

### **Enforcing the Quality of Medicines in a New World Order - Summary**

The European Union (EU), like the USA, has rules in place to ensure the Active Pharmaceutical Ingredients (APIs) used to make medicines meet current Good Manufacturing Practices (GMPs), to ensure that each medicine is identical to the product approved by the Health Authorities.

Last century, medicines were either patented or branded and were manufactured mostly in the West in-house and in compliance with GMPs. The world has changed, today driven by the demand globally for lower health care costs, off-patent medicines make up the majority of pharmaceuticals we consume – generics now fill 60% of the prescription drugs dispensed under managed benefit plans in the USA. 80% of the API volume used to make EU medicines comes from abroad, and not everyone is playing by the rules. This is putting the safety of our citizens at risk. Globalisation makes it harder to enforce the rules and has resulted in:

1. The emergence of off-patent API production in the low cost economies where regulations and GMP requirements are very limited compared to those in the EU.
2. More complex and fragmented supply chains increase the potential for contamination, mislabelling, or substitution of one substance for another; all of which increases the risk to patients.
3. Unprecedented pressure on prices and profit margins drive generic and OTC companies to buy formulations and APIs at the lowest cost – sometimes from API plants that have never been inspected by any health authority from the EU or the US. This pits quality and ethics against profits in an uneven fight. Without enforcement, the least scrupulous operator wins.

The compliant industry has to meet ever growing, tougher regulations. Meeting cGMP requirements adds about 25% to the cost of an API. These high costs make cGMP compliant manufacturers uncompetitive versus non-compliant manufacturers. The EU regulatory framework has not kept pace with these dramatic changes in the marketplace. The lack of effective oversight, inspection and law enforcement by the authorities has encouraged non-compliant, illegal trade, including the importation of APIs into the EU - mainly from Asia - via certain brokers and traders. This allows them to offer lower prices from a non-compliant cost base and to import sub-standard (often counterfeit) APIs with a low chance of being caught.

Oddly, the EU inspects API plants based on proximity not risk. Per year, European authorities may inspect 30-50 API plants in Asia, when Italy or France inspects a greater number in their own country. The few foreign inspections by the European Directorate of Quality of Medicines (EDQM) tell us something is broken:

1. All the suspended approvals were related to production in Asia. None were in the EU
2. All approvals that were withdrawn by EDQM related to filings in the name of middlemen (brokers, agents, traders and distributors)
3. Some of the suspended approvals are of APIs for old OTC drugs that could be exported to the USA and whose facilities FDA would not have inspected
4. Some of the suspended approvals and FDA warning letters seem to be related to API producers that receive "support" from middlemen.

Last month, EFCG asked the European Commission to improve the oversight and enforcement of the regulations for APIs by increasing inspection resources and enforcement sanctions; by adopting some of the systems that the US FDA has in place; by taking the leadership to regulate middlemen and seeking international cooperation.

Several supra-national bodies - European Parliament, USP and WHO - have recently recognised that more inspections are key to preventing non-compliant APIs from reaching the market. Unscrupulous players cannot be allowed to take advantage of uncoordinated jurisdictions that allow them to escape by crossing the “state line”. The generics and the OTC medicines that the world needs cannot continue to be regulated by 20th Century structures and resources; the answer lies in smarter enforcement and the global cooperation of national medicines’ agencies.