be made cheaply by a route which had already been disclosed. That this route formed the copper phthalocyanine undoubtedly helped them concentrate their efforts most effectively (36).

(35) I.D.G. 1148, 4 June 1935.

(36) W.A. Silvester (see above, note 34).

4. Manufacturing routes to phthalocyanine compounds

The significance of the lack of attention paid to the copper compound, and of the devising of routes for phthalocyanine as part of the analytic work, becomes clear when the actual manufacturing processes used are considered. Neither of the processes adopted, by ICI in the U.K. and by I.G. Farben in Germany respectively, was based on the patents taken out by ICI between 1928 and 1932. The process chosen by each differed, as each firm was in a different patent position. In Germany I.G. Farben operated a process that was a direct development of the observations of de Diesbach and von der Weid, and was based on the reaction of phthalonitrile, whose process was developed so that a continuous baking of phthalonitrile and cuprous chloride was possible (37). In the U.K., the initial process operated was based on heating phthalonitrile in trays with copper bronze or cuprous chloride, and thus followed the patent of Heilbron, Irving, Linstead and Thorpe of 1932. It is significant that, because the implications of de Diesbach and von der Weid's disclosure had not been fully appreciated when the patent was filed in 1932, it was necessary in the full specification to specifically exclude their process, to avoid the patent being opposed by the British Patent Office Examiner as already covered by the prior art (38). ICI's situation was thus that although it had patented its own process, it was unable to prevent any other manufacturer from using de Diesbach and von der Weid's process, or from developing it in ways not covered by ICI's patent.

In these circumstances, it was clearly beneficial to ICI to establish an improved and patented process, particularly designed for the copper compound. A completely new route was devised, in which phthalocyanine was produced by heating phthalic anhydride, urea and a substance which could yield copper. The reaction involved was not fully understood.

(37) B.I.O.S. 960, 33,36.

(38) See B.P. 410,814.

It may be represented by the equation:

$$4\ C_6H_4(CO)_2O + 4\ CO(NH_2)_2 + Cu \longrightarrow (C_8H_4N_2)_4\ Cu + 4\ CO_2 + 8\ H_2O$$

yet it was found to be impossible to use an amount of urea which corresponded to this equation, and the reaction was successful only when an excess of urea was used. The process was discovered by an ICI chemist, M. Wyler, in 1935, and was developed for production purposes (39).

The process was attractive mainly on account of the low cost of phthalic anhydride and the lower temperature required. In the initial report of the research, Wyler estimated that the urea process would produce phthalocyanine at a very considerable cost advantage over that based on phthalonitrile. The advantages stressed were "preparation from cheap intermediates immediately available in large supplies, instead of the necessity to lay down special plant in order to prepare special intermediates, and the ease of preparation". Much cheaper raw materials were used, so that the total cost was estimated to be reduced by over 60 per cent (40). The yield was lower than that of the phthalonitrile process, but was subsequently improved when it was observed that the materials of construction affected yield. Subsequent enquiry by Blackley chemists identified molybdenum compounds as powerful catalysts, which allowed the yield to be raised, or the temperature further reduced (41). Manufacture of copper phthalocyanine began, at Ludwigshafen in Germany by I.G. Farben, and at Manchester by ICI, in 1935.

In studying the way that work was conducted on manufacturing routes, it is hard not to feel that at least until late in 1932 the project lacked clear overall direction. The patenting of phthalocyanines was later characterised as having "proceeded by jerks" (42); there seems to have been inadequate collaboration to ensure that statements in journals of the

(39) M.F.S. Choate and M. Wyler, Dyestuffs Division Report B.1879 (1936).

(40) See above, note 39.

(41) A.R. Lowe, M. Wyler and W.E. Humphreys, Dyestuffs Division Report K.384 (1936)

(42) W.A. Silvester (see above, note 34).

academic work were already covered by patent; the significance of previous literature reports, in particular that of de Diesbach and von der Weid, does not seem to have been appreciated.

5. The importance of the D.G.R.C.

In general, attention seems to have been directed more to the academic questions associated with a new chromophore of remarkable properties than to the problem of whether a compound first made in 1928, or one derived from it, was worth producing, and if so what would be the best means to achieve this. In addition to the specific question of which pthalocyanine compound to investigate, several reasons for the lack of overall direction may be identified. The first is the character of the Dyestuffs Group Research Committee, which first took up the Grangemouth discovery, and to which Linstead reported his work. Its composition, with a considerable number of academic members, emphasised the more academically interesting question of the phthalocyanine compounds' composition, rather than the problems associated with commercial success. In this context, it is interesting to contrast the composition and actions of the Dyestuffs Group Research Committee with the committee which played a role of comparable importance in the development of bipyridyls twenty five years later - the Development Committee of Plant Protection. The contrast in names - between research and development - characterises the differences. The former, with its considerable number of academic members, was designed as an observation post, whose members would be able to note advances in chemistry which threatened the existing positions of the Dyestuffs Group, or which provided opportunity for these positions to be strengthened. If their activities are considered as a screening process, it was both wide mesh and widely targeted. As such, it was successful: the meeting with Michels would, by itself, justify all the activities of the Committee.

Its weakness, however, arose when the broad screen had indicated a use, and detailed development was required. The minutes of the D.G.R.C. provide little indication that the varied and interlocking problems of development were being systematically tackled. Indeed, it would be surprising had this occurred, for the composition of the Committee did not lead itself to this sort of detailed analysis. Whereas Plant Protection's Development Committee contained representatives of numerous functions and departments - research, development, marketing, patents, and production were all represented - the D.G.R.C. was predominantly staffed by men drawn from research activities.

The difference between the development of the bipyridyls and the phthalocyanines emerges particularly clearly from examining the analytic work that occurred in each project. The bipyridyl analysis was related closely to the overall aim of gaining acceptance of a herbicide in particular applications. Analytic techniques to identify the presence of diquat in minute quantities, for instance, were developed for particular substrates in which diquat might exist. Thus the techniques were refined to abstract and quantify diquat present in potatoes, the crop against whose haulm diquat was to be used. In contrast, analytic work to discover phthalocyanine's structure, as has been seen, was pursued with such vigour that other parts of the programme were delayed. The analytic tasks clearly differed greatly: for phthalocyanine, an unknown structure had to be elucidated, whereas for bipyridyls techniques had to be evolved to identify and quantify the presence of very small amounts of a known material. The significant contrast is not that between the type of analysis, but that between the relative contribution of analysis to the two projects.

The closest parallel within Dyestuffs Division to Plant Protection's Development Committee was probably the Interdepartmental Conference which

met to consider proposals to manufacture and sell products. In January 1937, for example, the decision was made to add manufacture and sell Monastral Blue GS Paste and Powder, based on the metal-free phthalocyanine pigment. This was considered by the Interdepartmental Conference, which received comments from Operating Department (on costs), from the Patent Section, from Research Department on forecast changes in technology, and from the Marketing Section on the uses that had been developed, and on the expected action of I.G Farben (43). When the decision to invest, produce and sell was made, care was taken to ensure that the total situation was assessed. The problems arose earlier, where the D.G.R.C. was not succeeded by a comparable development committee, whose task should have been to replace the broad, wide-mesh screen with ones of diminishing mesh size that were increasingly targeted.

6. Problems of obtaining phthalocyanine in the correct physical form:

A second explanation of the time that elapsed before the copper phthalocyanine was made the centre of development work may be found in the need to produce the compound in a form suitable for use as a pigment. In their pure and highly crystalline form phthalocyanine compounds are of little value as pigments. Their use as colouring agents therefore depended on converting them to a suitable physical form. The importance of obtaining phthalocyanines in a suitable physical form can be inferred from comparison of the early report on copper phthalocyanine, before much work had been devoted to transforming it to a suitable pigmentary form, and the report reached in 1935, when the decision was made to manufacture and sell the copper phthalocyanine. In the former, copper phthalocyanine was characterised as very fast to light, acid, alkalis and intercellulose solvents, but as dull in shade.

(43) I.D.C. 1337 S (1937).

The latter described copper phthalocyanine as: "a blue pigment dyestuff possessing all-round fastness properties ... and ... outstanding properties", and concluded that advent of copper phthalocyanine meant that "the demand for a blue pigment dyestuff instead of being most poorly served is now better served than that for any other colour" (44).

The existing pigments, shown in Table43, were clearly inferior. Prussian Blue possessed only half the tinctorial strength of copper phthalocyanine, and ultramarine less than one twentieth.

Table 4.3 : Fastness characteristics of blue pigments

	Light	Acid	Alkali	Solvents	Heat
Copper phthalocyanine	E	E	E	E	E
Iron Blue	E	E	P	E	G
Ultramarine Blue	E	P	G	E	G
Peacock Blue	P	P	P	F	P

E = excellent G = good
F = fair P = poor

Source: see note 44

The examinations differed in that the earlier screen examined not only the copper, but also the iron, phthalocyanine, but too much should not be made of this. The iron phthalocyanine, as reported in the original patent for example, was of comparable intensity to the copper phthalocyanine. The striking difference between the two conclusions is to be found in the fact that by 1935 methods of preparing the most suitable physical forms had been decided.

For although some work had been done in 1931 and 1932 to devise grinding techniques to reduce crude phthalocyanine to a suitable physical form, it did not prove successful. The process used - sand comminution - produced

(44) See Above, note 35.

the pigment in such a form that on drying it was even harder and less satisfactory than before (45). It was not until late in 1934 that this problem was tackled systematically, and a process developed to produce a powder which could be incorporated in oils. The need not only to obtain the correct compound, but also to obtain this compound in the correct physical form, complicated the screening process. It was not possible to conclude after producing a compound that unsatisfactory colouring properties in a test indicated definitely that the compound was unsuitable.

The importance of devising a process to produce the chosen phthalocyanine in suitable form was not confined to the need to identify the correct compound. There were important economic considerations as well. In the preferred process used, the conversion of crude copper phthalocyanine to a dry, pure powder added nearly 90 per cent to the original cost of producing copper phthalocyanine. That this problem remained unattended until 1934 is an indication of the extent to which questions of industrial and commercial significance remained unposed, and hence unanswered (46).

The means adopted to convert the phthalocyanine into the correct physical form was based on the well-known technique of acid testing. This may be represented as dissolving or suspending a dyestuff by filtration. To obtain satisfactory copper phthalocyanine pigment, it was necessary to rapidly dilute the sulphuric acid, preferably accompanying this with strong agitation. Alternatively, the original phthalocyanine crystal could be treated with sulphuric acid to form phthalocyanine sulphate, to yield a micro-crystalline pigment after filtration and hydrolysis.

(45) A.S. Gomm and A. Stewart, H 1002 D (1935).

(46) A.S. Gomm and A. Stewart (see above, note 45).

The water-wet paste thus made must undergo further operations, depending on the end application being considered. To make lakes, the water-wet paste is absorbed on extending agents like aluminium hydroxide, or barium sulphate. To yield a form which disperses in water to colloidal solutions, the paste must be further diluted and dried. To achieve a dry powder for dispersal in non-aqueous media, a special method is required to ensure that the pigment remains dispersed during the drying process. Without this, the pigment on drying becomes hard and gritty, and must be ground extensively to break it down into a suitable form.

Even after these forms had been obtained, problems occurred. It was quite quickly found, for instance, that in certain media the pigment obtained from acid-pasting was not stable. Aromatic solvents, contained in many paints, lacquers and enamels, were not suitable, since they weakened and dulled phthalocyanine's intense blue shades. To allow phthalocyanine to be used in these important applications, more stable forms had to be sought, either by grinding in such a way that a more uniform particle size was obtained, or by adding a suitable stabiliser (47).

7. The Conversion of pigment to dyestuff:

Once a suitable physical form had been achieved, copper phthalocyanine found many uses as a pigment. It could be used in printing inks, where its ability to absorb almost all wavelengths in the red region made it particularly suitable as an ink for three tone printing. It could be used in paints and enamels, where fastness to light and to lime made it particularly useful as a pigment for plaster. Its great heat stability enabled it to be used for plastics, whose high extrusion temperatures often made other colours unsuitable. Paper, rubber, linoleum, cement and soap could all be coloured by the pigments.

(47) A.J. Hailwood and W. Todd, Report H 2573 (1932).

But there remained large and important applications for textiles, which were difficult to colour with pigments. Some textiles could be coloured in this way. It was possible, for example, to use phthalocyanine to colour viscose in the mass, for its fastness to both acid and alkali allowed it to be incorporated into the liquid before its extrusion into the caustic bath. This sort of use, however, represented only a small part of the market for colouring textiles. The main market remained for dyestuffs, whose application to textiles requires that the dye should be soluble at some point in the dyeing process. The problems posed by the phthalocyanines were severe. A pigment, insoluble in water and organic solvents, had to be converted into a form temporarily soluble in water, from which it might be applied to a textile, and then had to be treated in such a way that the compound was no longer soluble. This had to be achieved without harming the textile and without destroying the chromophore. The achievement of this target, essential to the full use of phthalocyanine, was to take much effort, spread over years more than a decade after Dunworth and Drescher's initial discovery.

The success with which this target has been attacked may be recognised by the fact that there are now no less than six different classes of water-soluble phthalocyanine dyes. To chronicle the development of each class would not be a rewarding task. Moreover, such a chronicle would necessarily be incomplete, since more phthalocyanine dyes are still being discovered: between 1956 and 1965 more than 250 patents relating to one class - reactive phthalocyanine dyestuffs - were filed (48). It is, however, worth giving a brief account of the first really successful class of water-soluble phthalocyanine to be discovered since this illustrates the problems involved in bringing the innovation to fulfilment. The successful class - the ingrain dyes - was first marketed by ICI in 1947, the initial product having the name Alcian Blue 8 GS. Their discovery may be traced back to work started in

(48) G. Booth, Chimia, 19, 207 (1965), 17.

