AMJ
ISSN: 0005-2523

ISSN: 0005-2523
Volume 62, Issue 08, December 2022

A REVIEW ON QUALITY BY DESIGN VALIDATION APPROACH FOR ANALYTICAL VALIDATION OF ANTI AGING AGENT

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Abstract

In the recent decade, the pharmaceutical sector has grown quickly by concentrating on product quality, safety, and efficacy. Scientific technologies like QbD (Quality by Design) and PAT (Process Analytical Technology)have helped pharmaceutical companies boost the amount of new products they generate. There have been ICH recommendations on QbD application in API synthesis and formulation development, which have been discussed in Q8 through Q11. The ICH Q11 guidelines provide examples of the QbD technique used in API synthesis. The USFDA mandates that generic drug manufacturers use the Quality by Design (QbD) strategy when developing new formulations. It is still unclear what regulatory bodies want from analytical development in terms of AQbD (Analytical Quality by Design) and PAT (Process Analytical Technology). API synthesis process and analytical technique development may benefit from combining QbD and AQbD, as outlined in this study. Method optimization and development with DoE, MODR (method operable design region), Control Strategy, AQbD method validation, and continuous method monitoring are some of the most important AQbD tools. These include identifying ATP (Analytical Target Profile), CQA (Critical Quality Attributes), and risk assessment. Quality by Design (QbD) activities may be implemented simultaneously in both synthetic and analytical development, resulting in the best quality product while reducing risks.

Keywords: QbD (Quality by Design), ATP (Analytical Target Profile), CQA (Critical Quality Attributes), risk assessment.

1. Introduction

QbD has recently been established as a way to guarantee a certain product quality throughout the development of pharmaceutical procedures. As the QbD idea is completely incorporated into pharmaceutical processes and notably in the process control strategy, the focus on applying it to analytical procedures has intensified. A total of six QbD may be used to generate new methods and to identify a method operable design area. Numerous researchers have noted the need of

moving away from typical checklist implementation of, say, ICH Q213 or U.S. Pharmacopeia (USP), to one that emphasizes a method validation strategy that ensures a high degree of dependability for the methods being validated. This change is necessary to guarantee that the key quality characteristics (CQAs) of the medicinal product are adequately measured.**[1]** Assessing analytical techniques to determine if they are legitimate means looking at the methods intended use and proving that they fit established criteria in the analytical target profile (ATP). The primary goal is to establish the objective of the analytical technique being validated and its metric of suitability for that purpose (e.g., accuracy, precision, and so on). Actually, "to show that it is acceptable for its intended purpose" is the overarching goal of validation of an analytical technique. In order to determine if analytical procedures are legitimate, it is critical to consider the effect that the findings they produce have on the quality of the final goods. This is where the CQAs come in**.[2]**

2. Analytical Quality by Design (AQbD)

QbD is described by ICH as "a systematic approach to development that starts with established goals and stresses product and process knowledge and process control, based on strong science and quality risk management."

AQbD is a process similar to QbD in that the results are well understood and fit for purpose throughout the entire lifecycle. Method Validation, Control Strategy, and Risk Assessment are all part of an integrated approach to AQbD life cycle management. Other tools include ATP (Analytical Target Profile), CQA , Risk Assessment, and Continuous Method Monitoring.**[3]**

3. Scientific QbD Approach for Synthesis and Analysis.

ICH Q11 describes the QbD technique for developing API synthetic processes, but it makes no mention of AQbD specifically. QbD-based analytical method development, or AQbD, should be used instead. Equal time might be allocated to the development of these two scientific methods (QbD and AQbD). Figure 1 depicts the phases involved in API synthesis and QbD implementation. High-quality products may be made by using this strategy simultaneously. It might provide more useful information for the start-up of process analytical technologies (PAT)**.[4]**

