

GMDP for the 21st century: pipe dream or real-world possibility?

Part 1

by Hedley Rees

GMDP, as most readers will know, stands for good manufacturing and distribution practice. Readers will also know it is the quality management system (QMS) regulatory authorities mandate for companies developing, manufacturing and distributing medicines and other pharmaceutical products.

The 21st century has been with us for nearly 22 years now, so why am I writing about the chances of GMDP entering the 21st century? Isn't it already here?

That's what we are about to discuss, recognising that we will be comparing the performance of pharmaceutical companies, and their supply chains, with today's best.

We begin with a journey back in time to establish progress, or otherwise, in the 20th century.

Pharma in 1980

The question takes me back to my early days in the industry, working at a Bayer AG manufacturing site in Wales. When I joined in 1980, the Orange Guide was the equivalent of a young lad in short trousers, when compared to the giant tome it is today.

The industry was dominated by large, vertically integrated companies that carried out the research, development, manufacture and distribution of their own products. **Figure 1** (overleaf) depicts the industry structure.

Here we see a single company (acting as clinical trial sponsor and product licence holder) carrying out the entire development programme, submitting a filing to a regulatory authority for review and potential approval to sell.

The site of manufacture covered all conversion activities, from receipt of raw and starting materials at goods inwards, through the various manufacturing processes, to dispatch of finished, packaged products to wholesalers – often direct to hospital and community pharmacies too.

The site QMS, then missing the 'D' in GMDP, was under single ownership of the site. There was no mistaking who was responsible for compliance and corrective and preventive action.

The Site Master File was regularly updated and on hand for the inspections. It clearly outlined the company's policies and procedures with respect to site operations and quality.

Regulatory inspections and audits would start with a review of the Site Master File, followed by a physical plant inspection and review of all relevant documentation, such as standard operating procedures and batch manufacturing records. The entire development, manufacture and shipment of each product was carried out under one ownership, under one roof.

Shipments to countries ex-UK went direct from the plant, into Bayer owned warehouses for in-country distribution.

With this level of integration, customer complaints could be dealt with effectively. It was not unusual to receive the polystyrene packing piece from the top of a



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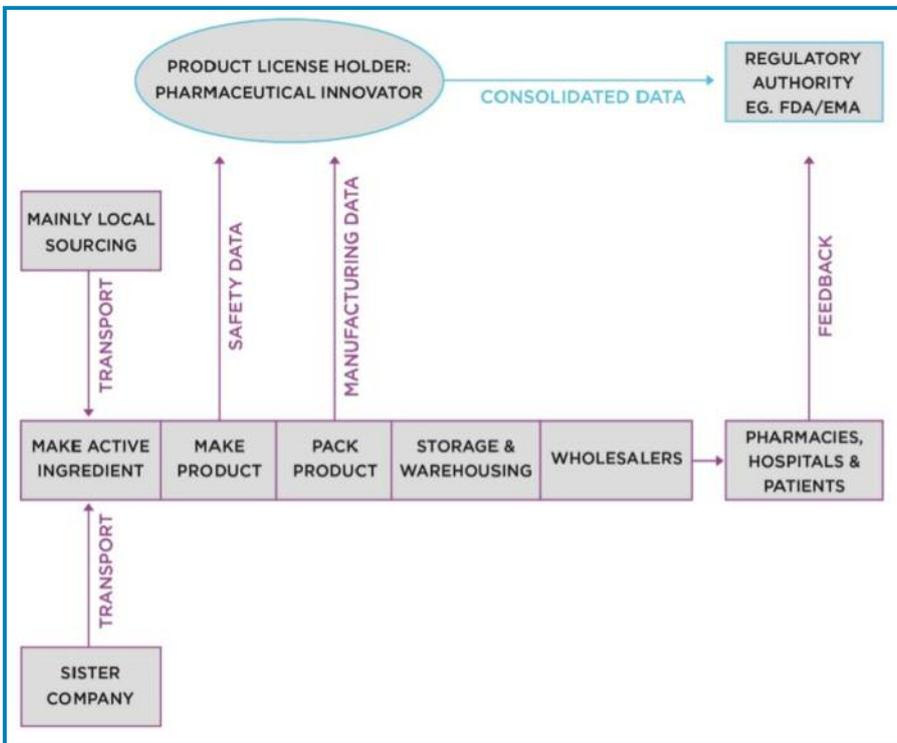


Figure 1. Industry structure 1980. (FDA: Food and Drug Administration; EMA: European Medicines Agency).

(glass) bottle of Alka Selzer from a customer, stating it would not dissolve! We were able to resolve the confusion in no time, often with a note of apology and complementary sample thrown in.

