Crisis in innovation

There is little doubt that R&D in the agchem industry, and to a lesser degree the pharmaceutical sector, is in the doldrums. **Dr Rob Bryant** contrasts the fortunes of both industries to find out why these science-based industries appear to be failing to innovate

It often seems that we now live in a new dark age of unreason in which the leading 'scientific' luminaries are politicians, legislators and economists, many of whom, are the promoters of highly suspect credos, including those of man-made global warming and the precautionary principle. Many powerful environmental lobbyists consider that recent technological progress ought to be rolled back to the golden age of a 'pre-chemical paradise' (the EU's REACH legislation is imbued with this type of thinking). In developed countries, the increasing affluent decadence of the population is matched by an increasing poverty of thought. Meanwhile, the world of man continues to be beset by real challenges. Feeding the ever-increasing world population by repelling the resurgent microbial attacks upon our food crops is one pressing example. And creating new treatments for the constantly evolving diseases that afflict human beings is another.

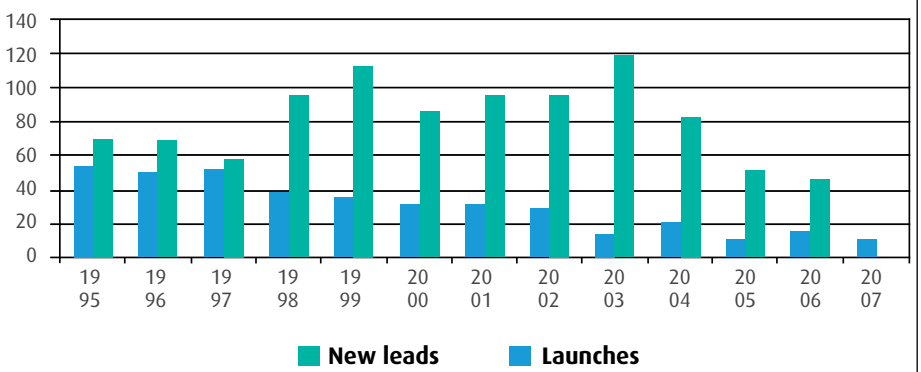
One particular facet of this general malaise is the bioscience industries' recent faltering ability to innovate. This crisis in innovation has grave implications for mankind's continuing ability to maintain the health and nourishment of the majority of the world's citizens.

The stark reality

Over the past 60 years, the agchem industry has created valuable inputs into agriculture, which have enabled the world to continue to feed its ever-growing population. Other contributions, including the use of fertilisers, farm automation and the development of higher-yielding crop varieties (using a range of plant breeding techniques), have all helped to greatly increase the volume of affordable food raw materials.

However, as the regulatory burden has increased in line with public fears about safety (only some of which are justified by scientific facts), the profitability and attractiveness of the industry has decreased. Egged on by romantic ideas about the superiority of 'organic' farming over modern practice, the majority of people in Europe (especially) now consider agrochemicals to be insidious poisons and GM crops to be capable of creating all kinds of health problems. This negative public perception has become enshrined in the regulatory burdens from which the industry now suffers. The upshot has been that innovation in the leading Western economies

Figure 1: New developments and launches of active ingredients (April 1995 – April 2007)



Source: Ag Chem New Compound Review (Vol 25) 2007

Table 1: Top agrochemical actives in 2005 (by consumption)

Common name	Consumption (tonnes)	End-use level sales (US$ millions)
glyphosate	182,000	5,250
sulphur	175,000	250
methyl bromide	72,850	110
atrazine	58,250	240
2,4-D	56,000	390
1,3-dichloropropene	45,000	90
copper salts	43,200	102
acetochlor	35,000	338
chlorothalonil	33,500	320
chlorpyriphos	28,200	395

Source: Crop Protection Actives (2006) published by Agranova

has been severely depressed (see Figure 1). Worse still, the regulators are forcing increasing numbers of registered products to be discontinued, thus removing the necessary armamentarium upon which growers have relied to control all manner of pests.

This inability to make a decent return on the research effort has driven companies to cut costs by consolidating and by outsourcing materials from the developing world. But still successful innovation remains muted, as does the steady decrease of new product launches. Indeed, as Figure 1 shows, the numbers of newly commercialised products appear to be heading for the baseline by the year 2012.

This dire scenario may appear to many to be acceptable, since the world has access to many established products. After all, the top selling agrochemicals, by volume, use mainly mature technologies, as shown in Table 1. It is true that the improved potencies of newer ais argues there to be a bias in this list, which is based on application volumes. Nevertheless, a list of the top selling products, by value, is also dominated by relatively mature compounds (Table 2).

