For nearly two decades, the US has been beset by critical shortages of key drugs and there are now similar issues within the EU. Here, Dave Elder explores the reasons behind the shortages and what processes are being implemented to resolve the shortfall.

Drug shortages are defined, a situation in which the total supply of all clinically interchangeable versions of a regulated drug is inadequate to meet the current or projected demand at the use level. There are many different, inter-related reasons for drug shortages, but quality issues affecting the complex supply chains of many of these medicines are the most common. The American Society of Health-System Pharmacists’ (ASHP) national drug shortages statistics for 2018 have identified the key reasons for drug shortages as being manufacturing (30 percent), supply and demand (8 percent), natural disaster (3 percent), raw materials (1 percent), discontinuation (10 percent) and unknown reasons (51 percent). In addition, there is often an over-reliance on single suppliers. A single supplier will often produce 90 percent of the total supply of a medicinal product. In addition, it is very common for these suppliers to have a single source for active pharmaceutical ingredients (APIs) and key excipients in their supply chains. Moreover, 80 percent of APIs are manufactured in India and China and 60 percent of finished products are made outside the US. This can exacerbate drug shortages when such companies fail to meet US/EMA cGMP requirements or exit the market entirely. For example, the recent issues with sartans caused by N-nitroso contamination can be attributed to the fact that the sartan supply chain was heavily dependent on small numbers of impacted API suppliers. Similarly, manufacturing issues with Hospira in 2017 led to shortages of many critical drugs, particularly injectable narcotics and local anaesthetics, eg, lidocaine. There are currently significant issues with sterile injectable drugs across all drug classes and with antimicrobials, chemotherapy, cardiovascular (particularly the sartans), CNS and nutritional fluids. There is also clear evidence that the situation is worsening; occurrences are increasing, duration is longer and public health impact is high. Some drug shortages have lasted for more than eight years, eg, liotrix tablets, with no imminent signs of resolution.

Ironically, some initiatives have had a negative impact on drug shortages. The US Food and Drug Administration (FDA) introduced the Unapproved Drugs Initiative (UDI) in 2006, which allowed companies to obtain regulatory approval and limited exclusivity for common, previously non-approved genericised drugs. Whilst the objective of the UDI was to improve overall safety and quality, it unintentionally increased drug prices resulting in drug shortages. Because many of the issues affecting drug shortages span multiple US agencies, an inter-agency task force was initiated in July 2018. An example of why this was deemed necessary is that the US Federal Trade Commission (FTC) isn’t currently required to assess public health considerations when assessing company mergers and acquisitions (M&A).

During drug shortages, market forces often exacerbate the issue by driving up prices of the existing suppliers. Similarly, hoarding of existing supplies can often be a result, again negatively impacting supply and demand logistics. Furthermore, the US pricing model for key drugs may be sub-optimal. For example, the current pricing model aims for maximal quality with lowest achievable cost; consequently, there is no spare capacity, there is a systemic underinvestment in manufacturing facilities and there are long and over-extended supply chains. Against this background, the FDA’s demands (via audit programmes) for improvements in quality will often result in suppliers exiting the market as it can be too costly to implement remedial actions.

The FDA held a public meeting in November 2018 for the purpose of “Identifying the Root Causes of Drug Shortages and Finding Enduring Solutions”. This will hopefully facilitate the implementation of robust resolutions to the problem in the US.