IJSRM
INTERNATIONAL JOURNAL OF SCIENCE AND RESEARCH METHODOLOGY
An Official Publication of Human Journals

Human Journals
Review Article
July 2023 Vol.:25, Issue:1

Annual Product Quality Review (APQR) and Overall Regulatory Compliance

IJSRM
INTERNATIONAL JOURNAL OF SCIENCE AND RESEARCH METHODOLOGY
An Official Publication of Human Journals

Arun Kumar L N[1*], Sanjeev Kumar Saxena[2]

[1]*Research Scholar Sunrise University, Alwar, Rajasthan, India*

[2]*Research Guide Sunrise University, Alwar, Rajasthan, India*

Submitted: 17 June 2023
Accepted: 15 July 2023
Published: 30 July 2023

HUMAN JOURNALS
www.ijsrm.humanjournals.com

Keywords: *APQR, overall regulatory compliance, FDA investigation reports. site deficiencies*

ABSTRACT

Annual Product Quality Review (APQR) is an important part of the overall regulatory compliance process. APQR is required to be performed for each product produced for the commercial market to evaluate data, trends and to identify any preventative or corrective action that would lead to product quality improvements and report them to management. Given the regulations are clearly detailed for the Annual Product Review, the compilation and usage of the APQR would be expected to be widely well entrenched and established in the organization. But recent FDA investigation reports site deficiencies in the Annual Product Quality Review and there have been warning letter issues containing references to poor or inadequate APQR. APQR provides very effective tools to look back on product performance to determine if changes are needed. An effective APQR process would help to fine-tune the product specification, ensure that changes made to the manufacturing or control processes are effective and/or ascertain further changes, establish the need for validation or revalidations, identify improvement opportunities, provide a high-level view to understand the cumulative effects of several small changes and a possible negative effect and lastly, it provides a good tool for the management to take cognizance of concerns or areas that requires corrective or preventive actions.

INTRODUCTION

APQR is an organized and comprehensive review of all production, analytical, stability, complaints, changes, deviations, recalls and customer data associated with a pharmaceutical product so as to monitor the drug product quality and improve where necessary.

Quality systems[1-5] call for continually monitoring trends and improving systems. This can be achieved by monitoring data and information, identifying and resolving problems, and anticipating and preventing problems. Quality systems procedures involve collecting data from monitoring, measurement, complaint handling, or other activities, and tracking this data over time, as appropriate. Analysis of data can provide indications that controls are losing effectiveness. The information generated will be essential to achieving problem resolution or problem prevention.

Three FDA objectives for performing the APQR are to determine the need to make changes in the manufacturing process, the manufacturing controls (e.g., in-process testing and monitoring), and product specifications.

The typical contents of an APQR are:

Time Period Covered

It is important to specifically identify the time period covered for the APQR. Typically, the APQR will include all batches manufactured or disposition (released or rejected) during a specific period, usually one year. Some firms choose to use a strict calendar year for reviews, while others stagger the dates to prevent an excess burden during any period of the year.

Product Description

It is also important to include a detailed description of the product under review. For example, you should state the product, and packaging configurations, and reference the control numbers in use to specifically identify the formulation in use. Any identifying references to production lines or equipment should be included if needed to differentiate products.

A. APQR (Annual Product Quality Review)[6-12]

APQR is an organized and comprehensive review of all production, analytical, stability, complaints, changes, deviations, recalls and customer data associated with a pharmaceutical product so as to monitor the drug product quality and improve where necessary.

Quality systems call for continually monitoring trends and improving systems. This can be achieved by monitoring data and information, identifying and resolving problems, and anticipating and preventing problems. Quality systems procedures involve collecting data from monitoring, measurement, complaint handling, or other activities, and tracking this data over time, as appropriate. Analysis of data can provide indications that controls are losing effectiveness. The information generated will be essential to achieving problem resolution or problem prevention.

Although the cGMP regulations require product review on at least an annual basis, a quality systems approach calls for trending on a more frequent basis as determined by risk. Trending enables the detection of potential problems as early as possible to plan corrective and preventive actions. Another important concept of modern quality systems is the use of trending to examine processes as a whole; this is consistent with the annual review approach. Trending analyses can help focus on internal audits.

