GMP Guidelines: 
What to expect 2014?

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One thing is for sure: It will not get boring in 2014. The further development of the EU Guide to GMP is a continuously ongoing process. Revised versions of a number of chapters were published as drafts last year. By now the consultation periods are closed and we can expect the corresponding final documents in the near future. A trend that has already been set in motion during the last couple of years continues: GMP requirements will more and more apply to suppliers by focusing on the responsibilities for quality assurance within the supply chain, e.g. for excipients and APIs. Which guidelines can be expected in 2014? We have put together information provided by the regulatory authorities and out of discussions with experts from the pharmaceutical industry. As usual, the GMP Conference also offered a comprehensive summary of the current status and an outlook. The results of the meeting held by PTS Training Service in Dusseldorf last December have also been incorporated. Find a brief summary below about new regulations and guidelines which can be expected in 2014. We will keep you informed in detail in following issues of our newsletter.

EU Guide to GMP

The revised Chapter 2 on Personnel will come into operation February 16, 2014. The changes were made in order to integrate the principles of “Pharmaceutical Quality System” as described in the ICH Q10 tripartite guideline. It contains precise definitions of responsibilities. The ultimate responsibility to ensure an effective Quality Management System is in place and responsibilities and authorities is with the senior management. Furthermore, new sections on the responsibilities of key personnel and consultants have been added.

Last year the European Commission closed the public consultation on the following chapters of the GMP Guidelines Part I and has published the comments:

- **Chapter 3 Premises and Equipment**  
  **Kapitel**
  The proposed amendments relate primarily to the prevention of cross-contamination and toxicological assessments. The requirements include the application of the principles of Quality Risk Management to avoid and control risks. The risk assessment should, among other parameters, include toxicological evaluations.

- **Chapter 5 Production**
  Here again a substantial change regarding the prevention of cross contamination and toxicological assessments was carried out. Furthermore new paragraphs on supplier qualification
have been added to ensure compliance with legal requirements and the production of APIs according to GMP. Therefore, the traceability within the supply chain has been included in the document as well as testing of starting material and conduct under supply shortages.

- **Chapter 6 Quality Control**
  The draft focuses in particular on new requirements regarding the transfer of analytical methods and modifies, for example, the requirements for laboratory reagents and media.

- **Chapter 8 Complaints, Quality Defects and Product Recalls**
  The revision shall ensure that the principles of Quality Risk Management are applied when investigating quality defects/complaints and when making decisions in relation to product recalls. Furthermore, the need for the causes of quality defects/complaints to be investigated and determined is stressed, and that appropriate preventive actions are put in place to guard against a recurrence of the issue. Expectations and responsibilities in relation to the reporting of quality defects to the supervision authority are clarified.

**Update on Annex 16:**

- **Annex 16: Certification by a Qualified Person and Batch Release**
  The European Commission published the changes to Annex 16 of the EU GMP Guideline last year as a draft, reflecting the realities of global supply chains and supporting the implementation of new control strategies for quality issues. The document focuses in particular on detailed responsibilities and accountabilities of the QP, the reliability of GMP certificates and the handling of unplanned deviations. The consultation period is closed. Several comments welcomed the revision. While in particular the principle change towards the specific core responsibilities and accountabilities of the QP got a very positive feedback, concerns have been raised regarding specific accountabilities of the QP. They were seen as unrealistic.

**EC: GDP for APIs**

In February 2013, the EC published the “Guidelines on the principles of good distribution practices for active substances for medicinal products for human use” for public consultation. The consultation period has been closed and the comments were published. The draft is based on the requirements of ICH Q7 or Part II of the EU GMP Guide. It clarifies activities that fall into the GDP area (e.g. importing, supplying or exporting APIs) and activities that are subject to the GMP Guidelines (e.g. repacking, relabeling of APIs).

**EMA Guideline: GMP for Excipients**

The comments on the new EMA Draft Guideline “Guidelines on the formalised risk assessment for ascertaining the appropriate good manufacturing practice for excipients of medicinal products for human use” were published last year. The 5 page document notes that adequate risk assessment for
excipients should be part of the Quality Management System of the product owner. Furthermore, companies importing medicinal products should have documentation on site showing appropriate GMP levels.

**PIC/S: GDP Guideline**

A PIC/S Expert Circle has prepared a PIC/S GDP Guide which is currently under consultation within the organisation. The document is based on the EU GDP Guide. It is a voluntary guidance for non-EEA participating authorities of PIC/S.

Annex 3 to the PIC/S Guide to Good Practices for the Preparation of Medicinal Products in Healthcare Establishments will be adopted after review by the competent Working Group of all comments to the final draft.

**FDA**

The FDA - in particular the Center of Drug Evaluation and Research (CDER) and Center of Biologics Evaluation and Research (CBER) - continuously pursues the path of internationalisation. In this context the two initiatives FDASIA (Food and Drug Administration Safety and Innovation Act) and GDUFA (Generic Drug User Fee Act) are relevant (more details in one of the upcoming LOGFILEs). The 21st Century Initiative will be further pursued, foremost the risk- and science-based decision making for challenges in the pharmaceutical industry. Over the last years CDER and CBER highlighted the two core principles for the discussion.

One could change a popular saying: “Only something backed by a risk analysis, is plausible.” A dependable risk analysis needs sound scientific data.

Furthermore, the implementation of the 21 CFR 4 “Combination Products” is of great importance for many companies. Next to compliance of GMP guidelines (21 CFR 210/211) organisations also will have to adhere to medical device guidelines (21 CFR 820).

**Summary**

The year 2014 will probably not unveil any transforming ideas. That being said, the industry has to do its homework regarding the following areas:

- Establishing a comprehensive Risk Management.
- Advancing the understanding of processes through scientific support.
- Improvement of quality oversights through clear definition of responsibilities and transparency in the production.
- Efficient monitoring of the entire supply chain.

Nevertheless, this year offers interesting challenges for all parties involved, for regulatory authorities as well as the pharmaceutical industry and their suppliers.

**Sources:**

19th GMP Conference, December 2013, Dusseldorf, held by PTS Training Service
New version of Chapter 2 of the EU Guide to GMP:
http://ec.europa.eu/health/files/eudralex/vol-
4/2013-01-18_chapter2_.pdf
Draft revisions of Chapter 3, 5, 6, 8:
Comments:
Draft Annex 16:
EC: GDP for APIs:
EMA: Guideline for Excipients
FDA: 21 CFR 4

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