A perspective on plant protection research in the private sector

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Introduction

Most members of our Society are employed by public sector organisations – Universities, Departments of Agriculture, and other government institutions – and their research activities in plant protection are generally well understood and widely publicised. A small number of equally important members, however, are employed in the private sector, but their various activities are less clearly understood or appreciated.

I hold the unusual distinction of having worked on "both sides of the fence", and I, therefore, have an appreciation of how both systems operate. My earlier career in the Victorian Department of Agriculture ended four years ago when I transferred to private enterprise to head the Research and Development (R&D) activities of Australia's largest multinational agrochemical company.

My aim during this address is, hopefully, to try to provide you with a better perspective of the nature of, and the rationale for the plant protection research which is undertaken by the private sector.

I would like to divide my presentation into two sections:
(1) International R&D generally, and
(2) The R&D activities which are undertaken in Australasia.

International R&D

Most multinational agrochemical companies are concerned primarily with the synthesis, evaluation, and development of molecules for use as chemical pesticides, although considerably more effort is now being directed towards biological control and other biotechnology related processes. Some of these companies also have significant seeds businesses.

When considering agrochemical companies, we tend to think of the well known players – Bayer, Ciba Geigy, Shell, Du Pont, to name but a few, but there are many other lesser known European and Japanese companies, e.g., Otsuka, Shionogi, Takeda, etc. who have major investments in the R&D of pesticides.

Scientists from many disciplines are employed (synthetic organic chemists, microbiologists, genetic engineers, biochemists, environmental scientists, process chemists etc.), and large sums of money are spent on the activities they undertake (ICI for example, spends about £100 million/year). Considerable importance is also placed on the patenting and long term protection of industrial property – a valuable commodity in commerce. At the end of the day, the aim is to produce and market a product or process which meets all the biological efficacy, environmental, and regulatory requirements, meets farmer needs, and provides an acceptable return to the shareholders of the company. This latter point is undoubtedly the major difference between the R&D activities of the public and private sectors.

As plant pathologists, we would like to think that fungicides play a more important role in world agriculture than do other classes of pesticides such as herbicides and insecticides, but in reality fungicides play only a minor role (Table 1). Most activity in R&D is directed at herbicides, as evidenced by the level of market penetration achieved by the various classes of pesticides in developed countries (Table 2).

Table 1 International market share by class of pesticide

Class of pesticide	% market share
Herbicide	70
Insecticide	15
Fungicide	10
Other[A]	5

[A] Includes nematicide, rodenticide, molluscicide, plant growth regulator, etc.

Table 2 Major agricultural chemical market sectors and the level of market penetration in some developed countries

Market sector and country	Class of pesticide	% total crop area treated
Rice, Japan	Insecticide	100
Rice, USA	Herbicide	98
Soybean, USA	Herbicide	94
Cotton, USA	Herbicide	90
Maize, USA	Herbicide	85
Grapevines, France	Fungicide	84

The amount being spent on R&D by the multinationals has increased dramatically over recent years (Table 3), and is currently running at about $US2000 million/year. This has been influenced by a number of factors, including:

- The poor success rate in synthesising biologically active molecules (1 in 1500 in 1960; 1 in 15 000 in 1990). Of every biologically active molecule, 1 in 100 eventually reaches the marketplace, and the likelihood of success is low.
- Increased requirements for regulatory and environmental data (Table 4).
- The added burden of regulatory re-registration costs incurred in the USA (e.g., $5 million for a single mesocosym study), and
- The requirements for new types of formulations and packaging.

During the 1970s, the international market was buoyant, with many new products being introduced each year (Table 5), but this has slowed, reflecting not only the reduced rate of growth of world markets (Table 6), but also the high cost of R&D on each successful product launched (Table 7).

