# Matching technical & market int

**Dr Rob Bryant** of **Agranova** looks at how buyers of agrochemical markets, products and chemical intermediates can select the information that best suits their specific requirements and offers some thoughts on how to match a company's needs with the market intelligence available

The business development and marketing groups of chemicals and fine chemicals companies continually need to assess the comparative merits of new opportunities. The selection of the most promising targets will depend upon a number of internal factors, such as the company's current business, its technical skills and its market presence.

Developing a reasonably reliable view of the external factors affecting the opportunity will always require access to several important sources of information, such as: customer(s), from whom the quality and reliability of information can vary greatly; published information, which is broadly distributed and widely varied in quality, and which may be scarce; reviews of subsectors of the market or technology; and, specially commissioned studies. Generally, a company will need to use a combination of all four to secure a really good picture of a specific product or market.

However, it is rarely cost-effective to carry out a full review on all possible leads. Specialist reports on narrow areas of the market are therefore often used to bridge the gap between a full review and a superficial one. These are particularly useful for undertaking a preliminary screen of likely candidates for deeper study. The challenge for someone using such reports is to assess the quality and value for money of the limited titles on offer. This article looks at how this type of information is produced in the field of agrochemical actives ingredients (AIs) and intermediates.

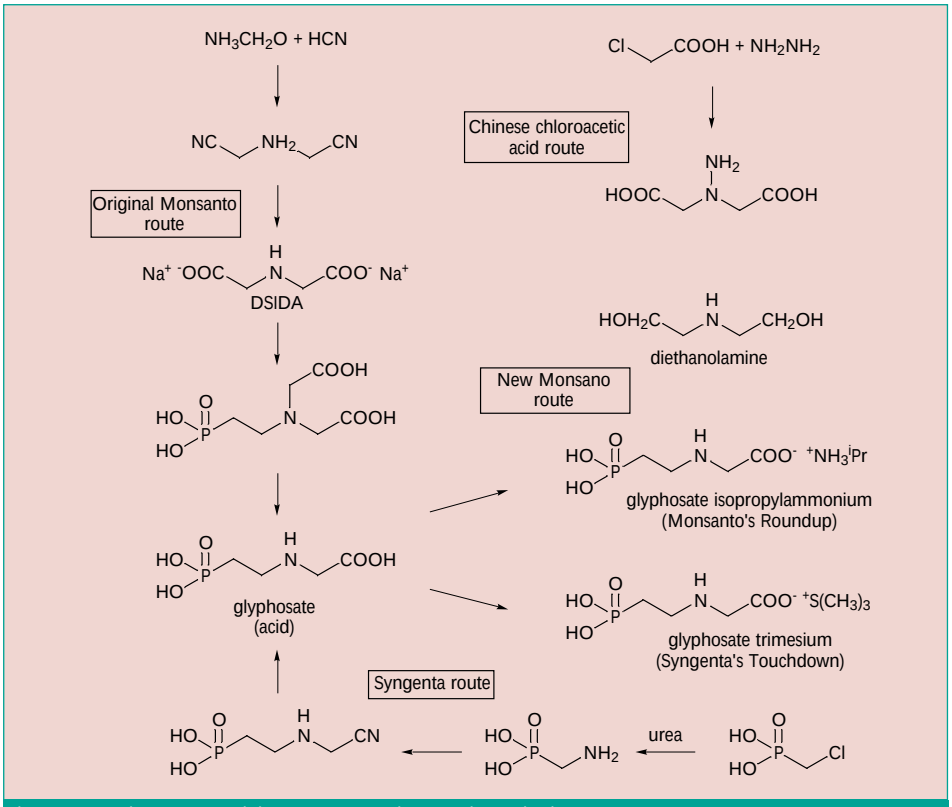



Figure 1 - Major commercial processes used to produce glyphosate

## Matching needs with resources

Many different users with differing perspectives and needs buy agrochemical information (see Table 1). Providing timely information for a broad range of clients at an affordable price is challenging. The decisions information suppliers need to make on the compromises needed to create reports for the maximum number of potential clients have become harder over the past five to ten years, as the customer base has dwindled. As a result, avoiding the type of compromise that creates a misleading result has become harder.

The split between the main sources of business for information providers is determined by the amount and quality of process information needed. Agrochemical companies tend to be far less interested in process technology - and much more interested in sales of finished products broken down as far as possible - whereas their suppliers are typically very interested in processes and intermediates.

