PITA Project: Policy Influences on Technology for Agriculture: Chemicals, Biotechnology and Seeds

Zeneca Agrochemicals monograph

Annex C16

TSER Programme

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[1]Joyce Tait and [2]Joanna Chataway

[1]Scottish Universities Policy Research and Advice Network (SUPRA)
University of Edinburgh
United Kingdom

[2]Centre for Technology Strategy
Open University
United Kingdom

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Introduction to the PITA Project

Technological innovation in the agrochemical, biotechnology and seeds industries and in associated public sector research establishments (PSREs) has the potential to deliver more socially and environmentally sustainable farming systems and to improve the quality of life of citizens in Europe. This is particularly true of farms on the most fertile land. However, although policies developed in different areas may all aim to improve the quality of life, in practice, in their influence on company and PSRE strategies, they frequently counteract one another and so attenuate the desired effect.

Market-related factors also influence decision making in industry and PSREs, the most important for this project being the policies of food processors and distributors and also public attitudes and opinion, which often set more demanding standards than those of national governments and the EU.

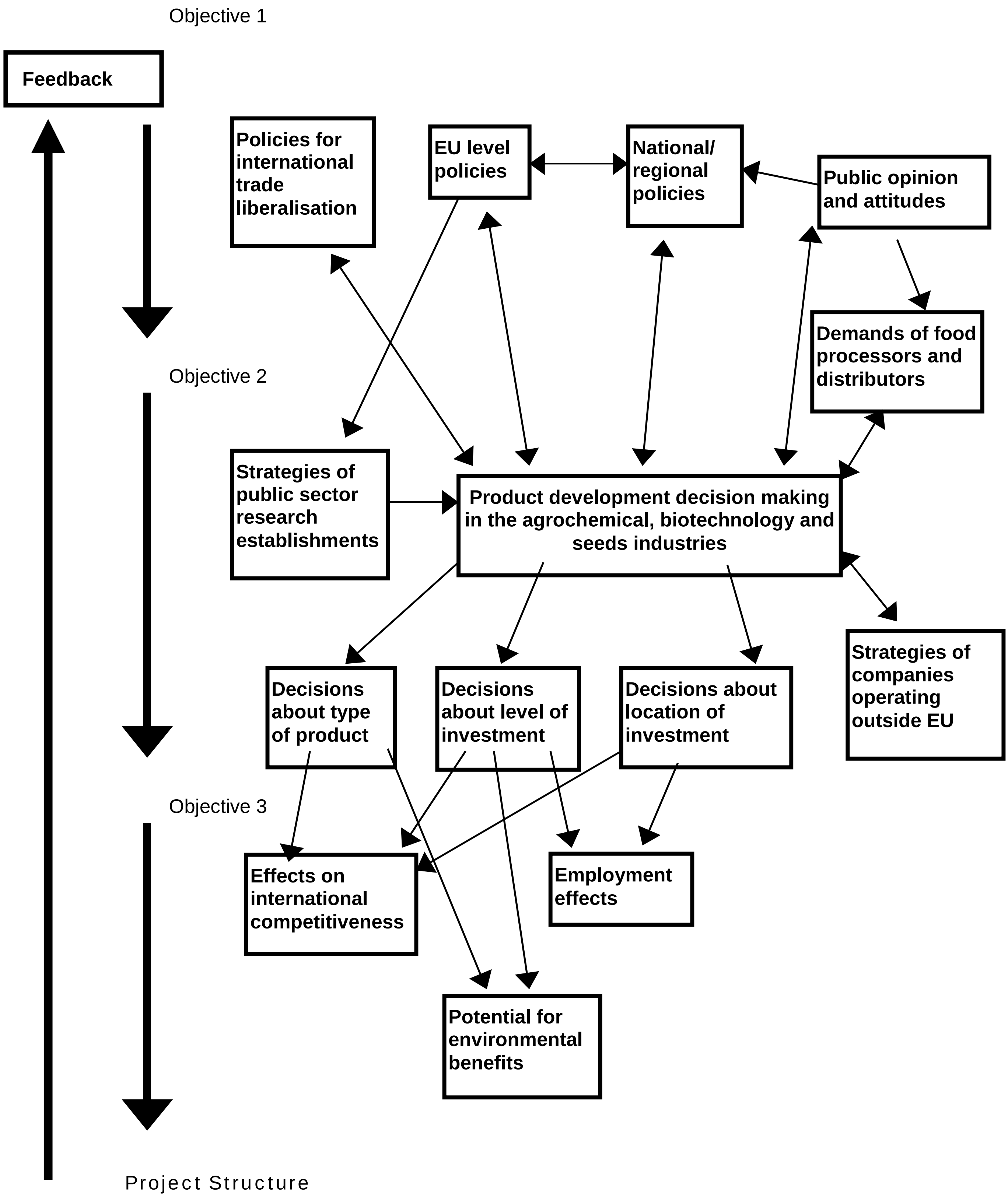
The PITA project (see Project Structure) is developing an integrated analysis of policies and market-related factors relevant to the agrochemical, biotechnology and seeds sectors. The core of the project is an investigation of the impact of these factors on the strategies and decision making of companies and PSREs and the downstream implications of these decisions on employment, international competitiveness and environmental benefits. The final outcome will be feedback of our conclusions to policy makers and company managers.

The range of policies and other influences studied includes:

- policies to stimulate innovation in the agrochemical, biotechnology and seeds industries;
- purchasing policies of food processors and distributors;
- policies for international trade liberalisation;
- policies for the regulation of industry and farming (for environmental protection and public health and safety, particularly for pesticides and biotechnology);
- agricultural and farming support policies, particularly for crop production;
- policies to promote environmental sustainability and wildlife biodiversity in arable farming areas;
- public opinion and attitudes.

The overall aim of the project is to contribute to the development of sustainable industrial and farming systems and an improved quality of life by encouraging the development and uptake of ‘cleaner’ technology for intensive agriculture. Its objectives are:

- to develop an integrated analysis of policies and market-related factors relevant to technological innovation in the agrochemical, biotechnology and seeds sectors, to study their interactions and to develop hypotheses about their impact on strategic decision making in industry and PSREs.
- to study the influence of policies and market-related factors on innovation strategies in the agrochemical, biotechnology and seeds industries and PSREs, and their impact on decisions about product development, levels of investment and location of investment.
- to study the outcomes of the industry decisions investigated under objective 2, in their effects on employment, on international competitiveness and on their potential to deliver environmental benefits.



Project Structure

Contents

1. Background data on Zeneca Agrochemicals

[Material in this section is based on information available from company publications, trade magazines and other press sources. Details of references are given in Section 8.]

1.1 Company history

Imperial Chemical Industries (ICI) was established in 1926 by amalgamating Britain's four largest chemical companies: Brunner Mond, Nobel Industries, British Dyestuffs Corporation, and the United Alkali Company. By the early 1990s it was selling 15,000 products in 150 countries. ICI was:

- the third largest chemical group in the world,
- the second largest agrochemicals producer and
- the fifth-largest seeds producer.

After an unsuccessful hostile take-over bid in 1991 ICI reduced its vulnerability to such events by splitting the company in 1993 into a chemicals company and a bioscience group, Zeneca (*FT* 31.02.92). The crossed Z of Zeneca's logo is derived from an alchemist's symbol, meaning 'to solve' and the Group's success is founded on its ability to provide solutions to customer problems (*AR 1997*).

The concept of life science synergies has always been an important part of the company's thinking and rationale (see Section 3.4). According to a journalist Zeneca 'became arguably the first company to evince its life sciences capabilities' (*PE*, Oct. 1998) The demerger linked pharmaceutical and agrochemical R&D, both of which 'depended upon the intimate intermingling of biology and organic chemistry'. This link was also regarded as useful for handling national regulatory authorities (Owen and Harrison, 1995: 137-38).

A range of other factors contributed to the rationale for the demerger. Like many other multinational companies at the time, ICI was over diversified. Some components had limited internal synergy and sometimes competed against each other, impeding a coherent strategy (*FT,* 03.08.92, 09.03.94). By reducing internal diversity, the new companies could more easily reach decisions and respond quickly to events. The 1993 demerger could thus be seen as attempting to avert an external threat, to overcome an internal impasse, and also to launch a life science based strategy.

The merger of Zeneca with Astra, announced in 1998 and completed in 1999, created a company with $10 Bn/yr sales which ranked second in European and in UK sales and third among world drug companies, after Merck and Glaxo Wellcome. The merger was driven by a desire to reduce costs (by $1.1 Bn annually, or 6000 jobs, mainly in administration), and to obtain better access to the US drug market (*AR 1998*: 13). Also, the companies pooled their strengths in anti-cancer drugs and anti-ulcer drugs. Zeneca argued for a life sciences model which includes agrochemicals but there was no apparent design for the agrochemicals unit in the merged company (see Section 3.4.3). Some trade journalists have been consistently skeptical about the life sciences concept (*PE*, Jan. 1999) and according to an Astra director, Zeneca's agricultural sector was an attraction but would bring no synergy with the pharmaceutical activities (*FT*, 10.12.98).

When we conducted our interviews, the company was structured as shown in Figure 1.1. Since then the formation of Syngenta has been announced, spinning off and merging the agrochemical and agricultural biotechnology divisions of AstraZeneca (39%) and Novartis (61%). Syngenta will be the first global, dedicated 'pure play' in agribusiness and is expected to realise $525M annual savings from the third year. The company will bear the $850M restructuring costs. The parent companies will now focus on the health-care sector. The merger is seen as a creative solution to declining pesticide sales (Daniel Vasella, Novartis

CEO); and a means to enhance value creation in agriculture at a time of substantial industry change (Michael Pragnell, Syngenta CEO Designate) (*CW* 08.12.99).

1.2 Acquisitions, subsidiaries and collaborations

Before the merger with Astra, the Devrinol herbicide business, outside North America and Japan, was sold to United Phosphorus in 1997. An organophosphate insecticide plant in the USA was also closed down as part of Zeneca's strategic approach to rationalising its agrochemicals portfolio (see Section 3.2.2). As noted in a trade article, the closure was aimed at creating a better quality business, as part of restructuring the specialty chemicals unit (*CMR*, 10.08.98). The molluscide Optimol was also sold to Pan Britannica Industries (*Agrow Review* 1998: 21).

A major agrochemical acquisition in 1998 was part of Ishihara Sangyo Kaisha Ltd (ISK), including its US based world-wide business in chlorothalonil (one of the world's largest selling fungicides) and international distribution rights outside Asia Pacific to the fungicide fluazinam, the nematicide fosthiazate, and the herbicides flazasulfuron and nicosulfuron.

Zeneca acquired a number of seed companies in the 1980s and in 1996 these were combined into a 50:50 joint venture with Cooperatie Cosun, called Advanta B.V., the world's fifth largest seed company (see separate PITA Advanta Monograph). Advanta has a role in the development of the new seed varieties with Zeneca (AgWorld Special Feature, 1998)

In 1997, Zeneca announced its intention to acquire Netherlands-based Mogen International, one of the world's foremost plant biotechnology companies, with strengths in genetic modification for fungal and nematode resistance and for the production of enzymes and carbohydrates in plants (James, 1998: 26) (See Section 6).

In plant biotechnology, Zeneca also has formal collaborations with over 50 academic and industrial partners, the following being regarded as particularly significant:

- The John Innes Centre and Sainsbury Laboratory, 1998 – Zeneca will provide $50M over 10 years to fund a new building to house 30 scientists. R&D priorities will be to use genomic information to improve the quality, yield and disease resistance of wheat for worldwide markets, along with an existing collaboration on starch biochemistry. Zeneca will have the rights to develop and market products from the research (Zeneca press release, 1998).
- Incyte Pharmaceuticals, Inc., 1998 – Zeneca will have access to Incyte's phytosequence and trade database, containing sequence information on crops such as wheat, corn and rice; and also to its micro-array technology, allowing study of thousands of genes or multigenic pathways in a single experiment (Zeneca press release, 1998).
- Maxygen, 1999 – Zeneca has made a $5M equity investment, plus $20M for R&D and licensing fees, in Maxygen (Redwood City, CA), a 1997 spin-off from Glaxo Wellcome which specialises in gene shuffling (molecular evolution). Maxygen will develop modified versions of Zeneca's oilseed, cereal and vegetable varieties. Traits include improved resistance to disease, herbicides and pests; also improved nutrition and starch content (*CW* 18.08.99).
- Cambridge Discovery Chemistry, 1999, for a defined period – this company will take over responsibility for Zeneca's chemistry facility within Zeneca's R&D centre in Richmond, California based on its expertise in combinatorial chemistry.
- Rosetta Inpharmatics – a joint venture will give Zeneca access to the Genome Reporter Matrix, a technique for selecting and optimising lead compounds for use in crop protection. Rosetta will provide chemical and biological profiles of Zeneca's research compounds (*CPM*, 31.03.99).

1.3 Company organisation and structures

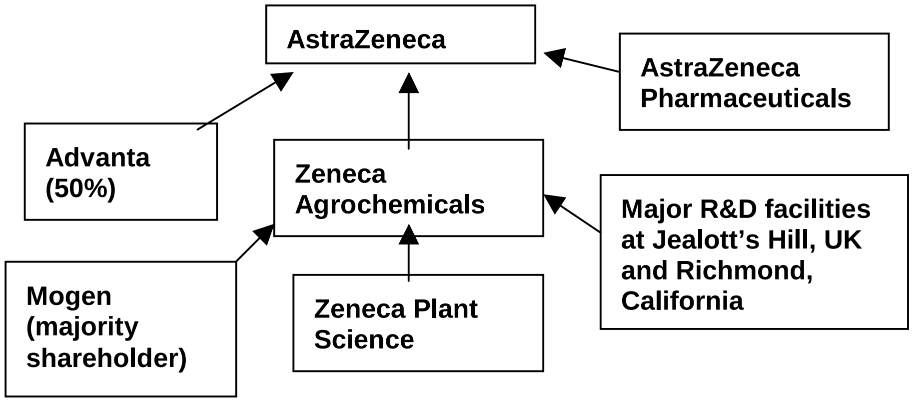


Figure 1.1 Structure and relationships of Zeneca Agrochemicals

Zeneca Agrochemicals is run by a business team based in Fernhurst (international headquarters). Their CEO sits on the main board of Astra Zeneca and there are eight senior managers and directors under the CEO who form the agrochemicals business team.

