IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

An Overview of the Design and Validation of Analytical Methods

Authors- Yogesh D Survase*, Mukesh S Patil, Ashish S Jain

M pharmacy [quality assuarance] , professor , principle

QUALITY ASSUARANCE

Shri D D Vispute College of Pharmacy and Research Center, New Panvel, 410206, INDIA

*Address for correspondence:

Mr Yogesh D Survase*

M Pharm Student

Department of Quality Assurance

Shri D D Vispute College of Pharmacy and Research Center, New Panvel, 410206

Analytical technique development, validation, and transfer are essential components of every pharmaceutical development programme. The establishment of efficient methods shows how laboratory resources can be optimized while ensuring that the objectives of each stage of drug development are met. High performance liquid chromatography is the most precise approach for both qualitative and quantitative drug analysis. The creation and validation of analytical methods are crucial for drug discovery, medication development, and pharmaceutical manufacture. It involves assessing the purity and toxicity of a pharmacological substance. A variety of chromatographic factors have been evaluated for the examination of method development in HPLC in order to optimize the techniques. A suitable mobile phase, column, column temperature, wavelength, and gradient must be developed.

This review article's primary goal was to examine the creation and validation of the process used for the drug from the beginning of formulation to the final commercial batch of product. When an analytical technique is used to obtain results for the quality of samples related to medicine, it is essential that the results be trustworthy. The requirements of good manufacturing practise (GMP) laws are adhered to in the pharmaceutical industry's validation policy, which is documented for how to do validation. Validation is crucial to the efficient operation of pharmaceutical companies.

Keywords: Validation, Method development, Limit of quantitation, Limit of detection, Linearity, Robustness, Ruggedness

Pharmaceutical analysis is particularly important for the quality assurance and control of bulk medications and pharmaceutical formulations[1]. The demand for novel analytical techniques in the pharmaceutical business has increased as a result of the global expansion of the pharmaceutical and drug sectors. Because of this, developing analytical processes has been the main focus of analysis. The development of analytical devices has led to recent advancements in analytical methods. Analysis expenses have been reduced, precision and accuracy have increased, and analysis time has been reduced because to the advancement of analytical techniques and tools. Therefore, most pharmaceutical companies are spending a considerable amount of money to set up specialized analysis laboratories. Excipients, medicinal products, degradation products, and related analytical procedures are examples of active pharmaceutical ingredients (API)[2].

The basic objective of any pharmaceutical industry is to constantly manufacture goods that are reasonable in price, have the right qualities, and are of high quality. A method needs to be established for the study, creation, and evaluation of medicines in pharmaceutical formulations. The main objective of this review paper was to investigate how the drug formulation process evolved and was validated from the beginning to the final commercial batch of the product. It is crucial that the results of an analytical technique used to assess the quality of samples relevant to medicine be reliable. In the pharmaceutical industry, validation policy is outlined for the sorts of validation that can be performed as well as the requirements for compliance. Any product or service needs analysis, and drugs are no different because they involve human life. Analytical chemistry is the study of the separation, measurement, and identification of chemical additives in synthetic and herbal materials made up of one or more chemicals or elements. The two main categories of analytical chemistry are qualitative evaluation and quantitative evaluation. Qualitative evaluation refers to the identification of the chemical additives present in the sample. Quantitative evaluation determines the amount of positive detail or compound present in the substance, i.e. the sample. Each year, there are more medications introduced to the market. These medications might also be brand-new things or slight structural changes made to the ones we already have. Medicines are supposed to be available in a way that guarantees their quality, bioavailability, adequate plasma concentration, desired timeframe, commencement of action, proper dose, safety, effectiveness, and stability during product storage. The development and validation of analytical approaches play crucial roles in the research, development, and production of pharmaceuticals. Obtaining

accurate, realistic, and consistent data is the major goal of an analytical measure. Validated analytical techniques are crucial to reaching this objective. Results from methodology validation can be used to determine the quality, consistency, and dependability of analytical findings, which are essential components of any same analytical procedure. Most laws and quality standards that affect laboratories require validation of analytical techniques[3].

ANALYTICAL METHOD DEVELOPMENT:

In the absence of established approaches, new methodologies are being developed for the evaluation of novel products. Innovative procedures are created to decrease the value besides time for higher precision and strength in order to explore the presence of either pharmacopoeial or non-pharmacopoeial product. Through test runs, these approaches have been improved and proven to be reliable. Alternative methods are developed and put into use to replace the current approach in the context of comparing laboratory data with all available benefits and drawbacks. Figure 1 depicts the life cycle of an analytical method.

NEED FOR THE DEVELOPMENT AND VALIDATION OF ANALYTICAL TECHNIQUES:

The identity, characterization, and resolution of the pharmaceuticals are displayed in drug evaluation when they are combined with organic fluids and dosage forms. The primary goal of analytical strategies at some point in the production process and drug development is to produce data about efficacy (which may be directly related to the need for a specific dose), impurity (related to medication safety), bioavailability (which includes important drug characteristics like crystal type, uniformity of drug release, and drug release), stability (that shows the degradation product), and effect of manufacturing parameters to confirm that [4].

Before the creation of new technologies, analysts should remember the following criteria:

- Does this method have the necessary sensitivity?
- Is this approach sufficiently selective to allow for direct application without hindrance from the sample's opposing element?
- Is it possible to use this procedure with accuracy and precision?
- Can the equipment and reagents needed for this procedure be found or purchased for a fair price?
- Is the amount of time needed to use this strategy appropriate?

- The available methods can be excessively expensive, time- or energy-consuming, or they might not be completely computerized.
- The current approach may have too many faults, be susceptible to infection, or be unreliable.
- An additional method may be required to corroborate analytical records that were initially obtained using current methods for criminal or scientific purposes.
- The particular pattern matrix won't have a procedure that works for a certain analyte.
- The current strategy might not provide enough sensitivity.
- It's necessary due to regulatory requirements
- Primary drug selection criteria for developing new analytical techniques:
- The medication or medication combination might not be recognized by any pharmacopoeias.
- Because of patent laws, a suitable analytical method for the drug could not be available in the literature.
- Due to the interference caused by the formula excipients, analytical procedures may not be available for the medication in the form of a formula.
- There won't be an analytical method for quantifying the medication in biological fluids.
- There won't be any analytical methods for a drug combined with other medications.