1939, when properties of copper tetra-4-pyridyl phthalocyanine, and its quaternised derivatives, were examined. It was found that the methyl methosulphate derivative was soluble in water, and possessed excellent affinity for cellulosic fibres. This discovery led to investigation of other similar compounds: quaternary ammonium and tertiary sulphonium groups were investigated as suitable means of conferring solubility on the phthalocyanine molecule. The different 'onium' groups showed differing reactions to changes in the acidity of the medium in which the dye was immersed. The affinity of the dye for cellulosic fibres was increased by raising the pH of the dyebath, by the gradual addition of alkaline materials. The solubilising power of the groups attached to the phthalocyanine, (whether pyridinium or some other) was overcome by this increase in alkalinity. Some groups were too stable, and the solubility of the phthalocyanine persisted until conditions had been reached which were unoperable; other groups were unstable under normal dyeing conditions, and precipitated out decomposition products before the dyestuff could become attached to the textile. The discovery of different groups, and their sensitivity to changes in the pH of their surroundings, suggested a new method of dyeing. The temporary solubility conferred on the phthalocyanine by its substituent group could be used, and then the dye fixed in the textile by increasing the alkalinity of the dyebath. (49).

Recognition of how a dye of this nature might be used concentrated the search on finding an 'onium' group which would become insoluble at a reasonable pH, and which would not alter the typical bright blue shade of phthalocyanine. To achieve temporary solubility for the phthalocyanine molecule, some way had to be devised of attaching solubilising groups without harming the phthalocyanine.

The details of the search are well documented. Briefly, it may be said that attention concentrated on the use of a methylene bridge; study of

(49) N. Haddock, 'Alcian Blue, a new phthalocyanine dyestuff', Research 1, 1 (1947-48).

'onium' groups attached via a methylene bridge showed that this could most easily be achieved by first preparing chloromethyl derivatives of phthalocyanine. This in turn required synthetic preparations to be evolved, since phthalocyanine's insolubility in organic solvents prevented normal synthetic routes being used. The 'onium' group was chosen so that the original turquoise phthalocyanine shade was maintained, and so that a small increase in pH would split off the solubilising group. A printing paste could therefore be formulated so that it was weakly acidic, but would, on treatment with heat or steam, become more alkaline. The solubilising group is thereby removed, leaving the dye fixed to the textile (50).

The steps involved in translating the original discovery were thus ended when the pigment was obtained in its correct physical form. It required twelve years from the introduction of the first phthalocyanine to the introduction of the first satisfactory phthalocyanine dyestuff. The first commercially useful vat phthalocyanine dyestuff was patented in 1948, twenty years after the first patent describing what was claimed as a new vat dyestuff.

8. Discussion

The history that has been traced in the previous pages is further removed in time from present events than the discovery and development of either halothane or the bipyridyl herbicides. Yet the conclusions that may be drawn from study of the phthalocyanines have important implications for those guiding research today. Some of the more general implications are best considered against the experience of the other two case histories: these are discussed in Chapter Five. Some specific points may, however, be made immediately.

First, any account of phthalocyanine's invention which describes it as an example of chance event alone is confining itself to a very small part of the totality of events comprising the innovation. The time between

(50) N. Haddock (see above, note 49), 688-689.

phthalocyanine's discovery and its introduction to the market was protracted: the discovery of 1928 did not become a commercial product until 1935 and use as a vat dyestuff did not occur until twenty years after the initial discovery. The movement from invention to innovation was tortuous: it involved two large chemical companies, academic workers, three different manufacturing routes and, to achieve the originally perceived target of a dyestuff, several development projects. The vicissitudes in phthalocyanine's fortunes from its discovery to its introduction as a pigment, were great: without the receptive organisation of the DGRC, without support from Thomas, or without the very considerable expertise devoted to process and product improvement the discovery might easily have foundered. Its right to exist may indeed have been declamatory, yet its survival was achieved only by dint of overcoming organisational and technological barriers.

Not only does an account of phthalocyanine's invention which concentrates on chance invention tell only part of the tale, but also it fails to answer two questions raised by examining the phthalocyanine innovation. Why was the discovery of 1928 significant when those made before had been abortive? And how did it occur that the commercial product was brought to the market almost simultaneously by ICI, responsible for the original discovery in 1928, and by I.G. Farben, whose work on phthalocyanines had not started until 1933? There are special features affecting the answers to these questions: technological and scientific advances provided opportunities for analysis and elucidation of complex structures that were not open to earlier workers before Drescher, Linstead and their colleagues. The German industrial workers were fortunate in possessing a patent-free route because of earlier work. Uniting the answers to these two questions, however, is the belief encapsulated in the remark that things happen because

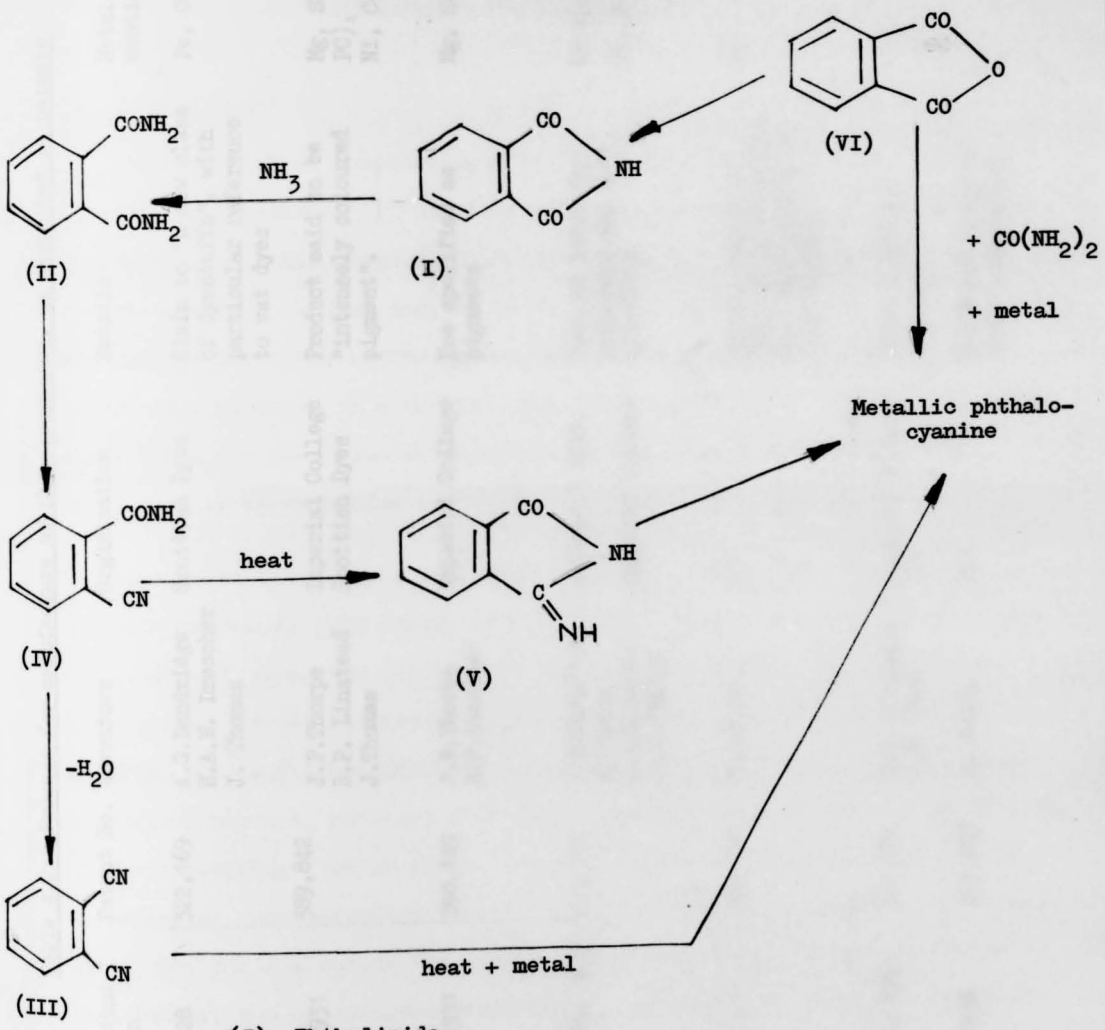
people make them happen. More significantly still, people act because they can see the benefit from acting. Dunworth and Drescher devoted some considerable work to the impurity because they could see the opportunity raised by their discovery. The chance event was significant because its significance was recognised, not because it was a chance event.

In similar fashion, I.G. Farben were so successful between 1933 and 1935 because they recognised the significance and importance of a discovery made elsewhere. The 1933 announcement to the British Association told that a remarkable copper compound had been discovered, that its basic unit suggested close affinity with a natural colouring agent, and that ICI was devoting considerable interest to it. The following up of this announcement would show that de Diesbach had ante-dated any ICI patents. The opportunity thus existed to improve the manufacturing route suggested by de Diesbach, without being constrained by ICI patents. It is interesting to observe that the I.G. Farben chemists, surveying the position anew in 1933, were able to draw conclusions which had escaped Linstead and his co-workers. Discovery brought with it the penalty of a wide range of possibilities, and possibly some pre-conceptions. The competitors arriving on the scene later were presented with a fuller initial account, could see the importance of the work described, and were anyway encouraged, if not forced, to seek alternatives. The I.G. Farben chemists concentrated so effectively because they recognised the opportunity so dramatically described in 1933. Again, not discovery, but the ability to appreciate the significance of discovery, was the key to the I.G. Farben success, as it was to the work at Grangemouth in 1928.

The importance not of discovery, but of recognising the significance of discovery, has considerable implications both for models of innovation and for the actual conduct of research. It suggests that models of innovation

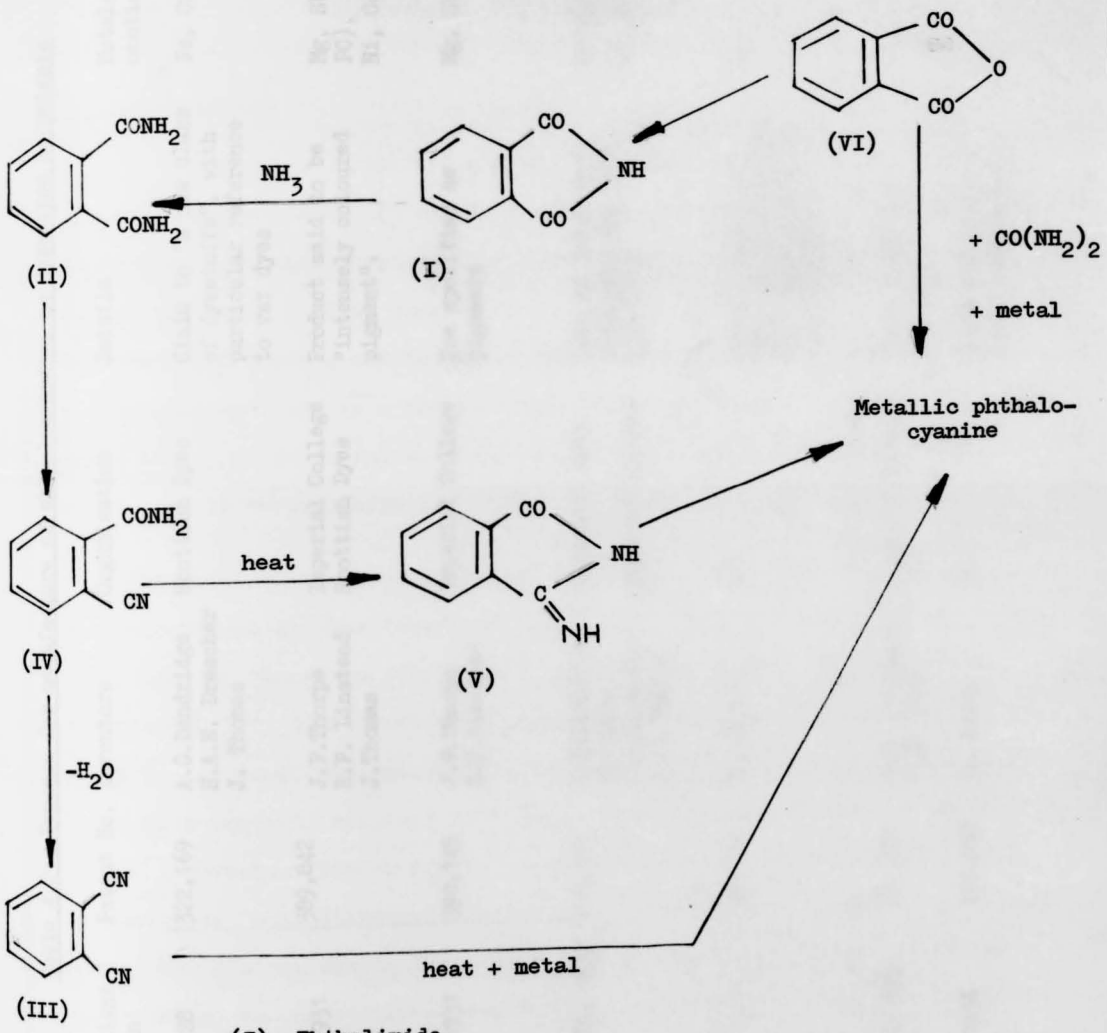
which presuppose that discovery is the original input in a linear process leading to innovation are incomplete, and may be seriously misleading as a guide to research managers and those conducting research and development. Dyestuffs Division's emphasis on academic contributions to their research programme is best explained by such a model, for throughout the development emphasis was placed on discovery: on discovery of a new colouring agent, of its chemical composition, of a new chromophore, and of various metals which could be associated with the chromophore. From 1928 until 1933 the emphasis of research was on the creation of new knowledge, and on the production of new phenomena. That this should be so in an organisation in which need and opportunity were both perceived shows that there may be a temptation to remain in science, rather than to attempt the translation from science to technology, and from new phenomenon to new product. The history of phthalocyanine suggests strongly that discovery does not provide an explanation of successful innovation, and that successful innovation may be realised by organisations or people other than those responsible for the initial discovery.