The main functional heads cover:

- finance;
- business support;
- manufacturing supply;
- research and development; and

product and territorial people are organized as:

- N. America;
- Asia + products (single director);
- Latin America;
- Europe + Middle East +Africa

Dating from before the merger with Astra, sales and other statistics for Zeneca's relevant business units are summarised in Tables 1.1 and 1.2

Table 1.1 Five Year Progression (£M)

Year	'94	'95	'96	'97	'98
Total Sales	4480	4898	5363	5194	5510
Americas	2047	2269	2579	2668	3042
Continental Europe	1351	1507	1665	1477	1553
UK	313	291	368	425	427
Pharmeceuticals sales			2435	2565	2811
Agrochemicals sales			1801	1631	1738
Operating Profit *	797	894	1043	1083	1097
Pharmaceuticals			757	786	815

Agrochemicals			224	223	216
Net Profit/loss before tax	659	619	1011	1081	1045
Total R & D expenditure **	518	549	602	653	708
Pharmaceuticals			390	440	483
Agrochemicals			162	163	172
Agrochemical sales	1521	1639	1801	1631	1738
Agrochemical Operating Profit *	130	144	224	223	216

*Before exceptional items

**Including ‘Specialties’

Table 1.2 Pesticide Sector Sales (£M)

Sector / Year	‘96	‘97	‘98
Herbicide	1033	1025	974
Insecticide	377	329	314
Fungicide	176	204	395
Other agrochemicals	98	73	55
Seeds*	117		
Total	1800	1631	1738

*Since 1996 Zeneca’s income from seeds via Advanta is included under ‘Share of operating profit/loss of joint ventures and associates’ (*AR 1998*: 84).

Zeneca Total Employees:

Total in 1997 – 32,100

Total in 1998 – 34,600

UK 40%

Americas 33%

Continental Europe 19%

Asia, Africa and Australasia 8%

Approximately 7000 staff work in Zeneca Agrochemicals’ business worldwide (Helping Farmers Feed the World).

1.4 Agrochemicals

For agrochemicals R&D, Zeneca has been investing significantly in enabling technologies to ensure that the company remains at the forefront of the industry. It is a leader in the application of high throughput screening to identify new crop protection chemicals and screened over 100,000 compounds in 1998. Combinatorial chemistry is used to provide the chemicals, and genomics to provide insights into plant and animal biology to enable rational targeting and design of pest control chemicals. These technology competencies, combined with specialised knowledge and resources in the agronomic, plant and environmental sciences, give Zeneca the capacity to succeed in biotechnology (AR, 1998, p26-27).

Under the heading ‘An Integrated Approach to Crop Production’, Zeneca Agrochemicals describes itself on its website as a world leading supplier of solutions based on chemical and biotechnology products designed to improve crop yields and food quality. The company also sees itself as a world leader in fungal control, a major player in non-selective herbicides and insect control, and investing in biotechnology to offer farmers alternative ways to protect and improve their crops. Table 1.3 lists the major agrochemical products and the main crops on which they are used (from Zeneca Agrochemicals' website, April 2000).

Table 1.3 Major agrochemical crops and products*

Crop treated	Horti-culture	Oilseeds	Corn	Wheat and Barley	Rice	Cotton	Others
Herbicides	Gramaxone Touchdown Fusilade Reglone	Gramoxone Touchdown Fsilade Reglone Flex Racer	Gramoxone Touchdown Surpass Mikado Eradicane Milagro	Touchdown Achieve Boxer	Gramoxone Ordram	Gramoxone Fusilade	Gramoxone Touchdown Fusilade Rglone
Insecticides	Karate Pirimor	Karate	Karate Force	Karate	Karate	Karate	Karate Ambush Cymbush
Fungicides	Amistar Bravo Anvil Impact Shirlan			Amista Bravo Anvil Impactr	Amistar Anvil		Amistar Bravo Anvil

*Gramoxone, Touchdown, Fusilade, Reglore, Flex, Racer, Scrupoiss, Mikado, Eradicane, Milagro, Achieve, Boxer, Ordram, Karate, Pivimor, Force, Ambush, Cymbush, Amistor, Bravo, Anvil, Impact and Shirlan are trademarks of a Zeneca Group company.

Zeneca Agrochemicals' main manufacturing facilities are at Grangemouth and Huddersfield in the UK, and at Cold Creek, Alabama and Bayport, Texas in the US. Acquisition of Bravo from ISK brought with it a manufacturing facility at Greens Bayou, Texas. Formulation, packaging and labelling is done at locations close to the principal markets.

Recent investments in pesticide production facilities include (cost of new plant):

- Gramoxone in Huddersfield (£40M) and Nantong (£42M);
- Touchdown in several countries, incl. UK in mid-1990s (£61M);
- Amistar plant in UK and USA (£31M);
- Karate and Force (pyrethroids) capacity was increased in 1998;
- Azoxystrobin capacity was doubled in UK in 1999 (£35M).

The product pipeline includes (AR, 1998, p 27-28):

Herbicides –

ZA1296/mesotrione, a pre- and post- emergence herbicide effective against broad-leaved weeds in corn. First registration submissions were made in 1998 and first sales are expected early in the 2000s

Insecticides –

a nematicide with a novel mode of action, to complement *Nemathorin*;

genetic approaches to nematode control (with Mogen);

high throughput screening to find new insecticide proteins which could be incorporated into plants to provide insect resistance

Fungicides –

ZA1963, from the same area of chemistry (strobilurins) which generated *Amistar;* anti-fungal proteins and other genetic fungal control mechanisms (with Mogen)

1.4.1 Herbicides

Zeneca's non-selective herbicides include:

Gramoxone, based on paraquat, the company's leading herbicide; sales have increased annually for the past two decades even though the patent expired in 1976 (C&I, 03/05/99).

Touchdown (glyphosate-trimesium), launched in 1989, registered in many European countries in the early 1990s; increased market share, especially in Latin America, partly through 'integrated weed control'.

Touchdown is intended to compete with *Roundup* for use on glyphosate-tolerant crops. Sales increased since the mid-1990s because it is used on set-aside land, which was increased by the CAP reforms. Sales increased by 30% in 1997, before any usage on Roundup Ready crops. Sales prospects depend upon its price and upon its advantage over Roundup (which is relatively cheap).

The selective herbicide *Flex*, originally for soybeans, was further developed to provide a broader range of weed control.

1.4.2 Fungicides

By the mid-1990s Zeneca planned to achieve a leading position in the global fungal control market and has expanded its fungicide product range across a wide spectrum of crops. Fungicide sales almost doubled between 1997-98. Amistar became one of the top-selling fungicides, just three years after its introduction, with global sales of £184M.

Azoxystrobin provides greater efficacy for all types of fungal diseases. Jealott's Hill staff discovered azoxystrobin by refining and testing 1400 analogues to natural strobilurins. Amistar was granted The Queen's Award for Technological Achievement in 1999 (*CPM*, 30.04.99). It is being registered and sold in all major global markets; and sales have increased in the USA and Europe. Production will be increased at a second plant in mid-1999. Azoxystrobin was one of several AIs included in the first Annex list of EU Directive 91/414 (*CPM*, 31.10.99).

Bravo (chlorothalonil) was acquired from ISK in 1998, although it is no longer patent protected. Zeneca expect that farmers will use it alternately with Amistar as a means to delay the onset of resistance (*FT*, 18.12.97).

ZA 1963 is a new strobilurin fungicide aimed at barley, wheat and apples; expected for market in 2002.

1.4.3 Insecticides

Zeneca increased its manufacturing capacity for its two main pyrethroid insecticides in 1998.

Karate, a broad-spectrum insecticide, is the insecticide of choice on GM cotton in the USA (*1997 Annual Report*). A micro-encapsulated formulation is expected to increase sales.

Force, for protection against corn rootworm; US sales increased in 1997-98.

Despite the increasing availability of Bt crops in many markets, insect resistance is not a panacea. 'There will continue to be a need for insecticides, so we'll be repositioning to concentrate on products that work with Bt crops. To succeed you have to manage genes and chemicals as a pair'. (Simon Bright, Technology Interaction Manager *CW*, 04.02.98).

Fosthiazate is a new nematicide aimed at flatworms, claimed to be more effective than organophosphates or carbamate insecticides. It started test-marketing in 1998.

1.5 Biotechnology and seeds

Zeneca estimates that the plant biotechnology market will grow substantially and has significantly increased the resources devoted to building a strong biotechnology platform. Its plant biotechnology programme benefits from synergy with the genomics capability, which is also used for researching new crop protection chemicals. This forms the foundation for research to identify and characterise genes which confer desirable traits (*AR 1998*: 27). They are developing an agri-genomics capacity, especially through collaborations with other companies and universities. This capacity is aimed both at new pharmaceuticals and also at novel traits for crops (*CW*, 09.12.98). Agriculture and drugs thus overlap; both Zeneca divisions use the same tools (genomics and combinatorial chemistry) and they contract with the same companies (David Evans, quoted in *The Economist* 11.09.99).

Table 1.4 summarises Zeneca's priorities in crop biotechnology, showing the predominance of output characteristics among their future plans. Nevertheless, an important component of the overall strategy is that these output characteristics will add value to the crop itself (changing commodities into specialties) and thus create an even greater incentive for the farmer to protect it from pests, weeds and diseases, either using biotechnology input characteristics or chemical pesticides. In this context, disease resistance combined with new-generation environmentally benign fungicides was an important component of Zeneca's strategy for a range of crops.

Table 1.4 Zeneca's R&D priorities in the biotechnology area

Crop Base	**Input characteristics**	**Output characteristics**
Corn	Anti-fungal characteristics	Nutrition in cereals
Wheat	Integrated pest management	Altered starch and protein crops
Rice		
Fruit	Non-BT insect resistance	Vitamins with anti-oxidant properties
Vegetables (bananas, potatoes, tomatoes)	Nematode resistance	Oils
Sunflower		Processing benefits (economic and quality)
Sugar beet		Improved colour characteristics
Oilseed rape		Plant-derived sweeteneing genes
		Animal feeds with improved nutritional characteristics, e.g. low phytate, higher oil, higher protein
		Projects based on chemical switching, e.g. anti-sprouting potatoes, control of timing of insect resistance

1.6 Patent Issues

Zeneca's gene patents integrate agrochemicals and seeds in distinctive ways.

In some cases, using chemical-molecular 'switches' which allow genes to lie dormant until needed, a transgene is temporarily silenced and chemical sprays (e.g. dichlormid manufactured by Zeneca) then activate the transgene to induce traits such as disease resistance, control of flowering time, delayed ripening or composition. These traits can provide a variety of benefits to the farmer and also minimise the potential environmental impact of GM crops.

This technique is also being developed for creating hybrids more efficiently (*Economist* 09.10.99). Some Zeneca patents cover agricultural input traits, e.g. resistance to herbicides, insects and disease.

Some transgenic insect toxins come from animals (scorpion, wasp, spider, snail) rather than from Bt.

Multiple herbicide-tolerance, e.g. to Gramoxone plus other herbicides, would allow use of different chemicals in the pre- and post-emergence stages.

The Derwent Biotechnology Abstract (a selection of patents by experts) includes the following numbers of patents relevant to Zeneca's agriculture-related interests:

Zeneca	77
Garst-Seeds	7
ICI	70
VanderHave	1
Total	155

In 1997 Zeneca terminated one of its glyphosate supply agreements with Monsanto and began producing its proprietry glyphosate salt herbicide, *Touchdown*, in the UK (*CW*, 12.08.98). In 1988 Monsanto claimed that Pioneer and Zeneca had infringed its patent on Roundup Ready (RR) soybeans because Pioneer had supplied them to Zeneca for testing *Touchdown.* Zeneca in turn sued Monsanto to establish its right to sell *Touchdown* for use on RR crops, contrary to Monsanto licences which prohibit farmers from using alternatives to Roundup. Zeneca sought to resolve the issue before obtaining US EPA registration for the herbicide in 1999. In the subsequent settlement, Monsanto licenced Zeneca to sell *Touchdown* for use on RR crops, in return for a fee (*FT*, 13.03.99). The companies have agreed to negotiate in good faith for Zeneca to have access to additional RR-crops in the USA and globally as each one is commercialised (*CPM*, 31.03.99).

1.7 Environment related issues

Zeneca's published environmental statements emphasise the company's own operations and also the agricultural use of its products.

The Zeneca Group supports the Responsible Care programme and the Charter for Sustainable Development of the International Chamber of Commerce, a top priority being to reduce waste by designing processes which are intrinsically cleaner (*AR 1993*: 25).