The current analytical methods might also call for exorbitantly expensive solvents and reagents. Additionally, it could involve laborious extraction and separation techniques that are unreliable [5,6].

CURRENT BEST PRACTICE FOR VALIDATION OF ANALYTICAL METHOD:

Validation should no longer follow a technique's evolution in a linear fashion. Therefore, the full process of developing and validating analytical methods can be considered, as it is depicted in the overall scheme. The performance characteristics of the method should entirely reflect the technique's intended use. Those include the analyte, its expected attention, the sample matrix, viable investigative materials, regulatory requirements, application (qualitative/quantitative), need for robustness, detection and quantization limits, accuracy and precision expectations, various types of system and the locations where the technique can be used, the analyst's capacity requirements, and so on.. before a device is utilized to verify a method, its performance must be verified. However, after technique development, it must be demonstrated that it meets the criteria, providing some level of assurance for its intended application [8].

DEVELOPMENTS OF NEW ANALYTICAL METHODS CRITERIA:

Drug analysis serves as the foundation for identifying the product. Between a medicine's release to the market and its inclusion in pharmacopoeias, there is frequently a lag in time. This is because there may be ambiguities in the sustained and extended use of these therapies, reports of novel toxicities, the emergence of patient resistance, and the introduction of improved pharmaceuticals by rival companies, as well as the launch of these treatments (Conners, 1994). In some cases, pharmacopoeias may not have the standard and analytical procedures for these drugs. New analytical techniques must therefore be created for these drugs. In a summary, the drivers for the creation of novel drug analysis techniques [9].

{ Figure 2 Criteria for the Development of New Analytical Method}

It's possible that no pharmacopoeias have approved the new medication or medication combination [10]. Due to patent laws, a proper analytical method for the drug may not be documented in the literature. The drug may not have analytical methods available in the form of formulation excipients. There could not be analytical techniques for a medicine when it is combined with other pharmaceuticals. It's possible that there are no analytical techniques for measuring the drug's concentration in bodily fluids. The current analytical processes could need pricey solvents and reagents [11]. Additionally, it could need laborious extraction and separation techniques, which might not be trustworthy. The steps in developing a method are: Beginning at the very beginning of the development process is documentation. There must be a method for comprehensive development study documentation [12]

HIGH PERFORMANCE LIQUID CHROMATOGRAPHY (HPLC):

High-pressure liquid chromatography is sometimes known as HPLC (high performance liquid chromatography). Any component present in a sample that can dissolve in liquid can be separated, identified, and quantified using HPLC. Adsorption is the major driving force behind liquid chromatography. Mobile phase is a liquid in this chromatographic method. This sample is a liquid solution. Sample is inserted into a stationary phase of porous material and a liquid phase column (mobile phase). A pump's high pressure delivery of the mobile phase causes the sample to move across the column. Sample elements move in accordance with how affine they are to the stationary phase. The component that is more attracted to the stationary phase moves more slowly. The component that moves more quickly has a lower attraction for the stationary phase. N-hexane, methylene chloride, chloroform, methyl-t-butyl ether, isopropanol (IPA), acetonitrile (MeCN or CAN), methanol (MeOH), and water are the most often used

solvents for HPLC (McPolin O, 2009). Efficiency (number of theoretical plates), retention factor, selectivity, resolution, and pressure are essential chromatographic factors. Chemical separation, purification, and identification are three uses for HPLC. Pharmaceutical, environmental, forensic, clinical food and flavour, and other applications of HPLC are among its many uses.

{Fig: 3 HPLC System}

Components of hplc as follows;

- Solvent reservoir, mixing system and degassing system
- High pressure pump
- Sample injector
- Column E. Detector
- Data recording system

Reservoir for the solvent, mixing apparatus, and degassing apparatus:

The solvent is kept in a reservoir (mobile phase). These containers are made of glass or stainless steel. Glass bottles are the most typical kind of solvent reservoir. In addition to dispensing mobile phase, the pump must mix solvents precisely and accurately. Low pressure mixing and high pressure mixing are two different types of mixing units. A degassing system eliminates air bubbles that have become trapped in the solution. Ultrasonication and filtering are used as degasser methods.

High pressure pump:

A liquid is forced by a pump to flow at a predetermined rate. Milliliters per minute (ml/min) are the unit used to measure flow rate. A flow rate of 1-2 ml/min is typical. The range of the pump is 6000–9000 psi (400-600 bar) Constant pressure pumps, syringe pumps, and reciprocating piston pumps are the three most popular types of pumps.

Sample injector:

Using a sample injector, the liquid sample is added to the mobile phase. Between the pump and the column is a sample valve. The sample can be injected into the continuously flowing mobile phase stream that transports the sample to the HPLC column by an injector (auto sampler). Sample quantities typically range from 5 to 20 microliters. There are two different types of injectors: manual and automatic.

Column:

The real separation of components happens in the column. Stainless steel makes up the column. Its interior diameter is 2.46 cm, and its length is 5–25 cm.

Detector :

The detector may turn the data into an electrical signal by identifying each component that elutes from the column. Specific detectors and bulk property detectors are the two types of detectors that are employed. The UV-VIS detector, photo diode array detector, fluorescence detector, and mass spectrometric detector are examples of particular detectors. Refractive index detectors, electrochemical detectors, and light scattering detectors are examples of bulk property detectors

Data recording system:

The output is recorded as a series of peaks and the area under the peak can be calculated automatically by the computer linked to the display.

