Markus Veit

GMP Focus

Data Integrity in the EU

Requirements for Quality Management Systems

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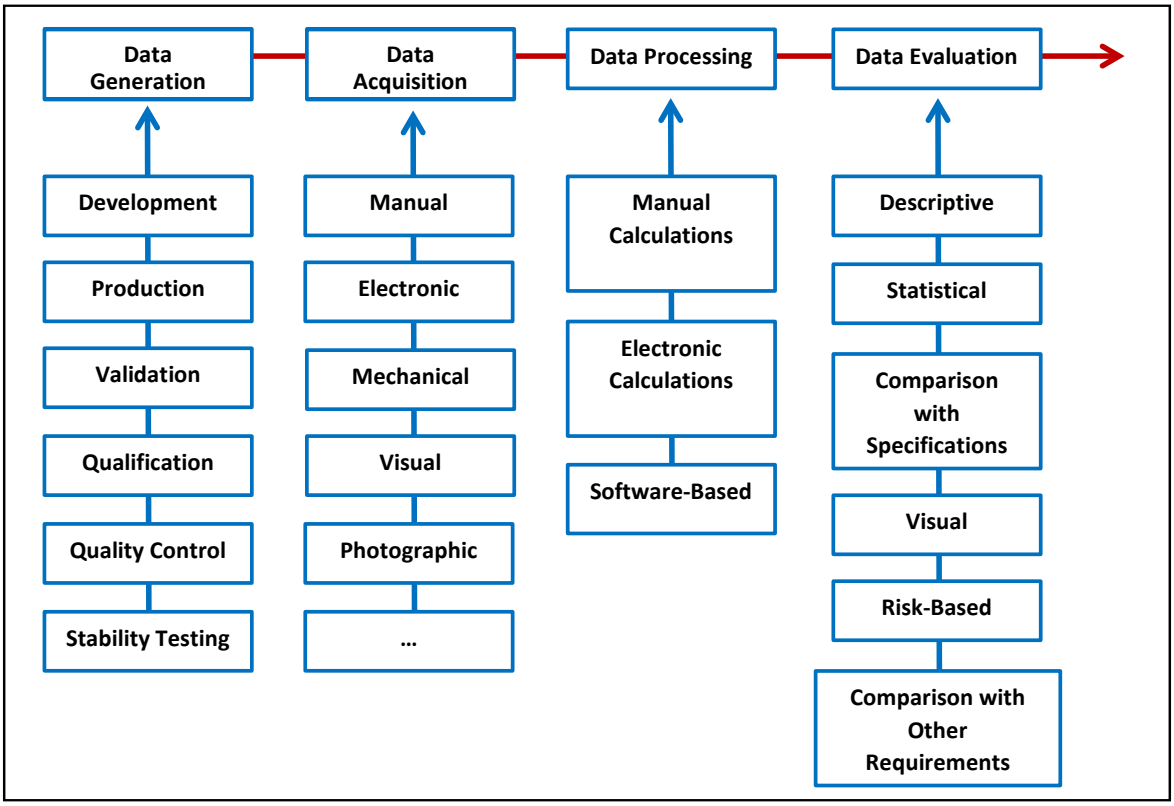
Introduction

The European Union's GMP Guidelines set a framework for protecting the integrity of data captured in the drug development and manufacturing process. Drugmakers doing business in EU countries – as well as their suppliers, contract manufacturers, contract testing companies and logistics companies – must meet these standards. But they also must be aware of other international policies and regulations governing data integrity, including the European Medicines Agency's question-and-answer document on data integrity, the UK Medicines and Healthcare Products Regulatory Agency guidance and the World Health Organization's guidance on data and records management.

In addition, they should apply a risk-based approach to data protection that complies with the principles of pharmaceutical quality risk management in ICH Q9. This includes regularly evaluating their practices and prioritizing areas that carry more risk. For instance, data used when making a decision on batch release is more critical than data not directly relevant to the release, such as warehouse cleaning records.

