Which European Guidelines will change in 2013?

By Thomas Peither

The New Year has barely begun as already the first draft amendments to the EU GMP-Guideline have been published. Furthermore, more news can be expected over the course of the year.

EU GMP Guideline
Adopted Chapters

The European GMP-Guideline will be revised continuously. On January 31, the new Chapter 1 “Pharmaceutical Quality Systems”, Chapter 7 “Outsourced Activities” and Annex 2 “Manufacture of Biological Active Substances and Medicinal Products for Human Use” will enter into force. Regarding Chapter 1, the life cycle of a product plays an increasingly important role, which must be reflected in the Quality Management System. Additional information was previously published by GMP-Publishing.

It has to be emphasized for Annex 2, that the requirements therein have to be seen in connection with Part II (active pharmaceutical ingredients).

Complaints, Quality Defects and Product-Recalls

The proposed changes to Chapter 8 of the EU GMP-Guideline Part I were published on January 17, 2013. It involves requirements in the field of

- Personnel and organization
- Procedures for dealing with quality defects
- Investigations, root cause analyses and corrective actions

The deadline for responses to this consultation paper is July 19, 2013.

Premises and Equipment

The proposed amendments to Chapter 3 have already been published on January 17, 2013 (end of consultation: July 18, 2013).

In this regard, the recently published Draft Guideline of the Safety Working Party (SWP) entitled “Guideline on setting health based exposure limits for use of different drug products in shared facilities” has to be seen, too. It applies to human medicinal products as well as to veterinary medicinal products.

The new requirements in Chapter 7 “Outsourced Activities” do not only relate to outsourced activities such as manufacturing or analytics but to all outsourced GMP regulated activities, e.g. environmental monitoring. At the same time a “Qualified Person” has to be involved, as this is not only a matter of contracts but also of change control systems used by a contractor and the examination for suitability and competence of a contractor. That way the particular responsibility of a contractor regarding the quality system cannot be evaded.

A substantial change can be seen in connection with Chapter 5 “Production” which relates to the prevention of cross-contamination and toxicological assessments.

Quality Control

The draft amendment of Chapter 6, Part I, was published on January 17, 2013 as well (end of consultation: July 18, 2013).

New requirements on technical transfer of testing methods but also other items such as laboratory reagents, media, etc. are modified.
Production

The following proposals for modification to Chapter 5 “Production” are of special interest:

- Cross-contamination
- Toxicological assessments
- Qualification of suppliers
- GMP-conformity of active substances
- Supply chain traceability
- Testing of starting materials

These changes have to be seen in context with the SWP Draft Guideline, as well.

Expected Consultations

It is expected that there will be changes to Annex 16 “Certification by a qualified person and batch release” over the course of the year.

The focus will be on:

- Detailed requirements on QP’s
- Reliance on GMP-confirmation of third parties
- Unplanned deviations

Annex 17 “Parametric Release” should be improved as well by formulating a more explicit applicability of Annex 17. In addition to terminally sterilized products it is planned to include biological drugs, APIs and intermediates in its scope.

Annex 15 “Qualification and Validation” will be revised, too, due to the numerous changes within the EU-Regulations since 2001 that have essentially influenced process validation and system qualification. Currently Annex 15 is improved by a working group with members of Great Britain, Germany, Ireland, Italy, Portugal and the PIC/S. This composition already indicates that the revision is carried out jointly with the PIC/S. A draft of a revised version of Annex 15 is expected to be published by the end of 2013.

Import of Active Pharmaceutical Ingredients (APIs) to the EU

The requirements for the import of APIs changed last year. Starting in July 2, 2013 all APIs imported to the EU have to be produced according to European GMP standards. This has to be confirmed by a certificate of the respective regulatory authority.

Excipients

Up to the present excipients are only regulated to a comparatively limited extent. However, it is planned to compile a Guideline for Risk Evaluation within Europe. Since the amendment to Directive 2001/83/EC Article 46 (f) has already made a statement to the risk assessment of excipients, the associated guideline is keenly awaited.

Currently the guideline is being developed by the EMA GMDP Inspectors Working Group, with participation of the authorities of Great Britain, Denmark and Hungary.

At present the working title is “Risk Assessment/Risk Management Guideline to Establish Appropriate GMP for Excipients Used in the Manufacture of Medicinal Products for Human Use”.

Right now, the guideline is expected to be with the European Commission for further review. A consultation date is not yet known.

Good Distribution Practice (GDP)

Industry is still waiting for the publication of the final GDP-Guideline. The last conferences did not give clarity on any actual time frame.

Meanwhile it has come to be known that there will be another Guideline to “Principles of GDP for Active Substances”. It is based either on requirements according to ICHQ7 or to Part II of the EU GMP-Guideline. A review by the European Commission is expected in the near future.

Conclusion

In 2013 the regulatory authorities will continue to improve the GMP-regulations and will further work on bringing them into line with the current requirements. The EU GMP-Guideline will change in Chapters 1, 3, 5, 6, 7 and 8. A revision is planned for Annex 15, 16 and 17. Moreover, we are soon expecting the new GDP-Guideline and Guidelines for excipients.
Source / Literature

Mortensen, Claus; Risk Assessment for Excipients; Danish Health and Medicines Authority; PDA/EMA Joint Conference 4-5 Dec 2012

Gray, Norman; Revision to Annex 15 Qualification & Validation, PDA/EMA Joint Conference 4-5 Dec 2012

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