Steps for Method Developments:

Various steps are involved in the development of an analytical method are as follows:

Characterization of analyte and standard

- All of the relevant information is gathered regarding the analyte and its structure, including information on its solubility, optical isomerism, and other physical and chemical characteristics.
- The standard analyte is obtained with a purity of 100%. To make the necessary arrangements for the right storage (refrigerator, desiccators, and freezer).
- In the sample matrix, when numerous components are to be assessed, the number of elements is observed, the information is presented accurately, and the standard accessibility is determined.
- However, once coordinated with the stability of samples, techniques include spectroscopy (UV-Visible, FTIR, atomic absorption spectroscopy, etc.), high-performance liquid chromatography, and gas chromatography, etc. [13]

Requirement of the technique:

Analytical requirements like linearity, selectivity, specificity, range, accuracy, precision, LOD, LOQ, etc. must be outlined in order to build up the analytical advantage [13]

Literature survey and prior methods:

With reference to pertinent books, journals, the United States Pharmacopeia/National Formulary (USP/NF), the Association of Official Agricultural Chemists (AOAC), and the American Society for Testing and Materials (ASTM) publications, all the literature related to the drug is reviewed for its physical and chemical properties, manufacturing, solubility, and applicable analytical methods. It is also very convenient to look at Chemical Abstracts Service automatic computerized literature [13].

Selecting the method:

By modifying the methodology as necessary, using the data gathered from the literature, the methodology is constantly changing. For analytes and tests, it may be necessary to develop, modify, replicate, and validate existing procedures using additional instrumentation. If the analyte to be investigated cannot be investigated using previous appropriate methods [13]

Proper instrumentation and initial studies:

An acceptable set of instruments examines the installation qualification (IQ), operation qualification (OQ), and performance qualification (PQ) of instruments relevant to research standard methodology[13].

Optimization:

Prior to using the trial-and-error method, a group of circumstances are differentiated and one parameter is changed at a time while undertaking optimization. This task must be completed based on an organized scientific method plan that covers all relevant elements and is well recorded in respect to dead ends[13].

Documentation of analytical results:

The true determined analytical values of benefit consisting of LOD, LOQ, cost, linearity and evaluation time and planning of samples, etc. are also recorded[13].

Evaluation of produced technique with actual specimen:

The specimen solution needs to prompt specific, complete recognition of the peak interest of the medication other than all different matrix parts [13] .

Calculation of the percentage of authentic samples that are recovered and an illustration of quantitative sample analysis:

The percentage of spiked, actual standard medicine recovered in a sample grid without any analytes is assessed. It must have been optimized for reproducibility of recovery from test to test. It is not always necessary to achieve 100% restoration as long as the results can be replicated and interpreted with confidence [13]

VALIDATION

The concept of validation emerged in the United States around 1978. The concept of validation has grown over time to encompass a wide range of activities, including analytical methods used for drug quality control and computerized systems for clinical trials. Validation is based on, but not endorsed by regulatory specifications, and is best viewed as an essential component of current good manufacturing practice (cGMP).

The term "validation" primarily refers to the process of evaluating a claim's plausibility or proving its feasibility. Validation is a team endeavor that involves workers from several plant departments. Any new or modified technique must be validated to ensure that it can produce trustworthy findings when used by many operators using the same or similar equipment in the same or other facilities [15]. The efficient evaluation of systems, facilities, and procedures with the goal of determining whether they carry out their intended capacity sufficiently and reliably as defined is known as validation, and it is a crucial part of quality assurance.

Validation should in this way be considered in the accompanying circumstances:

- Completely new procedure.
- Latest equipment.
- Procedure and equipment which have been adjusted to suit altered needs and,
- Procedure where the finished result test is a poor and undependable marker of product quality.
- Important stages in validation [14].

The action identifying with validation studies can be categorized mainly into three stages:

Stage 1: Pre-validation qualification stage is included in this, and it includes all activities related to product studies and improvement, formulation pilot batch testing, scale-up research, innovation exchange with business scale groups, setting up stability conditions, managing in-process, finished pharmaceutical formulations, qualifying equipment, master documents, and process limit.

Stage 2: This stage comprises process validation. In order to ensure that good products can be produced even in the worst cases, it is planned to verify that every installed restriction of the crucial process parameter is substantial.

Stage 3: is also known as the "validation maintenance stage" and calls for ongoing examination of all procedure-related records, including validation of review reports, to ensure that the production procedure has not been altered and that all standard operating procedures (SOPs), including change control procedures, have been followed. The approval team, which includes representatives from alcrucial departments, ensures that there have been no modifications or deviations that should have led to requalification and revalidation at this stage [14].

TYPES OF VALIDATION:

{Fig: 4 Validation types}

Validation of analytical methods:

Laboratory research is used to validate analytical approaches by demonstrating that the procedure's execution characteristics are appropriate for the suggested scientific application. Any new or modified technique must be validated to ensure that it will produce predictable and reliable results when used by different administrators with identical equipment in similar or completely different laboratories [21]

Method validation is a reported programme that provides a high level of assurance that the processing system will satisfy its projected acceptance foundation [16]

It generally comprises of five steps, which are as follows:

System qualification:

System qualification allows for the verification that the instrument is suitable for the intended investigation, the materials are suitable for use in analytical judgments, the analysts have the necessary skills and training, and the necessary prior documentation, such as analytical approaches and authorized protocols, has been reviewed. It will be challenging to pinpoint the problem's origin if the general requirements of a gadget are disregarded and problems occurs [22]

Sampling:

It helps in the selection of a representative portion of the fabric, which is then evaluated. The choice of an appropriate sampling technique is crucial because it ensures that the sample used to draw essential statistical

conclusions is actually representative of the data as a whole. There is a sizable body of work on sampling procedures in the statistical literature, but the relative costs and time involved with each technique should be evaluated beforehand [22]

Preparation of sample:

