LOGFILE Feature 03/2021

26th PTS GMP Conference - Current Topics Presented Virtually

by Doris Borchert, PhD

There is a first time for everything - in this case for the digital format of the GMP Conference, which PTS Training Service organised for the 26th time on 1 December 2020. A successful premiere, according to the unanimous feedback of the participants. The conference took place live - and that is exactly what made it very lively and authentic.

The current Corona pandemic not only ensured that the conference took place in a new format, but also that many speakers made reference to it in their presentations - even if they did not always deal with GMP aspects in the narrower sense.

In this article we especially compiled the conference news on GMP and GDP topics for you.

GMP Deep Dive (Interview)

Gabriele Wanninger, PhD, Head of the GMP/GDP Inspectorate, Government of Upper Bavaria in conversation with Josef Landwehr, PhD, PTS Training Service

Gabriele Wanninger took questions from the moderator Josef Landwehr and from participants. The most important questions and answers are summarised thematically below.

EU GMP Guide

- When can we expect the final version of Annex 1?
  Once again, a four-digit number of relevant comments have been received for the 2nd draft, which need to be processed. The main topics are rooms and equipment. There is an additional delay due to the Corona pandemic. The final version will probably not be available until the end of 2021.
- Why does the new Annex 1 now also apply to nonsterile products?
  Until now, there have been no zone concepts for nonsterile products; this gap is now to be closed. However, the specifications of Annex 1 for nonsterile products are only optional.
- What changes in monitoring?
  For microbiological monitoring, averaging will be dropped in the future; instead, each contamination must be identified at the species level. The reason for this change is that averaging, which was previously permissible, allowed real problems to be "averaged out".
- What is the status of Annex 21?
  The comment period was extended until 20 August 2020. The much discussed topic "fiscal import" was removed from Annex 21.

- What other revisions can be expected in the EU GMP Guide? In view of the increasing importance of the topic of data integrity, Chapter 4 Documentation and Annex 11 Computerised Systems are to be revised.

US FDA and MRA

The FDA no longer carries out routine inspections in Germany and has already queried many inspection reports. Conversely, it is more difficult to interpret FDA inspection reports. These only contain a list of deficiencies, but in contrast to German inspection reports, no clear statement on GMP compliance. Preapproval inspections (PAI) continue to be planned and carried out.

One participant asked about the rationale behind this approach. Although PAIs are also covered by the MRA, Gabriele Wanninger said, it was to be expected that the FDA would initially still conduct its own PAIs in Europe. This is because for PAIs - unlike for routine GMP inspections - certain aspects have to be taken into account. These include, for example, the deadlines in the approval procedure. In addition, a PAI focuses on a specific product for which the application for a marketing authorisation is being submitted. While routine inspections look at overall GMP compliance and only pick out documents on specific products on a random basis, a PAI also looks in particular at compliance with the marketing authorisation documents. In the current pandemic, however, the aim is to suspend PAIs in MRA countries.

Brexit

The UK receives read-only access to the EUDRA GMDP database. It is still unclear whether GMP certificates issued by the MHRA will be recognised in the EU after Brexit.

Editor's note and update: The EU and UK have agreed to the mutual recognition of inspections and certifications of medicinal products as part of the EU-UK Trade and Cooperation Agreement signed on 30 December 2020.

Impact of the Corona pandemic

The number of inspections was greatly reduced in spring 2020; in summer, priorities were set on acceptance inspections. These were partly carried out as hybrid inspections (e.g. only rooms inspected on site, documents virtually). Routine inspections were only carried out in urgent cases, preferably on site. Remote inspections in third countries were carried out occasionally for follow-up inspections. All GMP certificates were extended until the end of 2021. Audits could not and cannot be carried out as usual because of the Corona pandemic. The authority takes a pragmatic view, but expects those responsible to look for alternatives.

The significance of remote inspections or remote audits is questionable in Gabriele Wanninger's view. Video conferences and the exchange of digital data are available tools.

The topic is addressed, among others, in the "Notice to Stakeholders", a Q&A document of the EMA, the Heads of Medicines Agencies (HMA) and the European Commission, which describes the regulatory expectations for medicinal products for human use during the COVID-19 pandemic.

