Independents' day

Guy Villax, CEO of **Hovione**, argues that the role of the independent supplier of pharmaceutical fine chemicals is as important now as it has ever been

The dust has now settled after the exciting but turbulent years times two years ago that saw the chemical giants snapping up pharmaceutical fine chemical specialists for hundreds of millions of euros. Some €3 billion were invested in three deals alone, while all of the merger and acquisition (M&A) transactions listed in Table 1 add up to more than €14 billion. This includes DSM's acquisition of Gist-Brocades for €6 billion and, more recently, Roche's Vitamins & Fine Chemicals division for €2.5 billion.

The notable new entrants are the integrated chemical giants that have acquired or invested in GMP businesses. Some of the businesses that were acquired were great international brands - Archimica, ChiRex, Finorga, Gist-Brocades, Laporte, Profarmaco, Raylo and Torcan among them.

The drivers for the outsourcing of APIs remain unchanged and exclusive manufacturing of new chemical entity APIs remains a rollercoaster: approvals carry high rewards, product cancellations and withdrawals mean significant disappointments. The business models adopted by the various players fall clearly into two very different types, with different offerings and different strategies.

The original strategy of the chemicals giants was to bet on size and enter a high-margin, non-cyclical business that - apparently - had synergies with their existing operations. Some articles emphasised that the acquisition of API capabilities was strategically aimed at giving them total control over the key building blocks, which could be sourced internally. BASF advertised with the slogan "Backward integration is another form of forward thinking".

Meanwhile, the traditional players - like FIS, Hovione, Lonza, Omnichem, Orgamol, Siegfried and Sumika (see Table 2) - have remained independent and have taken no part in the M&A frenzy. In fact, they would all probably see M&A as a strength-diluting exercise which would debilitate one of their strongest assets - their company culture. Their annual growth, which has consistently been in double digits for the past ten years, remains purely organic and they enjoy stable ownership.

Many of them have continued to invest at a time when others are trying to sell. Orgamol, for example, is building a new pilot plant and synthesis unit in Switzerland, Siegfried has innovated dramatically in the GMP design of its own new facility (*SCM*, September 2002, pages 10-12), Lonza is placing very big bets on biotechnological API manufacture and Hovione has just commissioned its new Technology Transfer Centre in New Jersey (*SCM*, October 2002, page 5).

The independents strongly disagree with the assumptions that formed the strategies of the new entrants. They would ask why size matters when most APIs are produced at volume of only a few tens of tonnes/year, when there is a trend to more highly active compounds, when an API producer should be a generalist - able to carry out all of the relevant technologies - and not the lowest-cost technology specialist, and when early phase clinical materials supply requires service, service and more service, which is not traditionally a characteristic of large, multi-site companies

Backward integration only adds to an already risky business, whereas the independents have the whole world - including India and China - from which to source low-cost raw materials. Moreover, buying sites from Big Pharma with supply agreements often resulted in a low margin business, single-customer dependence and getting an old plant, which was often not multi-purpose and which was certainly not designed for quick change-over and evolving compliance standards.

The chemical giants seem to be keen on buying existing facilities, taking over business and discarding brands that were the result of much hard work, solid relationship building and customer focus. The independents, by contrast, design their plants themselves, build from scratch, 'gold plate' when it is important to do so but otherwise worry about the nickels and the dimes.

Furthermore, with their expansion into the API business, the chemicals giants risk antagonising their traditional customers, who would now perceive them as competitors and no longer as suppliers and partners. Hovione, for example, would now prefer to discuss its new catalyst needs with Engelhard rather than Degussa or Johnson Matthey, whom it has come to view as competitors.

Neither the analysts, the board members nor the shareholders considered any of these matters during the buying spree. Instead, management thought that it saw opportunities for making a difference in their shareholder value and the stock market supported it all wholeheartedly.

Perhaps it is not surprising that so many observers regard the chemicals giants as the most important players, when so much of the discussion focuses on them alone. At CPhI in Paris, for example, a special panel discussion gathered together five senior purchasing managers from Big Pharma and five senior executives representing most of the chemical giants that have designs on GMP manufacture of fine chemicals.

It was odd that major buyers of outsourcing services - such as Wyeth, GlaxoSmithKline or BristolMyers-Squibb - were not represented. It was also odd that, among the companies representing the API contractors, none of them except Lonza had GMP manufacture as a traditional core business. In fact, adding up all their GMP reactor capacity, their numbers of FDA filings and their sales in GMP fine chemicals, their grand totals are probably lower than those of any two of the companies in Table 2.

The usual list of topics was addressed and most of the discussion time was centered on price and open-book costing. Service - the most critical differentiator - was barely touched upon! No-one discussed how tax strategies, the one common manufacturing strategy that can be found at all Big Pharma companies, actually explain a great many purchasing decisions. The formality of the panel discussion did not allow for any of the individuals present to provide any insights to the otherwise well-attended conference.