Sampling aids in choosing an appropriate sample of the cloth, which is subsequently examined. In order to ensure that the sample utilized to generate important statistical conclusions is truly representative of the data as a whole, it is essential to use an appropriate sampling technique. There is a substantial amount of research on sampling techniques in the statistical literature, but it is important to first assess the relative costs and time commitment of each technique [22]

Analysis of sample:

The device used to extract qualitative or quantitative data from samples with a sufficient level of vulnerability is evaluated. Given that the gadget contains 3 interconnected core components an input, a converter, and an output—the inquiry may be rather foreseeable. The letters x and y are used to denote the input and output, respectively, and they stand for focus and reaction. Numerous factors, including as the chemical characteristics of the analytical species, the quantity of the analytes in the sample, the sample matrix, speed, cost, and so on, affect the choice of a particular analysis [22]

Assessment of data:

Information assessment's primary goal is to organize and accumulate knowledge using numerical and statistical methods into a particular informational index. Data analysis enables the extraction of useful information and the drawing of conclusions regarding the inputs, outputs, and particularly the validation process in general [22]

Cleaning validation:

A system or piece of equipment can be evenly cleaned to predetermined and specified criteria by using cleaning validation, which has been reported as having a high level of confirmation. A recorded method called cleaning approval shows how consistently and effectively pharmaceutical production equipment is cleaned. Examining the cleaning system's feasibility for the removal of product deposits, degradants, additives, excipients, or cleaning agents as well as in the prevention of potential microbial contamination is the aim of the cleaning approval process. For the reasons listed below, it is crucial to validate cleaning methods:

- Pharmaceutical products and active pharmaceutical ingredient (API) can be contaminated by other products and microbes.
- It is an administrative prerequisite in pharmaceutical product manufacture the worry is the same-guarantee that the equipment is properly clean and safety and quality is kept up.
- It is likewise guaranteed from an inside control and consistency perspective the quality of manufacture.
- To protect product integrity.
- To reuse the equipment.
- Necessity for cleaning validation To check the viability of cleaning techniques and to make sure that no risks are related to cross-contamination of API or detergents. Cleaning validation protocol
- The goal of the validation procedure.
- Obligations regarding performing and endorsing the validation study.
- Equipment details.
- The interval between the end of production and the start of the cleaning techniques.
- Cleaning methods to be utilized for every product, each manufacturing device or each piece of equipment.
- The quantity of the cleaning cycle to be performed continuously.
- Routine checking equipment.
- Sampling techniques, including the basis for why a specific sampling technique is utilized.
- Clearly defined sampling areas.
- Information on recovery studies, where suitable.
- Analytical techniques including LOD and LOQ.
- The acceptance criteria, along with including the method of reasoning for setting specified limits[23,24].

Importance of validation:

- Assured high quality.
- Time boundation.
- Optimization of the method.
- Minimum batch product failure, enhanced efficiency, manufacturing, and productivity.
- Quality cost decreased.

- Rejection decreased.
- Yield increases.
- Fewer complaints about process related issues.
- Fast and realistic start-up of new equipment's.
- Increased worker consciousness of the process [16]

ANALYTICAL METHODS VALIDATION (as per ICH R_1 (Q_2))

- Accuracy
- Precision
- Repeatability
- Intermediate Precision
- Reproducibility
- Specificity
- Detection Limit
- Quantitation limit
- Linearity
- Range
- Stability
- Robustness
- Ruggedness
- System Suitability

Accuracy:

The phrase "the proximity of check results achieved with the aid of that procedure to the appropriate price" can be used to define an analytical method's accuracy. Its variety must all be placed with this accuracy. Any of the following methods can be used to evaluate an analytical method's accuracy. Comparing the measured price to the "real" price after analyzing a sample of recognized awareness However, a well-characterized sample (such as a well-known reference) ought to be used[26]

A general method to addition. On this technique, a sample is analyzed, a known quantity of a pure energetic ingredient is added, and the pattern is analyzed once more. The difference between the 2 assays' results is shown by comparing them to the expected result. Restoration is defined in both procedures (preferred addition approach and spiked-placebo restoration) as the ratio of the actual end result to the predicted end result expressed as a percentage. A method's accuracy should be assessed at several phases of fortification since it can vary within the range of possible test values. At least three concentrations (80%, 100%, and 120%) must be covered by the accuracy within the desired range.

By comparing test results with those acquired using other validated test methods, accuracy can also be determined. The accuracy of dosage shape assays is typically 3–5% of the true value. According to the ICH files, accuracy should be evaluated with a minimum of nine measurements spread throughout a minimum of three awareness levels, overlaying the necessary range (i.e., three concentrations and three duplicated willpower for each attention)[27]

Precision:

It describes the degree of scatter (or proximity of settlement) between a series of measurements taken under the specified conditions using several samples of the same homogenous sample. Three levels of precision can be taken into account: repeatability, intermediate precision, and reproducibility. Precision within an assay is another name for repeatability. It is a measurement of the accuracy of evaluation performed in a single lab by a single operator using a single piece of equipment over an unexpectedly short period of time. RSD of reflect values is a measure of how much an effect has settled while experimental conditions are kept as constant as possible. The International Conference on Harmonization (ICH) recommends at least nine measurements covering the desired range for the technique (for example, three concentrations with three replicates as in the accuracy test), or at least six measurements at 100% of the check concentration for the evaluation of repeatability, which should be expressed as standard deviation, relative standard deviation (coefficient of variation), or self-beliefc programming language. By comparing the results of a method conducted in a single laboratory over a period of weeks, the ICH defines intermediate precision as long-term variability of the dimension method. Additionally, it is known as intraday precision. Reproducibility describes the accuracy of the evaluation of the same pattern by specialized analysts in

specialized laboratories under varying operational and environmental conditions that are still within the specific parameters of the method[29]

Specificity:

The capacity to accurately assess the analyte in the presence of additives that could be anticipated to be present is known as specificity. These often include degradants, matrix, contaminants, and so forth. Other aiding analytical methods may make up for a specificity deficit in a given analytical procedure (s).