This article is focused upon the needs of the fine chemical intermediates producer, whose prime interest is developing three key areas of information. In most instances, only the first two can be supplied within a report for sale to a broad range of customers. These three are:

- Global estimates of AI demand - actual or potential, depending on the stage in the product's commercial development - with market shares in key applications
- Existing or planned production processes used by key customers - usually the innovator or sub-contractor is the major manufacturer for the majority of newer compounds - and patent constraints on would-be producers
- Commercial intelligence on existing and planned suppliers of intermediates, share of business, pricing and contractual arrangements

Table 1 - Needs of different customers for agrochemical industry information

| Type of client | Key information needed |
|---|---|
| Agrochemical marketing company | Demand data (limited by product, by crop &/or by region) for formulated compuonds; information on new compounds; |
| Agrochemical discovery company | Information on new compounds; competitor & supplier information; competitor intelligence |
| Active Ingredient (AI) producer | Global demand for AIs; existing & potential customers; technology used & intermediates required |
| Contract manufacturer | Information on new & commercial compounds; technology used & intermediates required; information on less successful commercial products; market intelligence on new & existing production; competitor intelligence |
| Custom synthesis specialist | Information on new compounds; technology used & intermediates required; competitor intelligence |
| Chemical intermediates producer | Demand for specific intermediates & emerging opportunities for new ones that fit company's capabilities; technology used & intermediates required |

## Processes & intermediates

Experience shows that the quality of information available, even on the area most accessible to non-privileged investigation (patented processes), is unreliable. A prime example is the world's leading herbicide, glyphosate. There are many patented routes to the active ingredient, but only those shown in Figure 1 have actually been commercialised. Although glycine

# telligence needs with resources

has never been a significant starting material (outside of China, where the domestic price is significantly lower than elsewhere), you would think it was if you consulted most sources of information on the subject.

The reason for the difficulty in finding reliable information is that, in order to deliver a comprehensive report on as many compounds as possible, even the best qualified information providers tend to take short cuts. The most obvious pitfall is to base the process upon the initial patent. Discovery syntheses are rarely a particularly good guide in this sector, because getting the lowest cost process is almost always vital for the success of a new product. This means that a major process development effort is required to minimise production costs.

Subsequent process patents (often carefully written to deflect attention from their significance) are thus a better guide. Improved routes to older, successful compounds are likely to be developed during the product's lifetime so as to retain profits as prices inevitably decrease. All this mitigates against a 'clean' database of intermediates and AIs.

Even when the process is correctly identified, the intermediates required can often be far from clear, adding further doubt to the projected or real market for the compound. For example, in the original route to pendimethalin, 4-nitro-orthoxylene appears to be an essential raw material However, this has never been the case, because no-one has worked out a cost-effective way to nitrate orthoxylene in the 4- position without creating a vast amount of the 3-isomer. Separation of the unwanted material is only realistic as the corresponding anilines (after reduction of the mixed nitration product). In fact, 4-nitro-orthoxylene is a relatively highly priced intermediate, sold in small volumes for speciality applications.

Another reason why process information can be hard to determine reliably is that there can be multiple routes under operation, particularly for mature products like glyphosate and chlorothalonil (Figure 2). In these instances, getting the relative balance of the differing demands for the intermediates becomes a complicating factor, though this is preferable to calculating non-existent demand for the incorrect intermediate.

Providing reliable information on agrochemicals and their intermediates at reasonable cost remains a difficult challenge. Using experienced technical consultants is probably better than being guided by lower cost published reports, since these tend to be based upon the type of potentially misleading public domain information cited above.

## Demand for AIs

Discovery and marketing groups within agrochemical companies tend to be far more interested in consumption of the leading formulations, split by region, and crop demand than in global demand for AIs. Providers of commercial data for agrochemical consumption have therefore often set up extensive market studies to satisfy this demand (using data acquired from 'farm panels' in key markets).

Companies requiring less accurate - but not less reliable - information on AI consumption have tended to pay more for this than they would like to or to use published information to make estimates based upon finished product sales, much of it derived from agrochemical company information. Moreover, significant errors arise if this approach is not used with care. Double counting (by the reporting of sales at both finished and AI level and by inter-company transfers of AIs), pricing and mark-up differentials between different markets and (for mature products) under-reporting of sales in undeveloped markets can all help to generate unreliable figures. Another common problem is one of definition; for example, non-crop uses can be significant for some compounds, but these are often neglected in published data.

There are no simple answers to this problem, particularly at a time when the providers of 'farm panel' data are losing customers through industry consolidation. Information on global demand has recently become available at reasonable cost and it can be used as an initial guide to the demand for an AI. What should be borne in mind is that, for the purposes of a chemical or fine chemical user, the information needs only to be relatively reliable but not particularly accurate. Table 2 gives an example of information taken from Agranova's commercial databases, its *Crop Sector Reviews* (which is targeted at agrochemical companies) and its forthcoming *Crop Protection Actives* (a database for chemical intermediate producers).

