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Analytical Method Validation: ICH and USP Perspectives

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ABSTRACT

The development of analytical methods facilitates comprehension of the crucial process factors and reduces their impact on precision and accuracy. A confirmed systematic technique guarantees accurate, consistent, and dependable data. The metrics shown here are in accordance with ICH criteria and include linearity, range, robustness, accuracy, precision, specificity, and limit of detection, as well as the limit of quantitation. The selective method will produce repeatable, dependable, and consistent results sufficient for the intended purpose, thanks to method validation. As a result, it's essential to specify exactly what the technique is to be employed for as well as under what circumstances. Therefore, one of the most important steps a laboratory should take to develop trustworthy analytical methods is method validation.

Keywords: ICH recommendations, validation, accuracy, specificity, and precision.

INTRODUCTION

Analytical method validation is the process of proving that analytical methods are appropriate for the purposes for which they are designed. The process of proving through written evidence that the designated method will reliably yield correct test results that assess a product against its specified specification and quality features is known as analytical method validation. The approach should be robust, dependable, accurate, exact, transportable, and valid a table for daily tasks in the Quality Control setting. The method should not be put through the validation process until it is finished. Validation experiments must be conducted using qualified and calibrated equipment and apparatus, and they must be adequately recorded.

Development of Analytical Methodologies

A crucial step in creating a complex dose formulation with multiple chemically and therapeutically compatible medications of similar nature is developing an accurate assay method for each constituent. The analysis becomes even more complex when excipients, additives, and breakdown products are present. Because of this, analytical development is carried out for a small number of pharmaceuticals for which compendial methodologies are unavailable. Methods are developed for both new and old pharmaceutical goods. When official methods are unavailable.

Method development is done for

- New drug products
- Already existing products

methods are developed to save time and money while improving precision and durability. It begins with the developed studies' documentation. The laboratory note book contains all of the data pertaining to these investigations.

LITERATURE SEARCH AND RESEARCH METHODOLOGY

The search for literature and research methodology Conduct a literature review to gather all kinds of data about the analyte. Literature is produced on solubility, synthesis, physico-chemical characteristics, and pertinent analytical techniques. Chemical Abstract Service (CAS) automated computerized literature searches are reviewed in addition to books, periodicals, chemical manufacturers, and regulatory agency compendia like USP/NF and AOAC publications.

Analytical Standard Characteristics

a) All of the information that is currently available about the medication or analyte and its structure is gathered, including its toxicity, purity, solubility, stability, hygroscopic nature, and physical and chemical characteristics.
b) They get the standard analyte. The arrangements required for appropriate

STEPS OF METHOD DEVELOPMENT:

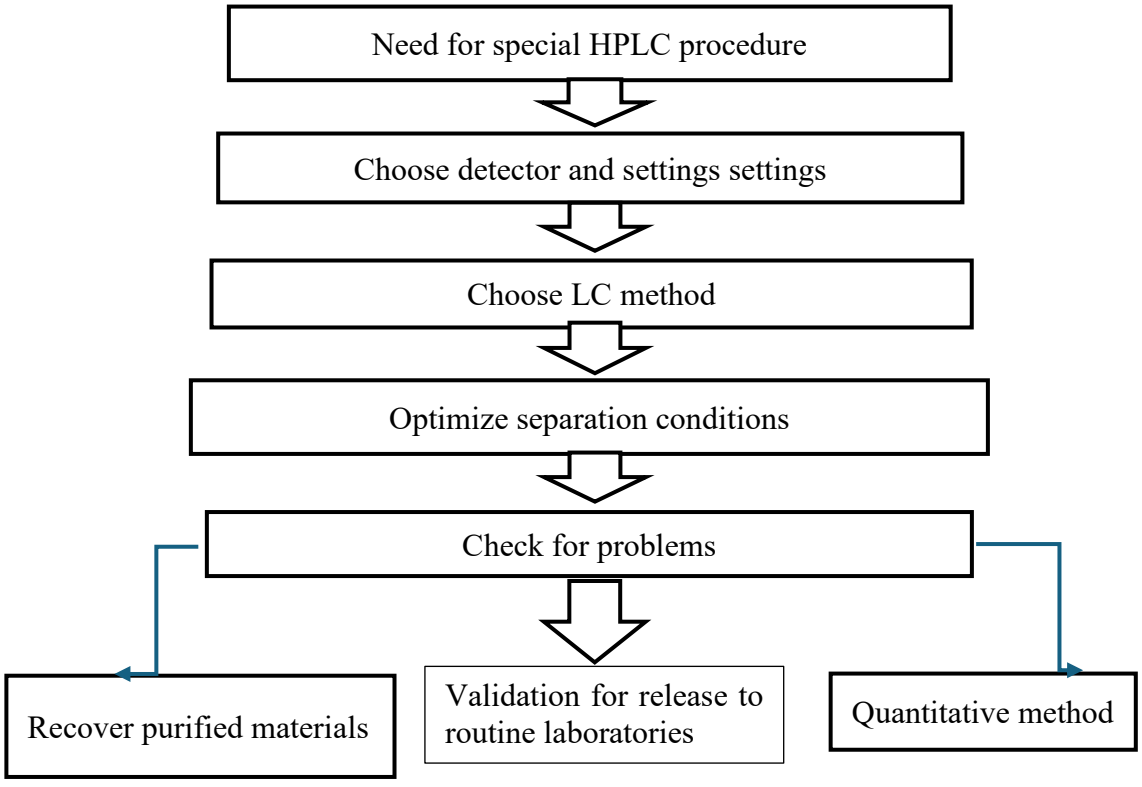

Fig No.1: Steps of method development

METHODS REQUIREMENT

The method's goal is specified. The necessary linearity, range, accuracy, precision, and detection limitations are specified.

SELECTING A TECHNIQUE

a) It is decided whether any described techniques from the literature can be modified to fit the present laboratory environment and upcoming requirements.

b) The methodology is modified based on data from publications and the literature. The procedures are adjusted as needed, and more current procedures are obtained for samples and house analytes.
c) Analogous compounds with similar chemical properties are studied and determined if there are no previous methods for the analytes in the literature.

INSTRUMENTAL SET UP AND INITIAL STUDIES

a) The necessary tool is ready. Utilizing laboratory standard operating procedures, the installation, operation, and performance of the equipment are examined.
b) New gases, solvents, and filters are always used.
c) The analyte standard is prepared in an appropriate injection/introduction solution with known concentrations and solvents. An authentic, well-known standard should be used as a starting point instead of a complicated sample matrix. Work with the actual sample can begin if it is quite similar to the standard (for instance, a bulk medication).
d) The method's feasibility is assessed in relation to the analytical figures of merit that were acquired.

OPTIMIZATION

Instead of utilizing a trial-and-error approach, optimization involves changing one parameter at a time and is carried out from a systematic methodological plan, with documentation of each step in the event of a dead end.

DOCUMENTATION OF METHOD DEVELOPMENT WITH ACTUAL SAMPLE

The sample solution should result in the absolute identification of the peak of interest apart from all other matrix components.

EVALUATION OF METHOD DEVELOPMENT WITH ACTUAL SAMPLE

The sample solution should result in the absolute identification of the peak of interest apart from all other matrix components.

DETERMINATION OF THE PERCENT RECOVERY OF ACTUAL SAMPLE AND DEMONSTRATION OF QUANTITATIVE SAMPLE ANALYSIS

Reproducibility of recovery from sample to sample and whether recovery has been optimized have been demonstrated. The percentage recovery of spiked, authentic standard analyte into a sample matrix that is shown to contain no analyte is determined.