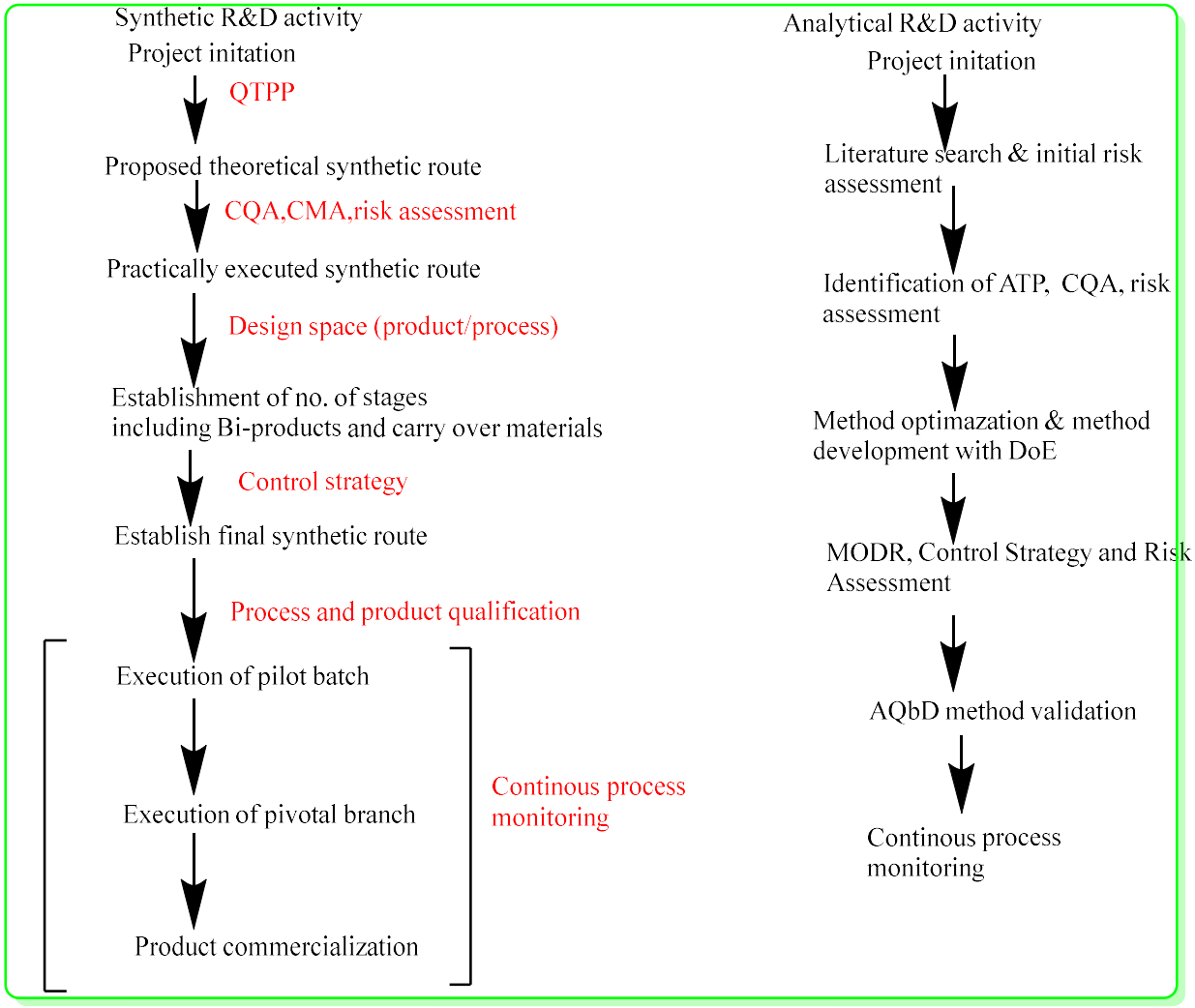

Fig 1: API synthetic development and AQbD approach.

3. Differences for Traditional and Scientific Approach.

Traditional and scientific approaches to the creation of analytical methods are vastly different. There is no statistical analysis or risk assessment in the traditional method. Method Validation, Continuous Method Monitoring, and AQbD Method Validation are all part of the scientific instruments that will be used in the AQbD approach**.[5]**