Because of the large costs involved, considerable effort is directed towards market research to establish the relative value of potential markets for which new pesticides could be developed. Within most major companies, an annual market of less than $50 million is not worth pursuing no matter how important the particular pest or disease might be to the individual farmer or industry. Major targets only are pursued, because it is uneconomic to do otherwise. In the case of potential new fungicides, the top five targets are perceived to be valued at $475 million annually in incremental business (in 1990 dollars) ranging from $50 million for control of rice blast to $150 million for a systemic fungicide to control cereal foliar diseases (Table 8). Now, there is increased competition with larger competitors resulting from amalgamations and acquisitions (ICI and Stauffer, Rhone Poulenc and Union Carbide, Du Pont and the US business of Shell etc.), i.e., there has been consolidation in the industry. Profitability within the agricultural chemical industry has declined by more than 20% in the last decade, adding further to the pressures on research budgets.

Ten years ago, it was possible to invent a new molecule, complete the necessary R&D, and have it achieving first sales in seven or eight years, and with a patent life of 20 years (16 in Australia), have a period of 12–13 years to recover costs and make a profit. It is now not uncommon to take 12–14 years to achieve first sales (particularly in countries such as Brazil where registration alone may take four years) and clearly, the profitability of a new compound relative to its R&D costs, is much reduced (Table 9).

Table 3 International expenditure on R&D of agricultural chemicals

Year	R&D spend $US × 10^6 of 1987	R&D spend % of sales
1974	800	5.5
1976	790	4.2
1978	1050	7.0
1980	1040	6.8
1982	1100	7.0
1984	1400	9.0
1986	1750	9.6
1988	1800	9.0
1990[A]	2000	9.2

[A]Forecast figures.

Table 4 Requirements for registration of pesticides in Australia, 1950 – 1990

Year	Mandatory requirement
1950	Acute toxicity package 30-90 day feeding study (rat)
1960	Acute toxicity package 90 day feeding study (rat) 90 day feeding study (dog) 2 year feeding study (rat) 1 year feeding study (dog)
1990	Acute toxicity (7 types of study) Sub-acute toxicity (4 types of study) Chronic toxicity (5 types of study) Special studies (6 types of study)

Table 5 Number of new agricultural chemicals introduced to the marketplace, 1974 – 1990

Year	New products introduced
1974	22
1976	17
1978	14
1980	14
1982	12
1984	12
1986	20
1988	18
1990	15

Once a new compound is introduced, it does not take very long (unless the area of chemistry is covered by an extremely wide patent) for competitive products to be available in the marketplace.

In the case of the triazole fungicides and the synthetic pyrethroid insecticides (first introduced in 1976 and 1977, respectively), there was a flood of similar molecules into the marketplace, each one having a

Table 6 World growth in the agricultural chemical market, 1980 – 1994

Year	Market growth index (1987 = 100)
1980	82
1982	90
1984	98
1986	100
1988	101
1990[A]	106
1992[A]	110
1994[A]	112

[A]Forecast growth.

Table 7 Industry R&D spend per product introduced to the marketplace, 1974 – 1990

Year	R&D spend/product $US × 10^6$
1974	35
1976	45
1978	70
1980	94
1982	108
1984	120
1986	90
1988	90
1990[A]	86

[A]Forecast figure

Table 8 Major market opportunities for new fungicides

Market opportunity	Value in Year 2000 $US × 10^6$ of 1990
Cereal systemic	150
Broad spectrum protectant	150
Wet diseases	65
Soilborne diseases	60
Rice blast	50

Table 9 The cumulative discounted cash flow for a typical successful new agricultural chemical

Years since invention	Cash flow $US × 10^6$	Major activity
0	0	First synthesis
5	– 40	Evaluation and development
7	– 60	First sales
10	– 40	Costs being recovered
15	+ 2	First profits
20	+ 40	Patent expires
25	+ 45	Product matures and new competitors

comparable spectrum of biological activity. The competitive edge held by the company which first marketed the new product was quickly eroded and lost (good for the farmer, but not so good for the shareholder) (Table 10).

