OPINION: Can Asia innovate?

Dr Rob Bryant discusses whether cultural norms are holding back Asian fine chemical companies

India and China are well established in the pharmaceutical ingredients market. To date, however, neither country has shown much enthusiasm for moving on from manufacture to innovation, in R&D or in manufacture itself, preferring instead to copy the inventions of the west and rely on outmoded processes. Many mature fine chemical technologists have experienced a feeling of deja-vu when inspecting Asian manufacturing plants that bear much resemblance to those that existed in Europe 30 years ago.

In order to uncover the reasons for this lack of progress in the Asian fine chemicals sector, it is necessary to look back to the origins of the modern pharmaceutical industry…

In the beginning…

Underpinning the establishment of western medicine were the beliefs of rationalism, which took root in Greece, were later all but extinguished by Christianity and then developed during the 16th century in the age of enlightenment. This shift in European thought led to the scientific and technological revolutions of the 17th-19th centuries, which in turn provided the conditions necessary to the development of the modern drug industry.

Europe led this development and until around 1960-1970 was pre-eminent in the invention and development of pharmaceutical products. Around that time, first the US (from the 1950s) then Japan (from the 1970s) emerged as leading markets for pharmaceuticals. As consumption in these markets grew, pharmaceutical manufacturing and subsequently, pharmaceutical R&D became established in these countries. But today, of course, it is India and China that are set to become very significant pharmaceutical markets.

China and India's role in the modern pharmaceutical industry is traditionally of supplier to more established pharma markets. Over the past 10-15 years, the manufacture of APIs and finished formulations in these countries has grown rapidly, fuelled by the increasing dependence on Asian fine chemical suppliers of multinational pharmaceutical and fine chemical companies. Although there is a degree of domestic demand predominantly from the generic medicines sector (particularly before these countries entered fully into TRIPS), it is export-led sales that continue to generate the best profits for Indian and Chinese companies (see Table 1).

Table 1: An historical view of the API manufacturing market

Period	Basic trends
1850 - 1940	Establishment of the modern pharmaceutical industry, centred in Europe. Increasing use of synthetic chemicals for medicinal use.
1940 - 1965	Explosion in the development of organic chemistry. Foundations of the modern pharmaceutical industry laid in Europe and US.
1965 - 1990	Separation of a distinct pharmaceutical fine chemical (PFC) industry, greatly stimulated by growth in the generic medicines sector. Italy and Switzerland specialise in API production. Establishment of regulatory controls on the manufacture of APIs – Good Manufacturing Practice (GMP).
1990 - 1995	Transfer of the production of raw materials and intermediates from Europe/US to India and China.
1992 -1998	India's rise in the API production market, especially of APIs for domestic and 'unlicensed' markets.
1992 - 2000	China's rise in the market for the production of intermediates for India and elsewhere.
2000 - 2005	Italian/Swiss producers change from supplying generic APIs and advanced intermediates to producing PFCs for the innovative sector.
2000 - 2005	India begins to dominate GMP manufacture of APIs. The custom research and manufacturing services sector (CRAMS) grows, led by European and US PFC and pharma companies.
2004 - 2007	China becomes a major supplier of APIs, increasingly to GMP guidelines.
2005- onwards	The continuing transfer of PFC production to Asia.

Despite the continuing transfer of PFC production to Asia, fine chemicals companies in the region remain conservative when it comes to improving their production processes. Could this conservatism be a matter of simple economics: that there is no need to develop improved processes if the existing ones are sufficiently efficient? Well, perhaps... and then again, not really.

The usual reason given for lack of development in this area is that, if a process was changed, the API would need to be re-registered and the cost of doing this would be prohibitive. While there is some validity in this argument, it is more of an excuse than an explanation.

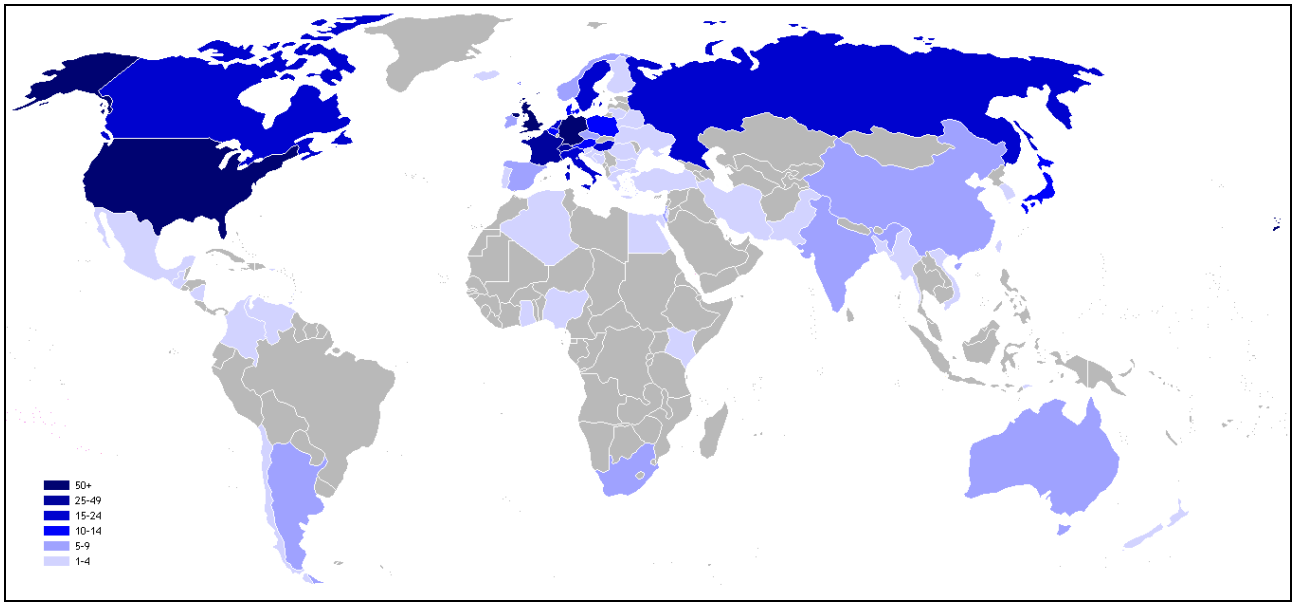
Given the far lower margins to which most Asian companies operate (bar those in Japan) compared to their European counterparts, improving the efficiency of processes would seem to be a good idea. Yet the majority of pharmaceutical manufacturing processes remain inefficient, often polluting and generally second-rate.