Good safety, health and environmental (SHE) management is seen as essential to Zeneca's continued success at all stages of development, manufacture, use and disposal. As part of this stewardship, Zeneca aims to ensure safe distribution of its products and also provides customers with information and training necessary to help them use products correctly and safely (*AR 1997:* 24-25)

The company emphasizes the environmental benefits and safety of its agrochemicals – 'Nature is the world's greatest source of toxicants, some with very specific and targeted activity. By studying the insecticidal and fungicidal properties found in nature, Zeneca scientists are developing new products with similar specific properties' (*Helping Farmers*, 1997). Integrated Crop Management (ICM) is seen as allowing the development of products which are safe to benefical insects, such as the lacewing, as part of sustainable farming systems (*Helping Farmers*, 1998).

The combination of biotechnology and chemicals is also expected to provide growers with integrated solutions to pest, weed and disease control. By locating genes which are crucial to the life-cycles of pests and disease-causing organisms, scientists can design highly effective and specific control agents which attack and interrupt the action of such genes (*Helping Farmers*, 1998).

DNA chips have been developed for toxicological screening of agrochemicals. Each chip contains a set of human genes involved in a specific toxicological pathway in order to test reactions at an early stage of R&D. This will not supplant the toxicology needed to satisfy the authorities but provides Zeneca with alerts to navigate its chemistry into safe areas (*C&I* 15.03.99).

Extensive studies also evaluate the potential effects of a new compound on the environment, with unsatisfactory products being discarded (*Helping Farmers*, 1998). Special laboratory facilities assess the environmental fate and effects of chemicals and effluents allowing registration in countries worldwide (*Brixham Environmental Laboratory).*

The fungicide Amistar, derived from a natural product found in mushrooms was the first product to be registered under the Environmental Protection Agency's (EPA) Reduced Risk Pesticide Scheme, which accelerates the approval of products with superior environmental and toxicological profiles. This EPA decision facilitated registrations in other countries (*AR* 1997) and also facilitated the export of US farm produce sprayed with Amistar.

Gramoxone and Touchdown have opened up the way for the extensive use of reduced/zero-tillage systems (*Helping Farmers Feed the World*), thus minimising soil erosion.

2. Interviews conducted for Zeneca Agrochemicals study

Interviews were conducted during the summer of 1999 with the following senior managers in Zeneca Agrochemicals, including Zeneca Plant Science and also Mogen:

- Global Research Director
- Director Research Planning, Chemicals and Biotechnology Strategy
- Head of Business Support, remit includes human resources, public affairs, business planning (long range strategic planning), and stewardship (cradle to grave ethical management of products)
- Biotechnology Strategy Manager
- External and Regulatory Affairs Group Manager
- Environmental Sciences Manager.
- Managing Director of Zeneca Mogen, based in the Netherlands.

2.1 Cognitive mapping technique

The technique of cognitive mapping is used in this monograph to summarise information from interviews. The maps follow the logic of the explanations given by interviewees. Cognitive maps are presented in the Appendix.

Rules for developing and interpreting cognitive maps are as follows[1]:

Concepts

Maps consist of concepts linked by arrows or lines. A concept is expressed as a short statement covering a single idea or notion, for example assertions about components of a strategy, causes of a problem or means of improving a situation.

[1] Based on the Reference Manual for Decision Explorer Software, pp8-14, Banxia Software Limited, 141 St James Road, Glasgow G4 0LT.

Concepts involve two contrasting parts or 'poles', i.e. they are bi-polar. Thus, where there is '…' in the middle of a concept, this indicates X 'rather than' Y, as perceived by the person who made the statement (e.g. friendly … distant). If the second pole of this relationship is not specified in a concept it implies 'X rather than not-X' (friendly … not friendly).

Links

Links describe relationships between concepts. Along with the concepts, they form a line of argument, a description of a problem or the components of a strategy.

They cover a range of different types of relationship, *causal, connotative* or *temporal*.

Causal links:

A → B indicates that concept A *leads to, or contributes to,* B or A *affects* B.

Connotative links:

A —— B implies that the two concepts are associated in an unspecified way.

Temporal links:

A → B (with a letter 'T' attached to the arrow) implies that B follows in time from A.

Positive and negative links:

Unless specified otherwise, links are assumed to be positive, i.e. the first pole of one concept leads to the first pole of the linked concept. Where a negative sign is attached to a causal link this indicates that the first pole of one concept leads to the second pole of the consequential concept (e.g. A leads to 'not-B).

3. Zeneca Agrochemicals' innovation strategies

[Section 3 is based on information provided by senior company managers in interviews.]

The Appendix includes a series of cognitive maps (3.1 – 3.5) summarising the innovation strategies of Zeneca Agrochemicals.

3.1 Overall strategy

3.1.1 Zeneca's strategy in comparison to other companies

The managers interviewed noted that the major issue for all agrochemical companies is the fact that the market has a relatively slow growth rate in real terms and they need to continue to invest in research to sustain their position. They also have to invest in a new technology (biotechnology) which will not generate returns for ten years. Managers question how sustainable is that position; how do they balance it? One possibility is to take a life sciences portfolio approach and invest seed R&D money in new technology as part of a regeneration of the business.

But that in general is not how Zeneca sees that some other companies are doing it. Monsanto have invested $9bn of shareholder funds in acquisition. Du Pont are quite close to that ($7-8bn, but very late in the day). These two are totally different from everyone else. Most companies (Novartis, AgrEvo, Zeneca) have been investing in technology with some acquisitions but a different order of magnitude. Monsanto is buying the 'channel to market'. Du Pont's big throw has been the stake in Pioneer. Zeneca invested in seeds mainly in the late 1980s at a time when you could buy companies for very different multiples. Novartis, Agrevo, Zeneca, Rhone Poulenc, and Dow have all got a reasonable 'route to market' base, but not as far downstream as Monsanto and DuPont. They are therefore not trying to capture value in the same way.

BASF, Bayer and American Home Products have been later starters with a different strategy for patents, technology and time to market. They are looking for benefits from their agrochemical businesses to help them to move into biotechnology. Zeneca is also doing that but not to the same extent.

There are thus three different camps within the industry who are approaching biotechnology quite differently. There are no other obvious candidate players who have the potential to get into leading market positions. Without the technology base or the 'channel to market' it would be very difficult. Of the top ten agrochemical companies today, four to six of them will make it as leading biotechnology companies in the future.

Zeneca's biotechnology business model has four components in the technology base (gene effects, enabling technology to get it into the crop, freedom to operate (patent freedom), and the germplasm base (seed company)); the fifth component is the channel to market; (see Figure 3.1). In their analysis, only the top ten companies are covering more than two of these components. Zeneca are starting to deal with some specialist, unique technology providers more than they did in the past but these are niche players in gene effects and enabling technology.

Niche players are also using their technology in the pharmaceutical area so they may remain independent with their technology spread over a number of businesses. In the case of the genomics company Incyte, Zeneca has access to their technology in both pharmaceutical and agriculture areas as separate deals (this is not sole access – Incyte also deals with other MNCs on a licensing basis). An alternative is for a company like Zeneca to start its own programme from scratch and that would then become a rate determining step in getting its technology to markets.

A key to success in the ag-biotechnology business is not to take the world as it seems now, even for a company on the edge of the technology, and to project forward 15 years assuming it will not change. In a new area of technology, those who make predictions are looking at a vision which is too narrow if it is just based on current knowledge. The technology has twisted and turned, and the view today is radically different from that of ten years ago.

Many people are involved in getting that breadth of vision and people are challenging one another. Zeneca tries to create an environment where a range of different ideas get out onto the table.

3.1.2 Foresight and Zeneca's overall strategy

The overall strategy of Zeneca Agrochemicals and the Plant Science subdivision is summarised in Map 3.1 (see rear of monograph). The three main components of the strategy are printed in bold at the top of the map: improving the competitive position; shifting the bulk of the future biotechnology income from crop protection features to crop enhancement; and increasing the value of the agrochemicals market. The lower levels of the map present the arguments leading up to these strategic components. These arguments and explanations are expanded in more detail below.

It was clear from our interviews that Zeneca had a sophisticated system of *Strategic Visioning*, looking ahead for 15-20 years, seeking crop-based leadership on a limited number of crops, and linking agrochemical and biotechnology strategies from commercial, technology and PR perspectives.

Figure 3.1 describes the components of Zeneca's Strategic Visioning process and the links between them. There are two Business Team members who sponsor Foresight in the company, on behalf of the technology and on behalf of the business. The Biotechnology business model looks at proposed R&D initiatives from the point of view of both the technology base and the channel to market.

As part of its internal Foresight exercise, Zeneca have selected Key Knowledge Topics such as animal nutrition or attitudes to food, organised as part of an electronic notice board system. The question “Should we put this gene into corn for feeding pigs?” would be informed by appropriate Knowledge Topics. All Knowledge Topics also get external views.

Eventually there is a single list of projects, for chemicals and for biotechnology, along with detailed information about the projects. Choice among projects has been fairly *ad hoc* in the past, but now Zeneca look at each project in terms of:

time scale

fit with strategy

economics

commercial risk (including consideration of public perception).

technical risk.

Projects are scored out of 10 as a way of presenting them to senior managers who will probably challenge the numbers (individual managers will often fight their own corners and may be unrealistic in their judgements). Projects are ranked and funded up to a certain line (there are usually five times as many projects as are funded).

Zeneca’s strategy is to look at its business by crop and to go for crop leadership by giving the market a superlative range of products for a limited number of crops, corn, wheat, rice, fruit and vegetables (particularly bananas, potatoes and tomatoes).

3.1.3 Zeneca target markets and their value

Zeneca’s estimates of the size of the agricultural biotechnology market also feed into the predicted overall value of the agrochemical/biotechnology sector of $75Bn by 2020, compared to the current agrochemicals world market of $30Bn. The future agrochemicals market has a relatively slow growth rate in real terms. Growth in agrochemicals sales to compensate for contraction elsewhere is expected to come mainly from developing countries where Zeneca has noted a 91% correlation between a nation’s growth as measured by GDP and its agrochemicals market. The Chinese market, for example, is expected to equal that of the US in 30 years. (See map 3.1)

In the context of biotechnology crops, Zeneca managers observed that input and output-related crop characteristics are different businesses, with ‘input’ having the grower as the customer while ‘output’ goes right along the market chain. However, on crops with output traits, farmers will also want crop protection elements, either genetic or chemical.

One market model is the changing of commodity crops into specialities which can be segmented in the market, providing an engine of value. The company thus gets its rewards in two ways: for the trait itself and also for protecting a more expensive crop. Farmers will want to see this all in one package so that input traits will complement agrochemicals.

3.1.4 Competition and collaboration with other companies

Zeneca had invested in some seed companies in order to acquire the germplasm base, some gene effects and patent rights, and hence the access to market. However the price of these investments had been more reasonable than investments made by some other companies because of the timing of the purchase. It was more characteristic of Zeneca’s approach to seek collaborations with other companies, as had been done in the development of the GM tomato and the tomato paste product, protecting the technology base and the channel to market by means of legal contracts with other players.

Some competitors have dealt with such issues by representing themselves very heavily in that chain, even buying processors. Zeneca will “stick to its knitting”. Partnering is seen as being more useful because it is prudent and also because the learning process comes from developing the partnership – each company has to learn something of the other’s business. For example, Zeneca did the development work on processing the tomato paste with Hunts in the US; Seminis was the seed company; and Sainsbury's and Safeway the retailers. Zeneca set up the collaborations.

As part of its Foresighting exercise, Zeneca regularly meets with food companies, usually processors (Unilever, Danone, Nestle) but also supermarkets. Senior managers in most food companies are seen to have a very positive attitude to biotechnology but marketing people are very nervous of anything that affects the brand.

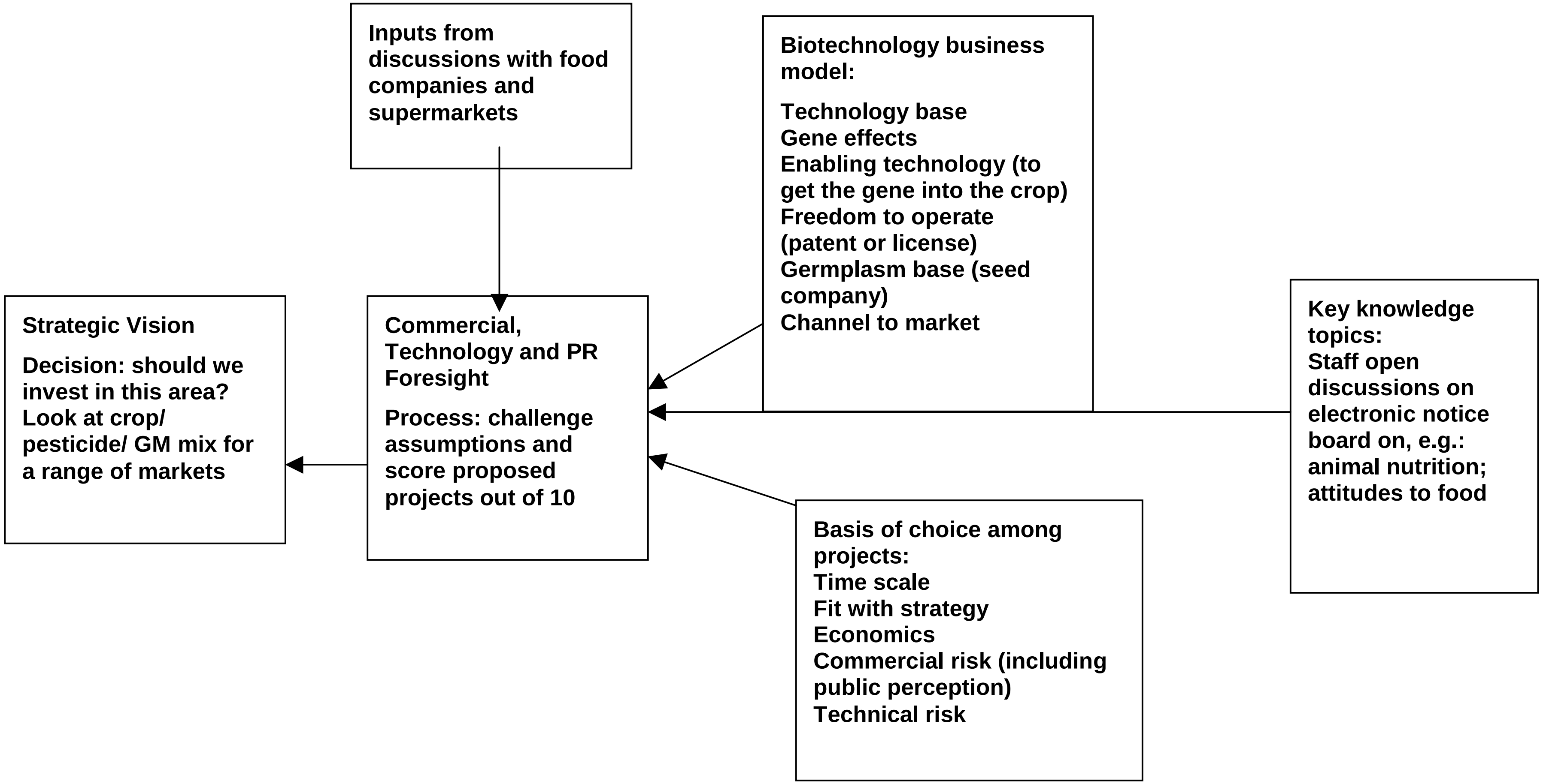


Figure 3.1 Strategic Visioning Process

3.1.5 Links with governments and trade organisations

For links with the press and in some cases government, Zeneca tends to use European Crop Protection Association (ECPA), the British Agrochemicals Association (BAA) and EuropaBio. This is partly in order to develop a consistent message and avoid fragmentation, particularly in the biotechnology area. In the US companies are encouraged to speak to Government but in Europe, particularly the UK, they tend to be criticised for doing so.