Analytical techniques to measure contaminants and drug product or substance content tests will be the emphasis of this study, as will also be two kinds of analytical methodologies (as defined in ICH Q2). Many of these techniques are approved on the basis of their capacity to measure the amount of contaminants or active ingredient in their matrix (drug substance or drug product). This is not, however, what they were originally designed to be for**.[6]** The ultimate conclusion will be based on the findings of the current research, and it is for this reason that the methodologies under consideration were chosen. Quasi-quantitative impurity tests' ultimate goal is to determine whether

or not a material or product is in compliance with the relevant product requirements. Impurity tests also have a similar goal: to determine whether or not a product is in accordance with its own specified limitations, as do content assays. Since these approaches are essential to the ATP, it is important to evaluate their fitness in light of these objectives**.[7]** The maximum allowable risk of incorrect assessments should be included in the ATP of various techniques. In order to determine whether these procedures are capable of meeting this ATP requirement, they need be validated. Method validation decisions should be made in line with the ultimate usage of these analytical methods in order to ensure the validity of the results**.[8]**

4. ATP (Analytical Target Profile)

Target analytes (products and contaminants), analytical methodology category, and product specifications are all considerations in ATP identification. To anticipate the method's needs and analytical criticalities, a preliminary risk assessment would be conducted. The following is the standard ATP for analytic procedures**[9]:**

- The selection of analytes (API and impurities)
- Techniques (HPLC, GC, HPTLC, Ion Chromatography, chiral HPLC, etc.),
- Conditions for the selection of a certain technique (assay or impurity profile or residual solvents).

a) **Target Analytes Selection**. ICH Q3 and all other regulatory guidance explained the consideration of impurities in the API synthetic route. Based on the above synthetic route (Figure 2), analytical target profile (ATP) impurities are as follows:

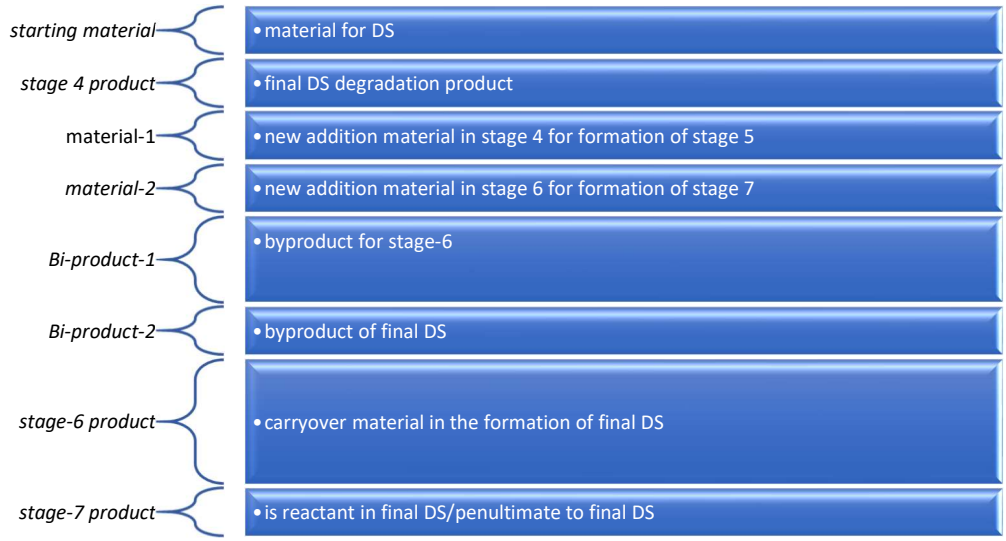

Figure 2: Synthetic route of target analytes selections

(b) **Technique Selection**. The nature of the analyte may be used to pick an analytical method since each one follows a distinct set of principles. In addition, the analytical test item and the goal of the test must be taken into consideration. Analytical test items and methods are as follows:

(1) impurity profile (Chromophore):HPLC with UV detector
(2) impurity profile (non-Chromophore): HPLC with RID/ELSD and so forth
(3) HPLC assay (Chromophore): HPLC with UV detector
(4) HPLC assay (non-Chromophore): HPLC with RID/ELSD and so forth**[10]**