A culture of innovation

Perhaps there is another reason why Europeans have continued to maintain their pre-eminence in both the invention of new drugs and the development of manufacturing processes. Given the fact that the scientific revolution took place in Europe, it is likely that the educational traditions and

culture of this part of the world are especially able to 'tolerate' innovation. Certainly, by one measure of inventiveness, the numbers of Nobel Prizes won by individuals of different nationalities, much of Europe punches very much above its weight (see Figure 1).

Figure 1: Nobel Laureates by country



Source: Wikipedia

From the figure, it seems that cold climates engender greater original thinking! Of course, there may well be a bias towards Europe, given that the prize is a European one. And we shouldn't forget that the US especially has benefited from the talents of many Asian émigrés. However, it does seem that there may be a cultural and educational basis for the weighting of this data. It is certainly intriguing that Asian social traditions tend to avoid intellectual confrontation and that people are educated to respect the status quo to a degree that Europeans could not tolerate. Recent history in the far east has, if anything, reinforced the need to avoid confrontation. For example, during the era of Mao Tse Tung all dissension led to 're-education' or even death. He died in 1976, so anybody brought up in mainland China now aged above 42 (a demographic including most people in positions of power in China today) will have lived through this period and learned not to 'ask questions'. In any case, respect for authority was already deeply embedded in eastern societies, including India.

Perhaps a talent for asking difficult, and even annoying, questions is one of Europe's competitive advantages in the pharmaceutical industry. If there is validity in this hypothesis, then it is one given too little attention when making international comparisons.

But does innovation matter in the development and production of pharmaceutical fine chemicals? And if it does, what does the lack of it mean for the development of Asia's industry in the 21st century?

It matters a great deal, since today's world demands greater care of the environment and the planet's limited raw materials. And in all pharmaceutical markets, the pressure for lower costs is becoming ever more intense. Western companies still have operational flab at the finished-product level that could be removed, but in India and China, where prices are significantly lower,

no such leeway exists. The best way to reduce costs and waste is to improve the processes for making APIs.

If the foregoing argument has merit, then there is a conflict between the continued growth of Asia's PFC sector and its need for better processes (and perhaps this conflict exists when it comes to the invention of new drugs too). Of course, many Asians receive a European or US education and therefore might be expected to take with them their western-taught ways when they return to their native countries. Yet things are never so straightforward in the face of strong cultural norms and the natural resentment that people feel when returnees try to change traditional, accepted ways of doing things.

If Asia was condemned to operate in a vacuum, then there might well be cause for concern. However, as the west reduces its fine chemical manufacturing sector, maybe Asian demand for western-trained process technologists and experienced project managers will attract Europe's experts to companies in China and India.

Europeans must be quick-witted enough to take advantage of this opportunity to continue to participate in API manufacture in this way. By inventing better processes to replace the older ones employed in Asia, they can participate actively in these countries' success and, where scale of manufacture allows, even compete successfully from a western production base.

Call for innovators

Global environmental and financial pressures demand a greater than ever contribution from innovators in all industry sectors. Current manufacturing operations need new ideas and technologies, especially in the chemical industry. Simply optimising a 20th century fine chemical manufacturing process, of (usually) doubtful provenance, is rapidly becoming unacceptable.

The answer is to design the processes from the ground up. This requires a mindset that does not hesitate to question the status quo. European inventiveness needs to be applied once more, to assist the development of cleaner and more efficient fine chemical manufacturing technologies in Asia. Furthermore, the same innovative approach is the best hope for the survival of the pharmaceutical fine chemical industry in Europe.

Dr Rob Bryant runs Brychem Business Consulting, a UK-based consultancy offering technical, marketing and operational advice to companies in the pharmaceutical industry. He is an organic chemist with a background in fine chemical process development and has recently been involved in setting up an Anglo-Chinese process development operation in Nanjing.

What do you think? Do Asian fine chemicals companies lack innovative processes? Let us know at scrip.publishing@informa.com.