Regaining supply-chain control: Is Pharma missing the target?

by Hedley Rees

Will regulations reverse the decline?

In the last four or so years, we have seen patients dying from adulterated materials (eg Heparin, 2008), shortages of life saving medicines, a catalogue of drug recalls and warning letters on manufacturing and supply issues, and a plethora of counterfeit products sold and consumed as the genuine article, risking the safety and well being of unsuspecting patients.

Given the above, it has become increasingly clear to all that there is inadequate control over the Pharma supply-chain. In an attempt to establish higher levels of supply chain integrity, governments and regulators have been swift to respond. Legislation has been enacted both in Europe and in the US. The EU has passed the Falsified Medicines Directive, leading to major revisions to Good Distribution Practice (GDP) and some revisions to Good Manufacturing Practice (GMP). In the US, the FDA Safety and Innovation Act (FDASIA) has been enacted into law, again with the intention of cracking down on illicit activities in the supply-chain, as well as encouraging better working practices. Mandatory ePedigree is now also actively under consultation at congressional committee level.

The vast majority of these measures are targeting finished product supply-chains making the journey from the final stage of production, through pre-wholesales, wholesalers, pharmacies, clinics and online ordering sites, into the hands of healthcare professionals and patients. Serialisation and authentication activity is now reaching fever pitch, as the various actors in the finished product supply-chain grapple with the associated cost, coordination and technology issues that must be solved in the next year or two.

All this pain of increased regulation will be worth it as we see an end to our supply-chain woes, won't it? Sadly no, and in fact there is a danger it will make matters worse, as the various actors in the supply-chain focus on interpretation of regulations that may make sense in theory but have not been tested in practice in the 'real world'.

It is not even as if the current regulations are deficient in any material way; the issue has always been one of adherence. For example, expectations on a third party logistics provider (3PL) for handling and storage *should* be clearly outlined in the Quality & Technical Agreement (QTA) between the licence holder and the 3PL and proper due diligence carried out in determining fitness for purpose of the 3PL's services. Any licensing of 3PL's, a possibility suggested in the EU GDP consultation, would appear to be duplication and undermine that basic duty of the licence holder. The massive inspection resource requirement would surely also be unsustainable.

This is not the end of it. There is also one glaring oversight that renders much of this effort useless. Most of what has gone wrong in the past has its roots in the manufacturing supply chain. The misbranded Heparin started life in the supply chain with an adulterated component material that was fully incorporated into the Baxter finished product. Authentication would have confirmed that lethal product as genuine. So too for the J&J/McNeil recalls – the issues were at supplier level and the risks to consumer well-being were incorporated into the finished product; and so too the many shortages associated with supplier quality issues such as glass vial delamination; and so too it goes on.

In a nutshell, stakeholders appear to be homing in, with laser-like precision, on that part of the supply chain where the problems present themselves. As any good physician would point out however, it is always necessary to look beyond the presenting symptoms into the underlying cause(s). So far, we do not appear to have completed the root cause diagnosis.

What are the root cause issues?

Let us first look at the symptoms – product integrity issues in the distribution channel. Why have issues presented here? Because this was the first area Pharma started the dis-connection process, as it abandoned direct links with its customers to the wholesaler network. That disconnection has been complete for decades and licence holders now have virtually no control over their products once they leave the site of finished production or their pre-wholesaler. The resulting no-mans land is a happy hunting ground for those wishing to make money from illicit dealings. There is so much movement of products between disconnected parties in the distribution channel, dark spaces are easy to find and capitalise on. Will more regulation remove the dark spaces? We will have to wait and see – personally, I'm extremely doubtful.

There are of course impending changes within GMP that aim to drive greater visibility of the supply-chain upstream of the finished product, and these are very welcome. However, in the same way strengthening the Highway Code would not automatically lead to better drivers, so more stringent regulations do not automatically improve supply-chain practices. The 'dark spaces' also need to be eradicated and this is where the issue lay. Pharma companies have been playing the same dis-connection game that it played with wholesalers – by outsourcing and off-shoring on a massive scale; and this game hasn't just been taking place in commercial manufacture, it has also been a favourite of Pharma R & D for quite some years now.

Drug developers seem to go all over the world for sources of supply and contract manufacture, creating complex, multi-stage supply chains that have no basis in common sense. Why would anyone buy raw materials in China, ship them to India