The term "specificity" is divided by ICH into two distinct groups.

Identity: to ensure the identification of an analyte.

Impurity tests:

These tests ensure that all analytical procedures used can accurately identify the impurities present in an analyte, including the presence of heavy metals, residual solvents, and other compounds.

Assay (content or potency):

To provide a precise result, this enables accurate declaration of the content or potency of the analyte in a sample. For specificity validation, analytical techniques that can measure analyte response while all sample additives are present must be used. It is not always possible to prove that a single analytical technique is the only one that works for a given analyte.

In liquid chromatography, specificity is achieved by putting the chromatographic conditions, mobile section composition, column temperature, and detector wavelength along with the most effective columns. The pattern education stage can be adjusted for except in addition to chromatographic separation.

Limit of Detection (LOD) and Limit of Quantification (LOQ):

The lowest concentration of an analyte in a sample that can still be detected analytically is known as LOD, while the lowest concentration of an analyte that can be quantitatively measured is known as LOQ.

Linearity:

An analytical method's ability (within a certain range) to achieve examination outcomes that are directly proportional to the awareness (amount) of analyte inside the pattern is known as linearity. A sequence of five to six injections of five or more requirements with concentrations ranging from eighty to one hundred twenty percent of the anticipated awareness variety is used to determine linearity. The analyte concentrations must be directly

proportional to the reaction's rate of occurrence, or the reaction must be proportional via a clearly defined mathematical computation. A linear regression equation used to predict the results must be ional selective [29] Mathematical calculation that is defined. A linear regression equation applied to the results must have an intercept that is no longer significantly different from 0. It must be confirmed that the acquisition of a large nonzero intercept has no bearing on the technique's accuracy [30]

Range:

The range of an analytical technique is the interval between the maximum and minimum concentration of an analyte in the sample for which it has been established that the analytical method has the necessary linearity, precision, and accuracy. The range is often expressed using the same units as the test results (such as percentages and parts per million) acquired by the analytical approach..

- For Assay - 80 to 120% of test concentration
- Content uniformity - • 70 to 130% of test concentration
- Dissolution - Q-20% to 120%
- Impurities - reporting level – 120% of impurity specification limit
- Assay & Impurities - Reporting level to 120% of assay specific
- Linearity is limited to 150% of shelf life specification of impurities
- Test concentration can be used to determine impurities
- To determine drug substance (assay) the test concentration must be diluted
- The range is 0 – ~ 150% of impurity specification[31]

Stability:

The balance of the solution is made up of the well-known and extracted sample answers (ready to inject) from the sample or matrix and analysed according to the precise methodology. The solution balance must be stored properly at room temperature and in a refrigerator depending on the consistency of the pattern and well-known solution. If the solution was refrigerated prior to investigation, it should have been thawed to room temperature before being tested for stability in both room temperature and the refrigerator. Two practise questions of the preferred and model answers should be written and examined.

Robustness:

An analytical system's robustness is a measure of its capacity to remain unaffected by subtle but intentional changes to the method parameters and provides a clue as to its dependability under routine use. In the context of liquid chromatography, examples of typical fluctuations include: cellular segment composition variations; variations in pH in a mobile section.

- Special lots and/or suppliers (unique columns)
- Glide price; temperature the waft rate, cellular segment composition, pH of a mobile phase, and the use of a special lot of LC column were the factors chosen for all the medications under study. The commentary will be condensed, and the validation record will index out the most important parameters.

Ruggedness:

The degree to which test results from the analysis of identical samples under a variety of test conditions, such as different laboratories, different analysts, using operational and environmental conditions that could differ but are still within the specific parameters of the assay, can be repeated is the robustness of an analytical technique. When the method is to be utilised in several laboratories, it is often advised to test the method's robustness. Ruggedness is commonly defined as the absence of operational and environmental factors of the analytical procedure having any impact on the check consequences. The degree of check result reproducibility is assessed as an aspect of the test variable to define ruggedness.

Suitability:

Machine suitability tests are a crucial component of chromatographic techniques, in line with the USP. These evaluations are used to confirm that the device's resolution and reproducibility are sufficient for the evaluation to be carried out. The main premise of device compatibility tests is that the gadget, electronics, analytical activities, and samples make up a single unit that can be assessed as a whole. System performance is checked to ensure system performance prior to or during the evaluation of unknowns. This is known as system suitability. Determined parameters are compared to the requirements established for the technique, including plate dependence, tailing factors, resolution, and repeatability (%RSD retention duration and region of repetitive injection).

The examination of a machine suitability "pattern," which may be a combination of primary additives and anticipated via-merchandise, allows for the measurement of those parameters. The use of software created

specifically for the purpose to offer a review of the separation and to provide a summary of the data pertaining to repeatability may be used to carry out the documentation of device suitability. The software is also employed for technique troubleshooting. To provide the feedback required to assess device performance, results saved in a relational database can be compared and summarized on a height-by-top or machine-by-device basis [34]

CONCLUSION

In order to demonstrate that a method is appropriate for its intended application, this article discusses how to build a method, what validation is, why it is important, the many types of validation, how to do the validation process, and its parameters. The main goals of developing analytical techniques are to identify, purify, and ultimately qualify any required drugs, etc. The creation of analytical techniques aids in reducing the impact of crucial process parameters on precision and accuracy. In order to ensure that quality work is done in the process that supports the creation of medicines and products, validation is a vital approach in the pharmaceutical industry.

Acknowledgement

I am thankful to Principal, Management and My Research guide of Shri D D Vispute college of pharmacy and research center for providing me all necessary facility for completion of this review work.

REFERENCES

1.Hema, Swati Reddy G. A review on new analytical method development and validation by RP-HPLC. Int Res J Pharm Biosci2017;4:41-50.

2.Ravisankar P, Navya CN, Pravallika D, Sri DN. A review on stepby-step analytical method validation. IOSR J Pharm 2015;5:7-19.

