

NAVIGATING THE OFF-PATENT COMPETITIVE LANDSCAPE

The managing director of UK-based Enigma Marketing Research, Dr Nigel Uttley, talks to Sanjiv Rana about strategies for competing in the off-patent agrochemical market

After a period of stagnation and even contraction, the global agrochemical market at around \$35,000 million rebounded last year to grow at close to 10%. Logically, the potentially larger pie in the years to come should result in rosy prospects for all players in the sector.

Dr Nigel Uttley feels that it all depends on which part of the pie a company operates in. He divides the agrochemical industry into three broad sectors:

1. Proprietary products with an enforceable patent, accounting for around 30% of the market.
2. Off-patent proprietary products, where the active ingredient is off-patent but the final formulated product: has some proprietary technology (such as a new delivery system, surfactant or safener); is linked to GM crops (such as Monsanto's Roundup Ready crops); is a mixture product containing a patented active ingredient; or has data protection issues that prevent generic manufacturers entering the market. These products account for the bulk of the market at 42.5%.
3. Generic products, accounting for 27.5% of the market.

Dr Uttley says that the market share of proprietary products has declined over the years. This is evident in the decrease in the number of new active ingredients entering the market each year. "The number of ais receiving an ISO common name has declined from an average of 20 per annum in the late 1990s to just seven in the last six years," he says.

The consultant with a doctorate in organic chemistry stresses that developing a new ai for the market is not a simple process. "It takes, on average, eight to ten years from discovery to registration for an agrochemical product, during which time, some 50,000 products will have been screened and discarded for the one that achieves commercial launch," he adds. "The cost of this exercise is put at more than \$150 million, excluding the costs of a new production plant and market launch."

He says that about 15 years ago, the new ai discovery industry had a great boost with the introduction of combinatorial chemistry and high-throughput screening, which significantly increased the number of new chemical entities available for testing. However, this new scientific dawn did not result in an increase in new products being introduced into the market.

The decline in the arrival of new ais has led the top six R&D-based companies to focus on and enhance the proprietary off-patent market. "Once an ai loses patent protection, it does not necessarily lose market share to generic competition, as the inventor company would have planned a post-patent expiry strategy long before the patent expiry," explains Dr Uttley.

defensive strategies

The defensive strategy can be multi-pronged. Explaining the EU registration process, Dr Uttley says that once an ai attains Annex 1 status under the EU agrochemical registration Directive (91/414), the data dossier submitted by a company receives data protection for ten years on new ais and five years for existing ais. Among 60 ais in Annex 1 that were in the EU review and had no patent protection, 35 have only one data submitter, which implies an absence of generic competition in the EU.

Dr Uttley gives the examples of products such as Dow AgroSciences' herbicide, fluroxypyr, and Syngenta's insecticide, lambda-cyhalothrin, both of which are off-patent in the EU but have no generic competition. "This, in effect, extends IPR [intellectual property rights] by an additional five-year period," he explains.

Another important weapon in the defensive armoury of a company in the EU is that of supplementary protection certificates (SPCs), which came into force in 1997. "The granting of an SPC effectively extends protection to commercialised products covered by a European patent if published later than January 1st 1985, by up to a maximum of five years," says Dr Uttley.

Out of 41 ais that Dr Uttley has profiled in his report on ais due to come off-patent in the near future, 35 have been granted SPCs, significantly extending their patent protection. He gives the example of BASF's fungicide, kresoxim-methyl, for which the EU patent expired in July 2007 but a UK SPC extended the protection until April 2011. Similarly, Bayer CropScience's insecticide, clothianidin, the patent for which is due to expire in November 2009, has received a UK SPC, extending its expiry by five years to 2014.

"SPC protection can also be availed by combining an [off-patent] ai with proprietary ais," he further elaborates. He gives the example of Syngenta's fungicide, cyprodinil, the EU patent for which expires in 2008, but which has a mixture SPC with picoxystrobin that extends the patent expiry to 2013. Similarly, BASF's herbicide, picolinafen, for which the EU patent expires in 2011, has a mixture SPC with flupyrsulfuron-methyl-sodium that extends the patent expiry to 2017.

One of the major ways a market can be protected against generic competition is to segment the market through mixture products. By combining an ai with one or more other ais, companies can claim novel synergistic effects, and mixture patents may be granted. "Mixtures can segment a market and extended patent rights can result either through an SPC from the original patent or the combination of the two or more active ingredients," he explains. Over the last 10–15 years, IPR for mixture products has become a very popular strategy and the generic sector has tended not to challenge the validity of these patents.

the generic landscape

Dr Uttley says that there are two major drivers that should result in increasing market share for the generic sector:

1. Increasing percentage of off-patent products.
2. Increasing global demand for agrochemicals, especially in markets such as South America, eastern Europe and Asia, where older established products have a large percentage of sales compared with newer chemistries.

But he also talks about barriers to generic companies' ability to take advantage of the situation. They include: a lack of critical mass to develop new generics; increasing cost of registrations; reduced product range due to more stringent registration systems; and a lack of market, IPR and registration knowledge.

Dr Uttley advises generic companies to take a holistic approach to choosing an ai by looking at: the marketing environment; process and manufacturing chemistry; IPR situation; and the generation of registration data.

Although the sales potential of an ai is important, Dr Uttley says that it would be inadvisable for a generic producer to opt for one without considering elements of the manufacturing process, such as the ease or difficulty of the process and the existence of any process patents or intermediates that could extend exclusivity of an ai.

In order to explain his point-of-view, Dr Uttley takes Nippon Soda's insecticide, acetamiprid, as an example of an ai that would be of interest to potential generic manufacturers. The ai is used for the control of sucking pests in fruit, vegetables, cotton and ornamental plants. Since its introduction in Japan in 1995, it has been registered in many countries for crop and non-crop markets. The European patent is due to expire in October 2010, but a UK SPC has been granted with a maximum expiry date of January 26th 2015.

The chemistry and technology involved in the manufacture of acetamiprid is said to be relatively straightforward and should be achievable by a number of generic and contract manufacturers. Already, he says, some 40 companies claim to manufacture acetamiprid and even though the actual number is likely to be considerably smaller, it indicates how easy it is to manufacture acetamiprid to the standard required.

"The ai is clearly a big opportunity for generic manufacturers but in the short term the available market may be restricted to those countries where registrations are relatively easy and cheap to obtain and where no extended patent protection exists," explains Dr Uttley.

Talking about Nippon Soda's defensive marketing strategy, he says that the company has licensed the development of acetamiprid-based products to many companies to maximise penetration of the crop and non-crop markets and many branded products exist in the market place. This strategy and the cost of registrations in major markets will assist Nippon Soda to protect certain markets but other markets will see strong generic competition in a post-patent environment.

strategies for generic success

His advice to any sizeable generic company with global ambitions is to choose markets where registrations are relatively easy to obtain. That would help generate income in the short term to pay for the more expensive registrations in the EU and US.

Another practical tip is to acquire products no longer of strategic importance to multinationals and develop "new" products through reformulation and mixtures with strong marketing strategies to create off-patent niche products. "This could be taken further by licensing ais to develop mixture products for niche branded markets, the way Makhteshim-Agan Industries is working with Bayer's fungicide, tebuconazole," he explains.

Gazing into the crystal ball, Dr Uttley foresees a trend towards consolidation in the generics sector. A weak generic lobby has allowed the drafting of registration legislation to favour companies with critical mass, he says. The result will be the smaller generic companies being squeezed out of markets and the creation of a big opportunity for larger generic companies with critical mass to acquire smaller companies and become global players.