FIGURE 4.1



(I) Phthalimide
(II) Phthalamide
(III) Phthalonitrile
(IV) o-cyanobenzamide
(V) Phthalimimide
(VI) Phthalic anhydride

FIGURE 4.1



(I) Phthalimide
(II) Phthalamide
(III) Phthalonitrile
(IV) o-cyanobenzamide
(V) Phthalimimide
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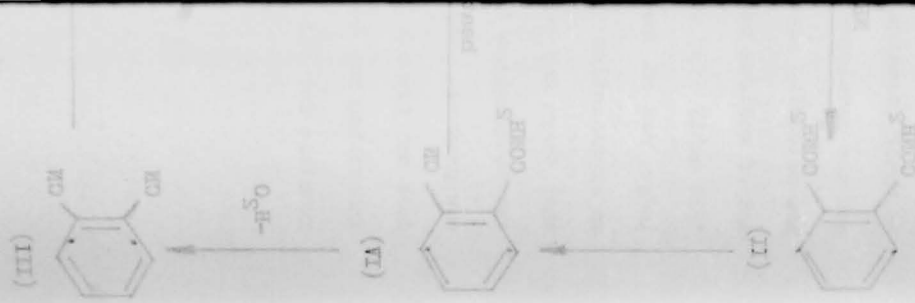


Table 4.2: Process for manufacture of phthalocyanine, as described in patents

Process	Date of patent application	Patent No.	Inventors	Organisation	Details	Metals specially mentioned
Ammonia passed into phthalic anhydride in prescence of a metal	May 16, 1928	322,169	A.G.Dandridge H.A.E. Drescher J. Thomas	Scottish Dyes	Claim to "a new class of dyestuffs", with particular reference to vat dyes	Fe, Cu, Ni
Heating orthocyano-amide with metal	June 20, 1931	389,842	J.F.Thorpe R.P. Linstead J.Thomas	Imperial College Scottish Dyes	Product said to be "intensely coloured pigment".	Mg, Sb (for metal free PC), Ni, Co Pb, Fe
Ammonia reacted with phthalic anhydride or phthalimide with Mg or Sb	June 22, 1931	390,149	J.F.Thorpe R.P.Linstead	Imperial College	Use specified as pigments	Mg, Sb,
o-anylenedicyanide (e.g. phthalonitrile) is heated, with or without agents yielding ammonia	November 16, 1932	410,814	I.M.Heilbron F.Irving R.P.Linstead J.F. Thorpe	Liverpool Univ. Imperial College	Uses as lakes for varnishes and inks specified	Cu specially mentioned Cu, Na, Zn,
Copper phthalocyanine may be made by heating a phthalic anhydride with urea & a substance yielding copper	July 10, 1935	464,126	M. Wyler	ICI	Details given of drawing in sulphuric acid and pasting to form pigment	Cu
Halogenation of phthalocyanines	August 14, 1935	461,268	R.P. Linstead C.E. Dent	Imperial College ICI	Green compounds obtained	
Metal halides used with phthalic anhydride & urea	June 4, 1936	476,243	A. Riley	ICI	Increased yield or lower temperature	

Chapter 5

CONCLUSIONS AND DISCUSSION

1. Introduction:

In the previous chapters, a model of innovation has been put forward and discussed. It was then used to examine three examples of innovation. In this chapter, there are two aims: to consider what changes the case studies suggest to be made to the model; and to discuss how the model can be, and has been, used to recognise and define problems encountered by those in a research laboratory. Before attempting either of these tasks, it is useful to recapitulate the essential features of the model, and to re-emphasize its differences from alternative theories.

The model adopted was concerned to explain three features characterising research projects: the length of time between conception and maturity, the likelihood of change in performance and in aims during this period, and the high probability of failure to produce innovation. On the one hand, a multitude of candidate compounds exist; on the other, at the end of the innovative process, solitary survivors emerge to contribute to the cash flow of the innovating firm or firms. Several questions are suggested by such an analysis: what distinguishes the solitary survivor from the many casualties? How can one ensure the survival of deserving candidates - and, as importantly, the expeditious despatch of those for whom prognosis is unfavourable? What are the likely ailments which may prove fatal, and how may these be diagnosed? What screens exist to distinguish between candidates, and how can these be used? Before considering the answers to the questions postulated, it is helpful to observe that they differ from those raised by many other analyses. The latter are frequently concerned with problems of creativity and of invention, with questions of individual creativity amid

the demands of an organisation, and with the choice of a portfolio of projects from a number of conflicting claims made on senior management's scarce resources.

The questions raised by the model that has been adopted and by other models differ clearly because the models themselves differ. The model that has been adopted views the protracted innovative process as being drawn-out because of the number of protagonists - individuals and organisations - involved in the elaboration of the invention into an innovation. The number of protagonists constituting an innovative chain, and a brief description of the different types of organisation which might be involved, are summarised in Figure 5.1.

It may be seen that the number of protagonists involved in the innovative process is likely to be particularly high for those innovations which start at some remove from the eventual end-user. This becomes significant in terms of the model, since the model postulates that each organisation or individual is likely to be guided by particular and unique criteria, and may pursue objectives that differ, perhaps to the point of incompatibility, with the objectives of others. The criteria guiding each group may be viewed as constituting a screen, through whose mesh a research project must proceed in order to survive. A prime responsibility of the original research scientist is therefore to define and comprehend the screens that his idea must pass in order to become an innovation.

The situation is considerably more complex than the simplified conceptual model shown in Figure 5.1 might suggest. Figure 5.2 shows in similar form the development of the bipyridyls. From this it may be seen that as well as several organisations being involved - Plant Protection Ltd., Dyestuffs and General Chemicals Division of ICI, farmers, registration authorities in

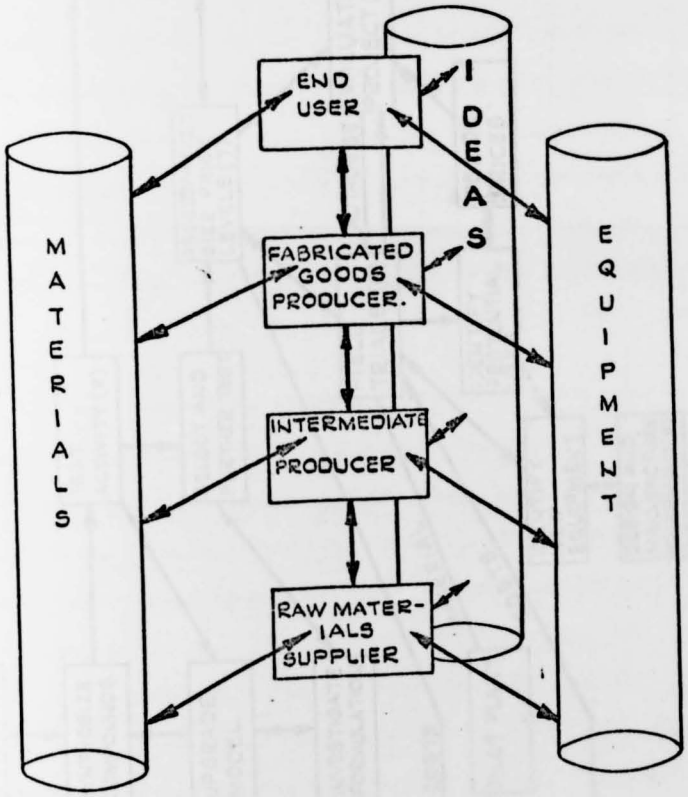
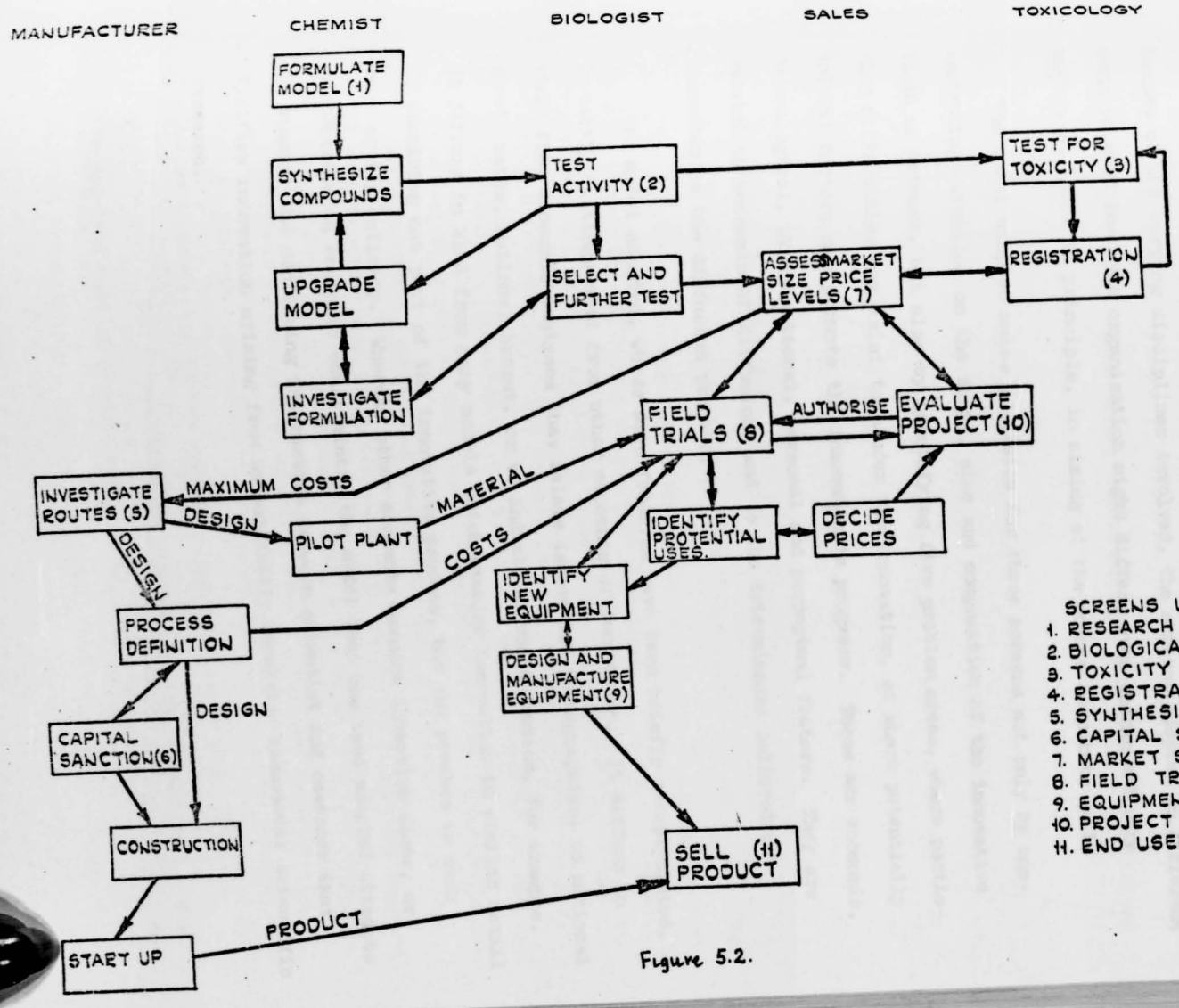

END USER
IDEAS
FABRICATED GOODS PRODUCER.
MATERIALS
EQUIPMENT
INTERMEDIATE PRODUCER
RAW MATERIALS SUPPLIER

Figure 5.1.



SCREENS USED:-
1. RESEARCH CHEMIST
2. BIOLOGICAL ACTIVITY
3. TOXICITY
4. REGISTRATION
5. SYNTHESIS
6. CAPITAL SANCTION
7. MARKET SIZE
8. FIELD TRIALS
9. EQUIPMENT MANUFACTURER
10. PROJECT EVALUATION
11. END USER

Figure 5.2.