3.. Patel A, Dwivedi N, Kaurav N, Bashani S, Patel S, Sharma HS, et al. Chemical analysis of pharmaceuticals: a review. J Med Pharm Innov2016;3:4-7.

4.FDA Guidance for Industry. Analytical Procedures and Method Validation, Chemistry, Manufacturing, and Controls Documentation, Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER). 2000.

5.Chauhan A, Mittu B, Chauhan P. Analytical method development and validation: a concise review. J Anal Bioanal Tech 2015;6:1.

6.PanchumarthyRavisankar, Ch. Naga Navya, D. Pravallika, D. Navya Sri; A Review on Step-by-Step Analytical Method Validation, 2015; 5(10):07-19.

7.Breaux J, Jones K, Boulas P., Understanding and implementing efficient analytical methods development and validation. Pharm Technol Anal Chem Test. 2003; 5:6-13.

8.ICH Q2 (R1), Validation of Analytical Procedures: Text and Methodology. International Conference on Harmonization, IFPMA, Geneva, 2005.

9.George Lunn, Methoxychlor, HPLC Methods for Recently Approved Pharmaceuticals, 1st Ed, 2005, 387.

10. International Conference on Harmonization (ICH), Validation of analytical procedure: Text and methodology, Harmonized tripartite guideline, Q2 (R1), Geneva, 2005.

11. Jay Br, Kelvin J, Pierre B, Understanding and Implementing Efficient Analytical Methods Development and Validation, 2003, Available from: http://www.pharmtech.com

12. Lloyd R, Snyder, Joseph J Kirkland, Joseph L Glajch, Practical HPLC Method Development, 2nd Ed., 1997, 179-184.

13. Ravisankar P, Navya CN, Pravallika D, Sri DN. A review on stepby-step analytical method validation. IOSR J Pharm 2015;5:7-19.

14. Jatto E, Okhamafe AO. An overview of pharmaceutical validation and process controls in drug development. Trop J Pharm Res 2002;1:115-22.

15. Mahar P, Verma A. Pharmaceutical process validation: an overview. Int J Pharm Res Biosci2014;3:243-62.

16. Lavanya G, Sunil M, Eswarudu MM, Eswaraiah MC, Harisudha K, Spandana BN, et al. Analytical method validation: an updated review. Int J Pharm Sci Res 2013;4:1280.

17. Verma P, Madhav NS, KR Gupta V. A review article on pharmaceutical validation and process controls. Pharma Innovation 2012;1:51-60.

18. Md Alamshoaib. Pharmaceutical process validation: an overview. J Adv Pharm Edu Res 2012;2:185-200.

19. Ahir KB, Singh KD, Yadav SP, Patel HS, Poyahari CB. Overview of validation and basic concepts of process validation. Sch Acad J Pharm 2014;3:178-90.

20. Nandhakumar L, Dharmamoorthy G, Rameshkumar S, Chandrasekaran S. An overview of pharmaceutical validation: quality assurance viewpoint. Int J Res Pharm Chem 2011;1:1003-14.

21. Bhardwaj SK, Dwivedi K, Agarwal DD. A review: HPLC method development and validation. Int J Anal Bioanal Chem 2015;5:76-1.

22. Araujo P. Key aspects of analytical method validation and linearity evaluation. J Chromatogr B 2009;877:2224-34.

23. Goyal D, Maurya S, Verma C. Cleaning validation in the pharmaceutical industry-an overview. Pharma Tutor 2016;4:14-20.

24. Lodhi B, Padamwar P, Patel A. Cleaning validation for the pharmaceuticals, biopharmaceuticals, cosmetic and neutraceuticals industries. J Innov Pharm Biol Sci 2014;1:27-38.

25. Murthy DN, Chitra K. A review article on cleaning validation. Int J Pharm Sci Res 2013;4:3317.

26. Tranfo G, Enrico P, Renata S, Daniela P. Validation of an HPLC/MS/MS method with isotopic dilution for quantitative determination of trans, trans-muconic acid in urine samples of workers exposed to low benzene concentrations. J. ChromatographyB, 67, 2008, 26-30.

27. Jenke DR. Chromatographic method validation: A review of current practices and procedures. Part II. Guidelines for primary validation parameters. Instrum. Sci. Technol 1998; 26:1-18.

28. G. Lavanya, M. Sunil, M.M. Eswarudu, M. ChinnaEswaraiah, K. Harisudha and B. Naga Spandana; Analytical method validation: An updated review; IJPSR, 2013; 4(4):1280-1286.

29. Tranfo G, Enrico P, Renata S, Daniela P. Validation of an HPLC/MS/MS method with isotopic dilution for quantitative determination of trans, trans-muconic acid in urine samples of workers exposed to low benzene concentrations. J. ChromatographyB, 2008'; 67:26-30

30. Vander HY, Nijhuis A, Verbeke JS, Vandegtnste BG, Massart DL. Guidance for roubustness/ruggedness test in method validation, J Pharm Biomed Anal. 2009; 24:723-53.

31. RajendraPatil, TusharDeshmukh, Vijay Patil, and KishanchandKhandelwal:Review on Analytical Method Development and Validation. Research and Reviews: Journal of Pharmaceutical Analysis; Volume 2014; 3(3):1-10.

32. Saranjit Singh and Monika Bakshi; Guidance on Conduct of Stress Tests to Determine Inherent Stability of Drugs; Pharmaceutical Technology On-Line APRIL 2000; www.pharmaportal.com.

33. Sanjay Bajaj, Dinesh Singla and NehaSakhuja; Stability Testing of Pharmaceutical Products Journal of Applied Pharmaceutical Science 2012; 02(03):129-138

34. Michel E. Swartz and Ira S Krull; Analytical method development and validation; Special Indian edition; Marcel Dekker, Inc.73-74.