Validation

Validation is a crucial step in effective quality assurance. “Validation is establishing documented evidence which provides a high degree of assurance that a specific process or equipment will consistently produce a product or result meeting its predetermined specifications and quality attributes.

Validation is the process of confirming that an analytical method or procedure is appropriate for its intended use, ensuring accurate and dependable results.

In order to ensure data quality, reproducibility, and regulatory compliance, this review paper highlights the significance and methodology of validation. We can ensure good laboratory practice, make informed decisions, and trust the results by validating analytical methods.

A pharmaceutical drug product needs to fulfill all of its requirements for the duration of its shelf life. It is necessary to validate the analysis method. To guarantee the product's safety and effectiveness during every stage of its shelf life, this is necessary.

1. **Pharmaceuticals:** Validation guarantees that finished pharmaceuticals adhere to current Good Manufacturing Practices (GMPs), ensuring the safety and quality of drug products.
2. **Medical Devices:** Validation is also vital for medical device manufacturing, conforming to GMP rules and verifying the safety and effectiveness of medical device.

Manufacturers can guarantee the following by putting validation procedures into place:
High quality products: Validation ensures that products full fill the necessary requirements.
Regulatory compliance: Validation proves adherence to pertinent rules and guidelines.
Patient safety: Validation eventually helps to ensure patient safety by guaranteeing the quality and dependability of items.

Objective of validation's
Validation's main goal is to provide a foundation for written production and process control procedures that are intended to ensure that drug products have the identity, strength, quality, and purity that they claim or are represented to have.
The product must also be built with quality, safety, and efficacy in mind. Controlling every stage of the manufacturing process increases the likelihood that the final goods will satisfy all quality and design requirements.
Analytical validation's primary goal is to guarantee that a chosen analytical method will produce repeatable, trustworthy findings that are sufficient for the intended use.
The goal is to show that the approach is appropriate for the intended purpose while guaranteeing the accuracy, consistency, and dependability of the analytical results.
Scope: Verifies assay, limit, identification, and quantitative impurity test procedures.
Regulatory Conditions: Method validation is required by the majority of regulatory and quality standards, including those issued by the FDA, USP, and ICH.

Validation Types
1. Prospective validation: carried out prior to the implementation of a new procedure or system.
2. Retrospective validation: applied to processes or systems that are already in place.
3. Real-time concurrent validation: carried out throughout the manufacturing process.

Importance of validation
1. Assures quality: Validation aids in making sure that goods and services fulfill the necessary requirements.
2. Lowers risk: Validation finds and eliminates possible dangers or mistakes.
3. Compliance: To guarantee adherence to industry standards, regulatory agencies frequently demand validation.

Advantages of Validation
a) Generates high-quality goods
b) Aids in process enhancement, technology transfer, validation of connected products, failure analysis, and raising staff awareness.
c) Lowering costs through improved efficiency, fewer rejections, longer equipment life, and the creation of reasonably priced goods.
d) Aids in process or method optimization.
e) Regulatory affairs-produces approved products and enhanced capacity to export.

Various agencies' definitions of validation
1. **The United States Food and Drug Administration** states that "validation is the process of establishing documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality attributes."
2. **According to WHO:** validation is the process of confirming that a system, activity, process, equipment, substance, or procedure produces the desired outcomes.
3. **EUROPEAN COMMITTEE:** Describes validation as the process of confirming that a system, material, process, or procedure genuinely produces the desired outcomes in line with GMP standards.

Validation of the Method
This procedure entails determining the method's limitations and performance qualities.

The equipment used to determine the method performance parameters is

1. Within the parameters
2. Functioning properly
3. Properly adjusted

Method Validation is required when

1. When a new method is developed, method validation is necessary.
2. Modification of the conventional approach
3. When different laboratories and analysts employ the same established methodologies, etc.
4. Methods comparison
5. When a procedure change is indicated by quality control.

There are various reasons why validation is necessary.

