Drug safety

ROUGHLY 80% OF THE KEY ACTIVE PHARMACEUTICAL INGREDIENTS (APIs) in drugs sold in the European Union are imported. The vast majority are made in factories in India and China, which are not inspected by EU inspectors. Unlike the US Food and Drug Administration (FDA), European health authorities do not have a foreign inspection service.

The situation is not helped by the fact that the API supply chain involves many middlemen (traders/agencies), not all of whom follow the rules. Some buy chemical grade products and sell them as pharmaceutical grade. The 'medicines' produced from these products can be harmful, even lethal.

In Haiti, more than 80 children died after taking cough syrup made with glycerine produced in China. Although labelled as pharmaceutical grade, the glycerine contained toxic diethylene glycol, related to the ethylene glycol used in car antifreeze. In a similar incident, about 130 people died in Panama. In October 2007, the *New York Times* broke the story that CPhI, a pharmaceutical trade fair in Milan, was attended by 82 Chinese companies that did not pass the authentication of their own country's regulatory authority SFDA (People's Republic of China State Food and Drug Administration). These companies were attempting to sell their API products.

There were also several reports last year of contaminated pet food, contaminated toothpaste and toxic paint on toys all emanating from chemicals made in China. But those in the west that deal with Chinese suppliers should have shouldered some of the responsibility, because either they did not check quality, or they bargained too much, or they chose not to see what was obvious - you don't get good products at cheap prices. If rogue players continue to operate, the risk of serious harm to patients will increase. At the same time, companies that do comply with regulations will not grow, they will lose profits and may go out of business.

Better enforcement should involve both sides, and companies should raise the standard and conduct enforcement ethically.

For the past year, the US Congress has been investigating whether the FDA inspects overseas API plants as thoroughly as those in US. The European Fine Chemicals Group (EFCG) participated as expert witness at a hearing of US Congress in November 2007, and expressed the view of the European API industry. Our suggestion was that Europe should set up the Foreign Inspection Service, and Europe and the US should mutually recognise the other's inspection reports. Rather than duplicating inspections at European plants, the FDA could then free up sufficient resources to perform around 100 inspections in Asia.

Recently, a Chinese expert told delegates at the EFCG's Seventh Active Pharmaceutical Ingredients Committee in Poland (www.apic.cefic.org) that China is considering regulations forbidding factories not in possession of a GMP certificate from producing APIs. These regulations would also stipulate that export APIs meet the standards and requirements*, for example, GMP, of the importing country. China GMP should follow ICH/Q7a, the GMP standard that the EU, US, Canada, Japan and Australia are now following. It is also soon to be adopted by the World Health Organization.

'In Haiti, more than 80 children died after taking cough syrup made of glycerine produced in China'

The pharmaceutical industry is fully globalised; enforcement must also be globalised. The monitoring agencies should get together to form a unified line. Medicines' agencies - FDA, SFDA, EMEA and others – must communicate with each other; understand each other and act together. Unless we work together, rogues will always find a way to get to where non-compliant APIs can escape inspection. After all, there is one objective: to secure a safe and effective drug supply for our patients.

There are rumours that China's SFDA is in discussions with the US FDA, but nothing has been disclosed publicly.

*Note: According to PRC law, API producers must have a GMP certificate for that product (a GMP registration number). APIs destined for export do not require a certificate. In the EU the situation is no different, hence the number of non-GMP licensed Chinese producers at the last CPhI in Milan. In the PRC, medicines can be made using only GMP-certified APIs – changing sources is possible provided the new source also has a GMP certificate, which explains why 'change control' is such an alien concept for China API producers.

An extract from the December 2007 issue of *Chemical China Frontier.*

Pharmaceuticals are a fully globalised industry; enforcement must also be globalised if patients are to have a safe and effective drug supply, says Guy Villax, ceo of Hovione, and member of the European Fine Chemicals Group