QUALITY CONTROL AND QUALITY ASSURANCE IN PHARMACEUTICAL INDUSTRY

Yadav Ravi, Piyush yadav ,Priyanshu Maurya,
Tushar Yadav, Rohit kumar.

Department of Pharmacy, Prasad Institute of Technology Jaunpur 222001, UP., INDIA

ABSTRACT:-

This brief review presents the international approaches to assessment of the content of geotaxis impurities (residual solvents and various inorganic and organic impurities) in pharmaceuticals. Nowadays, it has become necessary to provide not only purity profile but also impurity profile of a particular pharmaceutical product because of national and international regulations. These aspects along with significance of the quality, efficacy and safety of pharmaceuticals, including the source of impurities, kinds of impurities, control of impurities and regulatory aspects are discussed.The supply of essential medicines of good quality has been identified as one of the prerequisites for the delivery of health care system of any country as poor quality medicines can harm or even kill consumers. The presence of unwanted chemicals in a particular medicine, even in extremely small quantities, may influence its efficacy and safety. Unlike in other industries, a medicine is a dynamic product whose color, consistency, weight, and even chemical identity can change between manufacture and ultimate consumption. Hence, quality of pharmaceuticals has been a concern of the people of the whole world, and is now receiving critical attention from regulatory authorities .Impurities in pharmaceutical products are of great concern not only due to the inherent toxicity of certain contaminants, but also due to the adverse effect that contaminants may have on drug stability and shelf-life. In pharmaceutical and drug products, impurities are the unwanted chemicals (organic, inorganic and residual solvents) that remain with the active pharmaceutical ingredients (APIs), or develop/added during formulation, or upon aging. Organic impurities are the most common impurities found in every

API which get incorporated normally during the multi-step synthesis process despite proper care .

INTRODUCTION:-

An important goal of IPCC good practice guidance is to support the development of national greenhouse gas inventories that can be readily assessed in terms of quality and completeness. It is good practice to implement quality assurance and quality control (QA/QC) procedures in the development of national greenhouse gas

inventories to accomplish this goal.[1]This guidance establishes good practice consistent with the Revised 1996 IPCC Guidelines for National Greenhouse Gas Inventories (IPCC Guidelines). The QA/QC good practice guidance outlined here reflects practicality, acceptability, cost-effectiveness, existing experience, and the potential for application on a worldwide basis. A QA/QC programme contributes to the objectives of good practice guidance, namely to improve transparency, consistency, comparability, completeness, and confidence in national inventories of emissions estimates.The outcomes of the QA/QC process may result in a reassessment of inventory or source category uncertainty estimates. For example, if data quality is found to be lower than previously thought and this situation cannot be rectified in the timeframe of the current inventory, the uncertainty estimates ought to be re-evaluated.The terms 'quality control' and 'quality assurance' are often use are described as[2]:-

DEFINITION OF QA/QC

Quality Control (QC) is a system of routine technical activities, to measure and control the quality
of the inventory as it is being developed. The QC system is designed to:
(i) Provide routine and consistent checks to ensure data integrity, correctness, and completeness;
(ii) Identify and address errors and omissions;
(iii) Document and archive inventory material and record all QC activities.
QC activities include general methods such as accuracy checks on data acquisition and
calculations and the use of approved standardised procedures for emission calculations,measurements, estimating uncertainties, archiving information and reporting. Higher tier QCactivities include technical reviews of source categories, activity and emission factor data, and methods.

Quality Assurance (QA) activities include a planned system of review procedures conducted by personnel not directly involved in the inventory compilation/development process. Reviews,preferably by independent third parties, should be performed upon a finalised inventory following the implementation of QC procedures. Reviews verify that data quality objectives were met,ensure that the inventory represents the best possible estimates of emissions and sinks given the current state of scientific knowledge and data

available, and support the effectiveness of the QCprogramme.[3]

KEY WORDS:-

Introduction,Practical consideration in developing QA/QC system,Element of QA & QC ,Inventory Agency, QA/QCPlans, QA procedure, Q.Assurance,Review process Methodology..