1. **Assures Accuracy:** Validation guarantees the accuracy and dependability of data or findings.
2. **Prevents Errors:** By looking for discrepancies or inaccurate data, validation helps to prevent errors.
3. **Enhances Quality:** Validation guarantees that goods, services, or procedures adhere to the necessary guidelines and requirements.
4. **Compliance:** To guarantee adherence to industry standards and regulations, regulatory authorities frequently demand validation.
5. **Fosters faith:** By proving the correctness and dependability of the outcomes, goods, or services, validation fosters faith in them.

Validation parameters as per ICH/USP

- USP

1. Linearity and range
2. Accuracy
3. Precision
4. Limit of detection
5. Limit of quantitation
6. Ruggedness

Robustness

- **ICH**

1. Specificity
2. Linearity
3. Range
4. Accuracy
5. Precision
6. Limit of detection
7. Limit of quantitation
8. Robustness

Performance characteristics examined when carrying out method validation are

1. Accuracy / Precision
2. Repeatability / Reproducibility
3. Linearity / Range
4. Limit of detection (LOD) / Limit of quantification (LOQ)
5. Selectivity / Specificity
6. Robustness / Ruggedness

1. Precision Meaning: "The accuracy of an analytical procedure is the closeness of agreement between the values that are accepted either as conventional true values or an accepted reference value and the value found.

Assay for Determination

1. Substance used for drugs
2. A medication Impurities (measurement)
3. Accuracy Meaning: "The closeness of agreement (degree of scatter) between a series of measurements obtained from multiple samplings of the same homogeneous sample" .

- Repeatability
- Intermediate Precision.

Reliability and repeatability

Repeatability is the ability to convey precision over a brief period of time under the same operational conditions.

In order to evaluate repeatability, at least nine judgments within the designated range should be used.

4. The detection limit

It is the smallest concentration of analyte in a sample that is detectable but not always quantifiable.

5. Quantitative limit

It is the smallest quantity of analyte in a sample that can be accurately and precisely

quantified. Calculating LOD and LOQ

Determination of LOD and LOQ

- ✓ Limit of detection
- ✓ Method
- ✓ Based on visual examination.
- ✓ Based on standard deviation of response and slope.
- ✓ Signal to noise ratio 2:1 or 3:1

➢ **Limit of quantitation**

- Method
- ✓ Based on visual examination.
- ✓ Based on standard deviation of response and slope.
- ✓ Signal to noise ratio10:1

6. Specificity

Definition: Specificity is the ability to assess unequivocally the analyte in presence of components which may be expected to be present.

Determination

- Identification tests
- Assay and impurity test(s)

Impurities are available

Impurities are not available

7. Linearity

Definition: The Ability of the method to obtain test results that are directly proportional to concentration within a given range.

Method: dilution of stock solution/separate weightings

Minimum 5 concentrations are used

8. Range

Definition: The interval between the upper and lower concentrations of analyte in the sample that have been demonstrate to have a suitable level of precision, accuracy, and linearity.

Established by confirming that the method provides acceptable degree of linearity, accuracy, and precision.

Specific range dependent upon intended application of the procedure.

9. Ruggedness

Definition: The ruggedness of an analytical method is the degree of reproducibility of test results obtained by the analysis of the same samples under a variety of conditions, such as different laboratories, different analysts, different instruments, different days, etc.

Certain may include

1. Source
2. Concentration and stability of solution
3. Heating rate
4. Column temperature

Humidity

10. Robustness

Definition: "The robustness of an analytical procedure is a measure of its capacity to remain unaffected by small, but deliberate variations in method parameters and provides an indication of its reliability during normal usages.

Determination The evaluation of robustness should be considered during the development phase and depends on the type of procedure under study

Variations may include:

- ‣ stability of analytical solution
- ‣ variation of pH in a mobile phase
- ‣ different column (lot/supplier)

Guidelines for USP and ICH

Q2(R1)

A standardized framework for verifying analytical processes is provided by ICH Q2(R1), which outlines crucial parameters and acceptance criteria.

