What's New in Update No. 7/2017?

Dear Reader of the GMP Compliance Adviser,

failures occur – unfortunately, this is inevitable even in a well-controlled pharmaceutical process environment. The point is how to manage them and especially, how to find out the root causes in order to be capable of defining appropriate and effective actions. The new chapter on Failure Management outlines how to set up a failure management system and explains how to use root cause analysis methods and tools correctly. Don't miss the opportunity to make yourself familiar with failure management as an essential part of continual improvement!

Furthermore, we have updated the GMP-relevant parts of the Code of Federal Regulations Title 21 which are now current as of April 1, 2017.

Login and check out the new content of your GMP Compliance Adviser!

GMP in Practice	
Chapter 20 Continual Improvement	20.E Failure Management

GMP Regulations	
GMP Glossary	updated
Chapter D USA: CFR and FDA	D.1.1 21 CFR Part 210 Current Good Manufacturing Practice in Manufacturing, Processing, Packing, or Holding of Drugs; General D.1.2 21 CFR Part 211 Current Good Manufacturing Practice for Finished Pharmaceuticals D.1.3 21 CFR Part 11 Electronic Records; Electronic Signatures D.1.4 21 CFR Part 820 Quality System Regulation D.1.5 21 CFR Part 4 Regulation of Combination Products D.1.6 21 CFR Part 600 Biological Products: General D.1.7 21 CFR Part 606 Current Good Manufacturing Practice for Blood and Blood Components D.1.8 21 CFR Part 680 Additional Standards for Miscellaneous Products D.1.9 21 CFR Part 601 Licensing

GMP in Practice

Read the short summaries below to get a perfect insight into the new contents at a glance.

Chapter 20 Continual Improvement

20.E Failure Management

Root cause analysis should be integrated into the quality management system of a pharmaceutical company. It should be a formal independent process of continual improvement and should be used during the entire life cycle of the product. Root cause analysis mainly consists of reactive elements. However, if used properly, it also facilitates the identification of trends and use of timely proactive actions before failures occur (failure prevention).

When designing the process, flexible rules should be put in place so that the relationship between the complexity of a failure situation, the available product and process understanding, and the required rigour and formality of root cause analysis are taken into consideration. A number of different root cause analysis methods and tools are available that can have advantages and disadvantages for each specific failure situation. As a result, the method used should be chosen with great care. Scientific and technical expert knowledge should be used during root cause analysis when determining the direct causes, contributing causes and root causes of the failure and when specifying the resulting appropriate actions.

Based on the causes discovered, actions are taken that can be classified into different types. It may be necessary to define several actions for each cause of failure. Concrete textual and temporal objectives should be formulated for each action; this makes it easier to monitor their effectiveness. The affected process or system owners are responsible for ensuring that the actions are implemented properly, on schedule and in a professional manner. The implementation of actions should be planned and carried out in a controlled way. The quality organisation is responsible for the overall testing of effectiveness.

There are different root cause analysis methods and tools that are more or less suitable depending on their application. Some quality risk management methods can also be used for root cause analysis. It can be necessary to support the actual root cause analysis using basic tools, e.g. statistical methods. To facilitate a statistical evaluation, failure situations and causes should be classified in groups. Statistical methods are also extremely suitable for proactive root cause analysis. Graphical representations can be used to show cause-effect relationships that would not otherwise be obvious. The fundamental application of the different methods and tools is described. (Martin Mayer)

GMP Regulations

Chapter D USA: CFR and FDA Guidelines

The Code of Federal Regulations is subject to an annual revision. With the current Update of the GMP Compliance Adviser we provide the actual versions as of April 1, 2017.

The dates of the following CFRs have been updated without any further amendments:

- D.1.1: 21 CFR 210 Current Good Manufacturing Practice in Manufacturing, Processing, Packing, or Holding of Drugs
- D.1.4: 21 CFR 820 Quality System Regulation
- D.1.6: 21 CFR 600 Biological Products
- D.1.7: 21 CFR 606 Current Good Manufacturing Practice for Blood and Blood Components
- D.1.8: 21 CFR 680 Additional Standards for Miscellaneous Products

D.1.2 21 CFR 211 Current Good Manufacturing Practice for Finished Pharmaceuticals

- A new subparagraph (e) on the requirements of medical gas containers and closures was added to Sec. 211.94.
- Additional changes were made to Sec. 211.125 on labeling issuance: The last sentence in subparagraph (c) regarding labeling reconciliation was newly added.
- In Sec. 211.176 on Penicillin contamination the contact info for the National Archives (NARA) was added.

D.1.3 21 CFR 11 Electronic Records; Electronic Signatures

- Sec. 11.1 Scope was amended by two new subparagraphs (n) and (o) on non-applicability of 21 CFR 11.

D.1.5: 21 CFR 4 Regulation of Combination Products

- A new Subpart B – Postmarketing Safety Reporting for Combination Products was added to 21 CFR Part 4. It identifies postmarketing safety reporting requirements for combination product applicants and constituent part applicants.

D.1.9 21 CFR 601 Licensing Service

- A new subparagraph (f) on the applications for biologics licenses; procedures for filing was added to Sec. 601.2.

Service

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