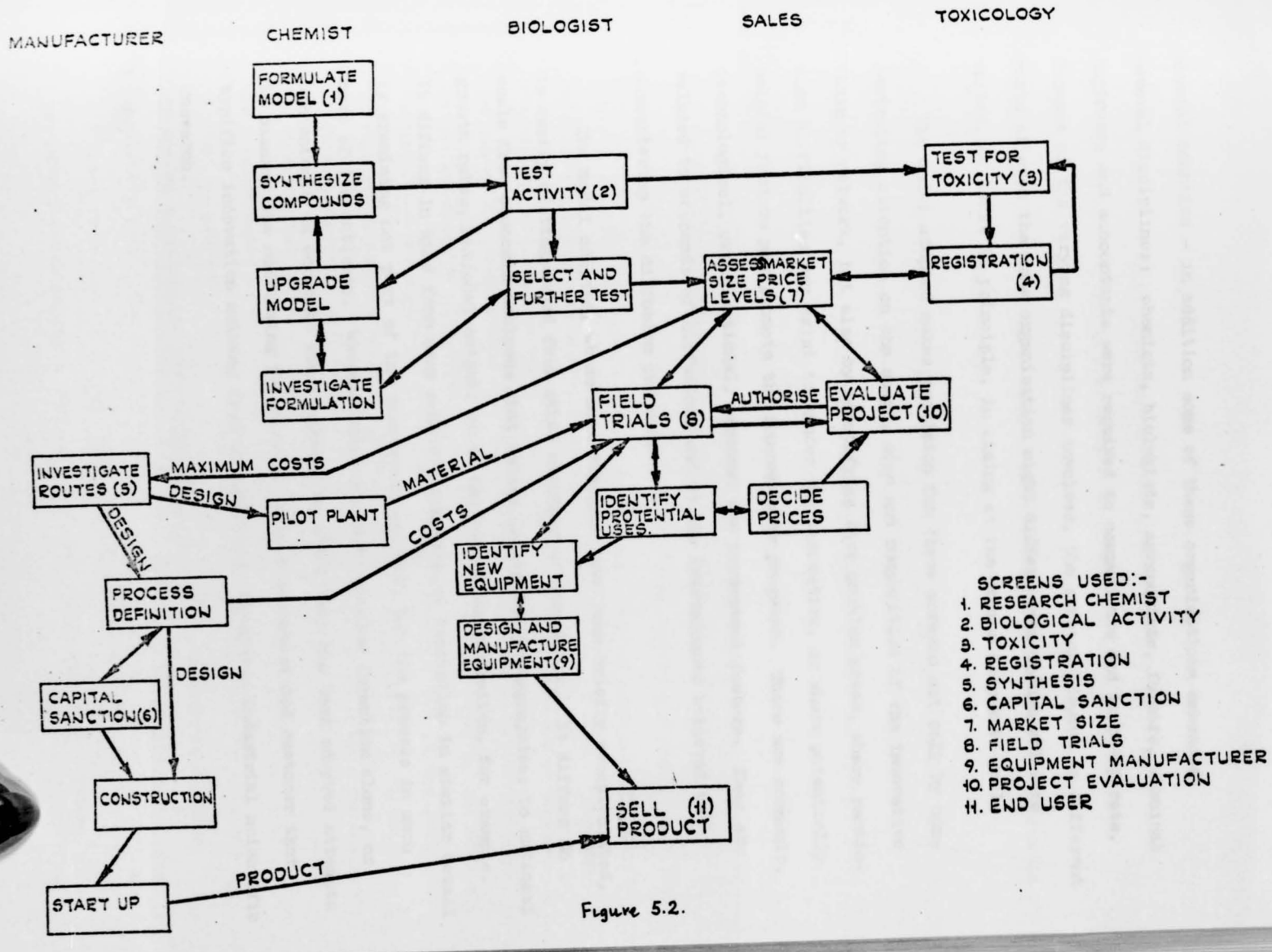

MANUFACTURER
CHEMIST
BIOLOGIST
SALES
TOXICOLOGY
FORMULATE MODEL (1)
SYNTHESIZE COMPOUNDS
TEST ACTIVITY (2)
TEST FOR TOXICITY (3)
UPGRADE MODEL
SELECT AND FURTHER TEST
ASSESS MARKET SIZE PRICE LEVELS (7)
REGISTRATION (4)
INVESTIGATE FORMULATION
FIELD TRIALS (8)
AUTHORISE
EVALUATE PROJECT (10)
INVESTIGATE ROUTES (5)
MAXIMUM COSTS
DESIGN
PILOT PLANT
MATERIAL
COSTS
IDENTIFY POTENTIAL USES.
DECIDE PRICES
IDENTIFY NEW EQUIPMENT
PROCESS DEFINITION
DESIGN AND MANUFACTURE EQUIPMENT (9)
CAPITAL SANCTION (6)
CONSTRUCTION
SELL (11) PRODUCT
START UP
PRODUCT
SCREENS USED:-
1. RESEARCH CHEMIST
2. BIOLOGICAL ACTIVITY
3. TOXICITY
4. REGISTRATION
5. SYNTHESIS
6. CAPITAL SANCTION
7. MARKET SIZE
8. FIELD TRIALS
9. EQUIPMENT MANUFACTURER
10. PROJECT EVALUATION
11. END USER

Figure 5.2.

several counties - in addition some of these organisations embraced several disciplines: chemists, biologists, agronomists, farmers, chemical engineers and accountants were required to communicate and to co-operate. Because of the varying disciplines involved, the screens adopted in different parts of even the same organisation might differ, even though all were united, at least in principle, in aiming at the common corporate goal.

The model adopted makes provision for these screens not only by concentrating attention on the shape, size and composition of the innovative chain or network, but also by identifying five problem areas, where particular difficulties may exist to hinder the innovation, or where potentially helpful factors may promote the innovation's progress. These are economic, technological, organisational, personal and perceptual factors. They are related to accounts of diffusion, and to the determinants believed to characterise the diffusion process.

The model adopted, whose main features have been briefly recapitulated, is easily distinguished from other accounts of innovation. It differs in scale from economic analyses that relate innovation to aggregates: to national growth rates, national output, or to industrial concentration, for example. It differs in kind from many models which examine innovation in similar detail by examining not part of the innovative process, but the process in much more of its entirety. Whereas other accounts examine invention alone, or concentrate on economic constraints, the model that has been adopted attempts to examine the continuing interaction between scientist and customer that typifies innovation arising from or explicitly involving industrial scientific research.

2. Changes to the model:

Now that the more important features of the model originally defined have been indicated, it is appropriate to consider what changes the case studies suggest should be made to the model. Theory having been tested against the reality of three sets of circumstances, alterations or additions may be made to strengthen the theory.

The first alteration suggested by such a testing may be deduced from contrasting the generalised model shown in Figure 5.1 with the specific model shown in Figure 5.2. The obvious difference between the two networks is the increased complexity of the specific over the generalised case. This elaboration of detail is entirely predictable.

2.1 Regulatory authorities.

Other differences are important, though less easily distinguished. The first is an addition to the innovative chain. A significant part is played by a body not directly involved, yet with considerable influence. For the bipyridyls, this is the registering authorities, which approve or reject the use of new herbicides. The example is not confined to the bipyridyls. In the development of halothane, a similar role was performed by the Medical Research Council Report on Non-flammable Anaesthetics. Nor is the influence of regulatory bodies, often government established, confined to innovations which are concerned with biological activity. Rather it seems more realistic to view the influence of regulatory bodies on biologically active compounds as a fore-runner of increasing influence over the end user's choice of product or process. The model of innovation must therefore be enlarged by adding a particular screen beyond the end user, established by some regulatory body. The screening adopted by this body is likely to be very different from that of the end user. Very often, it concentrates on one parameter, establishing a minimum standard: flammability of a fibre, or

emission standards for car engines. In addition, the type of measurement is likely to be very different. Whereas the end consumer may have a hierarchy of desires, and be influenced by many factors, including some unlikely to be measured easily by objective criteria, the regulatory body is by nature inclined to adopt standardswhich are definable by objective test. The definition of testing procedures is often the greater part of the specification of standards. The screen erected in this way is consequently an abstracted screen, and a compound may find different degrees of acceptability when measured against it and against the screen of the end user. This is illustrated by the conflicting conclusions on halothane that emerged from the end users, anaesthetists who experimented with the new anaesthetic, and from the regulatory body, the MRC Committee. The former were heavily influenced by the way in which halothane matched their needs, and particularly by the absence of the shock syndrome. The latter, investigating scientific phenomena amenable to objective testing, was unable to comment upon a matter decided essentially by subjective criteria. The conclusion reached by the two thus diverged. In general, the existence of a regulatory body may be expected to add an abstracted screen to those possessed by the end user. This screen will be at least an addition to those used by the end user, and may in some cases be in conflict with them.

2.2 Organisational Links

A second characteristic of the generalised model was the disregard of organisational ties between different protagonists in the innovative system. Yet in each of the innovations studied, organisational links were significant in connecting end user and intermediate supplier. The identification of a need, the provision of candidate compounds to satisfy this need, the extended testing of suitable compounds, the devising of application processes and the development of manufacturing routes were all predominantly performed within one organisation, for each of the innovations. It is therefore

important to consider what effect the addition of organisational links to the model will have. The significance of the organisational links in the innovative system is shown in two ways. The first is negative: when organisational links were absent, increased difficulties were presented to the innovation. In the development of phthalocyanines, the work undertaken by Linstead was ill-coordinated with the overall industrial objective of the research programme, and led to delay in producing the required product. In halothane's development, clinical trials that were made without very close contact with the earlier research were less favourable than trials conducted by Johnstone, who had the advantage of having already studied in some detail the results of trials on amimals. Both trials were independent, yet the trial conducted by the anaesthetist with greater knowledge of the new product yielded results which have been confirmed by subsequent events. In the development of the bipyridyls, there was potential conflict between the firms responsible for the sale of ancillary equipment, who wished to maximise their profits from equipment sales, and Plant Protection with its desire to maximise bipyridyl sales. Even when - as here - the objectives proved compatible, the involvement of several organisations is unlikely to avoid dispute over the divisions of profits. Within large organisations dispute over transfer prices of products between organisationally separate parts are not rare. Similar disputes may be even keener when it is no longer possible to claim that all profits, however divided for internal accounting purposes, will eventually be collected centrally within one firm. The existence of organisational links in the innovative system thus reduces the energy barrier between different parts of the chain (1).

(1) See also M.J.Peck, Competition in the Aluminum Industry, (Cambridge, Mass, 1961), 189-202.

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important to consider what effect the addition of organisational links to the model will have. The significance of the organisational links in the innovative system is shown in two ways. The first is negative: when organisational links were absent, increased difficulties were presented to the innovation. In the development of phthalocyanines, the work undertaken by Linstead was ill-coordinated with the overall industrial objective of the research programme, and led to delay in producing the required product. In halothane's development, clinical trials that were made without very close contact with the earlier research were less favourable than trials conducted by Johnstone, who had the advantage of having already studied in some detail the results of trials on amimals. Both trials were independent, yet the trial conducted by the anaesthetist with greater knowledge of the new product yielded results which have been confirmed by subsequent events. In the development of the bipyridyls, there was potential conflict between the firms responsible for the sale of ancillary equipment, who wished to maximise their profits from equipment sales, and Plant Protection with its desire to maximise bipyridyl sales. Even when - as here - the objectives proved compatible, the involvement of several organisations is unlikely to avoid dispute over the divisions of profits. Within large organisations dispute over transfer prices of products between organisationally separate parts are not rare. Similar disputes may be even keener when it is no longer possible to claim that all profits, however divided for internal accounting purposes, will eventually be collected centrally within one firm. The existence of organisational links in the innovative system thus reduces the energy barrier between different parts of the chain (1).

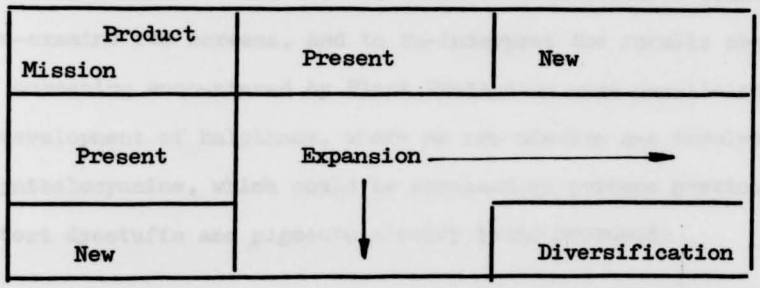
(1) See also M.J.Peck, Competition in the Aluminum Industry, (Cambridge, Mass, 1961), 189-202.

The second important way in which organisational links show their significance is more positive. For, in contrast to the way in which the absence of organisational links presented obstacles to the innovation, the presence of such links facilitated the formation of an innovative chain. Again, the case studies illustrate this. The benefits of organisational links were particularly important in the bipyridyls' development, and showed themselves in several forms. First, organisational links were important in spreading the risk involved in innovation over several organisations, rather than confining it to one. That research on manufacturing processes could be developed by Dyestuffs and Mond Divisions meant that Plant Protection was not forced to rely on its own much more limited resources. Organisational links were particularly strong and influential in paraquat's development. Plant Protection was a subsidiary of Mond Division. The heavy investment on new processes at Widnes at a time when very considerable doubts still existed on the product's eventual commercial success can best be explained by the positive desire of the parent organisation to protect its subsidiary. The benefits of organisational links do not mean that different parts of the same organisation may not rely on commercial links as well. A significant feature in halothane's development was the willingness of Pharmaceuticals Division to purchase halothane from Mond at a price that took account of the risk involved in developing a process for a product that had yet to establish itself. In this way the more enthusiastic member was able to overcome the doubts which existed elsewhere. The existence of organisational links are in no way incompatible with what may be regarded as normal commercial relationships between protagonists in the innovative system.

A second positive advantage accruing from organisational links is that a project which a single part of the organisation might regard as

involving completely new technology or marketing may be translated through organisational links, into more familiar business areas. In this context, the terms used by Ansoff are helpful (2). Ansoff distinguishes between expansion by a firm, which may take the form of selling more of the same product in the present markets (market penetration), or more of the present products in new markets (market development), or new products in the existing markets (product development), and diversification, which involves a new product sold to a new market. This is shown most easily in the diagram reproduced in figure 5.3, illustrating that diversification occurs only when new product is combined with new mission.

Figure 5.3: Diversification v. expansion



For Mond Division alone, the development of halothane would have involved diversification - the selling of a new product in a new market. The involvement of Pharmaceuticals Division ensured that, because of their combined skills, the project became essentially product development.

The significance of this change from diversification to expansion is not merely a semantic change of categorisation. It is possible to distinguish several ways in which diversification may influence the innovative system. The first effect of diversification, rather than expansion, is to make the design of screens more difficult. This may be observed in the three case studies, for the project involving the greatest degree of new

(2) H.I. Ansoff, Corporate Strategy (New York, 1965), 109-110, 128.

mission, the bipyridyls, caused most problems associated with the design of screens. The bipyridyls, while similar in many ways to other Plant Protection products, had an effect distinctly different from those of other herbicides. The initial screens which were used to test their effectiveness concentrated on particular parameters - persistence after application, and selectivity between different plants - against which the bipyridyls measured poorly. Their performance against these screens caused considerable effort to be devoted to altering the bipyridyls' properties to make them match the existing target. Yet this approach was unsuccessful, and it had to be recognised that the compounds under test would not satisfy the target that had been identified. Success occurred only when the existing target was abandoned, and a new mission, suggested by the bipyridyls' properties, was accepted. The acceptance of a new mission required Plant Protection to re-examine its screens, and to re-interpret the results obtained. The problems of screening encountered by Plant Protection were paralleled neither in the development of halothane, where no new mission was involved, nor in that of phthalocyanine, which could be assessed by screens previously established to test dyestuffs and pigments already being produced.