USP:

Provides detailed instructions for particular dosage forms in other chapters as well as in USP <1225> (on validation) and <1226> (on verification).

Comparison:

Although the ideas and parameters of the USP and ICH recommendations are similar, there could be minor variations in wording or emphasis. For instance, ICH utilizes

"intermediate precision" but USP uses "ruggedness".

Implementation:
To promote harmonization, ICH Q2(R1) acts as a basis for further guidelines such as USP, JP, and EU guidelines. The reliability and applicability of analytical methods employed in a variety of industries, especially the pharmaceutical sector, are essentially ensured by analytical method validation, which is directed by ICH and USP principles. Important distinctions and parallels:

Key Differences and Similarities:
Scope and Harmonization:
ICH Q2(R1) is a globally recognized guideline that aims to harmonize analytical method validation principles across different regions.
USP while aligned with ICH Q2(R1), is specific to the United States Pharmacopeia and provides more detailed guidance for validation parameters and procedures.

Validation Parameters:
Both ICH Q2(R1) and USP include essential validation parameters such as accuracy, precision, specificity, linearity, range, and limit of detection/quantitation.

Specificity:
ICH Q2(R1) defines specificity as the ability to unequivocally assess the analyte in the presence of potential impurities, degradation products, and excipients. USP includes similar requirements for specificity and also addresses the need to evaluate potential interference from placebo components.

Ruggedness:
While ICH Q2(R1) focuses on intermediate precision, which includes variations in different days, analysts, and equipment, USP explicitly mentions ruggedness as a parameter to be evaluated. Ruggedness refers to the reproducibility of the method when used under normal, but slightly different, conditions.

CONCLUSION

Both ICH and USP guidelines are essential for ensuring the quality and reliability of analytical methods. While ICH provides a broad, harmonized approach, USP offers practical guidance specifically for pharmacopeial methods and emphasizes system suitability testing. Understanding the nuances of both frameworks is crucial for pharmaceutical scientists and analysts to effectively validate their analytical procedures and meet regulatory requirements.

Declaration by Authors

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REFERENCE

1. Snyder LR, Kirkland JJ, Dolan JW. Introduction to modern liquid chromatography. John Wiley & Sons; 2011 Sep 20.
2. Validation of Analytical Procedures, International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, Q2 R1November, Step version 4.
3. Shinde M, Kumar S, Mallik A, Jyothi N. A Review on Hplc Method Development and Validation.2021 Chief Editor.
4. Kalshetti S, Rao KP. Development and validation of HPLC method for the quantification of clotrimazole in a gelatin film formulation. Future Journal of Pharmaceutical Sciences. 2021Dec;7(1):1-9.
5. Severina HI, Gubar SM, Bezruk IV, Materiienko AS, Ivanauskas L, Bunyatyan VA Kovalenko SM, Scupa OO, Georgiyants VA. Development and validation of hplc determination of related substances in a novel anticonvulsant agent epimidin. Research Journal of Pharmacy and Technology. 2021Jun 1;14(6):3223-31.
6. Raju MD. Development and Validation of HPLC Method for the Determination of Lasmiditan Drug in Bulk and Tablet Dosage Form. Journal of Pharmaceutical Sciences and Research. 2021 Mar 1;13(3):170-3.