3.2 Agrochemical product development strategies

3.2.1 The planning role in the agrochemicals business

Agrochemicals strategies had two major strands, developing the profit potential from existing patented and off-patent chemicals where this is feasible (see Map 3.3), and major investment in new technology to discover better new, patented products (see Map 3.2).

The existing chemical product portfolio is scrutinised for products with a poor ‘return on net assets’ and Zeneca has made major savings by withdrawing altogether from insufficiently profitable markets or by sales to other companies. By 2003, 85% of the agrochemicals business is expected to be in approximately 12 products, compared to 1994/5 when 50% of the business was from 40-42 products.

In the early 1980s the strategy was to try to get products in all market sectors, encouraging customers to buy most of their products from Zeneca’s range rather than that of a competitor. The reduction in the product portfolio is a direct result of their more targeted overall strategy, looking at specific crops, countries and uses, and benefit/cost ratios for farmers, which guides decisions on whether to develop, extend, defend or exit from chemicals in the existing portfolio (see Section 3.2.2). However, this new approach has to be limited because of the tendency of distributors to major on the products of only around five manufacturers, and companies still have to think about leveraging their range.

Zeneca managers commented that getting leads for new chemicals is relatively easy but the development process involves a huge attrition rate from about 200,000 down to 1. A successful molecule has to be able to survive the spraying regime (sunlight, rain, high temperatures); penetrate into a leaf; get to the target site and kill the plant if it’s a weed or not kill it if it is a crop; survive metabolism in the plant; be safe to non-target organisms from insects to cows; not be present in ground water to more than 0.1 ppm; beat the competition; be easy to make and in a safe chemical plant. The end result is therefore a series of compromises and trade-offs.

In the planning process, commercial people in the business think through what the business targets should be for research. Planning groups then manage the process; asking “What kind of portfolio do you want?” There are business inputs in all sections of R&D, beginning with contributing to deciding what the target is (set screens to meet the target), and continuing on a regular basis. This keeps a good awareness of market changes as products go through the development process.

The cost of bringing a new agrochemical product to the market is more than $100 M, which requires significant commitment and a long term view. The new strategy (Map 3.2) for the development of agrochemical products was based on spin-out technology from the pharmaceutical industry, in three main areas:

genomics to validate targets,

combinatorial chemistry to generate large numbers of new chemicals for testing and

high throughput screening to identify the most useful products.

Unlike most other companies, Zeneca carries out ‘in vivo’ tests for efficacy of new chemicals in the early screening stages, using both biotechnology and biochemistry to look for indicators for enzyme systems and to speed the development process.

These innovations enabled Zeneca to go from a screening system which tested 15,000 new chemicals per year to one which tested 200,000 per year, but the end result from the new system is still likely to be just one successful product on the market every one or two years. The high-throughput, more targeted screening is much more efficient at identifying potential new leads than previous systems and the end products will have the higher quality needed to meet today's more discriminating regulatory standards. The battery of tests needed to satisfy various regulatory regimes is so expensive that any molecule taken beyond this initial screening stage needs to have an 80% chance of success. Getting improved products to market was a key component of Zeneca's strategy for maintaining and increasing its market share.

Both the choice of screening target and the criteria for deciding on which products to take beyond the initial screening process are based on a decision process similar to that described in Figure 3.1, looking at countries, crops and uses. There are business inputs to the screening, registration and marketing development stages of R&D and all project teams have business people involved.

The lower section of Map 3.2 shows the contribution to the overall balance in investment of new applications to develop existing products, requiring compliance with additional regulatory hurdles over a 2-4 year period. In other cases there will be a need to ensure that existing products with a good potential return on net assets (see Section 3.2.2) continue to have a viable market. This will require a decision by Zeneca either to defend the product or to move out of that market over a 2 year period.

The upper part of Map 3.2 outlines the role of Zeneca's major new technological developments, based on spin-out technology from the pharmaceuticals area in the agrochemicals discovery process. It is too early to tell the eventual impact of these developments, but they are expected to change the balance between number and quality of new chemical leads, producing better products at the end of the development pipeline but not necessarily a greater number of products.

Producing 200,000 chemicals per year for screening is not possible by conventional synthesis. Synthesis is being automated using robotics, and 'boutiques' have been set up to provide 'combinational libraries' (e.g. Cambridge Discovery Chemistry, Section 1.2). These small companies operate outside Zeneca and take up 25-30% of the chemistry department's expenditure.

Map 3.2 does not show in detail the complex and expensive development process of testing for efficacy against various insect, disease and weed pests, and also for compliance with world wide regulatory systems, which lies between the initial screening stage and the arrival of a product on the market. This is where the 'serious money' investment starts.

The 'fast track' regulatory process developed by the US Environmental Protection Agency (EPA) under its Food Quality Protection Act allows new pesticides showing an environmental improvement over existing technology to proceed more rapidly through the EPA system (see map 4.2). This was used by Zeneca to gain approval for Amistar, its new strobilurin fungicide based on chemicals found in mushrooms. This is now one of the world's biggest selling fungicides from a standing start in 1997. Amistar is now being registered progressively for new crops in new countries.

Decisions to develop, extend or defend particular chemicals will be taken in the light of business targets already set up for particular countries, crops and uses as part of the overall strategy (see map 3.1), in the context of other financial objectives and the need to add shareholder value from technology investments.

Zeneca also recognises that some targets are better addressed by genes than by chemicals, for example soil pests such as nematodes. Chemicals either degrade in soil or are so persistent that they cannot be registered. Factors like this are cutting down the range of chemical targets but 90% of the market for chemicals is still there.

Given the general desire to find replacements for organophosphate insecticides, a new class of insecticides with a new mode of action is a major target and all companies are working on this. Zeneca has some leads in this area but nothing immediate. GM developments have not yet made a big difference in this area – major developments so far are all based on Bt. However, Zeneca is considering some alternatives to Bt (see Section 1.6.2).

3.2.2 Agrochemical portfolio management

To evaluate the existing product portfolio Zeneca uses a 2 x 2 matrix, £ invested against 'return on net assets' (RONA), the latter being a measure of the product 'quality'. They looked at the range of products in the portfolio and took the decision that RONA needs to meet a minimum standard.

On this basis managers decide how to deal with the existing product range, as indicated in the four boxes in Table 3.1.

In Box 1 are products that Zeneca would want to defend and extend.

In Box 2, there is a need to improve RONA, look at why the product is there and move it towards Box 1 if possible.

In Box 3, they would either grow the product or accept that it is a niche product in a high quality niche; in the latter case, they would probably exit from this product market later.

In Box 4, they would either improve the product rating or exit from that market.

On the basis of such calculations, in the last five years, Zeneca have removed about eight active ingredients from their portfolio, either by straight exit or by sale, representing approximately 20% of the total range of active ingredients, avoiding the need for three manufacturing sites world wide. For other products they were able to improve their rating in the matrix.

Table 3.1 Basis for decision making on product portfolio

£ invested ⇑	RONA ⇒	
	2. Improve RONA	1. Defend/extend
	4. Improve or exit	3. Grow niche; exit later

The strategy is to have a greater focus in the business. With the high cost of getting products to market and keeping them there, Zeneca cannot afford to be supporting small products. Products today have got to be bigger, to pay back more, and Zeneca have to be able to get them to market as fast as possible, and launch them globally.

Zeneca sees big opportunities for new technology in future markets. Amistar, for example has an environmental and toxicological profile which is superior to the competitive technology and was the first product to be registered under the Food Quality Protection Act in the US for 'reduced risk' pesticides. In future there will be more such products that can go on at lower rates with less effect on the water table and on non-target species.

If a company has new technology which is also better, there is no problem about getting market share. The number one driver for the industry is 'value for money for the farmer' and the farmer is paying for an effect – dead weeds, dead insects, dead fungi. The conventional wisdom is that, on a cost-benefit ratio, the farmer will probably pay about 1:4 or higher (for every $ spent he is looking to get $4 or more back). New technology is not necessarily more expensive to begin with but the older technology tends to get cheaper once the new technology arrives.

Zeneca's market research on price positioning shows that if they do not get their money out of a product early, the price is unlikely to go ahead of inflation. Price increases in the industry are roughly 50% of inflation so real value has been declining. Therefore the growth in value has to come from innovation.

Zeneca's screening technology and ability to generate new leads (see 3.2.2) gives the company the opportunity to keep investing in R&D. The number of new products developed from this is not greater because the screens are tougher environmentally and therefore investment hurdles are higher to reach the financial criteria for that investment. They have to generate 10 times the number of leads today to have the opportunity to generate the same number of products, but of a higher quality. The aim is to have fewer high quality products and become sector leaders.

In targeting exercises where commercial people are meeting the research people in planning groups Zeneca is therefore asking what is a 'better product', what is the benefit/cost ratio you want to achieve, does this product have a technical edge that justifies the price premium? Will the cost to the farmer be recovered in improved yield, better pest control or more acceptable pest control compared to competitor products which may be cheaper?

In 1990/91 Zeneca amalgamated the technical development department with product management (marketing) and created 'sector business teams'. The names have changed since then but the process has survived although the way they make decisions is changing.

> In the early 1980s the company identified all the market sectors and tried to get products in all sectors The aim was to have a broad range of products to offer the customer so that they would buy Zeneca's product range rather than another company's. Most distributors in developed countries will major on the products of about five manufacturers and cherry pick from others. A company wants to be one of those five, to leverage its range.
>
> To achieve this Zeneca needs to screen research targets from a business point of view much earlier than before. Instead of generating small products that do not meet the criteria, business people have to be intervening much more actively at an earlier stage in the research process to get the bigger products out. The whole targeting exercise has responded to a different view of the future of the business. Product groups became broader to have a mix of skills to make those decisions much earlier in the process.

3.2.3 Issues related to commodity chemicals

The overall concept in bold at the top of Map 3.3 indicates that Zeneca should only give support to off-patent products if they fit the company portfolio at certain stages of development, rather than across the whole product range. The question of how to continue to extract value from their products after they are no longer protected by patent and become commodity chemicals is a major issue for multinational companies. In this situation multinationals face competition from smaller generic manufacturers. Zeneca managers described how they see the generic sector continuing to grow and to squeeze the market (right hand side of Map 3.3), and gave two examples showing how multinational companies could counteract this trend.

An important factor in decisions about defending an off-patent product is the existence of special circumstances which would enable the company to retain control over it and prevent its becoming a target for commodity producers. The first example (left hand side of map 3.3) was Zeneca's decision to build a paraquat production facility costing $42M in China after the chemical had lost its patent protection. Relevant considerations in this decision were the rapid growth in GDP in East Asia; the Chinese policy of attracting foreign manufacturers; the fact that paraquat is strongly regulated world wide making it more difficult for generic manufacturers to produce; the need for large scale production to exploit economies of scale; and the likely important role for a chemical like paraquat in the early stages of development of Chinese agriculture. Zeneca saw a need here both to work in international markets and to have local manufacture where there are big opportunities.

The second example of an interesting commodity chemical issue, given by Zeneca managers, was the decision by Du Pont not to defend their herbicide cyanazine when it became due for regulatory review in the USA. The review would have been expensive and generic manufacturers would not have been able to afford to pay for it themselves. Also, Du Pont had an alternative product in their own portfolio. Unlike the pharmaceuticals market, where a product can lose 40% of sales in its first year off-patent, generic competition is less intense in agrochemicals (see right hand side of Map 3.3). This factor, and the high cost of regulatory review, will inhibit the growth in the generic agrochemicals sector. In the Du Pont case, lack of patent protection thus led to the disappearance of cyanazine from their portfolio and the opening up of a market opportunity for Du Pont's new, patented technology.