Product recalls were exceptionally rare and would place little strain on plant capability to carry out forward and reverse traceability – all movements were under the one roof, except for raw and starting material sourcing.

Industry structure as it is today

Figure 2 represents the industry structure as it is today. This picture

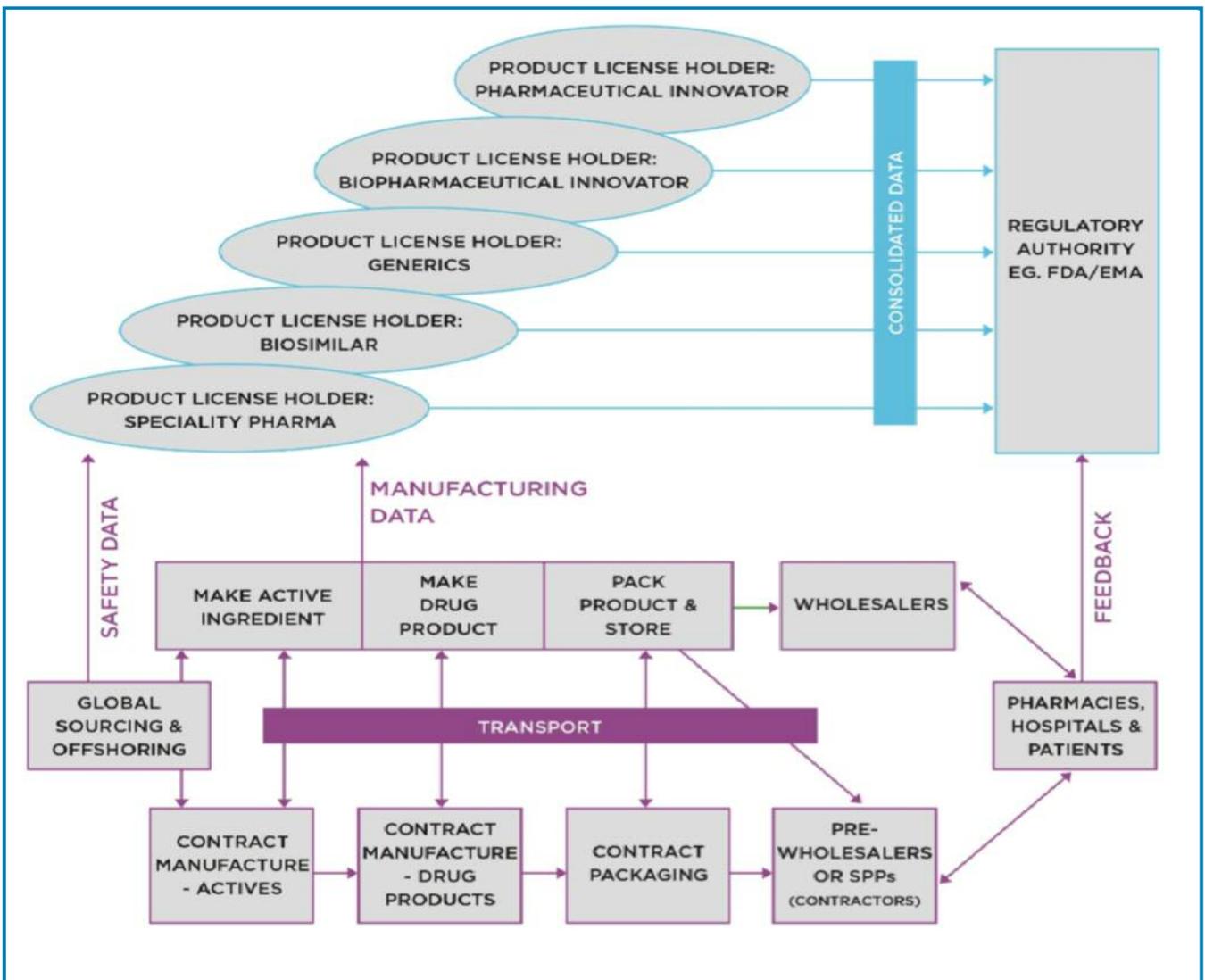


Figure 2. Industry structure 2021. (SPP: specialty pharmacy provider).