A second consequence of the move from diversification to expansion is the increased familiarity of decision-making processes. It is significant that in none of the three innovations was it necessary for managers in different parts of ICI to take decisions far removed from their previous business experience. Mond Division, for example, had to consider investing in new chemical production, not in deciding the relative merits of different anaesthetics or herbicides. The two examples were familiar to differing degrees: whereas the fluorine technology involved in halothane production was of a type of which there was already much experience, the complexity of paraquat manufacture represented a considerable advance from Mond's previous experience in predominantly simple molecules containing two or three carbon

atoms. In both cases, however, the uncertainty of the total project was divided, so that Mond Division management had to make decisions on problems in fields that were not totally new. Equally, Plant Protection's managers, faced with the weighty decisions on bipyridyl development, were able to relate these to their previous business knowledge. The decision to accept a lower overall profit target for Plant Protection, in order to support the research and development expenditure for paraquat, was facilitated by the familiarity of the decision and of the market to senior managers.

It is not only the decision-making processes that are more familiar. The principal protagonists are likely to be known. There has been considerable emphasis, particularly associated with Schon's identification of the part in innovation played by the product champion (3), of the way in which the innovation is judged by the character of the man supporting it as well as (and perhaps as much as) by the properties of the new idea alone. The three case histories illustrate this: Johnstone for halothane, Boon for the bipyridyls, and Thomas for the early stages of phthalocyanine played vital roles as product champions. For the latter two, the contacts already established within different parts of ICI before they accepted the responsibilities of product champion were important. Other ICI managers had previously had the opportunity of assessing their judgment, and the arguments in favour of the new ideas presented by Boon and Thomas could be, and were, related to previous experience of the product champions' abilities.

A further advantage of organisational links is obscured by either the conceptual or the realistic model. These show, respectively, what may occur and what has occurred in one instance. What cannot be depicted here are the

(3) D.A. Schon, Technology and Change (Oxford, 1967), 115-117.

problems encountered in creating the innovative system. Two particular problems may be identified when no organisational links unite the protagonists. The first is the problem of the organisation which has recognised the need, but does not possess the resources to satisfy this need. In the innovations discussed, this problem was overcome by use of internal organisational information flows. Thus Boon was able to identify the skills in sodium dispersion technology developed at Widnes, the skills in "hot tube" reactions of Billingham, and the organic chemical know-how and expertise amassed at Blackley; similarly Pharmaceuticals Division was able to identify Mond Division's skills in fluorine technology; and Mond, having decided to examine anaesthetics as an outlet for its well-developed fluorine knowledge, was able without difficulty to establish working relations with Pharmaceuticals Division. In each case, the identification of a development partner was greatly facilitated by organisational contact. Had these not existed, a very considerable problem would have been posed: how was relevant technology, or useful marketing experience, to be identified? A very considerable information barrier may occur between any stages in the innovative system, and one effect of organisational links is to reduce the size of this barrier. For not only is the organisation in search of information more likely to know where to search, but also the quality of the search will be different when dealing with other parts of the same organisation: needs may be explained more freely, confidentiality becomes a lesser problem, and a common framework of expression makes misunderstandings less likely.

A second problem encountered when different parts of the innovative chain comprise different organisations is how does the inventing firm assess the verdict on, and the price offered for, technology or ideas? A firm rejecting an idea or process may do so from a variety of reasons. Some of these will be quite general, applying to most, if not all, who might be

interested in the invention. But some will be particular to the firm to which the invention was offered: the idea may not be compatible with its existing technology; it may already possess a technique or product superior to that proposed. The firm whose proposal has been rejected has therefore to decide whether the grounds for rejection are individual and special, or whether they are general. When an idea is rejected by another part of the organisation in which it originated, the reasons for rejection may be discussed. The information obtained from the decision is much greater. The problem is repeated in slightly altered form when an offer is made for the invention. Often it is difficult for the inventing organisation to determine whether the price it has been offered is realistic. A positive benefit of organisational links is that more informed and less guarded discussion of prices is possible.

Of course, it must be made clear that in an ideal situation there would be no need for links, since all parts of the innovative chain would be united in close co-operation. In one sense, all links are palliatives. Such is the nature of innovation, however, that this ideal state is unlikely to occur, and hence palliatives must be sought.

The effect of organisational links may be summarised. Negatively, their absence leads to increased difficulties in co-ordinating research and in assessing projects. Positively, the effects on a large company are considerable: the risks may be spread, and the areas of uncertainty diminished, since various parts of the company may each contribute specific expertise. The movement from diversification to expansion (following Ansoff's terms) enables more realistic screens to be adopted, for decision-making to be related to previous experience, and for the personality and standing of the product champion to be judged. Perhaps most important of all, the presence of organisational links permits the building up of an innovative chain: the

the problems of creating the initial chain, and of knowing whether setbacks should be fought against or should be allowed to prevail, are reduced by organisational links. The initial theory made allowance for organisational problems. The experience gained by testing the model against the reality of these case histories suggests that organisational links should be further emphasised.

2.3 Types of innovation:

So far, the alterations to the model have not altered its basic form: an extra class of protagonist has been added to the innovative chain, and the significance of organisational links has been further explored. It is now intended to suggest an additional 'feature' which the model as previously defined did not include. This is the difference between different types of innovation.

The model as first formulated did not differentiate between types of innovation - between, for instance, product and process innovation. This distinction is one commonly adopted by writers on innovation, yet the form the model assumes suggests that the distinction may not be very helpful. One person's process innovation may be another's product innovation; product innovation is likely to involve new equipment, either to manufacture the product or to use it; new processes are likely to modify existing processes which either feed raw materials to, or take from, the new process. Each of the innovations studied considerably altered the process to which it was applied: to use halothane, anaesthetists had to adopt special equipment, and had to move from open- to closed- circuit administration; to use bipyridyls, farmers had to purchase new equipment, varying in complexity and cost from a simple spray to a direct drilling machine, and might have to change farming techniques considerably, depending on the particular application considered; to use phthalocyanine dyestuffs, dyers had to learn how to adopt their work to

new techniques considerably different from those used in vat dyestuffs. Similarly, for each product, the devising of economic manufacturing routes was crucial. Thus the interaction between new product and new process in each case was considerable. The distinction often drawn between product and process innovation is here deliberately ignored.

Another distinction, however, seems far more useful. This is based on the specification used to define the product. Here it is useful to consider the distinction drawn by Woodward between different types of product, and to examine the significance of this to research and development. The distinction was drawn between integral products, measured by engineering parameters such as length or diameter, and dimensional products, measured by weight, capacity or volume (4). Whereas the former are produced as discrete items, the latter are made up from small individual components, believed to be indistinguishable one from another, and divided into units only for ease of transport or application. Chemical products are typically dimensional products, recognised as such by Woodward. As Woodward's analysis would suggest, each of the three new products considered in the case studies was predominantly dimensional, rather than integral. Yet each product differed subtly, but significantly, in the extent to which mechanical properties were important. Halothane was the least complex, since the product was defined in chemical terms alone, with no specifications other than chemical purity. The bipyridyls represented a slightly more complex specification, since it was necessary to formulate the chemical with wetting agents and other additives to ensure that maximum effect was gained. The phthalocyanines were still more complex, in that their effectiveness depended critically on physical form,

(4) J. Woodward, Industrial Organization: theory and practice (London 1965), 38

particularly on particle size. Although all three compounds, or classes of compound, were mechanically simple, the phthalocyanines were the only class to possess any marked integral feature.

One important proviso is necessary. The treatment of a product as a homogeneous substance may merely be a measure of ignorance which, when resolved, shows the assumed homogeneity to be false. At one level it was possible to treat the insecticide 'Gammexane' as a dimensinnal product, of formula hexachlorobenzene. At another level, the shaping of individual molecules assumed great importance, since the γ- isomer is the only form to be commercially useful. Similarly, isomers of halothane are unsatisfactory anaesthetics. The belief that a product is dimensional must therefore be tempered by qualifying the scale of analysis.

The effect of an integral feature on the innovative process was considerable. When the compound possessed only dimensional features, screening could be conducted against chemical criteria: candidate compounds being screened for anaesthetic or herbicidal activity - providing there was no doubt connected with the compound's chemical purity - could be eliminated at an early stage. However, negative or unsatisfactory results gained from a set of experiments to test a particular phthalocyanine did not permit the conclusion to be drawn that the compound was useless: the absence of useful properties might be attributable to the physical dimensions of the compound tested rather than to its chemical composition. Thus when an integral feature influenced the usefulness of a compound which would otherwise be considered a dimensional product, the screening of candidate compounds became more difficult. The abstraction of screens was reduced, as the sufficiency of any experiment was diminished.

This may be phrased in a different manner, by saying that integral products require more detailed screening because the number of variables

is greater than would be the case with dimensional products. The manufacturer of PVC fibre, for example, may find that the properties of fabrics woven from his material are affected by any of four specific stages in the fibre's manufacture:

(i) The means of polymerisation may affect the physical properties of his PVC, resulting in greater or lesser stereoregularity in the polymer.

(ii) The shaping of the fibre from the polymer may affect its mechanical properties.

(iii) The fibre may be treated - by, for instance, drawing, shrinking or heat setting - to alter its properties.

(iv) The particular means used to convert fibre to fabric may make considerable differences to the fabric properties.

Thus there are four stages to which changes in the properties measured in the final fabric may be traced. Whereas some fabric properties may be related, via theory, to physical properties measured at an early stage, others such as handle or drape cannot be so related.

The consequence for the significance of an unfavourable screening result is that, whereas an unfavourable verdict on a screen testing halothane or a bipyridyl would cause the compound under test to be abandoned, a similar verdict on a fabric would not permit the particular chemical compound being investigated to be abandoned. The increased number of variables affecting integral products requires screens of greater detail, and of less generalisation. This loss of abstraction is not necessarily harmful. In achieving closely defined targets, integral products permit an approach much more akin to design than to invention. The specification of a research target for an integral product is likely to be in terms of mechanical operations - an automatic coupling device for rail trucks is an example - or of physical

dimensions - drainpipe compatible with existing drainage systems (5). In contrast, the research specifications for dimensional products are much more likely to be defined in terms of effects - herbicidal activity, or electronic properties - and design is a less clearly defined activity. In the process of devising a new integral product, the designer may proceed from an acceptable to an improved device by a series of logical steps, incorporating or rejecting components in the system he is designing. By carefully analysing how individual components function, or by assembling together components to perform a defined task, the researcher aiming at a new integral product may achieve his design. The model used in considering ways of achieving the final operation is more precise, because it is less abstract, than the model that was used by the research chemist synthesising candidate anaesthetic or herbicidal compounds. The feedback loop shown in Figure 5.2, relaying information from screener to synthesiser to upgrade the model guiding synthesis, is more likely to relay information on the success or failure of individual components used to make up an integral product than to suggest changes in the model used to select possible solutions to the problem.

The difference between integral and dimensional products has been observed, and the implications of this difference on the screening of potential new products considered. In general, the dimensional product may be screened by screens of greater abstraction than integral products. This argument may be extended by considering not just dimensional and integral products, but different levels of production, of which five may be distinguished:

(i) chemicals, defined in chemical terms
(ii) materials
(iii) devices.
(iv) manufactured products.
(v) complete systems.

(5) See, for instance, S.A. Gregory, The Design Method.

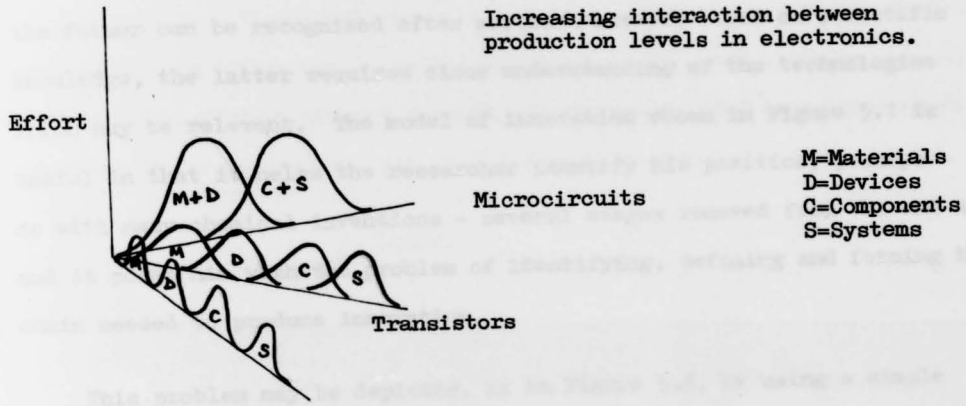
The analysis of products, and their assignment to the five levels described here, are useful for two purposes. First, it enables the applicability of the generalised and particular screens to be judged: abstracted screens are most useful in testing chemicals and materials, and least applicable to manufactured products and systems, where particular testing is required. The second purpose of such product categorisation is somewhat different. The readiness with which chemicals lend themselves to generalised screening might suggest that screening is therefore simple. An important countervailing effect, however, is the position of the chemical product in the innovative chain. Whereas the potential uses of the manufactured product or system will be well-defined, those of the chemical may be identified only with considerable difficulty. The identification of the innovative chain from the chemical to the end effects offered may often comprise a difficult task.