Whichever list is chosen, one might ask: "Surely, the most profitable agrochemical companies, those avoiding investments in innovation, can supply these older products for the foreseeable future?" Of course not! New diseases continue to arise, particularly among the lower orders of the natural world – viruses, moulds and other fungi, insects, mites and nematodes. The lack of new science to inform the creation of the new technologies to tackle the emerging problems that 21st century growers will encounter will be compounded by the dominance of companies that only make existing products.

Where is innovative research still being undertaken? The top agrochemical companies are still inventing new compounds, but in insufficient numbers and at such high development costs that the returns demanded by investors are not being created. They increasingly minimise their R&D costs by in-licensing and by jumping on the 'me-too' bandwagon, when new activity is discovered. Japan is an exception to this general rule and has emerged over the past ten years as a major source of new agrochemicals, as can be seen from the graph of Japan's share of new developments during this period (see Figure 2). There are probably several explanations as to why agrochemical innovation continues to be buoyant in Japan. Perhaps the most important is the greater long-termism that characterises Japanese business culture (which helps to underpin R&D). In addition, the smaller scale of most agrochemicals companies offers a more conducive environment for carrying out new compound development.

The other area of new technology, where good profits can be made, is in the development of GM crops (especially those with input traits such as herbicide tolerance and insect resistance). However, these undoubted advances can only offer a partial solution to the changing challenges of agriculture and the need for novel agrochemicals continues to be pressing.

Learning from pharma

What can be learned, if anything, from the experiences of the agchem industry's 'bigger brother', the pharmaceutical industry (pharma)? The pharma business model has evolved, in fact, in a very similar way to that of agchems. The large, multinational pharma companies also lost the knack of innovation as they grew in size and they, also, followed bad advice and went for acquisitions and mergers that were recommended by consultants and various financial groups.

Biotechnology was also heralded as the 'great new thing' that would allow pharma to re-invent itself and deliver the fantastic financial performance that it had enjoyed in the 1980s. To some extent, the biopharmaceutical revolution did create exciting new therapies and made fortunes for some of its pioneers. Nevertheless, no single technology can be expected to be a cure-all and, inevitably, the limitations of biopharmaceuticals are now becoming apparent (particularly their very high costs) and the industry is again searching for the tools to discover products for the many ailments that still lack cures or even palliatives.

Table 2: Top agrochemical actives in 2005 (by value)

Common name	End-use level sales (US$ millions)	End-use level sales (tonnes)
glyphosate	5,250	182,000
imidacloprid	730	1,850
azoxystrobin	635	4,750
mesotrione	425	7,385
pyraclostrobin	420	3,720
fipronil	420	925
tebuconazole	410	2,100
paraquat-dichloride	400	22,500
chlorpyriphos	395	28,200
kresoxim-methyl	394	3,310

Source: Crop Protection Actives (2006) published by Agranova

In Figure 3, the constant downwards decline in the annual number of global launches of NAS (new biopharmaceutical and small molecule actives) is reminiscent of Figure 1, which shows new agrochemical commercialisations.

The pharma industry enjoys a major advantage over the agrochemical industry, however. It has maintained a more positive public image than its bioscience counterpart. The reason for this is complex, but pharma's far greater marketing skills certainly have helped. Perhaps, also, people in Europe and the US take the availability of plentiful food for granted. Good health cannot be assumed with the same insouciance and so pharmaceutical investment is still considered worthwhile.

Whatever the reasons, the pharma industry has maintained a relatively positive image and has continued to find financial backing for the development of new active ingredients, albeit via a new type of entrepreneurial company, originally dubbed the 'biotech' sector, but now more accurately named the 'emerging pharma' sector. Over the past 10 to 15 years, after a shaky start, the small company sector has grown to become the powerhouse of modern pharmaceutical development

Figure 4 presents a breakdown of the proportion of newly launched pharmaceutical actives (biopharmaceutical and small molecule) that have been subject to licensing deals. It can be assumed that an overwhelming majority of the licenses granted have been to major pharma companies by the emerging pharma sector and research institutes.

The NASs marked 'no deal' represent in-house developments by major pharma companies. They account for around one-third of new commercial products, illustrating the major contribution now being made by R&D institutes and emerging pharmaceutical companies.

Of course, there are other factors why the current outlook for pharmaceutical innovation is not as gloomy as is the case for the agrochemical sector. For instance, it is arguable that the pharmaceutical discovery effort has taken advantage of the rise in the supply of technically educated Asians to enhance its discovery programmes. The main conclusion that can be drawn is that, unlike the agchem sector, the pharma industry has begun to reinvent itself in order to recover the successful innovativeness that is vital to its future.