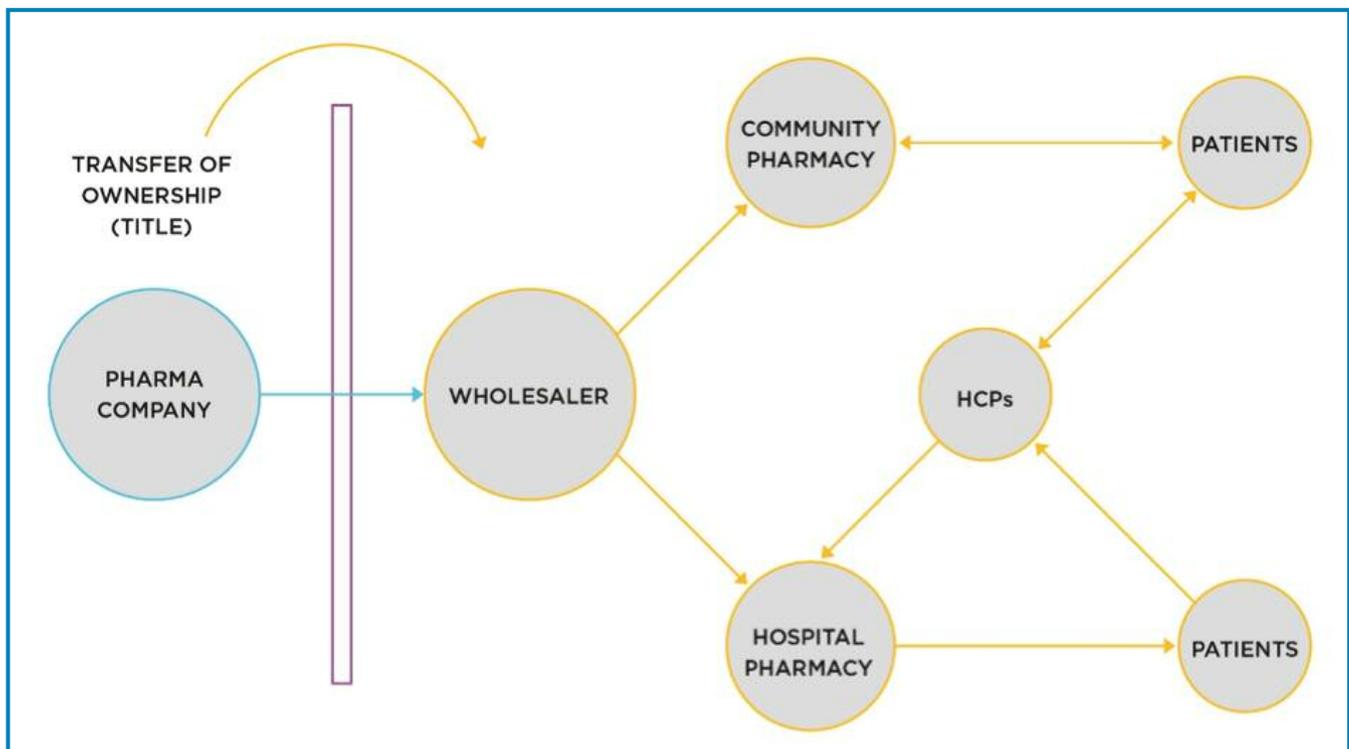


Figure 3. Transfer of ownership to the distribution channel. (HCPs: health care providers).

is very different from the 1980 version. The supply chain at the bottom of the picture has a large component of contract manufacture added to it, along with offshoring procurement policies. Transportation is running through every stage of manufacture, for both in-house and contractor owned.

We see there are also a lot more fingers in the pie when it comes to developing drugs, as the research and development-based innovator companies have increasingly outsourced early-stage development to small- and medium-sized enterprises. Along with that, biologics has grown like topsy, adding additional complexities such as sensitivity to temperature variation and process change.

For regulatory authorities, the picture has changed dramatically. In 1980, they dealt with a limited number of large, experienced pharmaceutical companies, with a known track record. Neither was able to pull the wool over the other's eyes. Today, the number of interactions with companies of all shapes and sizes developing drugs has grown exponentially, leading to shallower relationships and understanding.

Finally, and possibly the most disturbing element of the changes, is the relationship between pharmaceutical

companies and the distribution channel. **Figure 3** shows how it is today.

We see that wholesalers purchase finished goods from pharmaceutical companies with licences to sell. Once under the ownership of the wholesaler, the pharmaceutical company is not involved. Today, it's a case of 'never the twain shall meet'.

However, the holder of the product licence still holds responsibility for the quality of the product received by the end-users of its products.

Pipe dream it is then...unless?

From the above, it is difficult to conclude that GMDP can or will make the transition to 21st century industrial standards. Even in 1980 and before, there was conflict between strict regulations being imposed upon companies, and a company's ability to respond to happenings on the ground. The 'us and them' was present then, and it still is, only the complexity of the industry structure has mushroomed to the point where no-one appears to be in charge.

In part 2, we will explore a new way to approach GMDP moving into the 21st century, beginning with a completely new strategy for the industry.