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Practical implementation of the PQS

Excerpt form the GMP Series "The Road to a Pharmaceutical Quality System"

by Stephanie Blum

In addition to the preceding general statements on the PQS, Chapter 1 of the EU GMP Guidelines contains specific information on GMP for medicinal products and quality control. At first glance, this content appears to be the same as the requirements in the rest of the chapter and the annexes of the EU GMP Guidelines and therefore redundant. It stipulates, for example, that the analytical methods and critical stages of the manufacturing process have to be validated. It also prescribes that processes for the supervision of outsourced activities must be in place.

Furthermore, it is stated that the sampling process may only be carried out by authorised personnel. It is known that the same requirements are set out in detail in Annex 15 and Chapter 7 or Chapter 6 of the EU GMP Guidelines – together with a number of other requirements that are not explicitly included in Chapter 1 of the Guidelines. Why does Chapter 1 single out particular aspects of GMP?

This question is quickly answered when the points explicitly outlined in Chapter 1 of the EU GMP Guidelines are listed in a chronological sequence that corresponds to the manufacturing process chain of the medicinal product. From this point of view, these aspects clearly illustrate how a pharmaceutical plant uses a functioning PQS to achieve a situation that the ICH Q10 Guideline describes as a state of control, see Figure 1.A-8.

Figure 1.A-8 State of control: system for controlling/monitoring process performance and product quality in accordance with ICH Q10

State of control in the PQS
ICH Q10, glossary "State of Control": A condition in which the set of controls consistently provides assurance of continued process performance and product quality.
ICH Q10, Section 1.5.2, Establish and Maintain a State of Control: To develop and use effective monitoring and control systems for process performance and product quality, thereby providing assurance of continued suitability and capability of processes. Quality risk management can be useful in identifying the monitoring and control systems.

The GMP elements mentioned in Chapter 1 of the EU GMP Guidelines accurately reflect this requirement in the ICH Q10 Guideline. Broken down to the individual steps of the manufacture of medicinal products, this implies the following (the sections in parentheses refer to the corresponding sections in Chapter 1 of the EU GMP Guidelines):

- Suitable resources (premises, equipment, facilities, personnel) are available. (1.8 iii and 1.9 i)
- Medicinal products are designed and developed in a way that takes account of the requirements of Good Manufacturing Practice. (1.4 iii)
- All manufacturing processes are clearly defined, systematically reviewed in the light of

experience and shown to be capable of consistently manufacturing medicinal products of the required quality and complying with their specifications. (1.8 i)

- Critical steps of manufacturing processes and significant changes to the process are validated. (1.8 ii)
- Arrangements are made for the manufacture and use of the correct starting and packaging materials and it is ensured that they are supplied by qualified suppliers. (1.4 vi)
- All necessary controls on intermediate products and bulkware, and any other in-process controls and validations are carried out. (1.4 x).
- Samples of these products (as well as samples of starting materials) are taken by approved personnel and methods. (1.9 ii)
- The test methods used are validated. (1.9 iii)
- The finished products manufactured in this way contain active ingredients complying with the Marketing Authorisation or clinical trial authorisation, are of the purity required, and are enclosed within their proper containers and correctly labelled. (1.9 v)
- Sufficient reference samples are retained. (1.9 viii)
- Medicinal products are not released prior to certification by a Qualified Person. (1.4 xv, 1.9 vii)
- Good Distribution Practice (GDP) has been implemented: Medicinal products are stored and distributed so that their quality is maintained throughout their shelf life and any quality risk is minimised. (1.4 xvi, 1.8 ix)
- Any complaints and significant deviations are recorded, investigated with the objective of determining the root cause and appropriate corrective and preventive actions are defined and implemented. (1.8 vii and 1.8 xi)
- A system is available for recalling products. (1.8 x)

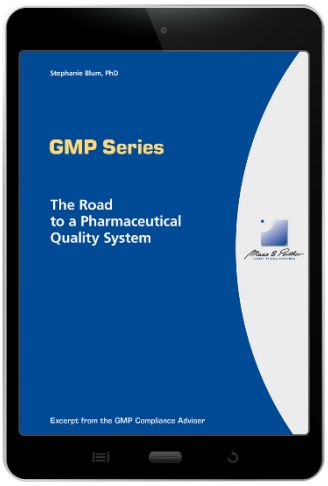
In addition, sections 1.8 iv–vi and 1.8 viii, 1.9 iv and 1.9 vi in Chapter 1 of the EU GMP Guidelines contain further general requirements. These relate to necessary records, personnel training and the correct implementation of the specified processes. Processes must also be in place for the management of outsourced activities [1.4 vii].

Without doubt, Chapter 1 of the EU GMP Guidelines contains historically evolved redundancies – within the chapter itself and in relation to other chapters and the Annex of the guidelines. This makes a reading of this chapter a little tedious at times. However, the selected aspects of GMP mentioned in Chapter 1 show in a practical way that the previously described PQS elements are not an end in themselves. Instead, the PQS, as set out in Chapter 1 of the EU GMP Guidelines, is meant to serve a single purpose only. The pharmaceutical quality system should ensure that the quality of the medicinal products meet the requirements defined in the authorisation documents, are safe and effective and as a result guarantee the safety of the patient.

Author

Stephanie Blum, PhD
Molecular Biologist, Consultant
E-Mail: stephanie.blum@cirQum.de

GMP Series – The Road to a Pharmaceutical Quality System



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