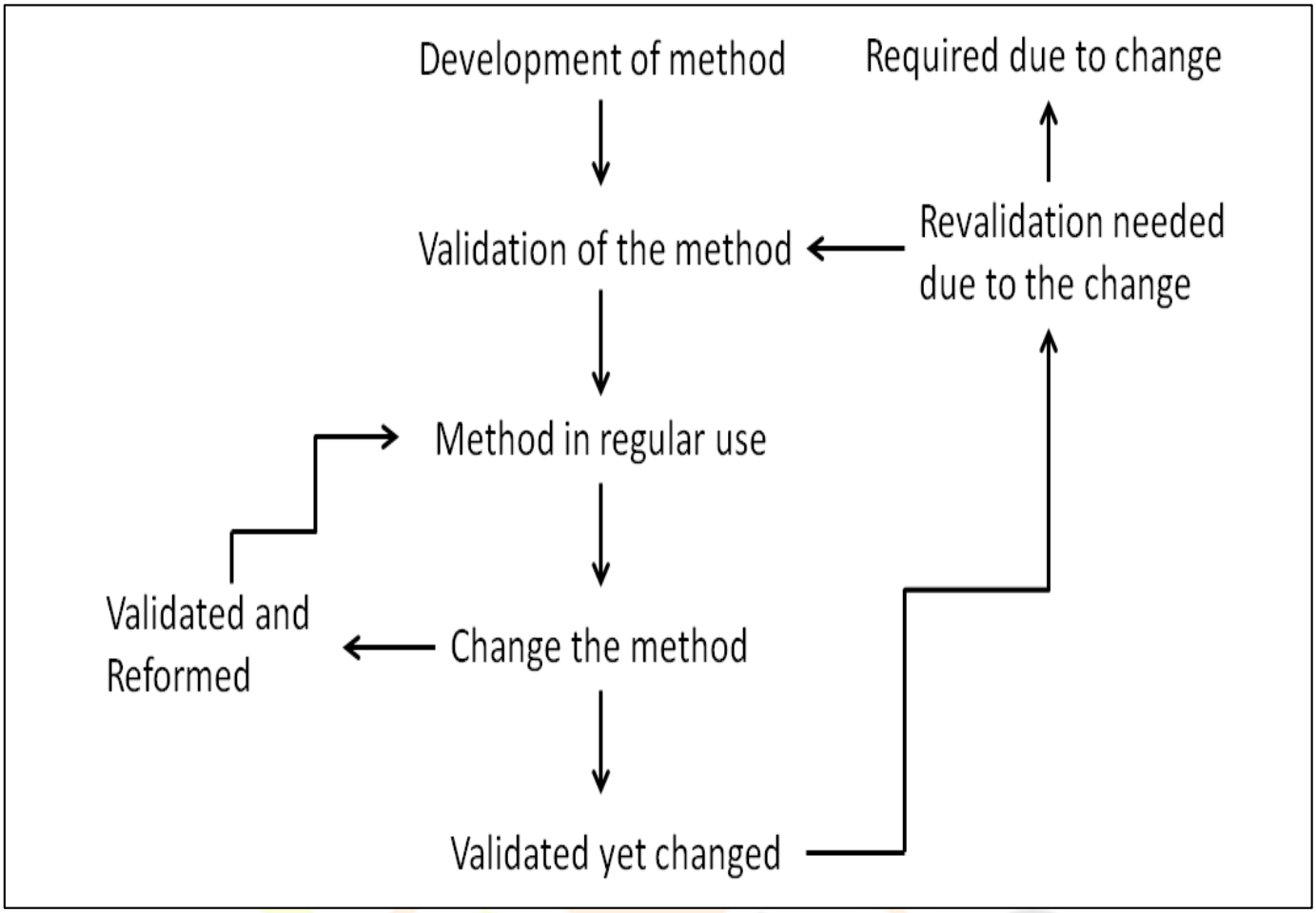

Fig 1: Life cycle of the analytical method

Fig 2: Criteria for the Development of New Analytical Method

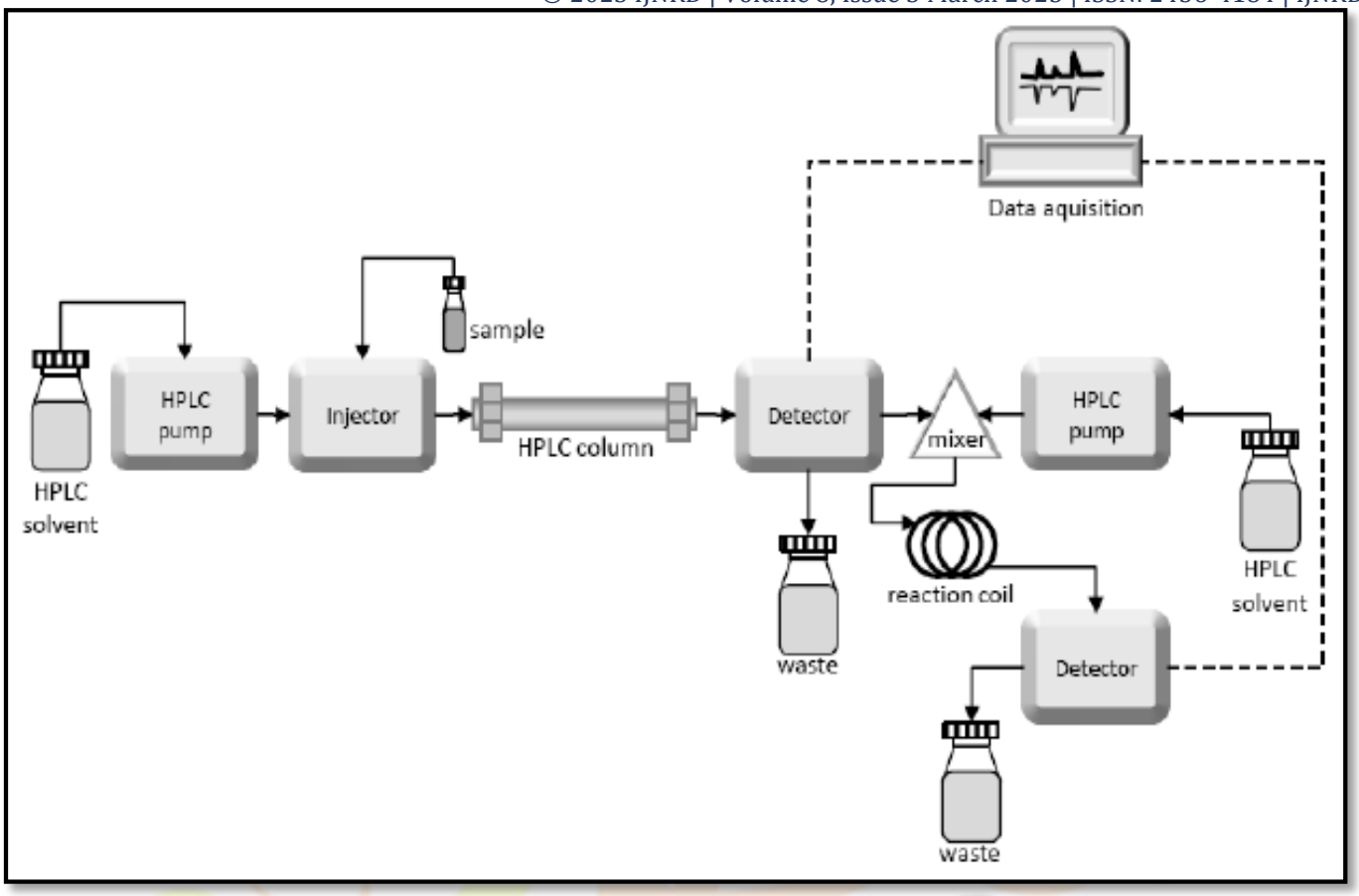

Figure 3 HPLC System

Fig: 4 Validation types