## Determining likely market size

Companies wishing to assess the potential value of a developmental AI usually rely heavily upon what customers tell them about its growth forecasts. However, it can be worthwhile attempting to generate one's own estimates. Such an exercise can be very useful in arriving at a decision whether or not to pursue an invitation to bid for a piece of business.

Crucial to this is making some kind of decision on the expected product volume and its lifetime. A modest success may be superior to a 'blockbuster', since the innovator may leave the production to a sub-contractor throughout its lifetime. What is 'small beer' for an innovator can be a 'nice little earner' for a fine chemicals producer.

Some questions need to be asked when making such estimates. What are the target crops and diseases? Are the application sectors sizeable and are they profitable? What is the value of sales for current treatments using established compounds? What are the leading treatments and their limitations? What is special about the new active? Is there other emerging competition? What lifetime is likely for the new compound? (The potential for disease resistance and the originality of the mode of action of the new AI are key factors here). Finally, is there potential for non-crop applications?

Getting at the necessary raw data is not so easy. Nevertheless, with a basic understanding of the value and volume of sales of existing AIs in the major crop sectors, a fine chemicals company has the basis for making some preliminary calculations. Agranova began working with Allan Woodburn Associates in 1998, in order to get access to reliable consumption information at an affordable price. The October 2003 edition of *Crop Sector Reviews* has profiles based on 1998-2002 data for nearly six hundred commercial agrochemicals. Agranova's newest publication, *Crop Protection Actives*, offers

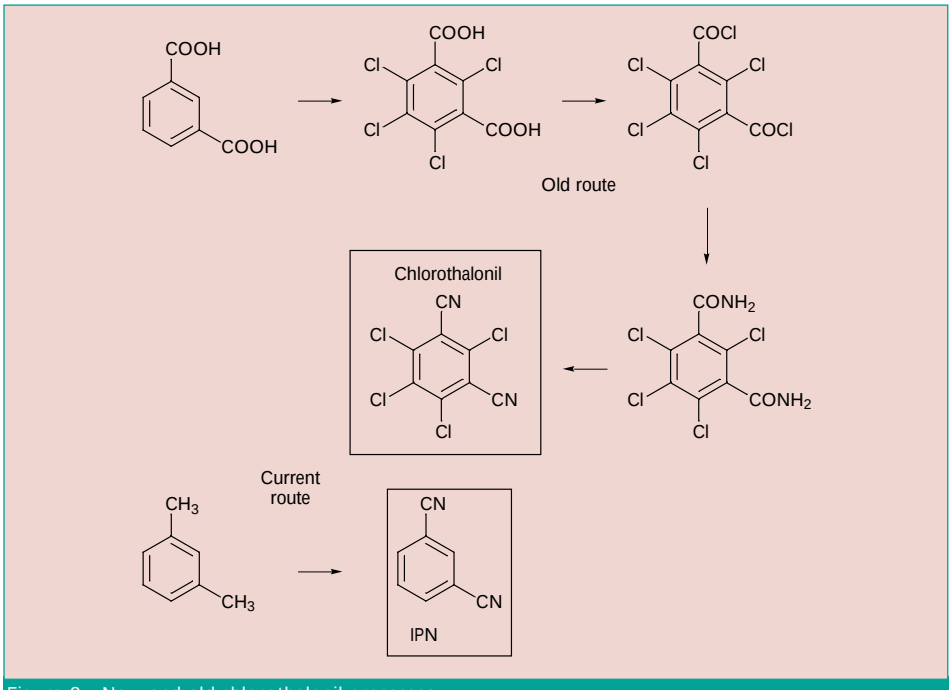



Figure 2 - New and old chlorothalonil processes

technical and market profiles on the latest agrochemicals that are constructed exclusively for fine chemical companies. Assessments of the process chemistry used are also included.

## Processes for new agrochemicals

Information providers also offer publications and advice to fine chemicals business development groups on selecting target agrochemical customers to approach. Technical reports based upon early patent submissions can offer a source of information for pre-screening new opportunities. However, their publication is often too late to be of much use as an alerting service. It is increasingly hard to predict which of the many new agrochemicals in development will become commercial products and carrying out exhaustive searches on patented processes tends to be prohibitively time-consuming and costly.

One useful approach, which can be offered at modest price to a wide range of customers, is to offer a sound analysis of what the likely chemical processes for development compounds might be, based upon the structure of the final AI. This can be done by experienced process chemists with a broad industrial experience. As an experiment, Agranova carried out a survey of the 40 or so new compounds in its annual *Ag Chem New Compound Review* that had been assigned structures. Subsequent research into the patent literature confirmed that this approach was very effective at identifying emerging intermediates.