For many years, the real rate of market growth internationally for plant protection chemicals grew at the annual rate of about 3–5%, but in recent times the continued prospects for growth have diminished considerably and the projections for the next five years indicate zero growth in most markets, and limited growth of 1–2% in a few countries (Table 11). The market is becoming mature. There are, however, still opportunities for growth, particularly in those markets which, to date, have been poorly penetrated. There are also opportunities for new products to replace older less environmentally acceptable products, e.g., replacements for fumigant nematicides such as EDB, 1-3,D,D-D, and DBCP.

Until comparatively recently, it was standard practice within the industry to ensure the biological efficacy of a new molecule as the prime activity in the development program. Clearly, if a new molecule was not biologically active, it was not developed, but if it was active, considerations of toxicology, environmental properties, persistence, etc. were determined later in the cycle.

In this system, millions of dollars could be expended before it was discovered that, on toxicological or environmental grounds for example, a particular molecule was not registerable and it was abandoned. (Such an experience occurred recently with a potential new grape fungicide which had been under evaluation for four years; the estimated loss was $10 million). Current practice is, at least in the major companies, to minimise or avoid this occurrence by conducting efficacy, toxicological and environmental studies in parallel using multidisciplinary research teams. The question of registerability is now determined much earlier than it was before. If particular areas of chemistry are known to cause problems (soil persistence, leachability, toxicity etc.), then the molecule is abandoned early in the cycle, even if the biological activity is outstanding (Figure 1).

Biological control of pests and diseases is being more widely promoted as a viable alternative to the use of chemical pesticides. Undoubtedly, there are opportunities for introducing biocontrol agents but, in reality, the prospects for their widespread commercial use are poor. ICI's estimate is that, by the year 2010, less than 10% of existing agricultural chemical products will have been replaced by biological alternatives. Until biocontrol agents are able to provide levels of control equivalent to that achieved by the use of chemicals, they will not be universally accepted by growers. It is likely that new biocontrol agents will face the same environmental, toxicological, and registration requirements as chemical products and they will probably be more expensive to buy. If the biocontrol agents have been genetically engineered, there may be additional impediments to their acceptance and registration. If you believe organisations such as the Australian Conservation Foundation, public acceptance of the use of genetically engineered organisms is totally lacking, and food products made from them may need to be so labelled, e.g., bread made from wheat engineered to resist a particular pest or disease. Nevertheless, productive research is being conducted in the field of biological control.

The cost of developing new molecules is becoming prohibitively expensive and, increasingly, more effort is being directed at improving the effectiveness and handling qualities of existing molecules, even if they are out of patent. New formulations such as water dispersible granules, water soluble sachets, and the use of micro-encapsulation all provide better, less hazardous products at lower cost than is required for new molecules. The risks to both the operator and the environment from the use of chemical pesticides can be further reduced by improved forms of packaging and handling (Figure 2), and by synthesising and producing new, specifically designed molecules which are more active at rates of application lower than those currently used.

Table 10 Rate of introduction of new competitors in two important areas of chemistry

Years after first introduction	Clustering of new product	
	Fungicide (triazoles)	Insecticide (synthetic pyrethroids)
0	1	1
3	2	5
6	2	7
9	7	11
12	14	17

Table 11 Relationships between market size and forecast growth rates for the top 12 country markets, 1986 – 1990

Sales value $US × 10^9	Forecast real growth % annually	Country
4.6	0	USA
2.8	3.0	Japan
1.8	2.5	France
1.1	4.0	USSR
1.0	5.6	Brazil
0.9	2.1	Germany
0.8	3.0	Italy
0.7	1.1	UK
0.6	2.1	Canada
0.5	4.0	China
0.4	6.0	India
0.3	5.0	Spain

Australasian activities

Relative to the international scene, the Australasian plant protection market, at 2% of the world market, is minuscule but nevertheless is valued at about $700 million. The local breakdown of market segments parallels that of the rest of the world with fungicides being of minor overall importance.

Research activities here (with one recent exception) are directed principally at the registration of new molecules and/or new formulations of molecules which are already in the marketplace.

