

# China emerges in APIs

China is becoming a major producer of APIs as well as basic intermediates. **Dr Rob Bryant of Brychem** has documented the process

Over the past 25 years, China's chemicals industry has developed strongly and has become a source of basic intermediates for fine chemicals around the world. In particular, it has become a major supplier of pharmaceutical fine chemicals. The industry's emergence as an essential source of increasingly advanced intermediates for producers of APIs based in Southern Europe and India has underpinned this growth.

However, the attention of major Chinese pharmaceuticals companies was not, until about two to three years ago, focused on the export of APIs themselves, since the opportunities for the sale of both APIs and finished formulations within the domestic market were generally very attractive.

Changes in the Chinese government's regulatory regime during the years 2005-6, which many commentators claim were encouraged by the multinational lobby, have prompted many companies to expand into the production of APIs (and finished formulations) for export, where incentives remain attractive.

Most Chinese production companies needed to revamp their plants and operations in order to make them acceptable to foreign customers and regulators. A new GMP certification system was set up for the benefit of both domestic and export producers in the late 1990s. An analysis of the certifications awarded to the leading 700 API producers reviewed in SNAPI, Brychem and WiCon's new database of Chinese API, shows that, between 1999 and July 2007, 6,914 certifications were issued, with a peak in 2004-5 of 2,820 (Figure 1).

As the numbers of applications for GMP licences grew so rapidly, the temptations to cut corners in order to keep up with the paperwork were clearly too great, creating the conditions leading to the well-publicised recent scandals at the State Food & Drug Administration (SFDA). Nevertheless, many

**Table 1 - Sales of selected Chinese API producers, 2005**

Company	Sales (€ million)
Shijiazhuang Pharmaceutical Group	529
Zhucheng Xingmao Corn Developing Company	427
Beijing Double-Crane Pharmaceutical	393
Huadong Medicine	298
Anhui BCCA Biochemical	279
Yung Shin Pharmaceutical Industries	253
Shenzhen Neptunus Bioengineer	227
Zhejiang Sunrise Fine Chemicals	171
Harbin Pharmaceutical (Sanjing Pharmaceutical Group)	151
Livzon Pharmaceutical Group Inc.	139
Zhejiang NHU Company	131
Hangzhou Minsheng Pharmaceutical Group	128
Lunan Pharmaceutical Group	116
Jiangsu Hengrui Medicine	100
Shandong Lukang Pharmaceutical	98
Zibo Xinglu Chemical	85
Jiangzhong Pharmaceutical	83
Henan Topfond Pharmaceutical	79
Shouguang Fukang Pharmaceutical	74
Zhejiang Hisoar Pharmaceutical	64

Source: SNAPI - Chinese database of APIs (Brychem-WiCon 2007)

companies have successfully established API manufacturing operations designed to comply with internationally recognised standards.

By July 2007, Chinese companies had lodged over 450 active DMFs with the US FDA, compared with Italy's 540 and India's 1,350. Although many of these DMFs have still to be 'referenced' (which would initiate an inspection), these numbers do reflect a real change in the quality of the plants to be found in China. Table 1 lists leading Chinese API suppliers by turnover.

There are now multiple Chinese producers for the majority of the world's top selling APIs. For example, the SNAPI database identifies 23 produc-

ers of amoxicillin, 15 each of paracetamol and simvastatin and 11 each of amlodipine and paroxetine. The largest number - over 45% of those reviewed in SNAPI to date - are located in Jiangsu and Zhejiang provinces near to Shanghai.

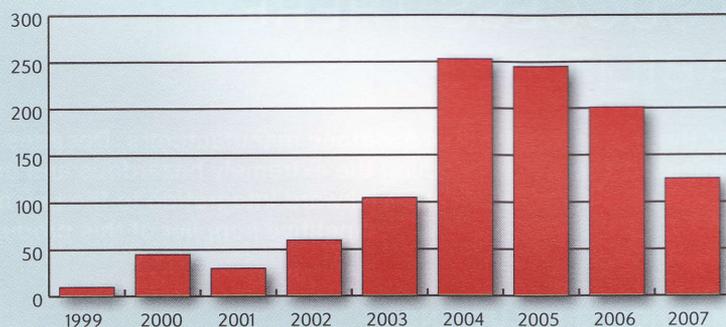
Detailed statistics on industry performance are gathered by the Chinese government. Estimates published by WiCon Pharma China report that sales of bulk drugs and APIs were valued at about €10.2 billion in 2006 at the ex-manufacturer level. Of this total, exports contributed about 40%.