PRACTICAL CONSIDERATIONS IN DEVELOPING QA/QC SYSTEMS:-

Implementing QA/QC procedures requires resources, expertise and time. In developing any QA/QC system, it is expected that judgements will need to be made on the following:
Resources allocated to QC for different source categories and the compilation process;

- Time allocated to conduct the checks and reviews of emissions estimates;
- Availability and access to information on activity data and emission factors, including data quality;
- Procedures to ensure confidentiality of inventory and source category information, when required;
- Requirements for archiving information;
- Frequency of QA/QC checks on different parts of the inventory;
- The level of QC appropriate for each source category;
- Whether increased effort on QC will result in improved emissions estimates and reduced uncertainties;
- Whether sufficient expertise is available to conduct the checks and reviews.[4]

ELEMENTS OF A QA/QC SYSTEM:-

The following are the major elements to be considered in the development of a QA/QC system to be implemented in tracking inventory compilation:

• An inventory agency responsible for coordinating QA/QC activities;

• A QA/QC plan;

• General QC procedures ;

• Source category-specific QC procedures .

• QA review procedures;

• Reporting, documentation, and archiving procedures.

INVENTORY AGENCY:-

The inventory agency is responsible for coordinating QA/QC activities for the national inventory. The inventory agency may designate responsibilities for implementing and documenting these QA/QC procedures to other agencies or organisations. The inventory agency should ensure that other organisations involved in the preparation of the inventory are following applicable QA/QC procedures.

The inventory agency is also responsible for ensuring that the QA/QC plan is developed and implemented. It is good practice for the inventory agency to designate a QA/QC coordinator, who would be responsible for ensuring that the objectives of the QA/QC programme are implemented.

QA/QC PLAN :-

A QA/QC plan is a fundamental element of a QA/QC system, and it is good practice to develop one. The plan should, in general, outline QA/QC activities that will be implemented, and include a scheduled time frame that

follows inventory preparation from its initial development through to final reporting in any year. It should contain an outline of the processes and schedule to review all source categories. The QA/QC plan is an internal document to organise, plan, and implement QA/QC activities. Once developed, it can be referenced and used in subsequent inventory preparation, or modified as appropriate (i.e. when changes in processes occur or on advice of independent reviewers). This plan should be available for external review.In developing and implementing the QA/QC plan, it may be useful to refer to the standards and guidelines published by the International Organization for Standardization (ISO), including the ISO 9000 series . Although ISO 9000 standards are not specifically designed for emissions inventories, they have been

applied by some countries to help organise QA/QC activities[5]

ISO AS A DATA QUALITY MANAGEMENT SYSTEM

The International Organization for Standardization (ISO) series programme provides standards for data documentation and audits as part of a quality management system.[6] Though the ISO series is not designed explicitly for emissions data development, many of the principles may be applied to ensure the production of a quality inventory. Inventory agencies may find these documents useful source material for developing QA/QC plans for greenhouse gas inventories. Some countries (e.g.the United Kingdom and the Netherlands) have already applied some elements of the IS standards for their inventory development process and data management.[7]

The following standards and guidelines published under the ISO series may supplement source

ISO 9004-1: General quality guidelines to implement a quality system.

ISO 9004-4: Guidelines for implementing continuous quality improvement within the organisation, using tools and techniques based on data collection and analysis.[10]

ISO 10005: Guidance on how to prepare quality plans for the control of specific project

ISO 10011-1: Guidelines for auditing a quality system.

ISO 10011-2: Guidance on the qualification criteria for quality systems auditors.

ISO 10011-3: Guidelines for managing quality system audit programmes.

ISO 10012: Guidelines on calibration systems and statistical controls to ensure Measurements are made with the intended accuracy.

