Supply Chain Security of Pharmaceutical Grade Excipients

- A core subject of IPEC Federation –

The Issue

Back in 1998, the World Health Organisation (WHO) stated that there were more than 500 deaths worldwide in the previous 60 years caused by use of falsified excipients. (1)

Since then further examples have occurred within the supply chain with dramatic impact (2), caused for example by criminal activity, contamination, mis-labelling, or upgrading of industrial grade material manufactured under non-GMP conditions.

As a result, the supply chain of pharmaceutical starting materials, in this case excipients, has been identified by regulators and industry as an important part of medicinal product safety. In a globalised world, excipients are supplied across continents and handled by an increasing number of different parties.

The increasing complexity of the global supply chain brings with it an increased risk in excipient security.

Purpose of the Position Paper

The purpose of this position paper is to provide support to all parties within the supply chain (e.g. pharmaceutical excipient manufacturers, distributors, traders, brokers, re-packers, carriers, warehouse providers) and to bring attention to tools available which ensure supply chain security and support global drug safety.

Supporting Background Information

Supply chain security means the protection of excipient quality, traceability and integrity from the excipient manufacturing sites downstream to the finished dosage form manufacturer.

Standards and regulations have been developed and implemented to minimize the risk of future falsifications incidents.

The WHO Good Trade and Distribution Practices for Pharmaceutical Starting Materials (GTDP, first published in 2003 and updated in 2016) was developed to provide guidance on how to assure security in the supply chain for pharmaceutical starting materials. Later, regulations were implemented by authorities to address the topic. For example, in 2004 the European Commission published the GMP (Good Manufacturing Practices) regulation for active pharmaceutical ingredients (APIs). The “Falsified Medicines Directive“(2011/62/EC), published by the EU commission in 2011, and subsequent guidelines mandate GDP for APIs (2015/C 95/01) as well as the assessment of the risk posed by the excipient supply chain complexity (2015/C 95/02). Changes to chapter 5 of EU GMP Rules and Guidance Part I explicitly describe supply chain security measures for the pharmaceutical industry. The Falsified Medicine Directive (FMD) was issued primarily to take action against falsified finished dosage forms in the market place.

Nevertheless, regulators became aware that falsified and sub-standard pharmaceutical starting materials were part of the risk for the patients and therefore incorporated related requirements into the FMD. With this enhanced regulation, Europe still has different regulations for both active ingredients and excipients. Drug manufacturers have to define the level of GMP to be applied by excipient manufacturers based on a risk assessment, but Good Distribution Practice (GDP) for excipients is not an explicit part of this regulation.

In the United States, the Food and Drug Administration Safety and Innovation Act (FDASIA) requirements include various supply chain control expectations. FDA is in the process of implementing many different programs related to improved supplier controls. FDASIA makes it clear that GMP requirements for drug products approved in the US include appropriate measures to verify the supply chain of excipients. FDASIA includes requirements for identification for all excipients used in approved drugs. FDA is increasing their surveillance programs of drug manufacturers related to excipient qualification.

IPEC Europe and IPEC-Americas first published its GDP Guide for pharmaceutical excipients in 2006 (3) (updated as an IPEC Federation Guide in 2017), to provide voluntary industry guidance tailored for the excipient supply chain together with the related GMP Guide (4). This GDP Guide is a tool to build appropriate links between the parties in an excipient supply chain and raise the required awareness for patient safety aspects of the supply chain. Furthermore, with the lack of an official European GDP guideline for excipients, IPEC's GDP Guide will help close that gap and help industry to apply appropriate GDP principles and thereby contribute to excipient security in the supply chain.

The GDP Guide was supplemented by an IPEC-sponsored certifiable standard for GMP and GDP for excipient suppliers – such as EXCiPACT (www.excipact.org) and the NSF/IPEC/ANSI 363. These standards contribute to the verification of supply chain security of pharmaceutical excipients and are aligned globally with the current paradigm of pharmaceutical regulation.

IPEC Federation Position

The entire excipient supply chain needs to be controlled from the excipient manufacturer to the medicinal product manufacturer.

Each party in the supply chain is responsible for its own specific area of activity within the supply chain. To establish and ensure supply chain security the IPEC Federation GDP Guide should be used as a tool.

In addition, there should be controls in place at each interface to ensure excipient security both upstream and downstream within the supply chain. The level of control can be established by the application of the IPEC Risk Assessment Guide (5).

This paper should be brought to the attention of all partners in the supply chain of pharmaceutical excipients.

References

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2007 - Panama Di-ethylene Glycol Contaminations
2008 - Heparin with Over sulphated Chondroitin Sulphate (OSCS)
2008 - Milk and derivatives with melamine
2009 - Nigeria Diethylene glycol contaminations
2010 - Melamine in milk containing products
2011 - Breast Implants made with industrial grade silicon
2012 - Sodium nitrite marked and used as Sorbitol
(3) IPEC Good Distribution Practices Guide for Pharmaceutical Excipients, 2017 (www.ipec-europe.org)
(4) IPEC PQG Good Manufacturing Practices Guide for Pharmaceutical Excipient, 2017 (www.ipec-europe.org)
(5) The IPEC Risk Assessment Guide for Pharmaceutical Excipients, Part 1 – Risk Assessment for Excipient Manufacturers, 2017 (www.ipec-europe.org)
(6) FDASIA – https://www.fda.gov/RegulatoryInformation/LawsEnforcedbyFDA/SignificantAmendmentstotheFDCAct/FDASIA/default.htm

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