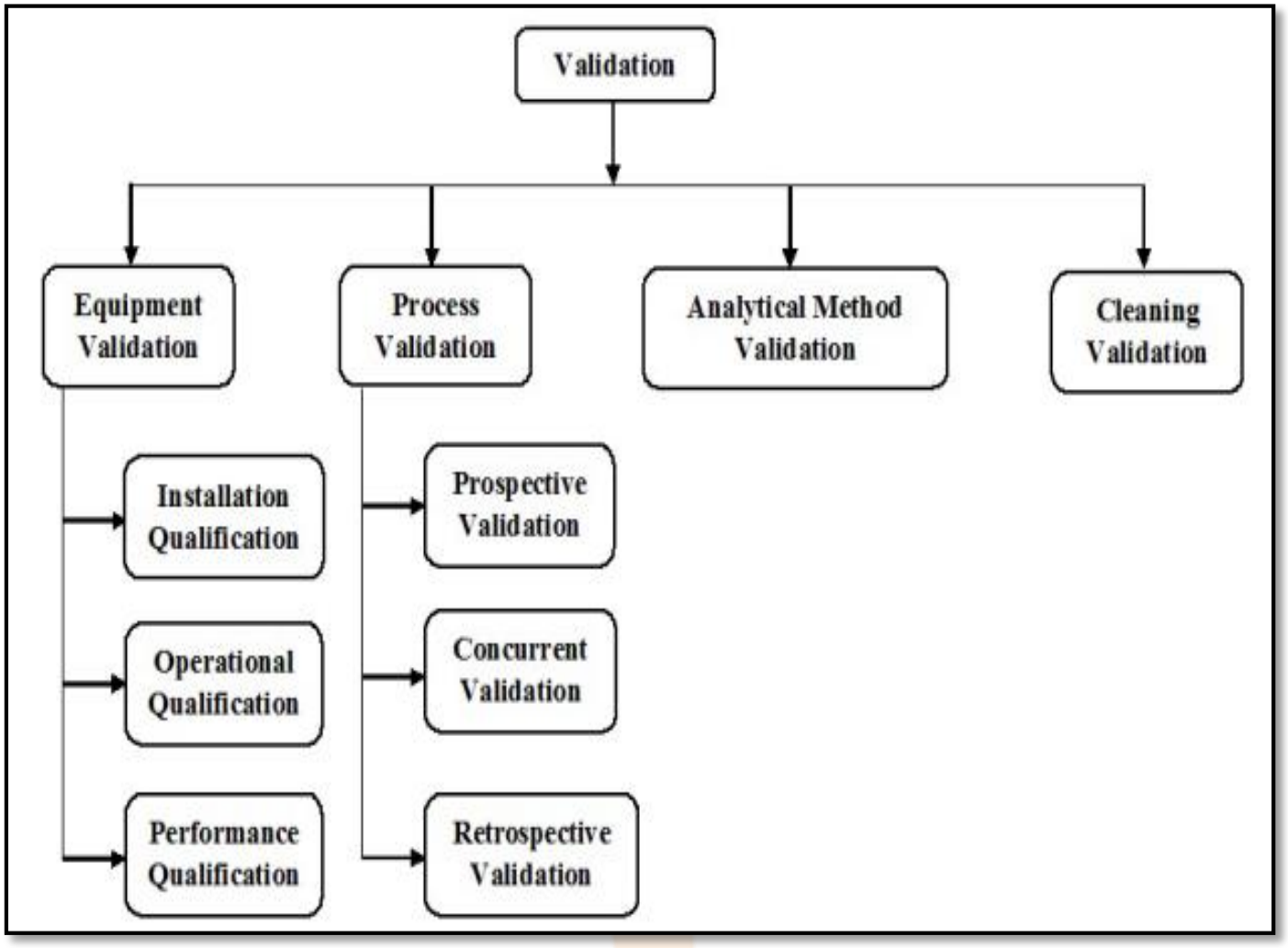

Figure titles and legends:

Fig 1: Life cycle of the analytical method

Fig 2: Criteria for the Development of New Analytical Method

Figure 3 HPLC System

Fig: 4 Validation types