You can find this document at https://ec.europa.eu/health/sites/health/files/human-use/docs/guidance_regulatory_covid19_en.pdf

GDP Update 2020

Thomas Porstner, PHAGRO (German Federal Association of the Pharmaceutical Wholesalers)

COVID-19 pandemic and GDP

Corona makes many things possible that were previously unthinkable - including more flexibility in the area of GDP. In order for things to continue at all, compromises have to be made - naturally with the claim that drug safety should not be jeopardised as a result. For example, in Germany the new regulation on ensuring the supply of the population with products of medical need allows deviations from the provisions of the German Drug Law in individual cases, if this is necessary to ensure the supply of medicinal products. Concessions are also made at the European level - this concerns, for example, the automatic extension of GDP certificates and time-limited wholesale authorisations until the end of 2021. There is also more flexibility for the responsible person: working in a home office, delegation of tasks as well as shortterm substitutions are possible, but subject to a number of conditions. The background for these decisions are staff shortages due to quarantine measures and cases of illness as well as stricter hygiene measures.

If you would like more detailed information, you will find all the important information in the following document:
NOTICE TO STAKEHOLDERS QUESTIONS AND ANSWERS ON REGULATORY EXPECTATIONS FOR ME-DICINAL PRODUCTS FOR HUMAN USE DURING THE COVID-19 PANDEMIC
(European Commission / Heads of the Agencies / EMA)
(https://ec.europa.eu/health/sites/health/files/human-use/docs/guidance_regulatory_covid19_en.pdf)

EU online pharmacies

Thomas Porstner put his finger on a sore point: compliance with temperature conditions when medicines are shipped by EU online pharmacies. Because these cannot be controlled at all or only insufficiently and considerable deficiencies are found in practice. The legal situation and the challenges are now also being dealt with by the scientific service of the German parliament. The problem: Irrespective of the question whether the respective EU member state provides for comparable safety standards, the shipment by the foreign pharmacy to Germany must be carried out in accordance with the German regulations on online-order sales. However, there is de facto no supervison of foreign pharmacies with regard to compliance with German regulations, because the supervising powers of German authorities are naturally limited to Germany. What remains is the recommendation to buy medicinal products directly from the local pharmacy or to obtain them from a German online pharmacy.

EU Counterfeiting Directive

The implementation of the EU Falsified Medicines Directive with the aim of preventing counterfeit medicines from entering the legal supply chain has created a lot of additional work for the industry. After a summary of the essential requirements from the GDP Guidelines, Thomas Porstner outlined the implications this has for wholesalers in particular. When must the authenticity of the unique identifier be checked? When is deactivation permissible or necessary? What must the wholesaler do in the event of a

counterfeit or a suspicion of counterfeiting? All this is clearly regulated and could be implemented in practice, but the system still suffers from technical deficiencies and operator errors.

Expertise of the responsible person

One of the prerequisites for obtaining a wholesale authorisation is the appointment of a responsible person who has the expertise required to carry out the activity. A degree in pharmacy is desirable, but not mandatory. The fact is that pharmaceutical issues are only part of the required qualification. In addition, however, the responsible person must also be able to assume professional responsibility for proper operation. Since the existing regulations do not precisely define the type and scope of the "required expertise", the German Higher Regional Court in Münster considers the competent authorities to be obliged to concretise the legal term. The yardstick for the legal interpretation is the respective scope of tasks and responsibilities of the responsible person. The expertise must be proven, e.g. by certificates of completion and/or further training certificates.

GDP Guideline for Veterinary Medicinal Products (EU)

A draft guideline is also currently being worked on for veterinary medicinal products. Thomas Porstner took a look at some specific contents. For example, the envisaged requirements for the re-turn of veterinary medicinal products with special storage conditions are much stricter than in the GDP Guidelines for human medicinal products. A distinction is also made between "required storage conditions" and "defined transport conditions", which implies a permissible deviation. With regard to vehicle and transport equipment, there is a need for improvement in the distinction be-tween requirements for temperature control, theft protection and traceability. It remains to be seen how these aspects will ultimately be regulated. Finalisation is planned for 2022.

GDP Guideline for Medical Products (WHO)

Last but not least, Thomas Porstner referred to the WHO guideline Good storage and distribution practices for medical products published in April 2020 (WHO Technical Report Series, No. 1025, 2020; Annex 7). The guideline defines "medical products" as "products including, but not limited to, finished pharmaceutical products, medical devices including in vitro diagnostic medical devices, and vaccines". The scope of application is thus broader than in the previous, superseded guidelines on good storage and transport practices, which are still listed as references in the new guideline.

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