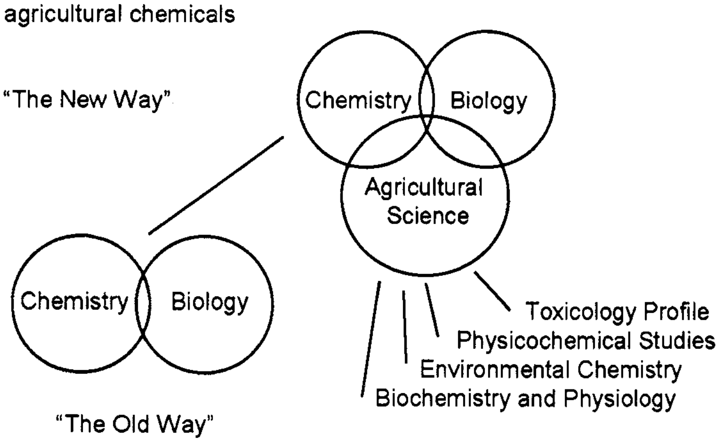
The nature of the research conducted by the various companies depends to some extent on their size, and on the extensiveness of their product portfolios. At one end of the scale, companies such as Nufarm devote their research effort towards the production of new formulations of generic products. ICI, at the other end of the scale, has a wider research base with activities ranging from invention and synthesis of new molecules (until recently), evaluation of biological and chemical actives, and the development of new and novel formulations largely of proprietary compounds. Companies such as Incitec, although they handle principally generic compounds, devote considerable resources towards formulation research in an attempt to differentiate their products from those of their competitors.

R&D budgets in Australasia are modest by international standards with ICI, as an example, spending more than $3 million per annum (probably the largest agrochemical budget).

The cost of research in Australia is less than that of similar programs overseas because of the attractive taxation concessions available here (150%, or equivalent to a cost of 19 cents in the dollar) but despite this, there is a reluctance by managers (most of whom are sales or marketing oriented) to invest more in long-term R&D. Research management is always under challenge, and when times are economically difficult (as now), research budgets are always first to be pruned. Vision is usually lacking.

In recent years it has become fashionable for public sector organisations to establish new business units to commercialise those areas of research which can be. Organisations such as Daratech in Victoria, and Sagric in South Australia for example, have achieved varying

Figure 1 The new multidisciplinary approach to the invention of agricultural chemicals



levels of success but it has not been an easy process. In one state Department of Agriculture, of 400 research projects being undertaken, four were deemed to have commercial value, a surprisingly low number. Good ideas can usually be put into practice only if they can be commercialised, and it is fair to say that in most R&D programs, 20% of costs are incurred in the research phase, and 80% in the development phase. ICI was offered the opportunity to commercialise a plant pathology diagnostic kit several years ago, but declined the offer on economic grounds. The science was good and the kit was sophisticated, but the product would never have made a profit. It was estimated that the market size was 1000 kits per year, at a bearable cost of, at most, $20 per kit, i.e., annual sales of $20 000. The estimated cost of producing a saleable product (suitable packaging, appropriate shelf life, production facilities etc.) was $160 000.

Commercial collaboration with public sector research organisations can be profitable if companies have the courage to invest. Collaboration can be by direct funding of projects such as ICI has done with the Victorian Department of Agriculture on biological control of *Fusarium* diseases, or by participation in projects supported by funds from the Industry Research and Development Board (GIRD grants). ICI has done well from such collaborations. In one current project with CSIRO, an investment of $900 000 (i.e., seed money) over five years, has resulted in an extended research program which has attracted total funds of more than $9 million.

Most Australasian R&D is conducted for the benefit of the national company (i.e., for the purposes of registering a product for use locally). A few multinationals, including ICI, undertake contract research on behalf of their parent companies. Such research, invariably has little direct relevance for the national company, and usually involves the early phase of evaluation of a molecule or process which has not yet been afforded commercial development status. Research here can be undertaken "out of season" in northern hemisphere terms, and provides the opportunity to obtain two years' results in one, thereby shortening the development cycle and achieving first sales and ultimately profits in the shortest possible time. There are, however, benefits in terms of "early hands on experience" from working with the molecule or process, which may be of value locally at a later date. ICI via its international network undertakes some 2500 replicated field trials of this type each year, and this is a massive undertaking by anyone's standards.