7. Paul K, BH JG, Shankar SJ, Reddy DN. Development and validation of simplified RPHPLC method for quantification of Darunavir in commercial tablets. Materials Today: Proceedings. 2021 May 14.
8. Gupta V, Jain AD, Gill NS, Guptan K. Development and validation of HPLC method-a review. International research journal of pharmaceutical and applied sciences. 2012Aug 31;2(4):17-25.
9. Shabir GA. A practical approach to validation of HPLC methods under current good manufacturing practices. Journal of validation technology. 2004 May; 10:210-8.
10. Papadoyannis IN, Samanidou VF. Validation of HPLC instrumentation. Journal of liquid chromatography & related technologies.2004 Jan 1;27(5):753-83.
11. Lindholm J. Development and validation ofHPLC methods for analytical and preparative purposes (Doctoral dissertation, Acta Universitatis Upsaliensis)
12. Prabh Simran Singh, Gagan Shah, Analytical Method Development and Validation, Journal of Pharmacy Research,4(7), 2011, 2330-2332.
13. Ravisankar P, Gowthami S, and Devala Rao G, A review onanalytical method development, Indian journal of research in pharmacy and biotechnology, 2, 2014, 1183-1195
14. Ravisankar P, Naga Navya Ch, Pravallika D, Navya Sri D,A review on step-by-step analytical method validation, IOSR J Pharm, 5(10), 2015, 7-19.
15. Ramamurthy M, Sarvana kumar K, pharmaceutical validation, The Eastern Pharmacist, 476, 1997, 45-47.
16. Agalloco J. Validation: an unconventional review andre invention, PDA J. Pharm Sci Tech, 49, 1995, 175–179.
17. Aleem H, Zhao Y, Lord S, McCarthy T and Sharratt P, Pharmaceutical process validation: an overview, J Proc Mech Eng, 217, 2003, 141-151.
18. Tangri Pranshu, Rawat Prakash Singh, Jakhmola Vikash: Validation: A Critical Parameter for Quality Control of Pharmaceuticals, Journal of Drug Delivery & Therapeutics,2(3), 2012, 34-40.
19. Sharma Ajay, Sharma Rohit, Validation of analytical procedures: a comparison of ICH vs Pharmacopoiea (USP) and FDA, International research journal of pharmacy, 3(6),2012, 39-42.
20. Validation of analytical procedure: Methodology Q2B, ICH Harmonized Tripartite Guidelines, 1996:1-8.
21. International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use ICH Harmonized tripartite guideline Validation of analytical procedures: Text and Methodology Q2 (R1) 6November 1996.
22. Ravisankar P, Anusha S, Supriya K, Ajith Kumar U, Fundamental chromatographic parameters, Int. J. Pharm. Sci. Rev. Res., 55(2), 2019,46-50.
23. Ravi Sankar P, Swathi Vaka, Srinivasa Babu Putta gunta, Shaheem Sulthana Md, Gouse peer SK, Current trends in performance of forced degradation studies and stability indicating studies of drugs, IOSR Journal of Pharmacy and Biological Sciences, 12 (6), 2017, 17-36.
24. Ravisankar P, Sai Snehalatha, Tabasssum Firdose Shaik, Srinivasa Babu P, Applications of HPLC in pharmaceutical analysis, Int. J. Pharm. Sci. Rev.Res, 59(1), 2019,117-124.
25. Ravisankar P, Madhuri B, Naga Lakshmi A, Pooja A, Bhargava Sai M, Suresh K, Srinivasa Babu P, Selected HPLC applications-Quick separation Guide: A Review, Int. J. Pharm. Sci. Rev. Res, 60(2), 2020, 13-20.
26. Ravi Sankar P, Sai Geethika A, Rachana G, Srinivasa Babu P, Bioanalytical method validation: A comprehensive review, Int. J. Pharm. Sci. Rev. Res, 56(1), 2019, 50-58.
27. Gaurav Tiwari, Ruchi Tiwari, Bioanalytical method validation: An updated review, Pharm Methods, 1(1), 2010,25-38.
28. Analytical Method Validation Pedro Lopez Garcia1, Ernesto Buffoni1, Fabio Pereira Gomes1 and Jose Luis Vilchez Quero2 1Instituto de Aperfeiçoamento Farmacêutico (IAF) 2Department of Analytical Chemistry, Faculty of Sciences

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