In the context of commodity products, Zeneca managers also made the point that growth in the biotechnology sector will contribute to the squeeze on some products in the agrochemicals market.

3.3 Biotechnology and seeds – development strategies

Zeneca managers made the point that when companies began to move into biotechnology in the mid-1980s they had some misconceptions about the nature of the seeds business and the future of agrochemicals and biotechnology as joint initiatives.

Seed producers had traditionally sold on the basis of improved yield but things changed because of Monsanto's strategy of selling crop protection rather than yield. Other companies were caught out by this and Zeneca, for example, did not have a stake in Bt. Monsanto was not strong in chemicals and so had nothing to lose; and having spent so much money in the biotechnology area they were driven down that track.

In making decisions about product development in the biotechnology area, Zeneca selects at two levels of detail. Some of the more interesting and creative thinking is done at the broader level, by global teams, looking at where a crop as a whole is going, what the outputs are used for, how farming is changing, what are the trends in the crop worldwide, what competitor companies are developing (see left hand side of Map 3.4). A different group then considers more detailed targets – candidate products, benefits, cost effectiveness and eventually looking at the crop/pesticide/GM mix for a range of markets.

> *A huge amount of time is going into company thinking about waves of product development from this technology, 5-10 years from now; 10-15 years from now. There will be no products from the current round of Zeneca's early investment for 5-10 years. The portfolio of products now in the final stages of research are expected to be launched beyond 2005 and these products will need a significant amount of development. A major planning exercise is now under way looking at the value of the biotechnology business over the next 20 years which is the necessary time scale for investment and this is expected to lead to an increased Zeneca commitment to biotechnology on a larger scale.*

Managers are looking for products rather than at the technology; output characteristics rather than input characteristics, e.g. nutritional characteristics of cereal products; trends in the food industry; asking what people are looking for. The number of products coming up the critical path depends on the number screened, as with pesticides. A company needs to decide at the beginning what scale of investment they are going to put into it, at what scale do they sequence genes, and this is influenced by the investment in basic science, the genomics revolution. A look at the full potential of the range of products that might emerge from investments in basic science feeds into a decision about the rate of growth of the potential business, rather than making individual product decisions at this stage.

Managers see the value coming out of Zeneca's investment in biotechnology as tiers of opportunity (output traits), or waves of different kinds of products (nutraceuticals, removing negative attributes), e.g. vitamin-enhanced bananas, modified starch crops (looking at starches across rice, wheat and maize, what kinds of new uses might be required).

> Zeneca are not thinking about plants as factories in the next 10-15 years, but short term there is a potential to change and to create specialty crops for the food industry. They are looking at oils, potential additives, vitamins with anti-oxidant properties.

Medium term opportunities are also seen in the area of integrated pest management (IPM), e.g. looking at programmes for fungal control, putting anti-fungal proteins into plants alongside chemical programmes, more effective programmes that will use less chemical and involve genes for fungal resistance within the plants themselves. This is how Zeneca designed the screens that they are using in early screening for new products. They need to consider what kinds of programme would be cost effective.

The tomato story

The tomato story is a very good example of a set of development decisions where the consumer did see a benefit. It has been on the market for 3 years. The developers did not launch 'biotechnology', they launched a product; it was labelled, people made a decision and used it. A lot of what Zeneca learned from the tomato case on the business development process was working with food companies and retailers and consumer and grower groups. That taught them a lot about what needs to be done to launch and get acceptance for a product. The same degree of close attention was not given by other industrial companies to the launch of soya bean in Europe and the tomato product has suffered as a result. The potential for the technology is to create more products like the tomato.

The tomato was Zeneca's first product because they found themselves with some very good technology and were wondering what to do with it at a very early stage. The tomato had been a model crop and they could see that influencing the texture of the product would have processing benefits. The big food companies were extremely interested in it because they could see that improving the processing conditions (reducing the boiling period in processing), along with the other natural benefits (colour, flavour) would improve the final product. The benefits of the technology were economic and in product quality. The decision was made in discussion with food companies to go for a processed, rather than a fresh product. They also had to do a lot of work with seed companies, farmers, retailers, regulators (this was the first product to come through the regulatory system) over a 5 year timetable.

Zeneca learned a lot from this prototype and a base is now established for future products based on plant derived sweetening genes, for example boosting lycopene. The company believed that consumers would be intrigued to have such choices and they have technology under research which will not necessarily be brought to market.

Other products and projects

For other products the benefits are mainly agronomic, for example improved animal feed. In the US, corn to feed animals costs over $10bn/yr, but poultry, pigs and beef each have different nutritional requirements. It is possible to design corn for each specific end use. However, if there is consumer resistance to the meat because it has been fed with a genetically modified grain, that may stop the development of the technology.

The US may be moving to a situation where GM in food products could create difficulties for consumers but Zeneca would be surprised if eating steak from an animal that was fed GM corn becomes a public issue unless there was real evidence of human health damage. It will not be an environmental issue because there is no environmental difference and antibiotic resistance marker genes are already being phased out by industry.

Zeneca are also developing animal feed products (e.g. corn) with the ability to reduce the environmental impact of the feed. The ‘low phytate’ gene improves phosphorus utilisation by the animal and therefore reduces the phosphate content of effluent from intensive pig and poultry production. This biotechnology product could potentially be combined with other genes to improve the nutritional profile giving higher oil or protein content, but in the public relations war no distinction is being made between different technologies.

Zeneca has no projects for which the intention is to stop farmers saving seed. It is difficult to make ‘terminator’ technology work at the moment; the development work could be done but it would be expensive and, given public worries and third world issues, companies will not spend the money.

Hybrid seed would give similar benefits and some crops (soya, maize) are mainly grown as hybrids because the quality is better. However the same is not true of cereals in Europe. If more crops were grown as hybrids, attitudes might change but wheat is difficult to hybridise.

There are also projects based on chemical switching where Zeneca wants to regulate the terminal output of the genes. One such example is anti-sprouting potatoes where a ‘switch’ is placed in front of the gene, regulated chemically or by some other means. For ware potatoes, the gene remains switched off; for seed potatoes the sprouting gene can be switched on when needed. This technology seems logical, legitimate and defensible but it has connotations of attempting to control farmers’ use of the crop.

Another possible example of the use of switching technology would be on Bt cotton. Rather than creating refugia to prevent the spread of insect resistance to Bt, the gene could be part of a controllable system and a chemical spray used to activate the gene to give better resistance management. If Zeneca were working on Bt, they would make it inducible rather than constitutive.

3.4 The ‘life sciences’ concept: synergistic and antagonistic interactions

Since the late 1980s multinational pharmaceutical and agrochemical companies, and some commentators on these areas, have been drawn to the idea that, by linking the skills of chemists with those of a range of biology-based scientific disciplines, innovation could be progressed more rapidly. The trigger for the emergence of the concept of a ‘life science’ based company was the prospect of new ranges of products based on biotechnology (see Map 3.5).

Among the multinational agri-biotechnology companies, Zeneca has been an enthusiastic supporter of this notion. However, external observers have been sceptical about the life science concept and its cost effectiveness based, for example, on figures showing that the Agrochemicals Division of Zeneca contributed 20% of operating profit from 32% of sales (Zeneca AR, 1998). Fifty percent of initial stage research investment (not R&D) is currently in biotechnology without significant income at this stage, compared to the $3Bn agrochemicals business.

In practice there are several distinct areas where there can be either synergy, antagonism or neutrality among the life science-based components of the R&D strategies of agrochemical/pharmaceutical companies. Zeneca managers gave some interesting insights into both the nature of the synergies and also their limitations.

3.4.1 Basic science

The really effective synergy was seen as arising in the basic sciences. The considerable investment in genomics, for example, is as relevant to the development of new chemicals as it is to biotechnology-based products. This was the basis of Zeneca’s decision in 1996, to a greater extent than some other companies, to combine the chemicals and biotechnology businesses.

> When commercial biotechnology became a reality they had to decide whether to continue to have a separate biotechnology business or whether to roll it into one

> business. They decided, to a greater extent than other companies, to roll it all into one business. The reason was largely because of the synergy in basic science. All the genomics (a huge spend) is as relevant to inventing chemicals as to new gene products. However, most of Zeneca's R &D is still in chemicals.

At the basic science level, there was also useful synergy between agrochemicals and pharmaceuticals, for example Zeneca was able to share information among scientists in the two divisions of the company (about science and also about the quality and credibility of scientists working outside the company).

In addition to the synergy between chemicals and biotechnology there is a wider synergy with the pharmaceutical company. The company benefited from these synergies to the extent of millions of pounds per annum, eg getting one licence rather than two. The scientists also synergised. There was a real synergy between businesses, agrochemicals, seeds and pharmaceuticals: all three used the same genomics companies, sharing information and finding out where the real progress was.

Zeneca Agrochemicals have had a genuinely give and take relationship with the pharmaceuticals division, with the flow mainly but not entirely from the pharmaceuticals to the plant sciences. Most successful agrochemical companies have pharmaceutical based parent companies. It is helpful but not obligatory. It is not the case in reverse. Also the pharmaceuticals division has been very concerned by the public protest about agricultural biotechnology.

The synergy works well where both partners are interested in sources of chemical novelty, but things are different in the gene area. Functional genomics, as a platform technology, can help both sides to invent secure chemicals, but unlike pharmaceuticals, the ag-biotechnology people also want to put genes into plants and this has a created a public reaction that can give rise to conflicts of interest.

3.4.2 Synergy between agrochemicals and biotechnology

The early vision of synergistic interactions between seeds and chemicals has not yet materialised. Contrary to early expectations, there have been only limited synergistic links between the chemicals and seeds products in the market place (See section 3.3.1).

There used to be a concern that, with two separate businesses, the gene business could damage the prospects for an interesting chemical. The view now is that, if Zeneca do not do this, somebody else will. This is synergy at the commercial level; given that there is no biological panacea it is better to have alternatives. Zeneca's strategy is to optimise the combination of chemicals, genes and information, as in the fungus resistance/fungicide combination. In fact this particular synergistic interaction was not planned that way from the beginning. The two components were being developed on separate tracks and were then brought together. The fungus resistance/fungicide example is closest to market but similar strategies are in place elsewhere, going for crop leadership on a limited number of strategic crops and having a superlative offer on these crops.

There is no doubt that biotechnology will knock out some products. In the context of Bt cotton, Zeneca did not have Bt and could not work in cotton, but they believe they have the world's best cotton insecticide so, prior to the launch of Bt cotton, they researched an integrated programme and positioned their insecticide molecule on it and their market share increased.

There will never be a plant that is totally disease or insect resistant. GM traits and chemicals will therefore go together. Within the company this is usually what is meant by integrated crop management, although it's actually a more powerful concept than just genes and chemicals.

The farmer is looking for an effect and if a biotechnology effect can be superior to a chemical effect, it is certainly going to be more convenient. It is not just the cost of the chemicals but the labour and expense of applying them. On bananas, for example, a large number of fungicide sprays are used each year and any contribution from GM control will be beneficial in terms of reducing use of chemicals and also allaying onset of resistance to chemicals. The aim eventually is to reduce fungicide inputs by 50% and also to provide a health benefit.

There will be a combination of chemicals and transgenic methodology (as opposed to conventional breeding) for decades to come. There is nothing technical on the horizon to replace herbicides – nobody is going to engineer the weeds, and biological control methods are not working.

The idea that some new GM-based output traits in crops would enhance the value of the crop, thus increasing the demand for crop protection chemicals, is one example of a synergistic interaction between biotechnology and chemicals at the market stage (see Section 3.1.3). Herbicide resistant crops are also an excellent example of a synergistic interaction between chemicals and biotechnology, although this trait did not feature highly in discussions with Zeneca managers.

However, the market itself is not well integrated. Companies like Zeneca deal with distributors, not directly with farmers, and in the USA chemical distributors are rarely the seed distributors.

There were also interactions between some chemicals and biotechnology in the case of pest problems such as nematodes and other soil pests which were seen as being more amenable to biotechnology than to chemical treatments. With a chemical it is very difficult to strike a balance between sufficient persistence to ensure effectiveness and rapid enough biodegradability to avoid residue problems.

Zeneca is developing a forum to consider interactions between crops, pesticides and GM technology and the likely impacts on future markets.

3.4.3 Synergy between agrochemical and pharmaceutical divisions

As noted above, synergies between agrochemical and pharmaceutical divisions of multinational companies have been mainly in the very early basic science stages of the R&D process. There has so far been no demonstrable synergy in the later stages of development. In the case of GM crops, natural and useful collaborations are likely to arise with food retailers and distributors rather than with pharmaceutical divisions of agri-biotechnology companies.

Synergies between pharmaceutical and agricultural areas of biotechnology were seen as potentially arising over a 20 year time scale, for example through the use of plants to produce drugs and also through the increasing emergence of health-related output traits.

> Further downstream, the strategy for GM crops is currently very much food, feed and fibre, only because of limited resources and the need to have focus. However, growing pharmaceutical products in plants is potentially exciting and in other circumstances some ag-biotechnology managers might sign on to this. By 2020 investors should be investing in the output trait businesses, even those that normally invest in pharmaceutical companies.
>
> *One area of possible synergy with pharmaceutical divisions could be through medicinal benefits from crop plants. However, linking medicine and diet is 10-15-20 years down the line and by that time it might be the case that agrochemicals and pharmaceuticals no longer have the link.*

4. Policy and other external influences on R&D strategies

[Section 4 is based on information provided by senior company managers in interviews.]