Local research needs are established not by researchers acting in isolation, but in collaboration with our commercial (sales and marketing) colleagues who identify new market niches and sales opportunities.

Figure 2 Ways in which risks to operators and to the environment can be minimised

Risk to operator: Low	→	High	Risk to the environment
Mini-bulk containers Water soluble packs Pressure rinsing In-field rinsing	Returnable or recyclable containers		Low
Water dispersible granules Direct injection	Water-based granules Induction hoppers Improved packaging	Manual open pouring Solvent-based formulations	
	Equipment decontamination Waste disposal		High

Once these needs are defined, programs and projects are usually prioritised on the basis of analysis using Nett Present Values (NPVs).

It has been suggested to me that research undertaken in the private sector lacks the rigour applied to research undertaken in the public sector; that because of the profit motive in the private sector, corners are cut and the research is superficial. I can't speak for all companies, but my experience does not confirm this view. Private sector researchers are usually well equipped, and the funds normally provided allow for flexibility of operation quite unlike that permitted in the public sector. Additionally, there are opportunities for attending international or national conferences, and for periods of secondment to work in company research establishments overseas.

Much of the private sector research undertaken is not widely published in the scientific literature, for obvious reasons. The data generated from such research may have commercial value, and this is why such importance is placed on secrecy agreements, industrial property, and patents. The quality of private sector research is, in my view, generally the equal of any conducted elsewhere, but it isn't widely publicised.

In ICI, every field or laboratory experiment undertaken is written up in much the same way as a paper for publication. Strict editorial standards are applied, because each report may ultimately form part of a submission for registration purposes – becoming a legal document in the event that something goes wrong and a damages claim is made. Every registration submission is expensive – $20 000 for a first registration, and $8000 for a label extension. Multiple registrations are preferred over single registrations, to spread the costs, and minor crop registrations are rarely economically attractive. State fees are in addition to these costs.

I would like to conclude with a few comments on environmental research. Environmental research with agricultural chemicals has not usually been undertaken in Australia or New Zealand. Most data have usually been generated elsewhere, and these have been accepted by our regulatory authorities. The time has come, however, where the authorities in many countries require local data, and failure to comply means that new molecules or processes are denied access to the marketplace.

In Australia this has not happened yet with fungicides, but it has been demanded for a new insecticide which ICI plans to market in cotton. The field program has been successfully completed (at a cost of about $800 000), but the quality of the results will ensure that the data can be applied elsewhere for the benefit of others.

Increased environmental demands for the safe use of agricultural chemicals provide an opportunity for progressive companies to gain an edge over their competitors.

The biggest single area for improvement, I believe, is the development and production of new, more active, safer-to-use formulations. ICI has recognised this opportunity and has invested heavily – going so far as to purchase an innovative formulation company in New Zealand. The technologies acquired, allow the production of water dispersible granules – probably the world's best such granules. A new state of the art production plant in Perth has been commissioned and is producing herbicides, while consideration is being given to the establishment of a similar plant to make fungicides and insecticides in one of the eastern states.

This new technology has several advantages:

- Formulations with high percentage contents of actives can be produced, thereby reducing storage, transport, and handling costs.
- The use of solvents is obviated, reducing the hazard of flammability.
- Disposable packaging (paper sacks and cardboard boxes) can be used, eliminating the problem of what to do with used steel and plastic drums.
- Accidental spillages can easily be cleaned up using a vacuum cleaner.

The benefits to farmers and to the environment are obvious, and there is little doubt that the technology has substantial commercial value. In this particular case, the technology can be exported, and already is, and this too generates further wealth for Australia.

In summary, I have tried to provide you with a perspective on R&D in the private sector, not only on the international scene, but also in Australasia. By international standards, R&D here has little significance elsewhere, but occasionally, developments do take place which make the international agrochemical industry sit up and take note.

Acknowledgements

Thank you for having provided me with the opportunity to be the President of your Society for the last two years. It has been a great honour.

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