Root Cause Analysis – An Essential Enabler

An excerpt from the GMP Compliance Adviser, Chapter 20.E Failure Management

8 min. reading time

by Martin Mayer

Root cause analysis as a quality management system enabler

Pharmaceutical companies (authorisation holders & manufacturers) should have processes and systems in place as part of their quality management system that support the identification of the causes of detected and potential failures. The processes and systems should encompass the identification and implementation of corrections, corrective actions and preventive actions as well as the monitoring of the effectiveness of the defined actions.

ISO 9000 defines **nonconformity** as the non-fulfilment of a requirement, whereas conformity is the fulfilment of a requirement. A failure is therefore a non-conformity. In a pharmaceutical company, the word failure means non-compliance with quality management system requirements, GMP Guidelines, etc.

Failures can be indicated or detected as a result of complaints, recalls, internal product rejections, deviations, process capability analyses, product quality analyses, trend analyses, audits, official inspections and other **indicators**.

Effective actions can only be identified if the exact cause(s) of the failure is/are known. Root cause analysis (RCA) requires a structured and methodical approach, and the rigour and formality of the approach should be appropriate for the respective failure. Root cause analysis should be based on scientific principles and comprehensive scientific and technical knowledge of the process and product.

If the causes of a detected failure are not analysed or if the causes are not discovered despite close examination, effective actions cannot be taken and the same failure (or a similar failure) will (re)occur.

The knowledge gained through root cause analysis should deepen the understanding of the process and the actions taken should lead to significant product and process improvements. The actions taken can include corrections, corrective actions or preventive actions.

Root cause analysis is an essential part of the continuous improvement process (CIP). Continuous improvement is the central requirement and objective of every pharmaceutical quality management system.

Root cause analysis is closely related to quality risk management/QRM. The methods and tools of root cause analysis can and should be anchored to the same points of the quality management system of a pharmaceutical company and integrated into the same processes as quality risk management.

As is the case with quality risk management, root cause analysis and the determination of appropriate actions should be used during the entire product life cycle.

The implementation of the root cause analysis process and the use of (formalised) root cause analyses is no longer just common sense or a requirement in the standards affecting quality management systems (e. g. ISO 9000, ISO 9001 et seqq.). It is now explicitly required by various GMP regulations and guidelines. Root cause analysis is, for example, listed as a requirement in Section 1.4 (xiv) of the EU GMP Guidelines and in ICH Q10 (e. g. Section 3.2), which is now included in Part III of the EU GMP Guidelines. Both documents include a description of the most important elements of a pharmaceutical quality management system.

Figure 20.E-1 shows the key elements, enablers and objectives of a modern quality management system. Root cause analysis is given a central role as an essential enabler.