ISO 10013: Guidelines for developing quality manuals to meet specific needs.[5]

QA PROCEDURES:-

Good practice for QA procedures requires an objective review to assess the quality of the inventory, and also to identify areas where improvements could be made. The inventory may be reviewed as a whole or in parts. QA procedures are utilised in addition to the Tier 1 and Tier 2 QC. The objective in QA implementation is to involve reviewers that can conduct an unbiased review of the inventory. It is good practice to use QA reviewers that have not been involved in preparing the inventory. Preferably these reviewers would be independent experts from other agencies or a national or international expert or group not closely connected with national inventory compilation. Where third party reviewers outside the inventory agency are not available, staff from another part of the inventory agency not involved in the portion of the inventory being reviewed can also fulfil QA roles.

It is good practice for inventory agencies to conduct a basic expert peer review (Tier 1 QA) prior to inventory submission in order to identify potential problems and make corrections where possible. It is also good practice to apply this review to all source categories in the

inventory. However, this will not always be practical due to timing and resource constraints. Key source categories should be given priority as well as source categories where significant changes in methods or data have been made. Inventory agencies may also choose to perform more extensive peer reviews or audits or both as additional (Tier 2) QA procedures within the available resources.[11]

QUALITY ASSURANCE REVIEW PROCESS:-

The QAR process ensures that a comprehensive review is carried out in accordance with international standards. Generally, it involves the standard four phases i.e. planning, conducting, reporting, and follow-up.

1 Planning Phase.

- Planning
    - Understand the OAGN or Audit environment
    - Define QAR
    - objective & scope
    - Identify key areas for QAR
    - Select appropriate audits for QAR Decide
    - methodology
    - Define roles and responsibilities
    - Estimate resources including time
    - Prepare QAR plan

2.Conducting Phase :-

In the second phase, the review team conducts the review using the QAR plan to guide the gathering of evidence.

- **Conducting of QAR**
    - Conduct entry meeting
    - Gather information
    - Record and analyse information
    - Discuss QAR findings with audit team

.3 Reporting Phase :-

The third phase is where the review team uses the outputs (preliminary findings and recommendations) of the conducting phase as inputs to prepare a draft QAR report.

- **Reporting of QAR**
  - Prepare draft QAR Report
  - Conduct exit meeting with
  - Finalise QAR Report

.4 Follow-up

The final phase is where the review team uses the action plan prepared by the audit line functions as inputs, and assesses the extent of implementation of the QAR recommendations and reasons for non-implementation, if any.

- **Follow up QAR**
  - Management
  - implements actionAssess
  - implementation of action plan
  - Prepare follow-up QAR Report[13]

METHODOLOGIES AND TECHNIQUES FOR CONDUCTING QA.REPORT:-

Methodologies and Techniques for Conducting QA Review Following methodologies and techniques can be used for conducting Quality Assurance
Review:

1. Interview is seeking appropriate information from the audit team. In the context, quality assurance team could ask audit team for information, listen to and consider their responses, ask follow-up questions and corroborate information, as appropriate. Interview technique can be also used to collect the information from the audited entity

2. Observation is looking at a process or procedure being performed by others. It provides evidence for that point in time and by them, which cannot be used to draw conclusions about matters that have occurred over a period of time.

3. Documentation review is reading records or documents either visually or electronically. Examples of records/documentation are correspondences, memorandum, minutes, reports, etc.

4. Re-performance is walking through or repeating operational steps. For example, to check the accuracy of efficiency measures, the auditor may replicate procedures used to measure efficiency. Replication can help the auditor confirm or deny the system or some part of it works as claimed.

5. Confirmation is a response, ordinarily in writing, to an enquiry, also ordinarily in writing, to corroborate information. It can be used to verify that an activity was carried out in the field.

6. Analysis visually or electronically identifies what is the same and what is different between two or more documents, tangible items or data. Analytical evidence should be derived by experts/people who are knowledgeable about the matters analysed and have the ability to make logical inferences and value judgements from the data collected. Different statistical tools can be used to analyze data or information.