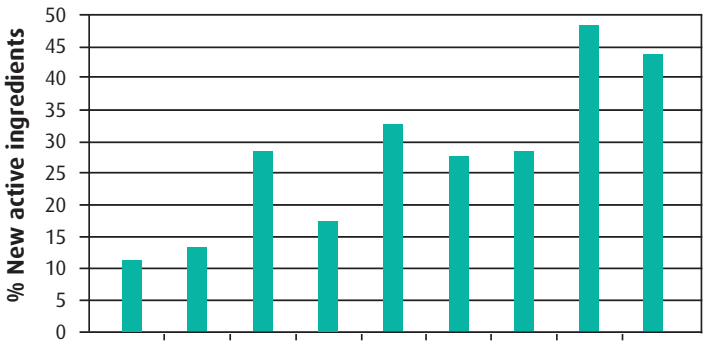
The challenge ahead

A small company innovative sector does exist in agrochemicals, but it has made little impact upon the slowing rate of invention (many developments from this sector are hardly serious – examples such as sour milk and aqueous sodium bicarbonate spring to mind).

This contrast between the pharmaceutical and agrochemical sectors could not be starker.

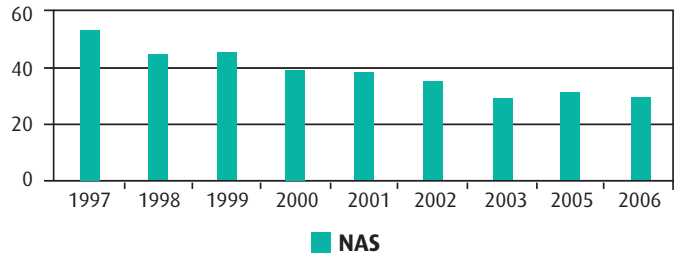
Since there appears little chance that the developing world will take up the mantle of innovation anytime soon, the challenge is to recreate a sense of renewed confidence in

Figure 2: Growing importance of Japanese innovation



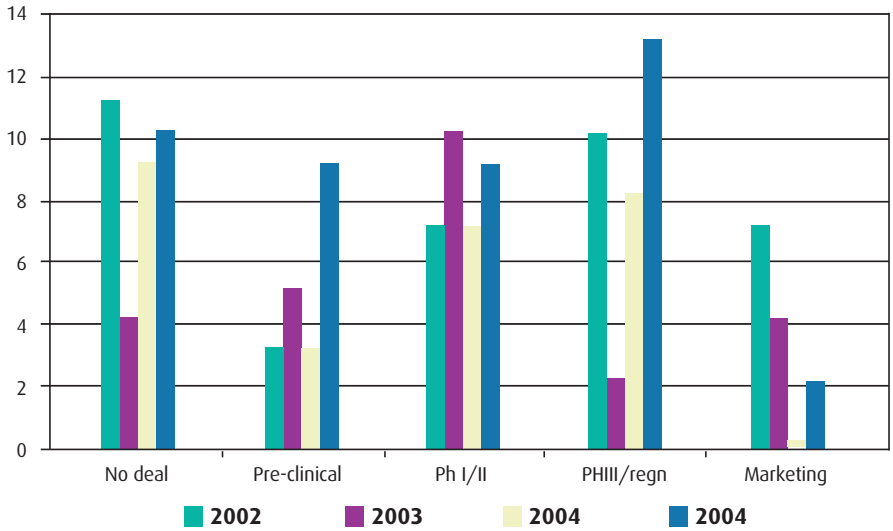
Source: Crop Protection Actives (2006) published by Agranova

Figure 3: Global launches of new pharmaceutical actives (1997-2005)



Source: IMS International

Figure 4: Development stage of pharmaceutical licensing deals (2002-2005)



Source: IMS International

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the agchem industry in Europe and the US. Perhaps by taking a leaf out of Japan's book, Westerners can rediscover an appetite for agrochemical innovation.

Life on this planet has always been in a state of continuous flux and it is clear that change is imperative for survival. Earlier advances in technology have been made possible by scientific innovation, which itself is the result of the creative activities of a few individuals over the past centuries. Recent technological progress in the life sciences began in such odd places as the fields around an Oxfordshire smithy (leading to the first geological map by William Smith), a Moravian kitchen garden (Gregor Mendl's discovery of the laws of inheritance) and on the heaving deck of a sailing ship following the coast of South America (on which Charles Darwin began to consider ideas on evolution). It can be argued that the results of the 17-18th century scientific revolution followed on from the enlightenment of the 16-17th centuries and gave rise to the technological advances of the 19-20th centuries.

So what will our descendants make of the 21st century? An era in which irrationality threw away the gains of the previous three centuries, or one in which logic and the practical application of scientific advances created new solutions to the never-ending challenge that characterises life on this planet?

What seems clear is that a positive outlook for the future will only arise from the triumph of reason over irrationality. These are interesting times.

Dr Rob Bryant runs a specialist consultancy, Brychem, which undertakes confidential studies on the fine chemical industry and its major customers. His other company, Agranova, publishes information on the global agrochemical industry.