Table 1 - New entrants in pharmaceutical fine chemicals

Remaining Brand/ Company	Merger / Acquisition / Investment with GMP orientation
Avecia	Hybridon, Boston Biosystems, Torcan
BASF	Takeda Vitamins
Bayer	Chem Design*, Novochem
Cambrex	Conti, Irotech, Nobel Chemi, Profarmaco, Biowhittaker
Clariant	BTP, PCR, Hexachimie, Archimica
Degussa	Laporte, Raylo, Inspec
Dow Chemical	Angus, Ascot, Haltermann, Hampshire, Chirotech
DSM	ACF Chemie, Andeno, Catalytica, Wyckoff, Gist-Brocades, Roche Vitamins & Fine Chemicals
Dynamit Nobel	Rohner, Sylachim, Finorga
Ferro	Pfanstiehl
Honeywell	PFC
Johnson Matthey	Macfarlan Smith, Pharm-Eco
PPG	Sipsy Chimie Fine
Rhodia	ChiRex, former Rhône Poulenc-Rorer plants in the UK
Solutia	Carbogen, Amcis

*Note: * - divested early 2002*

Table 2 - The independents

Company	Ownership
FIS	Private
Hovione	Private
Lonza	Quoted
Omnichem	Owned by Ajinomoto
Orgamol	Private/Foundation
Siegfried	Quoted, has a reference shareholder
Sumika	n/a

The climate is tough and nobody is giving away presents. Some of the pharmaceutical companies present at the event, who are facing patent expiries or have cancelled projects or withdrawn drugs, are vigorously pulling back previously outsourced business. In Europe, meanwhile, the EMEA has announced that it is cutting its annual budget by 7% in response to a 50% drop in the number of new medicines being submitted for authorisation.

Some of the chemical giants, with their empty GMP vessels, are now considering turning to generic APIs for a lifeline. If they imagine that these will offer sales in a two to three-year timeframe, I wish them luck. A generic API project needs six years to mature; gone are the days of the 'cowboy' generic bulk producer. Peter Pollak's Sertraline *directissima* story (*SCM*, September 2002, page 46) is a case in point. As a further confirmation, why not look at Ranbaxy's annual report and assess the significance of the 29 patents (US and PCT) their generic R&D programme has yielded in 2001 alone?

The next two decades of generics will be very different from the past 20 years. Everyone will try to avoid Captopril-type bloodbaths. Everyone will focus on how to manage to avoid overall price erosion after patent expiry; very significant R&D budgets are being invested right now to make sure that a generic does not equate to low margins. Companies such as Novartis, Pliva and Ranbaxy have made that crystal clear. Their accumulated market knowledge and long-term view should not go unnoticed. Again, there is no room here for opportunists.

In my view, the winning model in pharmaceutical fine chemicals would be a company that is simultaneously big enough and small enough. It should be big enough to have the critical mass that will support the diversified portfolio necessary to mitigate risk and a large process chemistry group able to develop several dozen simultaneous projects, to maintain the depth and breath of know-how and technology necessary to support multiple process validation campaigns every year and to assure long-term capacity.

At the same time it must be small enough to take decisions and communicate them quickly and to provide the highest levels of service, flexibility and transparency. I believe that the entrepreneurial, focused company without share-price concerns or peripheral activities to serve as distractions is likely to be a step ahead of the competition.

The constant need for large amounts of capital investment, the many years that projects take to mature from the development phase to commercial scale and the inherent risk of each project makes our business unfriendly to the stock market. Thus it should be no surprise that the key players have a reference shareholder able to look at the longer-term: whether it be Ajinomoto (in Omnichem's case), a family (Hovione) or a foundation (Orgamol).

Hovione's own normal growth has been boosted in the last 12 months by repeat business, projects moving beyond validation to the commercial phase and winning customers with Phase III projects. In our experience, customers with outsourced Phase III projects to outsource normally change suppliers for three main reasons:

1. They want a stable supplier for the long term, one that does not shop itself around constantly
2. They want assurance of capacity and of compliance - they are fed up of getting a different colour batch every time
3. They want to be 'in-the-loop', and not to be the last ones to know of problems or of process changes.

In the past few years GMP fine chemicals manufacture as an industry has been the object of far too much interest, and too many massive bets were placed with exaggerated expectations. Most are not pleased with their investments. The business is still out there. Despite temporary dips, the long-term market trend continues to show growth but it is just not as simple or as quick as many companies expected it to be.

Fines for non-compliance with GMP have reached a record $500 million for a single offending company and the FDA's most recent initiative 'Pharmaceutical cGMPs for the 21st Century' are just two examples that indicate that the scope for differentiation has increased yet again. The role of the independent specialist manufacturer of APIs has never been more relevant than it is today.

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