In a report published by Italy's Generic Pharmaceutical Industry Association (CPGA) in 2005, India and China were predicted to reach €6.9 billion and €3.3 billion in API sales respectively. However, these estimates need to be treated with some caution, since they include categories that are usually not included in Western estimates.

Thus, as the export breakdown shown in Figure 2 shows, vitamins and food acids (worth 30% of the total) are included in the exports sales. Under this definition, the top selling APIs in 2006 were citric acid, vitamin C, tetracyclin, penicillin, vitamin E, paracetamol (acetaminophen), heparin, erythromycin thiocyanate, monosodium glutamate and lysine.

In spite of these reservations, the value of exports is clearly large. With a growth rate of 25% between 2005 and 2006, the Chinese APIs industry is set to become one of the world's leaders within a very few years.

These sales estimates do not include information on pharmaceutical intermediates and raw materials. The number of non-GMP fine chemical pro-



Source: SNAPI database of Chinese API producers (NB - 2007 figure is 'annualised')

**Figure 1 - GMP certificates granted by SFDA to API producers, 1999-2007**

ducers in China is enormous. Official records show that the Chinese authorities issued manufacturing licences to over 9,500 fine chemicals companies up to July 2007.

The majority of these do not have GMP and sell only to local customers or through traders. These companies vary in size from major groups, such as Red Sun, to very small companies that employ fewer than 10 people. Dealing directly with such companies can thus be challenging for a foreign customer and the use of traders is therefore commonplace.

However, given the prevailing business culture in China, dependence on traders can be risky. The experience of receiving consignments of crudely mixed batches of differing qualities is partly a reflection of lower standards among Chinese intermediate producers and partly a reflection of the practice of multiple sourcing of material for a single order that many traders still operate.

The only solution to this continuing problem is to shorten the lines of communication. Large and medium-sized Western companies have set up local offices to help them to find and retain dependable suppliers and there are already over 1,600 foreign joint ventures covering pharmaceuticals, APIs and biological products in China. When one includes all joint venture companies supplying the pharmaceutical fine chemicals sector, this figure would probably top 4,000.

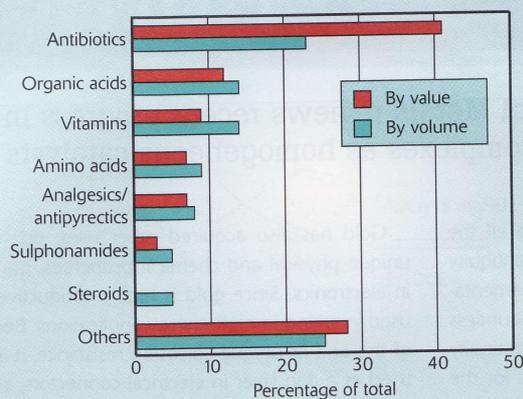
Inward investments by companies based in Hong Kong, Taiwan and the US, very often run by returning Chinese expatriates, head the list. However, India has also recently become an important investor and many of the top pharmaceutical companies now have joint ventures or long-term agreements to secure continuity of supply.

US and European investment in Chinese chemical and agrochemicals companies has been far greater than in the pharmaceuticals sector until recently, but this is rapidly changing as many more move into China or expand their downstream operations.

Whether setting up an office or locating a reliable manufacturing partner, access to reliable information in English can cut down the costs and improve the chance of success. This has been the reason why Brychem has teamed up with WiCon International to offer information and services to companies needing to find a way past the barrier of Shanghai and Beijing traders and select suitable companies that could be shortlisted for an initial meeting.

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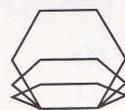


Source: WiCon Pharma China, China Pharmaceutical Guide 2007 (2nd ed.)

Figure 2: Type of bulk drugs/APIs being exported by China, 2006

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