The problems of tracing the generalised properties of the chemical forward through various production stages to the end effects conferred on the eventual consumer may be particularly intense when there are interactions between the different production levels. The problems which have to be overcome have been described by Morton, in the context of the electronics industry. He argues that whereas it used to be possible to separate different production levels, this is no longer possible. For earlier technologies, such as the production of tube valves, there was a vertical movement from materials to devices to components to systems, during which "at each interface, the number of options was small and new advances were infrequent". For later technologies, the interfaces became more blurred, so that "since the design and fabrication of transistors depended on the structure of materials at the atomic level, overlap in understanding and coupling of materials and device specialists became essential"; still more with recent technologies, such as the microcircuit "greater knowledge of materials, processes and device structures will be required, yet, at the same time, even more overlap in

understanding and effort between material and device specialists will be required (6). Morton's argument, which he depicts diagramatically in the way shown in Figure 5.4, is readily translatable into terms used by the model in this thesis.

Figure 5.4 (after Morton)

Increasing interaction between production levels in electronics.



The argument advanced by Morton shows that, in at least one modern technology, the manufacturer of a material will succeed only if he understands a great deal about the succeeding production levels lying between the material and the eventual system in which it finds its use. In terms of the model defined earlier to describe innovation, the feedback from end user, manufacturer and intermediate manufacturer has become so intense and so complex that simple screens of a chemical or material are no longer adequate. The interaction between fabrication processes and the chemical being formed first into a material, and then into a device, has grown to the extent that screening appropriate for dimensional products is likely to be insufficient.

Even when the interaction is not as intense as that described by Morton,

(6) J.A. Morton, "From materials to systems" in D. Allinson (ed), The R & D Game (Cambridge, Mass. 1969), 242-247.

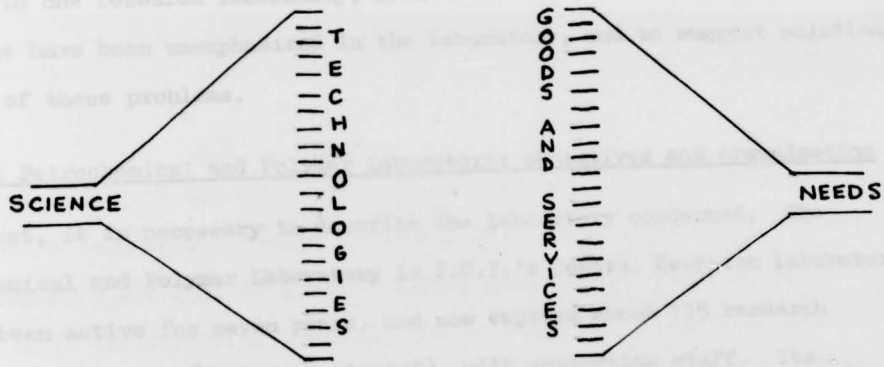
the problem remains of identifying the innovative chain which may be formed to connect the chemical or physical phenomena demonstrated by the chemical under study with the needs which may be satisfied by such phenomena, or by some system incorporating the chemical. In short, the problem is that of moving from an "interesting phenomenon" to a "useful property". Whereas the former can be recognised after abstract screens based on scientific knowledge, the latter requires close understanding of the technologies which may be relevant. The model of innovation shown in Figure 5.1 is useful in that it helps the researcher identify his position, perhaps - as with many chemical inventions - several stages removed from the end user; and it poses him with the problem of identifying, defining and forming the chain needed to produce innovation.

This problem may be depicted, as in Figure 5.5, by using a simple morphological analysis. The body of science lies on one side, the pattern of needs on the other: connecting, and hence separating, the two, across a space of differing width, is technology (7). The connecting of a specific scientific phenomenon with a perceived need is the act of invention. When the science and the need are separated, and hence may be linked, only by several stages of production the task of the inventor is made more difficult. Even when the chain is quite short, invention may be difficult enough. It is interesting to observe that in the innovations described in the three case studies, in none of which were chemical effects mediated by processing operations, only one candidate compound - halothane - was synthesised deliberately for the research programme to meet a defined need. The two other starting compounds were either made accidentally - as with phthalocyanine - or already existed - as with diquat. The example of diquat points the problem: given the existence in the Dyestuff Division specimen collection

(7) For a similar analysis, which however does not emphasise the problem described here, see the model proposed in W.H. Gruber and D.G. Marquis (eds.) Factors in the Transfer of Technology (Cambridge, Mass. 1969), 5.

collection of the bipyridyl later known as diquat, why was it not possible to suggest its usefulness as a herbicide? A similar problem is posed by phthalocyanine: why did de Diesbach and von der Weid not identify the usefulness as a colouring agent of the compound they had synthesised? Even with the short innovative chain from chemical to herbicide, or from chemical to pigment, the identification of a possible innovative chain is difficult. With chemicals which are to be incorporated in integral products, and with chemicals which must undergo several manufacturing processes before demonstrating their usefulness, the difficulties are greater.

Figure 5.5 The science: need interface



The distinction between integral and dimensional products, and the question of how is it possible to create an innovative chain, have thrown into prominence certain problems. The screening appropriate for dimensional products has been shown to be more abstract than that appropriate for integral products. It has been argued that integral products are more likely to be amenable to design methods. Most important of all, the position of the producer of chemicals has been shown to be often near the start of a protracted series of production steps, so that the properties observed in the chemical will be much mediated before desired end effects are achieved.

The model of innovation first described and now elaborated suggests that the most important problem facing the research chemist starting from new science is the identification of a suitable innovative chain.

3. Use of the model of innovation within one Laboratory.

The conceptual model of innovation first described has been compared with the reality observed in the three case studies. The additional complexity, the existence of regulatory bodies, the importance of organisational links, and the significance of the difference between dimensional and integral products have been identified as additions to and alterations of the original model. It is now proposed to show how this model has been applied in one research laboratory, both to identify problems which might otherwise have been unemphasized in the Laboratory, and to suggest solutions to some of these problems.

3.1 The Petrochemical and Polymer Laboratory: objectives and organisation

First, it is necessary to describe the Laboratory concerned. The Petrochemical and Polymer Laboratory is I.C.I.'s Central Research Laboratory. It has been active for seven years, and now employs about 115 research scientists (Ph. Ds or "Ph.D equivalents"), with supporting staff. Its research scientists are predominantly chemists, although there is a considerable and growing number of physicists and engineers. The Laboratory has an annual budget of more than £1.5 million. The Laboratory was established to augment I.C.I.'s long term research, and is unaffected by demands to improve day-to-day operations, although persistent problems experienced by I.C.I. Divisions, which are believed to be amenable to the skills of the Petrochemical and Polymer Laboratory, are occasionally referred to the Laboratory. The Laboratory Director is directly responsible to the General Manager, Research and Development, a central I.C.I. senior manager, who is in turn responsible to the I.C.I. main board director for research. The manufacturing

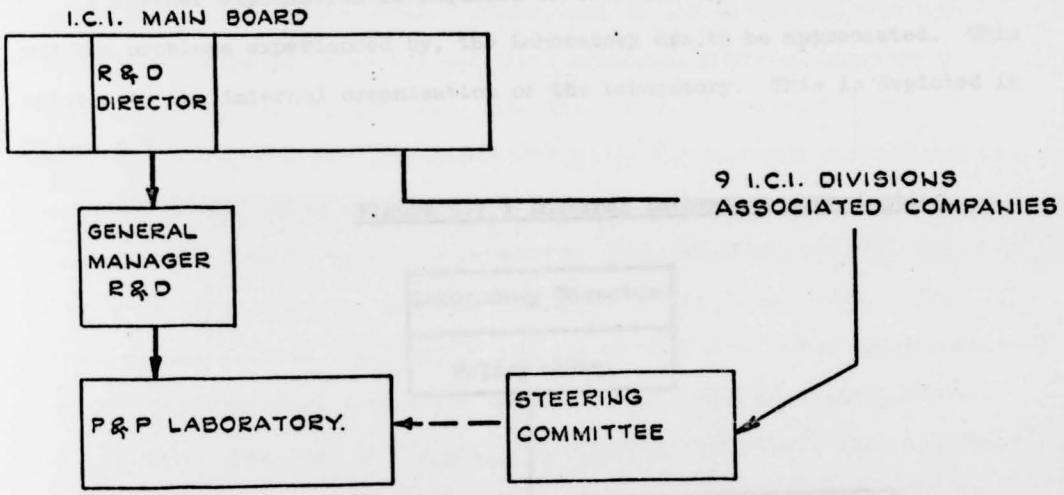
divisions of I.C.I., each of which possesses its own markets and technologies (and its own research and development department - some of which are very much larger than the Petrochemical and Polymer Laboratory), have no direct control over the choice of research projects, although a group of divisional research directors advise the Laboratory Director on policy. Figure 5.6 shows the position of the Laboratory within I.C.I.

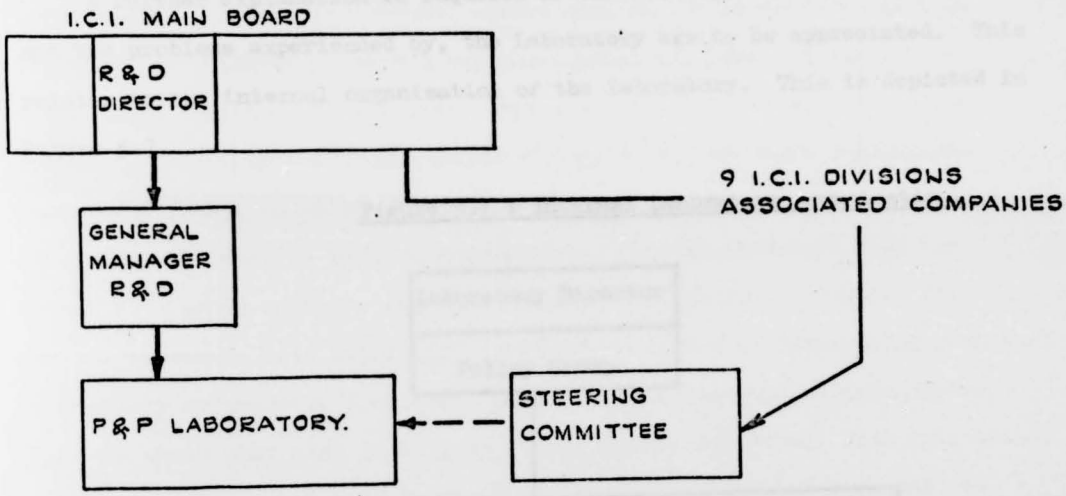
Figure 5.6 : P.&.P. Laboratory's position within ICI.

(see overpage)

Contact between the Laboratory and I.C.I.'s manufacturing divisions, each of which is largely autonomous, is closer than the diagram might suggest. The Laboratory Director is a senior I.C.I. manager with research experience in an I.C.I. manufacturing division, and so brings with him considerable divisional experience. Research scientists within the Laboratory, after a stay whose duration does not normally exceed five years, move to an I.C.I. manufacturing division or overseas company, not always in a research position. Most important of all, many of the research projects within the Laboratory are intended, either explicitly or tacitly, to be exploited by an I.C.I. Division. There is consequently considerable contact between Laboratory and Divisions on individual projects, and more formalised contact through various advisory committees on particular problems.

Enough has been said to illustrate that the Laboratory is not tightly constrained in its choice of research projects. The research projects

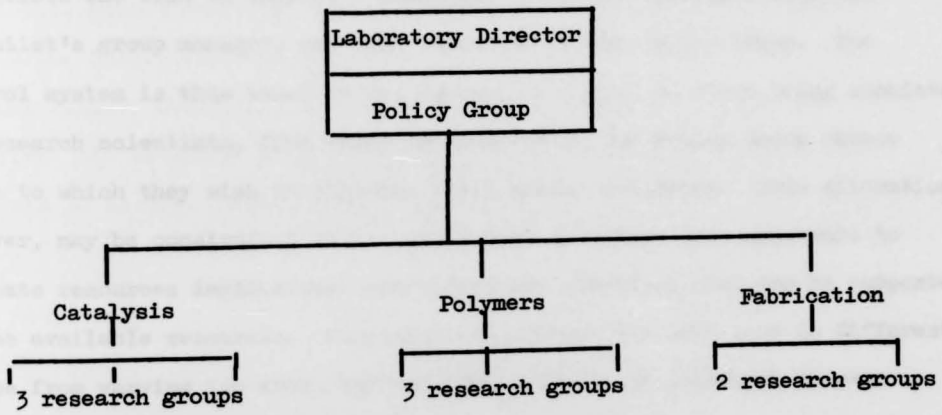

I.C.I. MAIN BOARD
R & D DIRECTOR
9 I.C.I. DIVISIONS ASSOCIATED COMPANIES
GENERAL MANAGER R & D
P & P LABORATORY.
STEERING COMMITTEE


I.C.I. MAIN BOARD
R & D DIRECTOR
9 I.C.I. DIVISIONS ASSOCIATED COMPANIES
GENERAL MANAGER R & D
P & P LABORATORY.
STEERING COMMITTEE

adopted vary greatly, ranging from process and product improvement for processes operated, and products manufactured, by I.C.I. Divisions; to new processes for established products, or new products closely connected with existing company business; to products and processes completely new to I.C.I. It may even choose to work in an area, technological or geographical, which I.C.I. has decided not to enter, intending either to reverse I.C.I.'s decision or to exploit inventions through licensing.

A further explanation is required if the full opportunites open to, and the problems experienced by, the Laboratory are to be appreciated. This relates to the internal organisation of the Laboratory. This is depicted in Figure 5.7.

Figure 5.7 : Internal Laboratory organisation.