By using this early alert service, producers of intermediates and sub-contracting specialists are in a better position to make a more timely approach to developers. A more detailed assessment might then be justified at a later point, when the project attractiveness becomes more apparent. Two examples of this type of initial analysis of how new, yet-to-be-launched, agrochemical actives can be produced will illustrate the value of this approach.

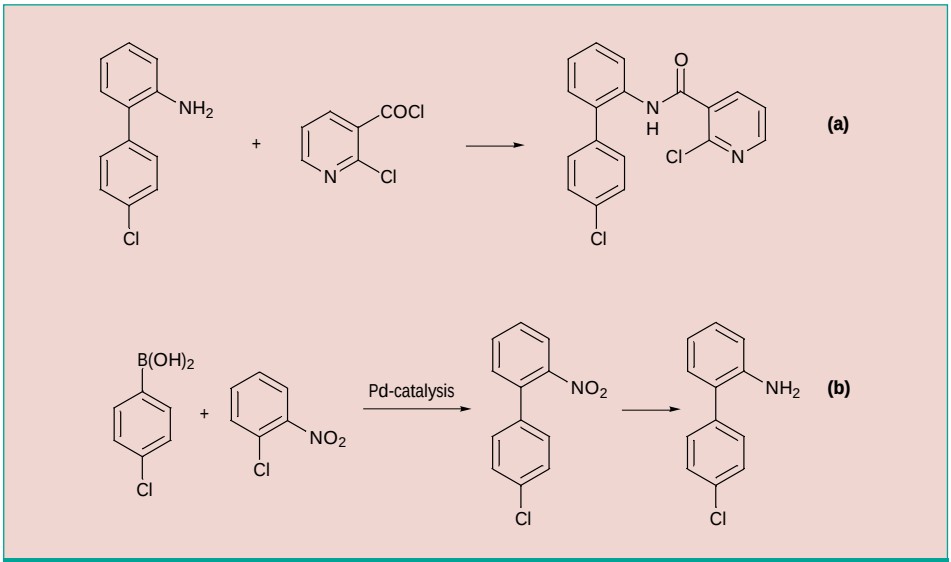



Figure 3 - Acylation reaction to BASF's boscalid (a) and Suzuki reaction to its disubstituted biphenyl (b)

## Boscalid & Spiromesifen

BASF's new nicotinamide fungicide, boscalid (BAS 510) is likely to be marketed in 2004. Examination of the original patents (submitted in 1992) confirms that the compound is made by a simple acylation reaction (Figure 3a). The 2-chloronictinoyl chloride is a large volume intermediate, which is already produced in France, India and China so this would not offer any novel chemical opportunities.

Production of the disubstituted biphenyl is a little more complicated. Traditionally made by the Ullmann reaction, biphenyls can also be made more efficiently by a range of metal-catalysed coupling reactions. The Suzuki reaction or one of its variants is likely to be the preferred route. Clariant's technology for producing the pharmaceutical biphenyls (especially o-tolylbenzonitrile) would suggest an obvious example of an industrial precedent for the Suzuki reaction. Indeed, a BASF process patent confirms that the manufacturing process may well use this type of chemistry (Figure 3b).

Bayer CropSciences' new insecticide, spiromesifen (brand name Oberon), is particularly effective in controlling whitefly. Its structure is a little more daunting than that of boscalid, but once the key disconnection is performed, the route becomes quite clear. Nevertheless, both starting materials, particularly ethyl 1-hydroxycyclopentanecarboxylate, require a little study before a complete process can be worked out.

The point of spending time and effort on putting together this type of analysis is that, so long as the basic picture can be worked out, a potential supplier can expect to have a better chance of winning a supply contract with it than without it. Even a slight edge is worth paying for in this increasingly competitive marketplace.