The lifecycle of data follows a consistent path: data generation, data acquisition, data processing, data evaluation and the subsequent use of data (or use of the related results) when making decisions, the storage of data and the deletion or destruction of data. Because data is always generated in order to make decisions or create specifications, data integrity affects many areas (see Figure 1). The first phase of the data lifecycle is subsequently used as a basis for decisionmaking.

Figure 1. First Lifecycle Phase of Data



Source: Maas & Peither AG

This report outlines the data integrity requirements of the EU GMP Guidelines and other regulatory policies, and explains how to ensure compliance with European standards. Copies of relevant documents are included in the appendix.

About the Author

Markus Veit is the Managing Director of International Drug Regulatory Affairs Services GmbH (i.DRAS) in Planegg near Munich and ALPHATOPICS GmbH in Kaufering, Bavaria. He is also a member of the Committee for Pharmaceutical Chemistry of the German Pharmacopoeia.

Doctor Veit is an expert in the field of pharmaceutical analysis. In the past 20 years, he has worked as managing director in companies providing services in the areas of drug development, manufacture, testing and approval for the pharmaceutical industry. At the same time, he developed and managed a number of different continuing and further training courses for persons working in the drug and medical devices industry.

Data Integrity in a GXP-Regulated Environment

Data integrity is a key element in the pharmaceutical quality assurance system. It is not a recent requirement, but is already anchored in the principles of the EU GMP Guidelines. However, the topic has become more important in recent years as a result of the ever-increasing flood of data, particularly electronic data.

The EU GMP Guidelines provide the most comprehensive data integrity standards for European nations in Chapter 4 – Documentation (see Appendix A) and Annex 11 – Computerised Systems (see Appendix B). But other regulatory agencies also have weighed in on the subject and, in some cases, provide differing opinions. To build a robust data integrity system, drugmakers must understand all requirements and know when to apply each.

The UK's Medicines and Healthcare Products Regulatory Agency (MHRA) published draft guidelines in 2015 (see Appendix C), defining data integrity as "the extent to which all data are complete, consistent and accurate throughout the data lifecycle." The guidelines go on to say that appropriate risk-based systems should be established "to ensure that data, irrespective of the format in which it is generated, is recorded, processed, retained and used to ensure a complete, consistent and accurate record throughout the data lifecycle." This data monitoring system "should address data ownership throughout the lifecycle." In addition, "the design, operation and monitoring of processes/systems" should be considered "in order to comply with the principles of data integrity including control over intentional and unintentional changes to information."

The World Health Organization also issued draft guidelines in 2015, finalizing them in 2016 (see Appendix D). In the same year, the European Medicines Agency (EMA) released a question-and-answer paper on the subject (see Appendix E).

General Principles

The basic principles of data integrity can be summed up in the acronym ALCOA. This widely accepted model – MHRA, EMA and WHO documents all reference it – defines the concept with five characteristics:

- **Attributable** – It must be possible to clearly attribute data to the person who generated it, to the device/equipment used to generate it, to a specific data record (e.g., a sample sequence) and to the software that was used for recording and/or processing it;
- **Legible and permanent** – Data must be permanently legible;
- **Contemporaneous** – Data must be current and/or recorded in a timely manner;
- **Original** – Data must be available in its original form or as a true copy.
- **Accurate** – Data must be accurate.

Because the five principles do not cover all aspects of data integrity, they are often enhanced and referred to as ALCOA plus. Data systems expert R.D. McDowall, in a 2011 article on ensuring data integrity in a regulated environment[1], proposes the following additions:

1 *R.D. McDowall, Ph.D (2011) Scientific Computing. Ensuring Data Integrity in a Regulated Environment*

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Any questions? Please contact us:

Phone +49 7622 66686-74 (Ms. Annette Crawford)
E-Mail annette.crawford@gmp-publishing.com