The Laboratory has a policy group comprising the Director and three colleagues which controls the activities of eight research groups, divided into three research areas: catalysis, polymers and polymer fabrication. Each of the eight research groups has a manager. The raison d'être behind research groups vary. Sometimes their existence may be related to an area of science - as, for example, electrolytic catalysis - sometimes to a type of product - as composite materials. Different groups have ties, some strong

and some weak, with I.C.I. Divisions, each of which is based on technological skills serving particular markets. The Fibres and Films Group has strong links with I.C.I. Fibres Ltd., and with I.C.I.'s interests involved in producing films; the groups concerned with polymerisation have strong links with Plastics Division, whose main business is the polymerisation of monomers.

The choice of research targets within the Laboratory is not heavily constrained. Indeed, the control system used in the Laboratory was deliberately established in such a way that individual research scientists should have considerable influence over the choice of research. The control system in theory is based on a common document, the research expenditure memorandum (REM), which is prepared by the individual research scientist or scientists who wish to work on a programme. This is discussed with the scientist's group manager, and then submitted to the Policy Group. The control system is thus based on the concept of a flow of ideas being submitted by research scientists, from which the members of the Policy Group choose those to which they wish to allocate their scarce resources. This allocation, however, may be constrained to an extent that is not at once apparent: to allocate resources implies that more ideas are submitted than can be supported by the available resources. Similarly, to prevent the work load in different groups from varying too much, the existing division of personnel between groups must be considered when allocating resources.

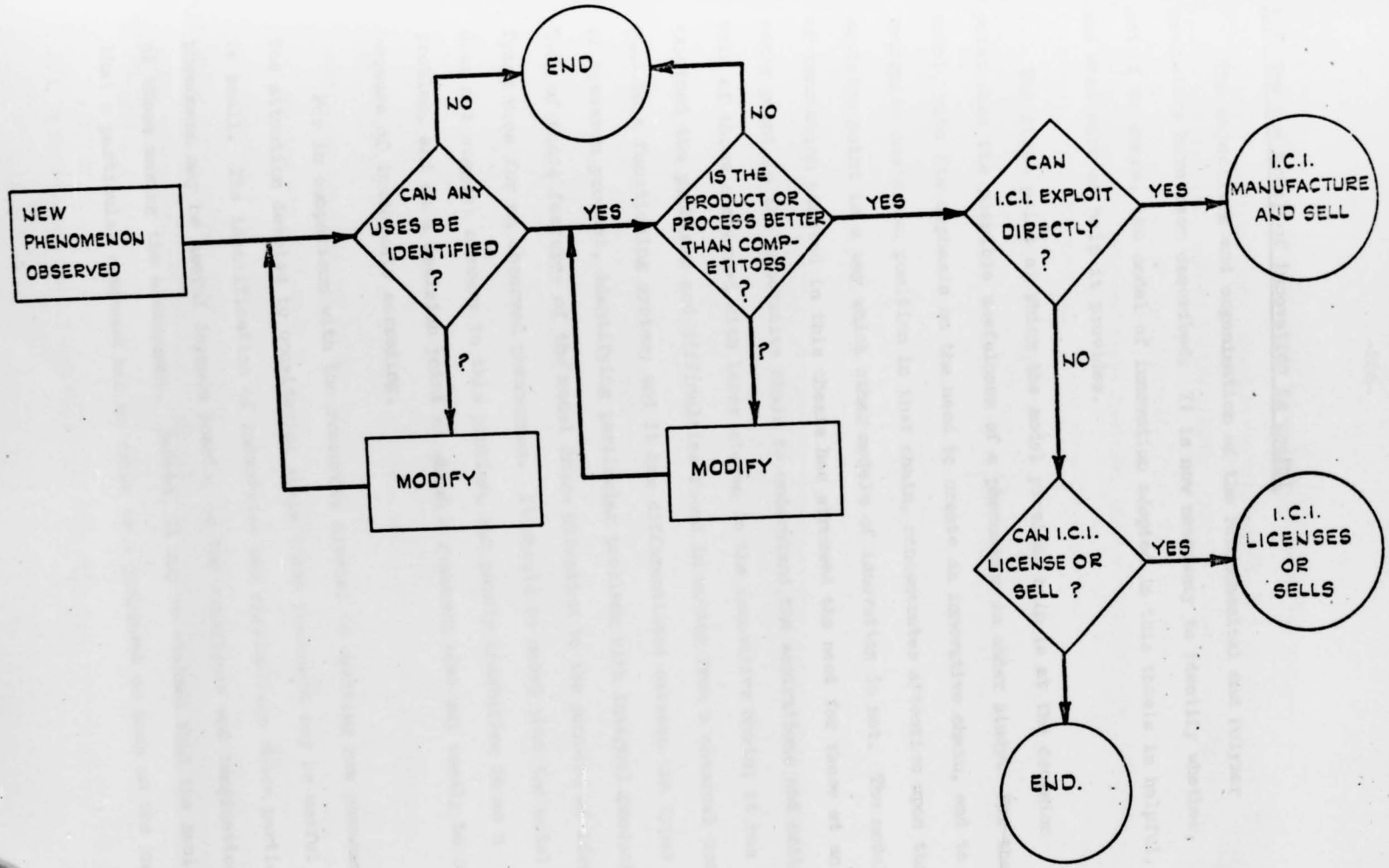
The creation of ideas, and their assessment, thus starts with the individual research scientist. The consequences of this are several. First, because of the scientific background and expertise of research scientists in the Laboratory, they tend to define the research targets and opportunites in scientific terms. A second consequence of the flow of ideas from research scientists to the Policy Group is that many of the ideas submitted are based on the activity of one or two research scientists, and do not often require or request large research teams. Because of the individual origins of

research proposals, the proposals themselves are rarely addressed at problems where needs are identified, or where a combination of differing skills are required. In terms of the science-needs interface depicted in Figure 5.5, the movement is from far left to right, from science towards needs.

The movement from science to need must include several decision points. Once a phenomenon has been observed, it must be examined to identify its potential utility, if any. If possible uses are identified, the solution suggested by the phenomenon under study must be compared with other possible ways of satisfying the needs being studied. The last decision point comprises a group of questions, designed to examine the ability of the Laboratory, or of another part of I.C.I., to successfully exploit the idea under study: can I.C.I. Manufacture and sell the product? Is it possible to license? Should the Laboratory merely publish the results of its work, and take no further steps? Overall, the process may be depicted as a flow-sheet of activity, all of which is triggered by the observation of a phenomenon believed to be new. This is shown in Figure 5.8.

Figure 5.8: Flow sheet of decisions to progress a research project in the Petrochemical and Polymer Laboratory.

(see overpage)


NEW PHENOMENON OBSERVED
CAN ANY USES BE IDENTIFIED ?
NO
END
YES
?
MODIFY
IS THE PRODUCT OR PROCESS BETTER THAN COMP-ETITORS ?
NO
YES
?
MODIFY
CAN I.C.I. EXPLOIT DIRECTLY ?
YES
I.C.I. MANUFACTURE AND SELL
NO
CAN I.C.I. LICENSE OR SELL ?
YES
I.C.I. LICENSES OR SELLS
END.

3.2 How the model of innovation is useful

The objectives and organisation of the Petrochemical and Polymer Laboratory have been described. It is now necessary to identify whether, and if so where, the model of innovation adopted in this thesis is helpful, and what sort of help it provides.

The first point at which the model provides help is at the decision point when the possible usefulness of a phenomenon is under study. For the model, with its emphasis on the need to create an innovative chain, and to recognise one's own position in that chain, concentrates attention upon this decision point in a way which other models of innovation do not. The model of innovation adopted in this thesis has stressed the need for those at an early point in the innovative chain to understand the aspirations and criteria of those concerned with later stages in the innovative chain; it has examined the problems and difficulties found in moving from a chemical compound to a functioning system; and it has differentiated between the types of research product, identifying particular problems with integral products. Each of these features of the model draws attention to the problem of identifying uses for an observed phenomenon. It should be noted that the model does not suggest answers to this problem, but merely identifies it as a problem, and as a decision point at which a research idea may easily be halted because of inadequate screening.

For in comparison with the resources devoted to creating new phenomena the attention devoted to considering where these phenomena may be useful is small. The identification of industries and applications where particular phenomena may be useful depends heavily on the experience and imagination of those making the assessment. Indeed, it may be claimed that the decision that a particular compound has no value is a judgement as much on the know-

ledge and determination of those assessing it as on the properties possessed by the compound. Examples of failure to forsee uses, like undetected murders, cannot be described. Yet the examples already described of diquat and of phthalocyanine show that the detection of utility is often delayed. Nor are these isolated instances within the chemical industry. It took some five years from the first synthesis of polyethylene to the moment when it was suggested that its dielectric properties should be measured to discover whether - as is now well-known - it might provide an adequate substitute for gutta-percha. An even more striking example is provided by Gammexane - γ- hexachlorobenzene - which, when first tested as a repellent, was rejected since it did not repel the wireworms against which it was tested, but rather killed flies in the laboratory environment. Successful identification of this property, and hence of the use of the compound as an insecticide, had to wait a further two years (8). In both instances, no mediating operations were required to process the original compound; yet both suffered considerable delay before a bridge was established between the science-based phenomenon and a potential use. Polythylene's history is particularly rewarding of study, since not only was there considerable delay between the discovery of the waxy polymer and the identification of where it might be useful, but also gutta-percha, the first use identified, now comprises only a small part of the total uses of polyethene. The original linking of science and need which led to the gutta-percha substitute was repeated by the identification of many uses for a bulk polymer. Yet polythene's influence on research management has been more to emphasise the importance of basic research, of the sort which led to polythene's first being made, rather than to stress the importance of the "use-recognition" step, which occurred not once, but several times, in polythene's development. Indeed, the attention paid within the Petrochemical and Polymer Laboratory

(8) M.W. Perrin, 'The story of polythene', Research (March 1953), 111-118.

to "phenomena-generation" relative to "use-recognition" may be directly linked to a belief that inventions of polythene's significance will occur only if science is manipulated to produce mutations. In its effect on research management the polythene syndrome has been a powerful influence.

The problem of moving from a scientific phenomenon to a need satisfied by some system to which the phenomenon contributes may be identified as particularly important in two parts of the Laboratory. The first circumstance occurs when the contribution of the phenomenon to satisfying a need can be evaluated only as part of a much larger system. Here the difficulty of constructing an innovative chain is great: for a product which is to find its use, only after one or more fabrication operations, in a complex system used in an industry - perhaps as an enabling invention, probably as one component among several - the problem of "use-recognition" is great. Groups within the Laboratory whose products are of this type are thus particularly vulnerable to inadequate attention being paid to identifying uses for the research ideas. The second circumstance in which the identification of needs likely to be satisfied by the research idea is especially difficult is when the group within the Laboratory has no counterpart in I.C.I. The organisational links that were seen to be so significant in the case studies provide no help. The cost of acquiring information with which to assess the idea is thus higher, and the probability of wasted resources is increased, either because ideas are inadequately assessed before rejection, or because it takes longer to acquire information to reject unpromising projects.

The model of innovation adopted in this thesis stresses the innovative chain. The first use of the model within the Petrochemical and Polymer Laboratory was to indicate the importance of a problem - that of "use-recognition" - neglected by traditional models of innovation. The model

adopted does not in itself solve the problem of moving from science to need. Rather the model has called attention to this problem, hitherto neglected by the implicit models of innovation extant in the Laboratory. There are obvious implications for resource allocation and for recruitment within the Laboratory.

The second use to which the model has been put has been to aid the assessment of new technologies or technological components against existing systems, materials or devices. To accomplish this, as shall shortly be described, it has been necessary to consider questions contained in the second and third decision boxes shown in figure 5.8., that is to consider whether the product was superior to competitive products, and to examine whether and how I.C.I. might exploit it profitably. This use of the model of innovation adopted in this thesis has been achieved by two means. The first is by adapting, for individual projects, the generalised concept of an innovative chain to a particular example and to the individual circumstances of a particular project. The second means adopted has been to convert the generalised concept of the innovative chain into a more specific, but still generalised, check-list of questions apposite to innovative projects. By combining the two approaches, it has been possible to examine research projects both with developing knowledge of the particular environment in which the innovation must survive, and also by judging the completeness of the innovative chain against the touchstone of questions that experience suggests to be important.

The first approach, the constructing of an innovative chain, is best illustrated by considering the evolution of knowledge about a specific project. In the interests of confidentiality, details of the project must necessarily be suppressed. It is possible however to indicate that the research programme was aimed at producing a photosensitive film, using a novel photosensitive

material. This material was to be applied as a coating to standard film base, and the coated material then required several subsequent operations before a complete film in a form suitable for receiving images was produced. The eventual use for the film was for a novel communication system, which competed with other systems.

The original model of innovation is shown in figure 5.1. The Laboratory's position in the example indicated above can be seen to be that of raw material supplier, in that the invention related to a new coating material, but did not originally include a developed process to produce a complete film. The generalised model could be converted into a specific innovative chain by identifying the subsequent operations required to convert the chemical into a film that could be used. The various stages identified are displayed in figure 5.9. From this diagram, various points emerge:

(i) The contribution of the chemical to be used as a coating material can be seen to be only a small part of the total technology needed to produce a complete film.