B. Complaint Program

Any non-conformances to physical or quality attributes with respect to predefined specifications of an API/intermediate which are observed at the customer end can be handled through an effective complaint program.

C. Internal Audit Program

In the arena of pharmaceuticals quality plays a major role as it affects the safety of the patient. If the Quality of the products is not met to the standard then probably patient health is under threat.

Pharmaceutical companies need to comply with multiple regulations imposed by various Health Authorities and organizations. These regulations enforce strict quality standards on

pharmaceutical companies to ensure the safety and benefits of the products made by the organization.

Quality systems control the mechanisms that develop and deliver products and services to customers. If the company rely on the customers to tell the effectiveness of the controls it would be unethical as they would not come to know how the process is being taken place inside the company.

In order to check the conformance to the standards, a process has been established to check the quality of work done in the company. An effective quality system will contain constant checks, tests and system for corrective action. However, all of these need the support of independent checks of the organization from within the organization. These independent checks are called Quality audits.

Audits are an essential management tool to be used for verifying objective evidence of processes, assessing how successfully processes have been implemented, for judging the effectiveness of achieving any defined target levels, to provide evidence concerning reduction and elimination of problem areas. For the benefit of the organization, quality auditing should not only report non-conformances and corrective actions, but also highlight areas of good practice. In this way other departments may share information and amend their working practices as a result, also contributing to continual improvement**.**

A quality systems approach calls for audits to be conducted at planned intervals to evaluate the effective implementation and maintenance of the quality system and to determine if processes and products meet established parameters and specifications. As with other procedures, audit procedures should be developed and documented to ensure that the planned audit schedule takes into account the relative risks of the various quality system activities, the results of previous audits and corrective actions, and the need to audit the complete system. Procedures should describe how auditors are trained in objective evidence gathering, their responsibilities, and auditing procedures. Procedures should also define auditing activities such as the scope and methodology of the audit, selection of auditors, and audit conduct (audit plans, opening meetings, interviews, closing meetings and reports). It is critical to maintain records of audit findings and assign responsibility for follow-up to prevent problems from recurring.

The quality systems model calls for managers who are responsible for the areas audited to take timely action to resolve audit findings and ensure that follow-up actions are completed, verified, and recorded.

D. Documentation Management System

The pharmaceutical industry has a complicated structure and depends heavily on research and documentation. Throughout the life cycle of the drug, it is under constant surveillance by regulatory bodies that require various documents to be submitted. Reviewing each of these documents and ensuring accuracy is difficult. Ascertaining that right documents are filed for approval from amongst multiple versions floating in the organization further add to the complications.

Pharmaceutical companies are highly information sensitive with respect to how documents and records are managed, making efficient document reviews critical not only from a regulatory standpoint but necessary for organizational efficiency as well. Stringent regulations have made compliance managers take a serious look at their document review practices.

QMS[13-17] provides a comprehensive solution that makes the process of reviewing critical documents simple and efficient. The solution leverages the role of authors, editors, reviewer, compliers, etc. by ensuring that documents and records submitted to the regulatory authorities, like the FDA, are complete and accurate. The solution also ensures a reduction in cost and facilitates information reuse by implementing best practices for document management and reviews.

Summary of Review

A summary statement early in the APQR will serve to provide an overview of any key observations made. For example, you might use this section to state that a large number of deviations were observed that might indicate a shift in the process. This section might also be used to note any unexpected results.

Recommendations and/or Corrective Actions

It is usually prudent to mention early in the APQR a listing of recommendations or corrective actions resulting from the review. This will aid the reader to focus on these

key aspects of the review. In addition, some readers (i.e., management) may only read the first page or two of the APQR, so it is important to highlight issues and concerns early.

Finished Product Results

Finished product results must be presented. Though the GMP regulation allows the use of "a representative number of batches," most firms choose to review all batches produced. Presentation of data can be in any form desired. However, all key analytical and physical parameters must be included in the summaries presented.

In-Process Results

In-process results could be even more important than finished product results. A close review of these data may provide clues regarding the integrity and consistency of the process. The APQR should include both in-process analytical/physical results and critical processing parameters. For example, it may be more important to track the average time of drying to achieve the required moisture levels than the actual final moisture. Time may be more indicative of the process control than final moisture.