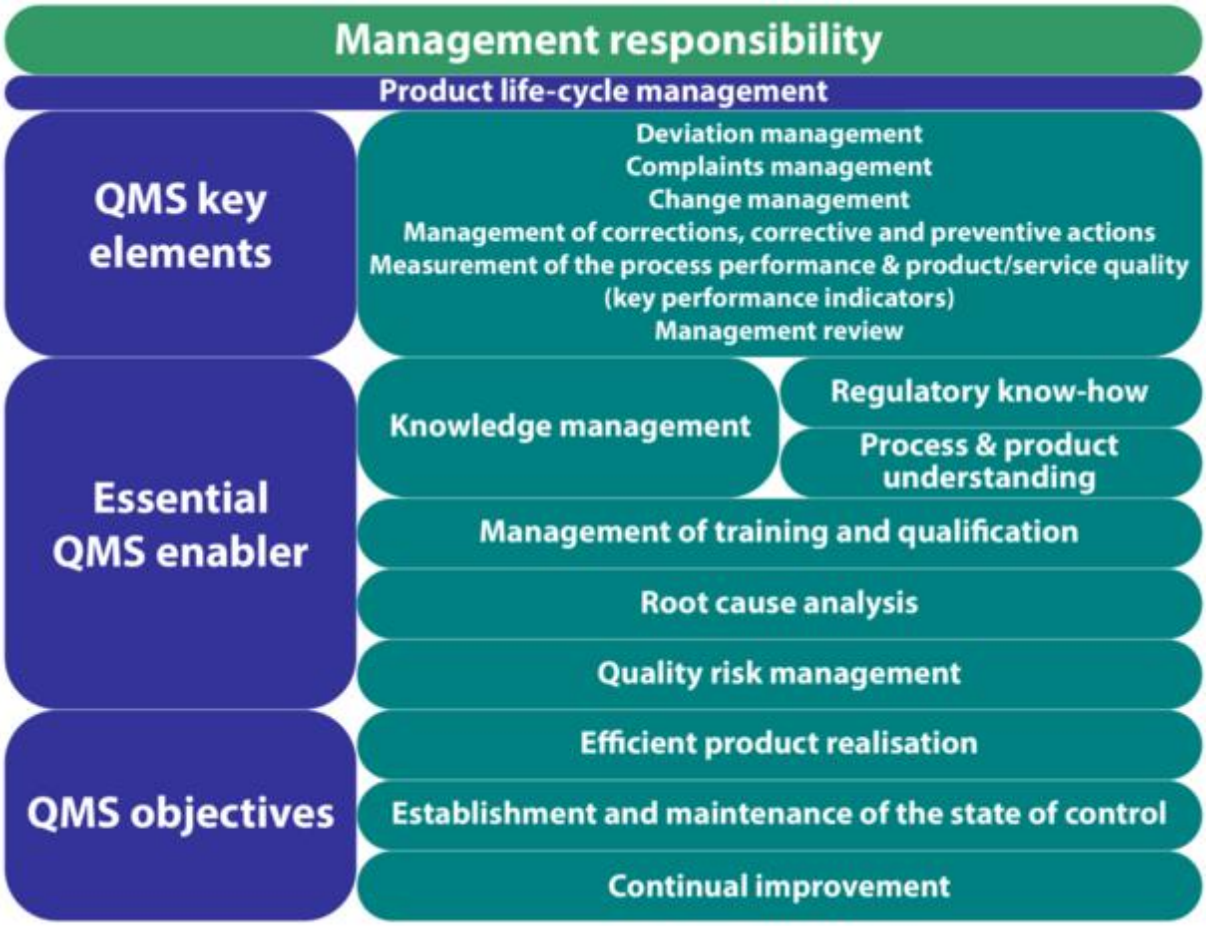

Figure 20.E-1 Root cause analysis in a pharmaceutical quality management system – an essential enabler

Root cause analysis in the product life cycle and pharmaceutical QM system

The life cycle of a medicinal product can be divided into four phases:

- pharmaceutical development
- technology transfer
- commercial production and marketing
- cessation of commercial production and marketing

As the individual phases of the product life cycle are passed through (see Figure 20.E-2), the understanding of the product and process increases and the subsequent cost of a failure is minimised. This is a result of increased knowledge acquired through practical experience.

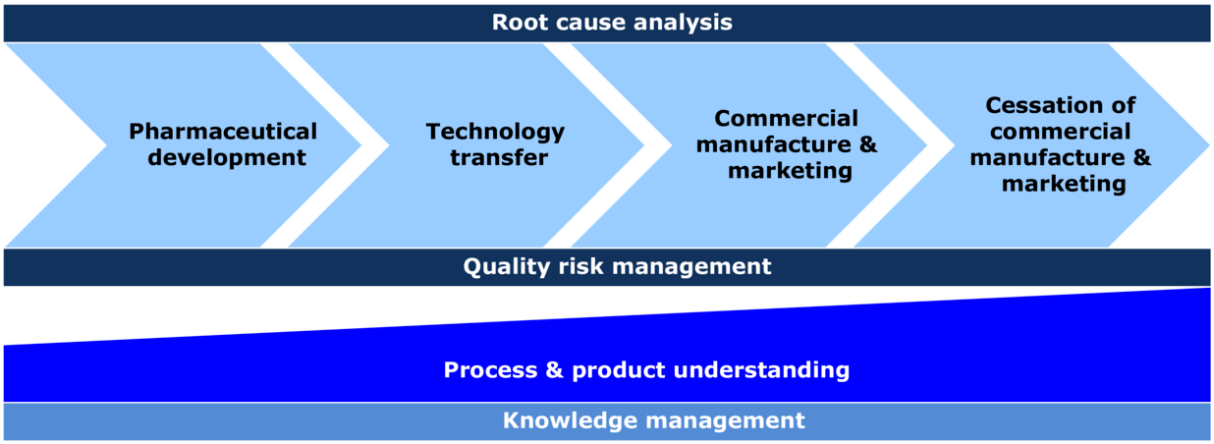

Figure 20.E-2 Root cause analysis in the product life cycle

The earlier a root cause analysis is carried out during a product life cycle, i. e. the earlier the causes are eliminated, the lower the subsequent cost of a failure (see Figure 20.E-3).

