Practical Issues on Supply Chain and Good Distribution Practice

A summary of the GMP DIALOGUE at the GMP-BERATER Tage 2017

by Susanne Sailer

Medicinal drugs and active agents do not only have to be manufactured appropriately, they have to be stored and transported in an expert manner as well. This is the only way to ensure their high quality and the patients' safety. The Guidelines of Good Distribution Practice (GDP) meet this need. The uncompromising implementation of GDP constitutes a necessity for everyone involved. Having the entire supply chain under control, however, means much more.

In the following, you can read a summary of the questions and answers that arose during the discussion at our GMP conference, the GMP-BERATER Tage 2017. GMP inspector Dr Petra Rempe and Juergen Ortlepp, Chemical Technology Engineer at Infraserv Logistics GmbH, responded to questions from interested GMP Publishing customers.

Medicinal products and their starting materials are manufactured and shipped through-out the world. After leaving the manufacturing site, they continue to be exposed to numerous influences during their transport to the patient that may have a strong impact on product quality. In addition, there is a risk that counterfeit drugs are introduced into the legal supply chain.

The pharmaceutical distribution network is becoming more and more complex and includes many stakeholders, such as e.g.:

- manufacturers (domestic and abroad)
- wholesalers (domestic and abroad)
- importers
- parallel importers
- pharmaceutical entrepreneurs
- wholesale trade (partial line, "pharmacy wholesale trade")
- wholesale trade (full line)
- external warehouses
- contract logistic service providers (carriers, retailers)

By the way, the supply chain does not only include the direct logistics or the logistics involving various stakeholders from the manufacturer to the pharmacy, but also reverse logistics. For it may absolutely happen that e.g. returned medicinal products are reintroduced into the supply chain after a detailed examination.

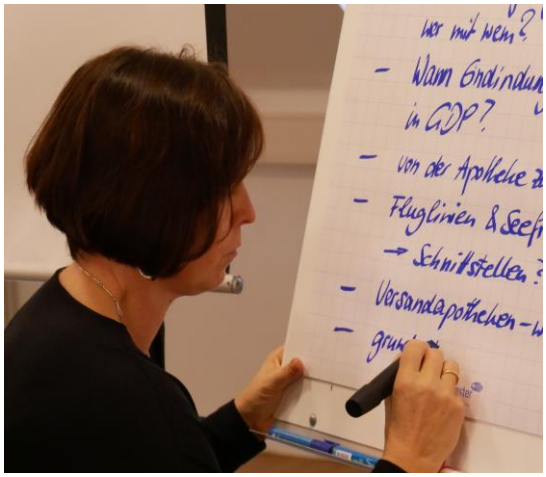
Which qualification does the responsible person need for the wholesale trade?

As stated in the GDP guidelines, a pharmaceutical training would be desirable. Unless otherwise prescribed by national legislation, however, it is not absolutely required. German law gives ample scope and does not prescribe any formal qualification or defined expertise for the responsible person. It only claims reliability and GDP knowledge. In case of inspections, the responsible person's curriculum vitae often gives an initial clue in order to obtain information of their experience in the sector. Moreover, a certificate of a GDP seminar or training is requested in most cases. The decision as to which qualification is required also depends on the product portfolio, for example. The risk of a company that exclusively does wholesale trade with disinfectants is different from that of a company trading with cytostatic agents.

Where should the data logger be located during transport?

There is no general answer to this question and there are no definite rules either. As a matter of principle, a data logger should be placed there where the highest variations of the critical parameters - generally the temperature - are to be expected. This place must be determined on the basis of the risk. Apart from that, data loggers can not only control the temperature, but for example gather other parameters as well. Risk analyses can be used to determine the critical parameters for a product.

Tip from among the participants: It has proven successful in practice to not only have one data logger, but two (failure, disappearance of a logger, etc.).



How to deal with deviations of temperature?

The GDP service provider must see to it that the storage and transport conditions are complied with. It is, however, rather improbable that the holder of the wholesale distributor authorisation has sufficient data at hand to be able to assess the potential effect of a deviation on a particular product. This is why, in the end, the manufacturer must decide on the consequences in case of a deviation of temperature. The assessment should be carried out on the basis of the risk for every individual product.

Let us take a look to related sectors: Self-control is effective in the food sector where identical standards apply throughout the EU. For example, chilled product will not be accepted if the defined temperature range was not complied with during storage and transport. The self-control tool does not work (yet) in the medicinal products sector.

The use of the mean kinetic temperature (MKT) was clearly denied by the experts. It must not be used to compensate for bad storage conditions. The determination of the MKT could give an indication for an assessment in rare and extraordinary cases of a deviation of temperature and in particular in the absence of further information on the product only.

Approaches and options of validation of supply chains?

If you follow a medicinal product or an active pharmaceutical ingredient, e.g. from a contract manufacturer in Asia to Europe, you may easily count more than 50 points of intersection during transport. Each of these points of intersection contains a potential risk. Practice shows: Such processes involve many insecurities (customs, runway, weather, etc.) and their validation is virtually not possible. It is, however, possible to describe the process chain, define points of intersection, go through different scenarios in advance, perform risk analyses according to the supply chain and thus to identify the greatest risks.

Monitoring long-distance transports (air and sea freight)

Both international airports and sea ports and container ships contain numberless "black boxes" areas. It is true that, at the airport, for example, there are qualified warehouses and guidelines for the staff. It is beyond control, however, how long and on which conditions goods stay at the customs or on the runway or where exactly a container is positioned on a freighter. Thus, in the end, the storage and transport conditions can only be monitored using data loggers for routine transports as well.

Who has to conclude contracts on the delimitation of responsibilities with whom?

General rule: The person who charges others with the transport or storage, will be responsible for GDP compliance as well. In order to make things clear with respect to responsibility, however, the parties involved should conclude contracts on the delimitation of responsibilities.

A contract manufacturer will only be responsible for the transport and the selection of the carrier if they are committed and/or commissioned to do so by contract. A customer may still charge contract manufacturers with the organisation of transports. In this case, it is advisable to name qualified carriers, for example in the contract on the delimitation of responsibilities, that may be charged (the list should be updated at regular intervals!). It is then again incumbent upon the customer to check the correct handling upon receipt. By the way, this also applies to in-house transports, for example when goods are transported within a parent company between two different branches. The responsibilities in case of in-house transports must be defined in the context of a contract, a matrix or the like as well.

By the way: GDP knows no Incoterms (International Commercial Terms)! This is a series of voluntary clauses customary in the logistics sector for the interpretation of usual terms of international trade. Incoterms cannot establish any GDP responsibilities.

When will pharmacies be integrated into GDP?

In Germany pharmacies do not have to comply with GDP, but the German Ordinance on the Operation of Pharmacies (Apothekenbetriebsordnung) applies that exactly defines the storage of medicinal products. Thus, the transport and the storage of medicinal products and active pharmaceutical ingredients is strictly regulated by legislation until they are handed over at the counter of the pharmacy. It is true that medicinal product packs contain clear information for patients on how to store a product, but, for understandable reasons, the way patients actually handle medicinal products is beyond control. This is why, as a person taking part in the discussion thinks, it is reasonable to leave to the customer the greatest possible amount of the stability reserve existing for medicinal products.

Author:

Susanne Sailer
Freelance Science Journalist
Schopfheim, Germany