Deviations/Investigations/Rework

The APQR must include all product or process deviations, investigations conducted for deviations or nonconforming situations, and any rework conducted. Some firms summarize all corrective actions derived from these events and include a status of the actions. The key to this section is to highlight concerns that did arise and provide evidence that actions are underway to correct the problems.

Stability Results

A key indicator of the control and consistency of any process is the stability data collected to support a product. A good APQR should list any stability trends,

deviations, or shifts apparent since the last review. These data can also be a good indicator of hidden process or product concerns.

Complaint Results

A summary of all product complaints is a required component of the APQR. Any trends or problematic batches should receive an additional review.

Returned Goods

A summary of all products returned for quality concerns should also be included in the APQR. This can provide valuable information not normally evident to the quality unit regarding product concerns or problems.

Recalls

If any product recalls occurred, they should be listed in the APQR. The reasons for the recalls and corrective actions taken should be summarized.

CONCLUSIONS

Any conclusions regarding the product should be listed in this section. Some examples of typical conclusions include: no revalidation required, no product or process concerns noted, etc. Any recommendations for changes should be included in the "recommendations" section, along with responsibilities, and a timeline for corrective actions.

.

Approvals

Finally, the APQR must include appropriate approvals. Usually, representatives from Production, Quality Control (QC), and Quality Assurance (QA) will approve the APQR. However, it may be desirable for others (such as Validation, or Regulatory) to have the authority to approve the APQR, depending upon its content or recommendations. The organization of the company may also dictate the approval process. In any event, a member of the quality unit must review and approve the APQR.

REFERENCES:

1. Gupta, A., 2000, "Quality management practices of ISO vs. non-ISO companies: a case of Indian industry" Industrial Management + Data Systems. Wembley: Vol. 100, Iss. 9; pg. 451.
2. Kitazawa, S., and Sarkis, J. "The Relationship Between ISO 14001 and Continuous Source Reduction Programs," International Journal of Operations and Production Management, 20, no. 2, 2000, 225–248.
3. Reid, R. Dan and Nada R. Sanders, Operations Management, New York: John Wiley & Sons, Inc., 2002.
4. Hammer, M. and J. Champy, Reengineering the Corporation: Manifesto for Business Revolution, New York: Harper Business Publications, 1993.
5. Aguayo, R. (1991). Dr. Deming: The American Who Taught the Japanese About Quality. (1st ed.). New York: Fireside.
6. Barra, R. (1988). Mobilizing for Quality, The Journal for Quality and Participation (11), pp. 28-33.
7. Brown, M.G. (2006). Baldrige Award Winning Quality: How to Interpret the Baldrige Criteria for Performance Excellence, 15th edition. New York, NY: Productivity Press.
8. Dale, B.G. (1994). Managing Quality, London: Prentice Hall.
9. Frederick, W T. (1911). The Principle of Scientific Management, New York: Haper
10. Besterfield, D., C. Besterfield-Michna, G.H. Besterfield., and M. Besterfield-Sacre. Total Quality Management. 2nd ed. Upper Saddle River, NY: Prentice-Hall, 1999. Read more: http://www.referenceforbusiness.com/management/Pr-Sa/Quality-and-Total-Quality-Management.html#ixzz2IsLXRq4S
11. "Hand book of total quality management" R.P. MOHANTY.
12. EN ISO 9000: 2000 "Quality Management Systems – Fundamentals and vocabulary", published December 2000
13. Kotter, J. (1996). Leading Change. Massachusetts: Harvard Business School Press
14. 9001 Quality (2010a). CAPA: Corrective action - the ISO 9001 Standard requirements. CAPA- Corrective preventive action. Retrieved from http://www.9001quality.com/capa- conective-preventive-actionl53-corrective-action/80-capa-corrective-action-the-iso-9001- standard -requirements. Htm I
15. 9001 Quality (2010b). CAPA: Preventive action - the ISO 9001 Standard requirements. CAPA-Corrective preventive action. Retrieved fromhttp://www.9001quality.com/capa•cOlTective-preventive-actionl55-preventive-action/84-capa-preventive-action-the-iso- 9001-standard-requirements.html
16. Cummings, T. & Worley, C. (2001). Essentials of Organisation Development & Change (7th Ed). South-Western College Publishing
17. ICH Q7a: "Good Manufacturing Practice (GMP) Guide for Active Pharmaceutical Ingredients (APIs)", published November 2000