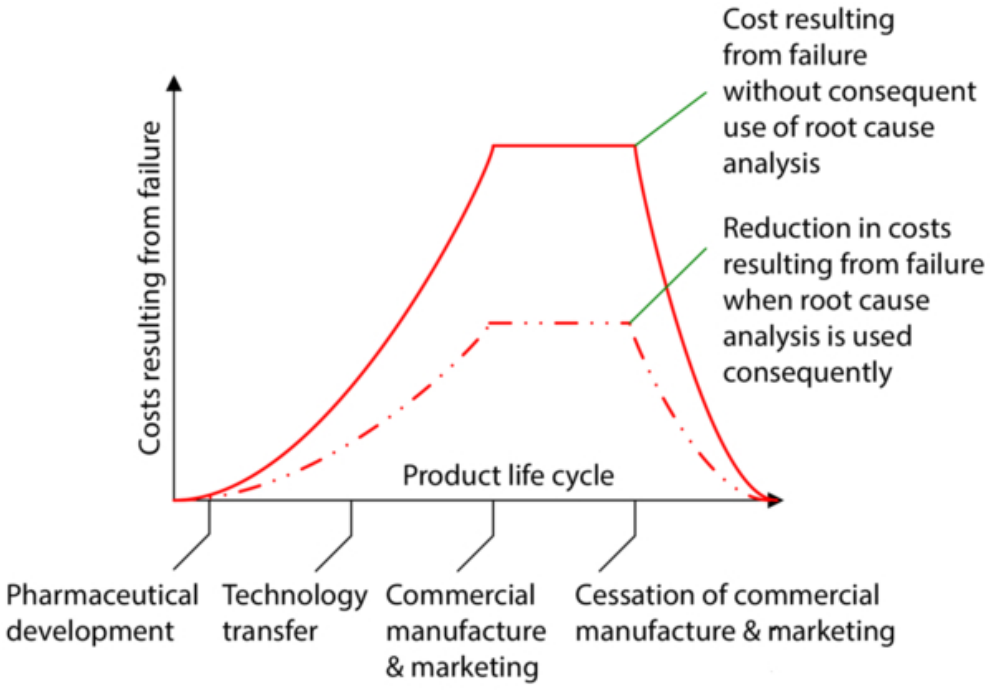

Figure 20.E-3 Reducing the subsequent cost of a failure in the product life cycle through consequent use of root cause analysis

A formalised process (root cause analysis ➜ definition and implementation of actions ➜ monitoring of effectiveness of the actions) and the use of specific formalised methods and instruments for root cause analysis in combination with quality risk management (QRM) is the basis for effective knowledge management.

Quality risk management (QRM) and root cause analysis have, in principle, identical elements and similar objectives. QRM and root cause analysis are proactive and reactive tools. Root cause analysis focuses on understanding the causes of potential and detected failures, and quality risk management deals with the detection of potential failures and their (potential) impact and with the (potential) impact of detected failures.

The methods and tools of root cause analysis should be anchored at the same points of the pharmaceutical quality management system (QMS) and integrated into the same processes as quality risk management. In general, root cause analysis should be carried out every time there is a deviation from a state of control affecting any process or system.

Some of the methods and tools used for root cause analysis are also suitable for use in quality risk management and are often incorporated into QRM processes. Although the focus of QRM and root cause analysis processes differ, it is possible to integrate the two separate yet interconnected systems into the QMS.

The risk control measures that result from the risk assessment and the corrections, corrective actions and preventive actions that result from root cause analysis (CAPA) can be monitored in the same system.

This system can also be used to implement actions from other processes, such as:

- management review
- continual improvement process (e. g. process capability analyses using key performance indicators)
- change control/change management
- trend analyses (out-of-trend)
- qualification of equipment
- validation of processes and computer systems

Elements of QRM and root cause analysis can be combined; e.g. QRM principles can be used to prioritise the processing of identified actions.

Different situations can occur during the individual life-cycle phases and sub-phases of a medicinal product in which the methods and tools of root cause analysis should be used.

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