This section considers managers' views of the range of policy and other external influences outlined in the Introduction that could affect the R&D strategies of multinational companies. Some of these, such as climatic factors, Common Agricultural Policy (CAP) reforms and the

Millennium Round of negotiations in the World Trade Organisation (WTO) are likely to influence company strategies indirectly via the market for pesticides and GM crops (Section 4.1). Others such as formal regulations for pesticides and biotechnology, and changes to these regulations, will have a more direct impact (Sections 4.2 and 4.3). Public opinion could impact directly on company decision making and also via markets in food processors and supermarkets as well as on farms (Section 4.4). Section 4.5 looks at the nature of 'environmental discourse' within Zeneca – how the company discusses environmental issues in general and how they are perceived as influencing strategy.

The appendix includes a series of cognitive maps (Map 4.1 – 4.3) summarising policy and other influences on Zeneca Agrochemicals' R&D strategies.

4.1 WTO, CAP and climate influences on the market for pesticides

Map 4.1 illustrates how a range of factors, short and long term, related to policy changes in the WTO and CAP, and also climate fluctuations, can influence decision making on agrochemical products. Bold arrow 1 at the top of this map indicates that the broad environmental and policy objectives decided by the corporate planning department, as described in Section 3, are still the major influences on the decision path for an agrochemical product. However, the range of factors feeding into arrow 2 on Map 4.1 also have an influence on these decisions by affecting the Business Team's view of future product groups and sectors.

4.1.1 WTO and CAP reforms.

The Millennium Round of WTO negotiations may succeed in making European farmers more reliant on world crop commodity prices and less reliant on EU subsidies for their income. Planned reforms to the EU CAP could have similar impacts, regardless of the outcome of WTO negotiations (see centre left strand in Map 4.1).

WTO and CAP reforms will have an impact at a trans-continental level on where particular crops are grown and hence on the range of pest problems to which they are exposed, altering the level of demand in some existing pesticide markets and opening up new demands in others. These reforms will also affect the profitability of different farming systems to varying extents and hence, theoretically, the extent to which farmers can afford to pay for crop protection products or more expensive GM seeds. Zeneca will want to have both products and distribution channels relevant to its target range of crops in the regions where these crops will be grown in future.

CAP developments are likely to affect markets in Zeneca's European region and the company watches the debates carefully to see where the CAP is going. For example, the downturn in the agrochemical industry in 1991 was an over-reaction by the market to a CAP change. Those companies who predicted this development and put their houses in order were in better shape than those who did not.

World Trade Organisation negotiations are the responsibility of Zeneca's commercial people but some other managers see them as a source of conflict which could exacerbate public concerns about GM crops (see Section 4.4).

The 'set-aside' policies of the EU also created a new market for herbicides and Zeneca benefited from having anticipated this (see Section 1.4.1, *Touchdown*).

4.1.2 Climatic effects

Zeneca managers discussed climate effects, long term and short term, only in the context of pesticide sales and development. GM crops were not mentioned in this context.

Long term climate change, as with WTO and CAP policy developments, could have the effect of shifting the location of cultivation of some of the world's major commodity crops, making them more susceptible to new ranges of pest problem, opening up opportunities and also closing options in some existing markets. However, global climate change was considered too distant a factor and too uncertain in its impact to be taken into account, except possibly in the case of major potential shifts in cultivation patterns. (See left hand side of Map 4.1.)

Zeneca has to predict where the major crops are going to be grown in future and hence what their product requirements will be. If climate change creates a shift in the wheat belt in China, this will create a market for new crop protection products. Similarly, because soya beans are mainly grown in South America, companies do not have a good range of products for soya bean in Europe. If policy or climatic factors were to lead to soya beans being grown in Europe, Zeneca would want to develop relevant products for the European market.

Short term climate fluctuations in major commodity crop producing areas can have a dramatic impact on crop harvests and on plant protection needs and have a bigger impact on the Business Team's view of product groups and sectors than long term climate change (see central strands of Map 4.1). For example poor spring weather in the USA in 1999 led to a reduction in sales of agrochemicals. This was compounded by the fact that there were two good commodity grain harvests in 1997 and 98 which increased holdings of commodity stocks. This, coupled with the financial crisis in Asia, reduced the demand for imports and led to low commodity prices, reducing the incentive for farmers to use crop protection products and hence reducing sales.

A related factor, illustrated in the bottom right hand corner of Map 4.1, is the observation by Zeneca managers that the world runs on an alarmingly small forward cover of approximately six weeks on commodity grains. This is leading to a situation where relatively small fluctuations in the level of reserves can have a major impact on commodity prices. When stocks are high and prices are low, in Zeneca's experience farmers will spend less on crop inputs. If the stock goes below six weeks, panic sets in and the price shoots up. If it gets to ten or twelve weeks, prices are on the floor. These short term fluctuations in supply and demand also have a dramatic effect on the short term business.

However, there were seen to be limits on the extent to which farmers could cut down on their inputs, even when times were hard. For pests like boll weevil or potato blight, pesticide sprays would be necessary every year. Farmers could take the risk and cut down on the protective use of pesticides for other more sporadic pests which perhaps only created problems every third year.

4.2 Pesticide regulation

4.2.1 The European and US regulatory systems

Both the European and US pesticide regulatory systems were mentioned by Zeneca managers as having an impact on R&D strategies but only in a routine sense (See map 4.2). For wheat, a largely European crop, the European regulatory system was very relevant to Zeneca's decision making and the area was regarded as well regulated. For most crops the European system was less relevant than that of the USA.

Overall Zeneca has no problem with the standards in the policy framework for conventional pesticides in Europe and N. America. Where a product has some environmental advantages, the policy and regulatory environment is improving in most places. However, Europe is dragging its feet in the area of re-registration of pesticides.

The USA are pragmatic and they tier their legislation. Within the EPA there will certainly be a problem with some of the more acutely toxic organo-phosphorus insecticides, in the context of regulations and also import tolerance – to import into the US one must meet their standards.

Harmonisation of regulatory systems world-wide is an issue in which the agrochemical industry has long been interested. However, progress in this has been very slow and there was an air of resignation in Zeneca that this was unlikely to happen in the foreseeable future.

In theory there was still seen to be a central registration system in Europe but in practice, following the emphasis on subsidiarity in the 1990s, each country still regulates on the basis of local issues. In fact in both the EU and the USA the legislation tends to be driven by individuals. In the USA many people do not realise that, despite the strong federal system, the states themselves are often more important and have their own interpretation of policy.

One aspect of the European regulatory system that was seen as inhibiting was the Drinking Water Directive – because of the very low limit set and the fact that it does not take any account of the relative toxicity levels of the chemicals involved, it was tending to exclude some potentially very useful and environmentally beneficial products from the market place. Amistar, the first product to be registered under the US ‘fast track’ system, initially faced rejection by Zeneca at an early stage in the screening programme for this reason. The new emphasis in the EU regulatory system on pesticide metabolites will make it even more difficult to develop new compounds.

4.2.2 The impacts of regulation on technology and employment

Proposals by the UK Government and by the EC for imposing environmental taxes, for example on pesticides, were seen by Zeneca as a concern for industry. Farmers’ incomes are at a low level and there is not much ‘recreational’ use of pesticides at the moment. Farmers are looking to shave rates and avoid sprays if possible. But if a potato grower gets blight, he has to use pesticides and the outcome of a pesticide tax would be an increase in the price of potatoes. Taxation is an inappropriate and blunt weapon and industry would like to see an efficient system.

Zeneca saw pesticide regulation as having the capacity to create markets, but managers were critical of early attempts to do this as they did not incorporate any incentives for industry. In the early 1990s regulators were trying to get greener products with no levers or rewards. People have always imagined that a more modern chemical will replace older chemicals in the market but there is very little evidence for that.

The need to re-register older pesticides has created some market opportunities for better, more environmentally benign chemicals (see, for example Section 3.2.3). However, the US Food Quality Protection Act (FQPA) was seen as potentially the most effective instrument in improving the environmental and health performance of new pesticides. The FQPA has changed the basis of competition from individual safety assessment to comparative risk analysis; this is leading to greener products rather than products directed to a specific market. Companies compete on product performance and lack of restrictions on use. There is a ‘risk cup’ and once it is full there is no more room for ‘me-too’ products. In R&D planning companies therefore need a lot of market data. They need to look at how their new product will shunt out others (their own and other companies’).

These factors have a knock-on effect on the rest of the world because the US sets the import tolerance levels for the world and there’s no doubt that a molecule that comes through that system is safer. It is also registered faster which gives it a market advantage and, just as important, the breadth of its label will give it a commercial advantage. So getting a compound now which has got ‘safer’ status will knock out or will limit by definition the impact of what is already on the market.

This is a paradigm shift in the way companies look at things. Whereas in the past, coming to the market late with a product which mimics an existing product but is less safe in EPA terms, would have been possible, now it is just a waste of time. This has pushed the industry towards a block-buster strategy – marginal developments are not worth taking forward.

Another reason for this shift in emphasis is the heavy safety/health/environment requirements on new chemical plant, so you no longer see a dribble of small molecules coming to market. This has been Zeneca’s strategy since 1991.

Food processors and distributors were also seen as having an important impact on pesticide use by farmers. Zeneca managers estimated that approximately 30% of pesticide sprays were specified somewhere along the food chain.

Pesticide regulation was also seen as a generator of employment in the industry, creating a need for a great deal of environmental science expertise in a range of disciplines. Zeneca employs 250 environmental scientists.

4.3 Biotechnology regulation

Zeneca managers contrasted strongly the biotechnology and pesticide regulatory systems in Europe. The continuing regulatory uncertainty in biotechnology could have a potentially serious impact on R&D strategies, particularly of European companies. They will have to make some hard decisions. They have too much research and not enough money coming back and there is a real indecision problem around the European regulatory system which is feeding back in the US. Managers were pessimistic and predicted that the problems with the EU Directive 90/220 would not be solved until the fourth quarter of 2000. Also, at the time of the interviews there was no threshold for the food industry and no guidance on feed regulation. It was seen as a political problem not a regulatory one.

The advisory system in the UK is also seen to be in a state of turmoil. The Advisory Committee has been reconvened with no ‘issue group’ involvement and it is hard to find good academics that do not have links to industry. Also some academics have refused to put themselves under that sort of pressure. The changes mean that the UK is moving towards a more European agency approach. There are pluses and minuses but it removes national choice and the democratic step.

Zeneca’s experience trying to get approval to grow its GM tomatoes in Europe was seen as an example of the failure of the European system. They wanted to grow the tomatoes in Europe for processing to avoid the need to transport them from the US (thus saving on fuel). They submitted the environmental application in November 1997 and it was held for a year in Spain where they were making some internal political decisions between the Ministry of Health and the Ministry of the Environment on how they should deal with the tomatoes as a ‘novel food’ rather than from an environmental perspective. No technical information was requested.

Subsequent stages in the process became very confused and a qualified majority vote was lost by three votes. The EU system was then stalled for several months and a decision was considered unlikely in time for the 2000 planting season. Supermarkets are also out of stock of the tomato paste.

This is a very good example of how regulatory indecision affects all parts of the industry. For companies, it is difficult to see how one can get consensus among fifteen member states when some are opposed on principle. Zeneca felt any attempt to influence the decisions of the EC under these circumstances would have been misguided.

Despite this experience, Zeneca managers did not feel that they were seriously affected in the long term by the problems with the European biotechnology regulatory system, provided similar problems did not spread to other parts of the world. After the GM tomato their next product will not be on the market for some time.

There was a strong feeling that many of their products did offer environmental and health benefits (see Section 4.5), but reluctance to believe that these factors would actually be influential on European public opinion, for example that the European public would buy a banana whose real benefit is less pollution and less hardship in Honduras and Costa Rica.

4.4 Public opinion influences on biotechnology

4.4.1 Ethical issues

Where genes are being transferred from one plant to another Zeneca managers felt that ethical issues were not really relevant. This, and the arrival of new crops with beneficial output traits could possibly over-ride consumer resistance but such choices would not be available for some time. Nutritionally enhanced products for an ageing population are seen as a huge growth area, particularly in pre-prepared food, and Zeneca are in active dialogue with food companies on these issues.

Much of the European debate about GM crops and food was seen to arise from a combination of misinformation and lack of information. The ethical dimension was thus in the deliberate misinformation of the public and in the failure to inform them about changes in their food supply about which they were entitled to know. People do not understand the science and technology behind GM crops and a lot of information was forced on people in a very negative environment, rather than there being a logical build-up to the debate.

Also the European public do not like not being told what is in their food. They did not even know there was soya in most of the food they were eating and perceptions changed suddenly from no knowledge to ‘it’s in everything’. People also feel negative about the fact that companies like Monsanto make money out of GM soya, rather than there being a public benefit, and pressure group involvement has contributed to the negative information environment. This contrasts with Zeneca’s GM tomato puree which was labelled as a GM product from the beginning, which was cheaper than the conventional product and which was outselling it.

As a result the European public agenda has become ‘We’re not having it’, rather than ‘Let’s make sure it’s safe’ and the regulatory system has ground to a halt.

4.4.2 Influence of public opinion on Zeneca strategies

Public opinion was a major current concern among Zeneca managers involved in the development of GM crops and seeds. Companies had been taken by surprise by the level of public protest. With such a huge investment over such a long timescale (the need to invent and to make it work) it causes concern if people might not want the technology at all.

However, these problems were not yet affecting Zeneca’s investment strategies. They are proceeding in the short term on the assumption that a stable regulatory environment will emerge in Europe and there will be a gradual acceptance of GM crops within a robust regulatory environment. They have been investing in new pieces of the jigsaw throughout 1999 and there were other deals in negotiation, making sure they have routes to market. But companies cannot sell a technology, they can only sell products.