7. Focus group discussions are a selection of individuals brought together to discuss specific issues on audit topics. They are primarily used to collect qualitative data and information. Focus groups techniques are used to obtain information on the implementation and impact of government programs based on the prospective of the beneficiaries and other stakeholders.

8. Seminars and hearings can be organized to obtain knowledge of specialist area, discuss problems, observations and find out possible solutions. The participants of seminars may be interested parties, stakeholders and experts.[14]

QUALITY ASSURANCE IN REGULATORY AFFAIRS OF PHARMACEUTICAL INDUSTRY:-

A regulatory affair as it is mentioned on the heading the first thing that strikes us on the word regulatory is regulation and laws. In this section we are about to discuss on how does quality assurance is related to the regulatory affairs department and how they work hand in hand for the betterment of the particular pharmaceutical industry to give a better profit to the industry. Regulatory affairs particularly deal with the regulatory aspect of a medication and pharmaceutical industry thus in the regulation aspect also QA documentation in order to obtain clearance on any related regulatory issues.] The overview on the job scope in the regulatory affairs is working close with the authorities to ensure product is registered according to the regulation guideline. Dossiers is a very important aspect in a regulatory affairs department , this dossiers are generally used to register the manufactured products in other countries.[14] This dossier should contain details about every aspect of the drugs; the major aspect in a drug dossier is the Quality assurance details and the Certificate of Analysis (COA). The dossier prepared is sent to the specific countries authorities for registration of the drug in that particular country. It will nearly take 2 years for a drug to be registered in a different country in a export basis. Every detail

of analysis and assay that is done in the QA department is given in the form as report to be attached in the drug dossier before it is sent for registration.[15]

Two Types of Dossiers

- Common Technical Dossier (CTD)

- Asean Common Technical Dossier (ACTD)

The CTD is used for registration of drugs in countries that are not included as Asean, this is the general format that is used. In CTD QA documentation plays a very important role, due to the fact that every authorities are more concern on the drug quality, thus when the drug has a good quality then it has high chances of getting the drug to be registered in the particular country.[16] These directly bring a big amount of revenue to the industry. ACTD is a common format of drug dossier which is used to register the drug in Asean countries, looking at this format of dossier also the QA documentation ia an important aspect that is required, if the drug has a very good quality then it has high chances of the drug to be registered

in Asean countries.[16] In addition to this, by having drugs registered in various countries makes the company to gain a good benefit and also gain good profit. This clearly shows that how Quality Assurance contribute to the drugs that are about to be registered in other countries and how it contribute to the revenue of the particular pharmaceutical industry.[17] If the drug is registered in a particular country and if any amendments to be done on the drug, then the authorities of the country should be informed about the changes and we have to obtain the approval from the country. This has clearly explained the correlation between the regulatory affairs and the quality assurance. [17]

CONCLUSION:-

As a conclusion on the entire discussion it clearly shows that quality assurance is somehow related to all the departments in a pharmaceutical industry, and it plays an important role in each department to enhance the process of that particular department. As how the title mentions that the quality assurance plays vital role and it is said as the backbone of a pharmaceutical industry. Quality Assurance they emphasize on customers satisfaction and also based on the guidelines which have been set up by the authorities. As the thalidomide incident which took place long ago it shows a clearly failure in the quality assurance and the clinical trial phase which lead to such a big disasters which caused teratogenicity (Phocomelia). The drug was first invented for morning sickness problem in the pregnant women's. Due to lack of proper analysis and quality check it has cause a black history, thus this also clearly proves that the quality assurance has a very important role in production of medication. Quality assurance is not only implemented or emphasize in pharmaceutical industry whereas it is emphasize on every production industry which is related to every feel. As it was said that QA works based on customers satisfaction, customer is the main source which gives profit and revenue to any industry. If the product does not have qualities then it will a big failure to the industry.[18] QA has its role in every part of a industry which is inter-related, QA can form many branches of

department "under their Umbrella" to increase the efficacy and the standard of the quality by ever means and methods.

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