Table 2 - Global agrochemical sales (in 2002) for all uses

| Active ingredient | Global Volume (tonnes) | Global Sales* (US$ millions) |
|---|---|---|
| Glyphosate | 178,600 | 4705 |
| Imidacloprid | 1,840 | 920 |
| Azoxystrogin | 3,310 | 472 |
| Malathion | 35,100 | 412 |
| Kresoxim-methyl | 3,050 | 408 |
| Paraquat-dichloride | 10,630 | 405 |
| Fipronil | 805 | 366 |
| Pendimethalin | 15,220 | 350 |
| Acephate | 17,800 | 330 |
| 2,4-D | 10,850 | 325 |
| Glufosinate-ammonium | 2,720 | 310 |
| Acetochlor | 16,000 | 304 |
| Diquat dibromide | 3,570 | 301 |
| Chlorpyriphos | 9,850 | 295 |
| Trifluralin | 22,400 | 294 |
| Carbofuran | 8,750 | 283 |
| Imazethapyr | 380 | 282 |
| Atrazine | 45,600 | 280 |
| Lambda-cyhalothrin | 480 | 275 |
| Permethrin | 1,800 | 270 |
| S-metolachlor | 8,200 | 244 |
| Deltamethrin | 510 | 238 |

*By value at the end-use level

## Conclusions

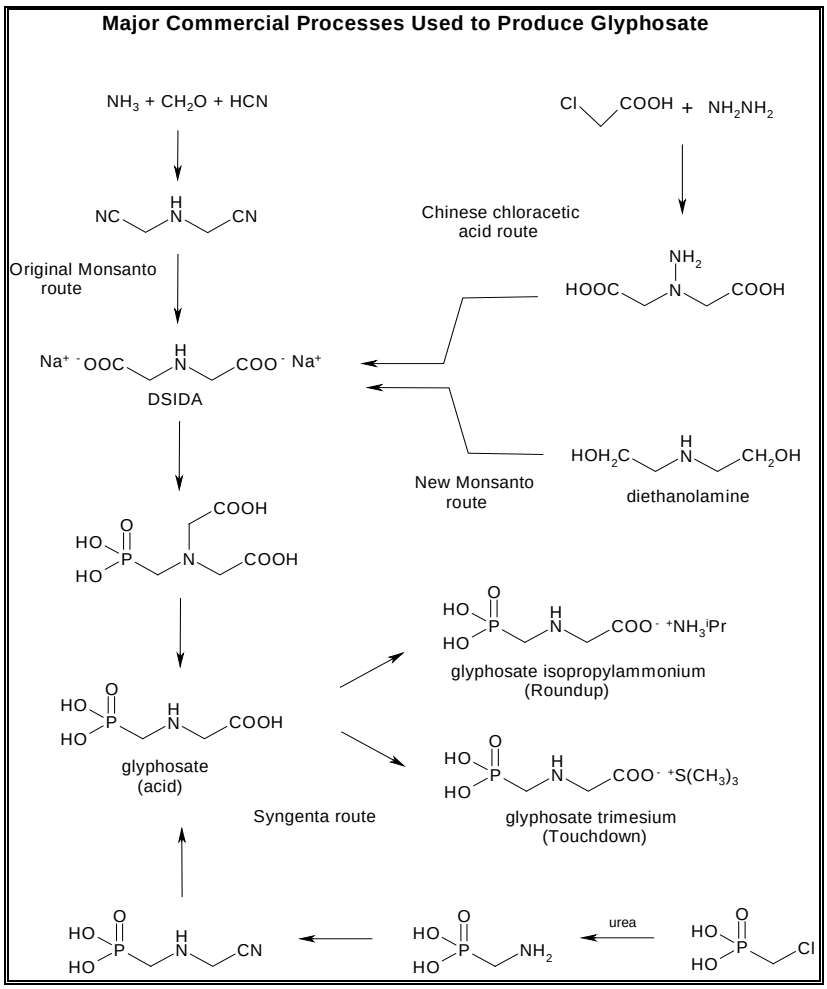
The prime motive in this article has been to present some of the challenges of preparing reliable techno-economic reports on agrochemicals. From previous experience in technical and commercial roles within the fine chemical industry, it does seem that many business development projects are based upon too little information.

The quality and reliability of business and market reports and databases being sold is often disappointing, making them less useful than they ought to be. This is probably more to do with the authors having made poor decisions on the necessary compromises needed to produce a saleable product than lack of competence. It is simply not possible to undertake a sufficiently thorough appraisal of the issues involved and make a reasonable return on the cost of the time and resources necessary.

Under these challenging market conditions, information providers must focus on the real needs of their customers and use greater ingenuity in creating reliable business intelligence. By offering carefully focussed analysis, rather than attempting to create suitcase-fuls of paper, useful reports can be created at reasonable cost. With affordable business research, chemical intermediate producers are then able to gain the improved insight into new business opportunities required to improve their chances of securing new supply contracts.

For more information, please contact:
Dr Rob Bryant
Agranova
34 The Drive
Orpington
Kent BR6 9AP
UK
Tel: +44 1689 600501
E-mail: agranova@compuserve.com

# Original Diagram for Glyphosate Processes
***(includes missing arrows)***




# Spiromesifen Process Outline (omitted from final draft)