Zeneca seemed prepared to hold on in Europe for a further two years. Beyond that point, decisions about possible re-location, with all the attendant implications for employment, would depend on the trajectory of the conflict in Europe and also in the rest of the world. Zeneca are one of the bigger players and could move research investment out of the UK and put it in the US. Others could do the same, taking biotechnology research jobs out of the EU. If all first product launches are in N. America why should Zeneca have all their development people in Europe? They need assets and buildings in N. America and why should they duplicate this? The research should be close to where the business will be and they would only locate in the UK if there is a business in Europe.

It was seen as unlikely that the American public would become as concerned about biotechnology as Europeans. The scenario has to be considered by the industry but there is a lot reinforcing acceptance in the US. The national media are different; they are more localised. There is no evidence of harm from GM soya and no difference in its chemical make-up. It is helping farmers and there is no evidence of any change in the environment. US agriculture is different – whole states are like big factories. The question becomes, has the American public had its debate in the 1980s, and do they have a different view of the technology? Research suggests that the American public feel they have a better understanding and greater confidence in the technology.

Another relevant issue in the GM debate discussed by Zeneca managers was ‘What constitutes GM free food?’ They emphasised the difficulty now of obtaining food products which are totally GM free. One hundred percent GM free crops probably already do not exist, and the chance of creating them, other than in crops which have never been modified, is slim. There is a difference between GM/non-GM and GM free/non-GM free and labelling and choice will be important issues. The EU policy is different from the US at the moment and the US Food and Drugs Administration (FDA) was seen as unlikely to change its policy of not labelling.

The important question for managers was, "What becomes mainstream food, longer term?":

using pesticides, along with non-GM crops (this seems to be the currently acceptable approach);

using pesticides along with GM crops (prognosis unknown); or

organic crops (without pesticides or GM crops).

Subsidiary questions then were:

how many of these sectors do you have and how big are they;

what types of GM are acceptable (e.g. extra carotenoids in food);

does the company have something which provides a recognised benefit.

4.4.3 Dealing with public opinion

The strength of the negative public reaction to GM crops in Europe in early 1999 had been unexpected. Given the heat of the debate, some managers saw no point in trying to enter public discussion until there were products available with clear consumer benefits.

Zeneca managers saw themselves as having a responsible and non-confrontational approach to public concerns. They do respond to public opinion but hopefully not by turning down viable projects within the company. They support regulation, point out the benefits and provide choice. They meet with other sides of the argument to explain their position.

An example of this approach was their handling of discussions with a local organic farmer who was told by the Soil Association that he would lose his organic accreditation because he was within the six mile exclusion zone from Zeneca's trial plots. Zeneca invited him to the site and spent a day talking to him about farming, not politics. He became convinced that there was no risk to his crops and that some genetic engineering developments could benefit organic farming.

Zeneca also favoured information provision, about the benefits and costs of the new technology and its products, and also about the underlying science. For all their products, the public should be given full information and a statement of the benefits. Some think that the industry hasn't spent enough time explaining the benefits. This was seen as difficult in the case of herbicide resistance but if one understands the economics it is there. (If it is cheaper, in a free competitive market, it will have an impact on the market).

Another important factor, which has been neglected, is choice – the public should have absolute choice. If any international body does not provide choice, that would be wrong.

Most important is the need to expound everywhere, from schools to public debate, the principles of scientific method. Peddling beliefs stains the reputation of science and has caused a large amount of public distrust.

The question of trust, particularly in the regulatory system, was given a high priority. On the other hand, for some, the days of trust in industry were seen to have gone.

The big issue for most consumers was seen to be whether GM food is safe to eat. However, robust toxicological screening of foodstuffs would be difficult as there are no rigorous methods for testing novel foodstuffs. Unlike drugs, one cannot do chronic toxicity testing – animals grow poorly if you feed them nothing but bananas. The research would also need to compare the novel food with the traditional and there are not yet methods for doing that. A cost/benefit analysis or a cost/uncertainty analysis is needed before industry can demonstrate 'substantial equivalence'.

4.5 Environmental discourse in Zeneca

As noted in the Introduction, the central question underlying the PITA project is whether technological innovation has the potential to deliver more socially and environmentally sustainable farming systems and if so, how do European policies affecting pesticide, biotechnology and seed companies facilitate or inhibit that outcome. In our interviews, all the managers we spoke to, regardless of function, were equally at home discussing environmentally relevant issues. ‘The environment’ was seen as highly relevant to their decision making across all functional areas, and was becoming more so with time (see Map 4.3).

A major planning exercise was under way in the autumn of 1999, looking at the potential rate of growth of the business as a whole over a 20 year time scale, and the most productive combinations of targets, rather than looking at products on an individual basis. In this process, Zeneca subscribed to the classic business sustainability model of the ‘triple bottom line’ which looks not only at the financial aspects of a company’s performance but also at social and environmental aspects.

> If Zeneca looks at its business in sustainability terms, long term, they need to be addressing all these issues. They are trying to co-ordinate a programme that recognises and addresses all these issues. The question of agricultural sustainability is a subset of business sustainability which implies that farmers can continue to farm crops on an area of land so that, in a generation’s time, their children can farm crops on it - protecting the sustainability of the land for future generations.

4.5.1 Triple bottom line: financial sustainability

Most of the aspects of financial sustainability have already been discussed in Section **4**. Without financial sustainability, a company will go out of business and social and environmental aspects then become irrelevant. However in discussions with Zeneca, managers emphasised that food production involves a long chain of business enterprises, linking those who supply the inputs for the farming systems, the farmers themselves, food distributors and processors, retailers, and eventually the consumers. Every link in this chain has to be financially viable for the food production system as a whole to function effectively. In this sense therefore, agricultural sustainability was seen as a subset of business sustainability, protecting the sustainability of the land for future generations being an important component of that.

The issue of organic farming was discussed in this context. While organic farming was seen to have a role to play in promoting social and environmental sustainability, it could never provide more than a partial answer. From a financial perspective, perceived problems with organic farming included the need to have a mixed arable farm, the need for flexible crop rotations to minimise endemic pest problems, the unresolved difficulty of weed control on organic farms and the yield and, in some cases, quality penalty.

From an environmental point of view, it is important to make sure that all non-natural interventions, chemical or cultural, do not affect non-target species, biodiversity or the soil. Conventional, integrated and organic farms could all contribute to this end.

Whichever farming system is involved, unless there is sufficient income for long term viability, the land will be put to other uses, for example golf courses.

4.5.2 Triple bottom line: social sustainability

In the social context, managers referred to a range of societal groups with a legitimate interest in, and concern about, the company’s activities.

The most high-profile aspect of this within the company currently is dealing with public concerns about GM crops, as described in Section 4.4.3. A range of other interest groups was also involved in discussions with Zeneca in a variety of contexts:

- various stakeholder groups involved in discussions about product impacts
- neighbours living near Zeneca facilities, e.g. the organic farmer described in Section 4.4.3.
- company employees
- peasant farmers and the impacts of Zeneca activities on their farming systems
- impacts on social infrastructure

4.5.3 Triple bottom line: environmental sustainability

Several issues relevant to environmental sustainability are included in earlier sections of this report.

However, as indicated in Map 4.3, the rationale underlying Zeneca's combined strategy for the development of pesticides and GM crops includes an important strand of environmentally relevant justification. The strategy of using new technology to develop more environmentally benign chemicals can contribute to environmental sustainability but, in producing pesticides, companies still need to use non-renewable resources in a variety of ways:

- energy to build a factory
- energy and organic chemicals from oil to produce the pesticide;
- energy to distribute the pesticide and to deliver it to the crop.

The factory also produces effluents and there will also be some environmental impacts from the addition of pesticides to the environment.

Using GM technology combined with pesticides, pesticide usage can be reduced, avoiding the addition of chemicals to the environment. A major additional sustainability benefit comes from avoiding the need to manufacture the chemicals and to distribute and apply them, using less energy and natural resources and avoiding the production of effluent from the factory, and in some cases even avoiding altogether the need to build the factory. (Development of manufacturing facilities for pesticides is one of the most costly aspects of pesticide development.) This amounts to using the energy of the sun to substitute for non-renewable sources of chemicals and energy.

5. Zeneca Mogen

[Section 5 is based on an interview with a senior company manager in Zeneca Mogen.]

5.1 Zeneca Mogen background and structure

Mogen started as a daughter company of the US based company Molecular Genetics when they decided in 1985 to set up a subsidiary in Europe focusing on plant ecology research. The research building became operational in 1987. Molecular Genetics then took a strategic decision no longer to be involved in plant biotechnology and Mogen, with money from several investors and also from the government, became independent in June 1987. They operated as an independent company until they were acquired by Zeneca in June 1997.

Zeneca now owns the majority of the shares and Mogen are operated at arms length through a supervisory board. The Management Board consists of three people, the Mogen chairman and two co-directors from Zeneca. This is also the direct link with Zeneca.

Mogen operates as a centre of excellence for Zeneca and has had strong growth in the size of the research effort since June 1997 and also an increase in the capacity of the site. This is important as a small company does not have the means to access the big technology developments in genomics and bio-genetics.

Mogen still have strategic collaborations with a limited number of other companies but that will eventually disappear. In the acquisition by Zeneca, Mogen looked after the interests of existing contract partners but decided not develop additional contracts with other companies. If it is considered to be of strategic importance to have a collaboration with another company in future then that would be organised by the controlling partner.

Mogen also have collaborations with the Universities of Leiden and Wageningen and with universities in England.

5.2 Mogen product development strategies

5.2.1 Before the link up with Zeneca

Before the link-up with Zeneca, Mogen had the typical business interests of an SME – to have up-front money to pay for the research cost and in the long term to have royalty income on the products being developed.

Mogen's technology base, supported by a strong patent portfolio and with contracts involving all the major seed companies, included:

crop protection;

fungal and nematode resistance;

output enhancement (producing specific enzymes in seeds, eg low phytate);

and yield enhancement.

> The basis of Mogen's fungal programme was a number of strategies to develop broad spectrum resistance, mainly in tomato and potato crops. Success in these areas could then be extended to other crops, but it was up to contract partners to develop the technology in their crop of interest because Mogen could not work simultaneously in all crops.

Companies must also balance carefully the needs for innovation and for pragmatism. High risk, fundamental research takes place in universities and research institutes and companies are involved, if at all, through collaborations.

> It is important to be creative but this should be incorporated in the normal process of doing research, with some room for creativity and people working on projects which may not immediately have a clear benefit. The really high risk projects will be progressed in a collaborative set up rather than spending in-house effort on those areas. This is the normal approach. It is a very important task to focus the in-house research efforts on the most important areas for the company.

Mogen previously had a business department but its reach was limited. The strategy was to sell contracts and operate on a research contract basis, generating up-front money and also some royalty later on. Mogen were able to make contracts with all the major seed companies in the world for their fungal programme and through those business contacts they had a good feel for what companies were seeking in the bio-technology area.

5.2.2 After the link up with Zeneca

The activities of Zeneca and Mogen were highly complementary but the strategy of Mogen has changed so that research is now primarily on contract to Zeneca and in line with their biotechnology strategy. Fungal and nematode resistance remain the prime areas of focus. Work on transformation of the potato and crop enhancement projects were also a valuable asset for Zeneca and were continued and strengthened.

Fungal resistance has been one of the main biotechnology targets of all the big companies but the easier projects were done first and fungal resistance is a more complex target. For herbicide or insect resistance a single gene will provide the trait but to develop broad spectrum fungal resistance it is necessary to find the right combination of genes to provide durable, broad resistance.

Research in the Netherlands and Jealotts Hill is now focused mainly on different crops. For example, Mogen had been working on tomatoes but most of that work is now concentrated at Zeneca's site at Jealotts Hill. There is also a shift in Mogen towards work on cereal crops.

In planning and carrying out the research programme, managers and researchers at the fore-front of research are not very aware of downstream needs and changes in markets. They need good and regularly updated information on what the end product should look like and whether there will actually be a customer. Very early in a research project, an understanding of the virtual product profile is needed, followed by further analysis over the years as the product develops to make sure that the virtual product profile is accurate and that there will actually be a market when a product is ready. This means having good up to date knowledge about agricultural practices, for local areas and for regions because that can influence the degree of success. The first product should be applicable in broad areas and later on when success is there the company will explore the niche areas.

To achieve this, there is a triangle of interactions between the research, business and patent departments. In discussion with the business people researchers get information on the needs from the business perspective – how the product should look, what is the market. The business people can also contact other potential companies who may be potential buyers of the product or a strategic partner in a joint development of the product. The patent department's input is on whether the products and the technology will have 'freedom to operate'. The research component of the triangle sets out the strategy to deliver the prototype product (see Figure 5.1).