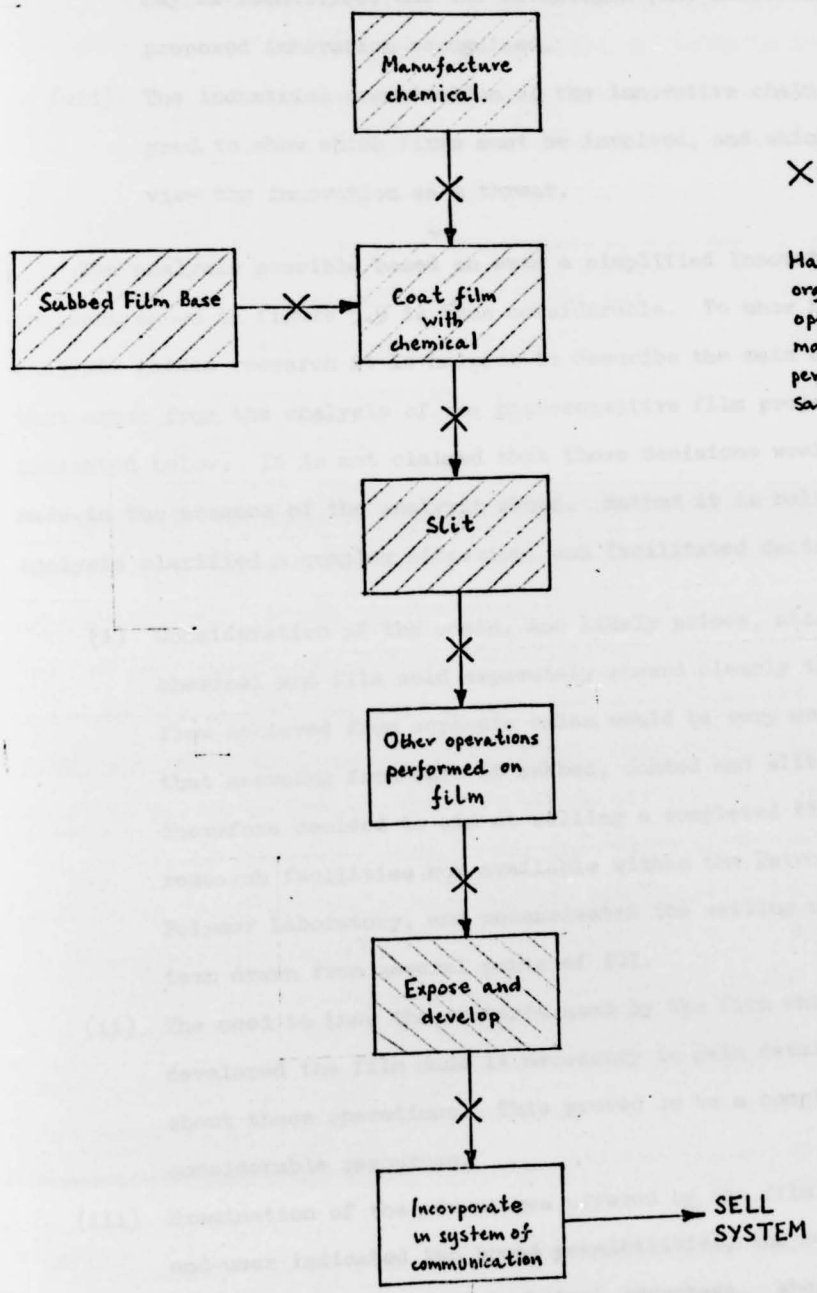
(ii) Those operations, and the complementary products, within the control of ICI may be identified.

(iii) The possible points of sale can be identified, and each may be considered against the resources required to achieve it. The resources required, including marketing capability, may be compared with the value added.

(iv) The innovative chain allows the properties required in the initial photosensitive chemical to be defined: the exposure characteristics, development time, and mechanical properties required are brought to the research chemist's attention.

(v) The co-operation needed from other firms (here shown as "other operations performed on film") may be seen, and firms capable of doing these identified.

Figure 5.9. Simplified innovative chain for novel photosensitive material.



(vi) The criteria by which the product will be judged at each stage may be identified, and the advantages (and drawbacks) of the proposed innovation recognised.

(vii) The industrial organisation of the innovative chain may be analysed, to show which firms must be involved, and which firms may view the innovation as a threat.

The analysis possible based on even a simplified innovative chain of the sort shown in figure 5.9 is thus considerable. To show how such an analysis guides research it is helpful to describe the main decisions that arose from the analysis of the photosensitive film project. These are indicated below. It is not claimed that these decisions would not have been made in the absence of the analysis shown. Rather it is believed that the analysis clarified a complex situation, and facilitated decision-making.

(i) Consideration of the costs, and likely prices, attainable for chemical and film sold separately showed clearly that the cash flow achieved from separate sales would be very much less than that accruing from sale of subbed, coated and slit film. It was therefore decided to aim at selling a completed film. This required research facilities not available within the Petrochemical and Polymer Laboratory, and necessitated the setting up of a project team drawn from several parts of ICI.

(ii) The need to know the criteria used by the firm which exposed and developed the film made it necessary to gain detailed knowledge about these operations. This proved to be a complex job, demanding considerable resources.

(iii) Examination of the advantages offered by the film system to the end-user indicated two broad possibilities, the one a minor cost reduction, the second a technical advantage. Whereas the former would be significant to the firm responsible for developing and

exposing the film, it was unlikely to have any effect on the cost of the final film to the end- user, nor to persuade the end-user to adopt the communication system using the novel film rather than a totally different system. In contrast, the technical advantage offered by the novel film was likely to increase the competitiveness of the communication system incorporating it. To gain information on exposure and development operations, an early approach was needed to the firm responsible for these operations and an early decision on price was necessary. The analysis, whose skeletal arguments have been indicated, facilitated this.

In coming to a decision on pricing policy, an additional analysis was useful. This added to the simple innovative chain information on a series of cost centres, so that the contribution of each operation to the final cost of an exposed and developed film could be identified. At the same time, a comparable analysis was made of cost centres both for the existing film used, and for other competing novel films. From these analyses, it was possible to answer both the question of how the new film system would satisfy the demands of the protagonists in the innovative chain, and also how the film being developed in the Petrochemical and Polymer Laboratory compared with competitive systems.

Examination of the various films that were, or might become, available showed important factors that were not discernible from the analysis of the Petrochemical and Polymer film. It disclosed, for example, that one other competitive film could compete on cost with the proposed film, but that the competitive film would not be able to use existing equipment for the film exposure. The firm responsible for exposing and developing whatever film would be used would therefore risk more by using the competitive film, which would require special equipment appropriate to that film alone, than

than by using the film from the Petrochemical and Polymer Laboratory which could be processed on existing equipment. Examination of the cost centres for existing and proposed films disclosed that the developer costs for the Petrochemical and Polymer Laboratory film would severely affect its competitiveness. This presented a clear research target.

The example of the potential new film has been used to illustrate how systematic and developing analysis of the innovative chain concentrates attention on research targets of importance. Two points should be made. First, it is not claimed that the approach adopted necessarily makes the research scientist tackle problems that would otherwise be neglected. Indeed, all the decisions here described would have to have been made at some stage as research progressed. Rather it is believed that the use of the innovative chain ensured that problems were identified soon rather than late; and that attention was soon attracted to important research targets. Second, the simple form of the innovative chain shown makes it easy to miss some potential advantages, and some problems. In the example considered, the times and duration of events were not examined at first, and this resulted in a failure to predict the full requirements for the photosensitive coating material. Only after detailed examination of the production processes depicted on figure 5.9 as "expose" and "develop" was it possible to define the total pattern of properties required in the film. It is worth emphasizing that the systematic analysis, of which the first steps have been described, is an examination that leads through repeated cycles. The organisational chain shown in figure 5.9 led to a cost analysis, which in turn identified further important research targets, and important centres of uncertainty.

The evolving innovative system, an example of which has been described above, is the initial analysis, from which detailed enquiries may follow.

One danger discovered in defining the innovative chain is that insufficient detail may be achieved: the very simplicity of the systems approach described above may deceive the research scientist into believing he has adequately defined the system at a time when important information is still lacking. It is important to repeat the conclusion of others who have examined similar approaches: the necessary knowledge of the technology and business, present and future, of other protagonists in the innovative chain is difficult to obtain, and requires considerable resources (9).

The danger described above is the reason for the second means adopted to answer the questions of how competitive is the new idea, and how might it be exploited. The second means adopted was the devising of a series of checklists, to act as an aide memoire . The specific innovative chain for any new idea may thus be supplemented with a list of questions, which the experience of several innovations suggests may be relevant. By checking the innovative chain against these questions, a wider frame of reference is provided, and points omitted in the initial analysis may be added. The checklist, with comments where necessary to define the relevance and context of the questions, is shown below.

A. The Product:

	Question	Comment
i)	What need does it satisfy? Is this an existing need? If a new need, why has it arisen?	e.g. need for improved blue dye New technology, price changes, income changes, organisational change
	If an existing need, how is it satisfied at present?	Can be satisfied by completely different technology: cf. paraquat with ploughing.
	How else might the need be satisfied? Is there anything unsatisfactory with present products? What are the particular advantages of present products?	Technical performance, cost, cost fluctuation, variations in supply, difficult to use, reliability of single supplier, labour availability.

(9) See M.F. Cantley, "Long-range planning in chemical industry", in New Horizons for Chemistry and Industry in the 1990's (London 1970), 167.

ii) At what price does the existing product sell?
Can the marginal cost of the existing product be estimated?
Is product demand price elastic?
What could affect the relative prices of the new and existing products?

Retail, wholesale, bulk discounts.

Raw material costs, import levies, purchase tax, labour charges, transport costs, economies of scale.

How is price measured?

£/ton, or £/operation; see B ii for further questions.

iii) What stages are there in manufacturing the product?

raw material, semi-fabricated articles, completely fabricated article.

What stages are there in distributing the product?
What are the possible points of sale?

Merchants, retailers, etc.

For each, what skills and resources are required?

Complementary products, production knowhow, merchandising skills, distributive network.

iv) How long does the product last before it must be repurchased?
How long is the product expected to last before it is superseded?
Is it liable to seasonal variations?
When is it bought?

B. The Customer:

	Question	Comment
i)	Who are possible customers? How are they identified?	see A iii) e.g. Profession, geographical area, use of existing product or process.
	How are they contacted?	e.g. Existing selling organisation, advertising, via merchants.
	Is the person whose needs will be satisfied by the product the only person to be identified, contacted and satisfied?	
	Who actually decides to purchase the product? Who else is involved?	Government regulations, labour practices, equipment suppliers, raw material suppliers.
	What advantages and disadvantages exist for each organisation?	Profit margin, market share, new technology, new organisation
ii)	How does the customer define his needs? What parameters does he use?	Relative advantage can be shown in these terms.
	Do the product advantages match his needs as he defines them? Does he define his needs explicitly? Will the customer need educating to use the process?	Effects of time on product Change criteria of choice; some organisational change may be necessary: new technology.
iii)	Can the customer experiment with the new product or process? How much is he risking by using the new product? How much is he risking by not using the new product? Is the product compatible with existing processes?	Is existing equipment easily adjusted? Is much capital required? New product may only contribute a small property to overall system. Competitor's action, considerable effect on total system. New production skills may be needed; equipment may be written off; new design or technical skills may be needed.
iv)	How many customers are there? Do any or many have long-term contracts? Will product demand be affected by customer income? What markets are the customers supplying? Are customers' products successful?	What part of the product life cycle has been reached?

C. Competition:

Question	Comment
i) Who are existing competitors? Who could become competitors?	Raw material suppliers, intermediate suppliers, equipment and machinery manufacturers, end-users integrating vertically.
What advantage does the product possess over competitors? What could competitors do to strengthen their position?	Price reduction, quantity discount, quality improvement, technical service, reallocation of purchases.
ii) Are there complementary products offered by competitors? Are there technical services offered by competitors? What delivery and credit terms are offered?	Define product range
iii) Are there patented advantages? Is there know-how?	

By using these checklists, the research scientist may guard against the danger of superficiality in his analysis of the innovative chain. In the example of the new photosensitive film, particular points that were raised included the problems of cost fluctuations in the existing product, which used a raw material liable to large price variation; the correct parameter against which to measure cost, and the problems associated with agreeing this parameter with the customer; the importance of compatibility between the new and existing film; and the advantages offered to the customer's customer by the new film.

There still remains a danger of superficiality. For clearly it is impossible to construct a comprehensive and useful checklist of questions for an activity as unprogrammed as innovation. The questions listed above are intended to reduce the danger of superficiality when a particular innovative chain is being investigated. The checklist is therefore an aid to, but cannot be a substitute for, the systematic enquiry into an innovative chain.

4. Conclusions:

The purpose of this chapter has been two-fold. First, to examine and modify the original simple model of innovation in light of experience gained from the three case studies; and second, to examine the utility of the model in one environment, a particular research Laboratory in the chemical industry. The second purpose may be viewed as the justification of the model. The ideas proposed in this thesis cannot be rigorously proved. What can be shown, however, is that the application of these ideas is helpful to practising research scientists. Obviously, albeit unfortunately for the author, it is not feasible to conduct control experiments to show how research projects would fare without the application of the ideas developed in this thesis. What is claimed, however, is that the model of innovation has led to changes in the way in which research in one Laboratory is pursued. In particular:

i) It has resulted in more attention being paid to the problems of identifying the utility of new phenomena, and hence to less resources being devoted to the generation of new knowledge and phenomena.

ii) It has shown that the problems of identifying usefulness is particularly severe for research groups aiming to produce new integral products, or for those which have weak organisational links with ICI.

iii) It has led to a systems approach to innovation which facilitates research, by identifying important problems quickly.

iv) It has provided a checklist of questions, to ensure that important problems are not neglected.

The model has thus had both overall significance for the Laboratory - effects i)and ii) above - and has aided the assessment of individual projects - effects iii) and iv). A further effect, not predicted when this research

began, has resulted from the explicit definition of a simple model of innovation. This has been the discussion occasioned by this definition. For it has forced research management and research scientists to make explicit the theories of innovation which lay behind their previous patterns of behaviour and work practices; and it has caused a more searching comparison of the effectiveness and usefulness of these theories.