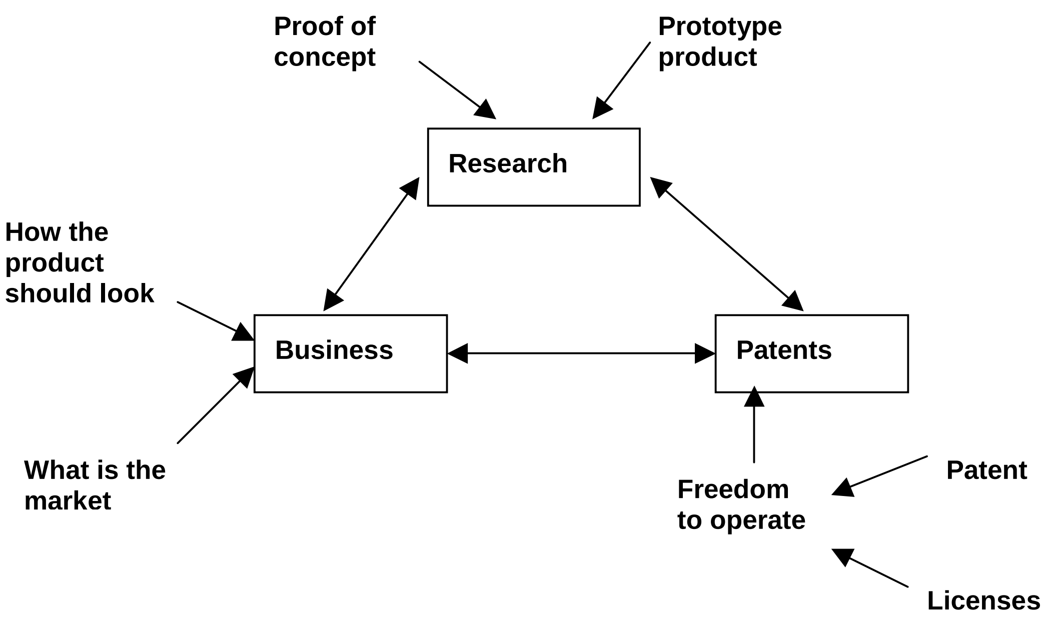


Figure 5.1 Mogen's 'triangle of interactions'

There is an interaction between a business that understands the market, scientists who have ideas, how to deliver a certain trait or whether it is possible to develop such a product, and the patent person who ensures that whatever is being developed will be properly protected but also knows who is in the field, having

> other patents, creating the need to take a licence. Zeneca, for many years an agro-chemical company, know the markets and what is important. With the opportunities from biotechnology the strategy might be re-directed but in the end a company sets out a certain strategy and then research will try to deliver the products, and this is not easily changed overnight.
>
> Managers look for the target ten years from now that is recognised throughout the world (for example Septoria tritici resistance in wheat). In a project there is a need for the breeder's input, then it is up to the research to demonstrate that the chosen strategy is viable, providing the proof of concept, and then to ask the breeders to evaluate the material. There is always a grey area when there is a handover of the project to the breeders but the concept should involve the downstream partners at a very early stage.

In the context of interaction with plant breeders, Mogen's links with Zeneca and its breeding subsidiary Advanta gave it better access to plant breeding knowledge. They still have to do the invention part and to be able to develop proof of concept. When they have a successful strategy then they contact the breeders and say "Look we have interesting technology, we'd like to move into your breeding". They need to consider what is the right germplasm to introduce the transgenic event because most of the proof of concept support is done in varieties which can be transformed easily, and not necessarily varieties that are used for the commercial market.

> An important factor in the attraction of Mogen to Zeneca, in addition to its patents and programmes, was the staff working on the projects and they have been successful in retaining the staff. Zeneca has a clear strategy to look after employees and they have a competitive benefit package. There have been a lot of positive outcomes for staff from Zeneca being the new owner of the company. Projects were strengthened and the employment conditions improved. Also, international career opportunities increased compared to what Mogen could offer its employees.

5.3 External influences on strategy

5.3.1 Innovation policies

When Mogen was operating as an SME, they could get access to EC funding. This supported some programmes but it was not something they could build into their business strategies because the funding was limited. In the later Framework programmes the conditions became more disadvantageous for companies like Mogen. For Framework 4, Mogen was very concerned about intellectual property being accessible to competitors and decided to find money to support research in other ways.

> The bureaucracy around EC programmes is such that companies should think seriously about joining. If it is an area which is of strategic importance, where the groups joining are at the front end of science then it is worthwhile but it should not be entirely in the company's core area. In that case it would be strategically far more important to develop a bilateral collaboration to strengthen the area.

Mogen knew of examples of EU projects where it took so long to negotiate consortium agreements that the agreement was not signed until the programme had finished. There were also projects where a company stepped out during the negotiation process and the programme fell apart.

In a relatively undiscovered area where there is a lot of basic research to be done, EC Framework collaborations were seen as appropriate. However, if the research is moving to the applied area companies will have conflicts of interest and the programme will not be successful if multiple companies join or particular companies stay out. It is a lot of work for participating companies and for the scientists, so the time investment should be paid back from the outcomes of a project.

Companies are very active in setting up bilateral collaboration with universities and research institutes. The costs are higher than for an EU programme because there is no government subsidy but the influence of participating companies on the research and on the targets set is far greater. The interaction and communication among the scientists also strengthens the overall research effort. Universities have been forced by the reduction in revenue from governments to operate in a more professional way and to undertake more collaborative research.

Universities are also now more aware of the need for a formal contract as the basis for any collaboration with a company and also the need to safeguard any IP generated by the project. However, not all the IP generated will be a valuable asset. Most universities think that if they safeguard the IP that will generate a lot of money in the short term – they have unrealistic expectations about the value of the intellectual property being generated. They also have a lot to learn about how to secure the IP in the best possible way. A patent which only gives protection in one country is not useful at all.

Mogen commented on the fact that, on the one hand, economic affairs in the Netherlands are promoting biotechnology and the start up of companies, and at the same time they are discussing a moratorium on GM trials and products. This is seen as a disconnection. Where policy makers do not understand the subject or they are manipulated so that they cannot have a consistent policy this is a big concern. In the end the company will hold back in making investments in this area. Ernst & Young analysed the impact of bio-tech on employment in Europe – it will definitely have a significant effect on the number of jobs.

5.3.2 Antibiotic resistance markers

Mogen commented on companies' decisions not to develop any new products that include antibiotic resistance marker genes. Companies are working on alternatives to these markers but this is slowing down research while they re-focus their efforts. While it might be technically possible to do this in one or two crop species or as a demonstration project, it may take another ten years for other crops. It is also not easy to remove such a gene at a later stage in product development because generally such genes are linked to the trait. The first such products will have a selectable marker gene linked to the trait which is not an antibiotic resistance marker gene. All these factors will slow down product development.

5.3.3 GM regulation and the impact of GM crops on pesticide use

The research and development programme for GM crops was seen as having a range of potential effects on pesticide usage on European crops:

- The fungal resistance project aims to reduce fungicide use in agriculture. Biotechnology will not be the only answer to all fungal problems so there will be a combination of the use of novel pesticides applied at lower doses along with transgenic traits. The end result of this will be reduced use of fungicides in agriculture, something that European regulatory and other efforts have so far failed to achieve.
- With herbicide resistant crops, many studies have shown that herbicide use has not been increased and in some cases there has been a reduction in use. More interesting is that the plants in the field perform better and grow more uniformly, giving a higher yield. This could reduce the amount of herbicide used per yield of crop.

  Companies often use the term integrated crop management – the total package you have to provide: the high quality seed or the high quality germ plasm; the traits that go with it; and also the knowledge to grow that crop in the best possible way. This differs from area to area and also in the use of different types of agrochemicals to get the maximum benefit. In good agricultural practice it will always be the target to limit the use of chemicals.

Considering the current difficulties with the regulation of GM crops in Europe, the situation was seen as having serious effects on the rate of development of the technology. In the end a company will work with the regulations, but if there is not some clarity then it will be an unworkable situation. Europe is approaching that situation now and that will have to change in the interests of clarity to the company but also to the consumers. There are not a lot of scientifically valid arguments to ban certain products from the market until 2003; however, the European Committee is not ready or not willing for political reasons to take certain decisions.

In the farming industry there are also opportunities which are being slowed down. Development time in the agricultural area is longer than in the human health area because it is a different type of business. But also because of the unclear regulations, financial investors are hesitating to invest in agricultural bio-tech. That is something Mogen experienced as an independent company when they were looking for financial investors to support the business. In the US companies can generate much more money than here because of the clarity of products being accepted. Without that clarity there will be immediate negative feedback on opportunities for these start up companies.

5.4 Development of SME sector in biotechnology

Mogen also commented on the trajectory of biotechnology SMEs as they begin to grow and to be successful. If they grow to a certain level of success then somebody will buy the company and the end results of the start-up company will never be seen because they will be integrated into a multi-national company at a certain moment in time. In the US sometimes the big multi-nationals allow a spread of companies to generate business and see whether they can be successful as a small independent company before taking them over.

6. Conclusions

6.1 Zeneca Agrochemicals

Zeneca Agrochemicals has a complex and sophisticated strategic planning process. From the perspective of the PITA project the major strands of this strategy are the financial components and the inter-linked environmental and policy aspects. As with any commercial company, strategies to maintain and retain a strong market position, satisfying the demands of shareholders, are always dominant. However, in this case, environmental policies and issues were often an integral component of these financial strategies, rather than being a *post hoc* justification.

The major strategic issues faced by the company were seen to be:

- the fact that the agrochemicals market was expected to be relatively static in future and Zeneca's desire to stay among the leading companies operating in this market; and
- the need to continue to invest in new technology (GM crops) when no significant income was expected for several years in the future.

Environmental and other policy issues were aspects that the company needed to take into account in its strategic planning in a variety of ways, either as problems or opportunities. The only issue which could be described as a major cause for concern was the European public reaction to GM crops and the consequent EC regulatory impasse. Even here, this would only become a serious issue for Zeneca if it persisted in Europe for more than two years or if the concerns and the regulatory consequences spread to other major market sectors.

6.1.1 Commodity chemicals

A considerable amount of strategic planning effort goes into decisions about the development of the product portfolio for agrochemicals already on the market – deciding which products to retain and support and which to drop or sell to another company. Once products have outlived their patent protection, regulatory and environmental factors play an important role in these decisions, for example impending regulatory review and the cost of undertaking this, balanced against the likely competition from commodity producers and the size of the market.

6.1.2 New pesticides

The development of new technology, from chemistry, biotechnology and biochemistry, to enable Zeneca to screen greatly increased numbers of potential agrochemical products each year was driven both by increased competition within the industry sector and also by the steadily increasing stringency of regulatory systems worldwide. New pesticides generally have a better profile from environmental and public health points of view than those which have been on the market for some time.

The US Food Quality Protection Act and the associated ‘fast track’ system for the registration of new pesticides through the US EPA was the most effective regulatory driver, even for European companies, in encouraging these changes. On the other hand European governments’ planned imposition of pesticide taxes was seen as an inefficient and in some cases ineffective approach. Likewise the EC Drinking Water Directive was in danger of preventing some products with an otherwise good environmental and public health profile from reaching the market because it focuses exclusively on the physical amount of residues in water and ignores their toxicity relative to other products.

6.1.3 GM crops and seeds

The main focus of Zeneca’s strategy for GM crops was on output traits, many of which would be largely irrelevant to environmental and sustainability concerns. However, an important strand of the *commercial* justification for development of both input traits and new pesticides was the assumption that farmers would have a greater incentive to protect such higher-value crops from pests.

Some of the output traits on which Zeneca was working would have a direct environmental benefit, for example ‘low phytate’ animal feeds and feeds tailored to the nutritional needs of different species would reduce the environmental impact of animal husbandry systems.

Input traits (insect and disease resistance) were assumed to have the potential to reduce greatly the use of pesticides. However, they were not expected to do away with the need for pesticides altogether. Zeneca is considering combined strategies for the development of crops involving both GM technology and pesticides.

Herbicide resistance, while not directly reducing pesticide usage did alter the nature of the herbicides used and, commercially, was changing the balance of power among competing companies. Glyphosate and glyphosate trimesium (Touchdown), used with Roundup Ready crops, would greatly reduce the need for ploughing in some farming systems with a vulnerable soil structure. Zeneca Mogen also made the point that herbicide resistant crops were generally more uniform and higher yielding, reducing the use of herbicide per unit of output.

Much of the justification for the GM crop strategy and its interaction with pesticide strategies was thus based on a sophisticated interplay between commercial and environmental factors.

6.1.4 Sustainability issues

Summing up the concept of agricultural sustainability, Zeneca managers made the following points:

- the agricultural system has got to work the biology has got to be right

it has to be sensitive to the environment

it has to be socially sustainable

it also has to be economically sensible – every link in the chain has to make a return or it doesn't continue.

In discussing environmental and sustainability issues, in the context of pesticides, the need to build a factory which complied with all the relevant safety, health and environmental regulations, manufacture the pesticide (with some inevitable production of effluent), distribute the pesticide to its markets and apply it to crops (with attendant use of fuel and pesticide residues in the environment) were all seen as factors potentially affecting the overall sustainability of Zeneca's operations. GM crops with insect and disease resistance input traits were seen as having the potential to reduce the need to manufacture pesticides and so would contribute to improving this aspect of sustainability.

6.2 Zeneca Mogen

The interview with Zeneca Mogen was particularly interesting for the insights it gave into the issues facing a biotechnology SME working in the agriculture area. Zeneca Mogen referred to the inevitability of the transition from being an independent company to being a subsidiary of a MNC if an SME's research strategy is successful. The advantages of this change to the SME include improved access to resources, no longer having to look for venture capital and to spend energy seeking new contracts, and improved conditions and opportunities for staff.

Zeneca Mogen gave an interesting perspective on the strategic planning cycle as a subsidiary of Zeneca, describing a triangle of interactions between business, patents and research functions **(Figure 6.1)**. In the research role, whether as an SME or as a subsidiary of Zeneca, there were strict limits on how far Mogen could go down the route of 'blue skies' research. This was seen as more appropriate to universities or research institutes, probably in collaboration with a company. The research strategy of a commercial company on the other hand had to be driven by more immediate market-based objectives.

The question of EC strategies for the promotion of innovation was also relevant to Zeneca Mogen whereas it had been of much less concern to Zeneca. The EC Framework Programmes were seen as of limited value to an SME and Zeneca Mogen commented on the discrepancy between the policies of some countries to promote the setting up of biotechnology SMEs on the one hand, and regulatory actions which impeded their chances of success on the other.

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Appendix

Cognitive maps based on Zeneca Agrochemicals interviews