5. CQA (Critical Quality Attributes) and Risk Assesment

i. **CQA (Critical Quality Attributes)**. Analytical method CQA comprises the features and parameters of the analytical technique itself. The CQA varies depending on the method being used. In high-performance liquid chromatography (HPLC), critical quality attributes (CQAs) include mobile phase buffer, pH, diluent, column type, organic modifier, and elution mode. Gas flow, oven temperature and programme, injection temperature, sample diluent and concentration are some of the CQA procedures used in gas chromatography (GC). HPTLC is a process. TLC plate, mobile phase, injection concentration and volume, plate development time, colour development reagent, and detection technique. The CQA for the creation of analytical methods, such as solubility, pH, polarity, charged functional groups, boiling point, and solution stability, may be defined by the nature of impurities and DS[11].
ii. **Risk Assessment**. Method parameters and material qualities may be identified using the science-based approach of risk assessment (ATP). Performing a risk assessment is possible at any point of the method development process, including the early design phase. Risks are identified early on in the development process using the AQbD method, and then plans for risk mitigation and management techniques are put in place. Use an Ishikawa fishbone diagram to identify and evaluate risks. See Figure 3 for an example of a fishbone risk detection technique for a typical analytical test[12].

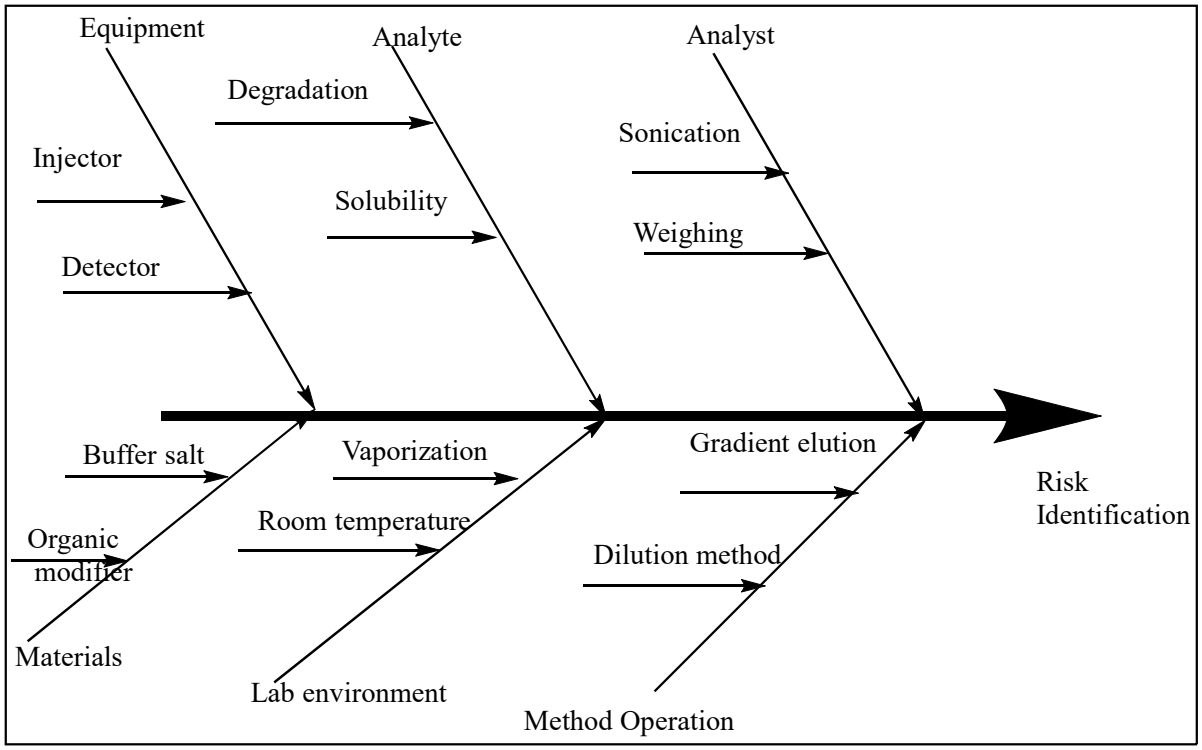

Figure 3. Fishbone for Risk identification.

6. Design of Experiment (DoE)

DoE may be used to confirm and fine-tune critical method variables based on statistical significance after initial risk assessment defines possible and crucial analytical technique variables. Method variables and their interactions and responses may be analysed at the unit level or in conjunction with other methods (critical method attributes). Using this method, it is possible to test a large number of situations in a short period of time. In order to find crucial method variables and the proper ideal ranges for the method variables where a robust area of the critical method characteristics may be produced, data assessments utilising statistical methods are necessary**.[13]**

For the purposes of the ICH Q8 guidelines, "ability of a process to accept variability in materials and changes in the process and equipment without detrimental influence on quality" is specified. The robustness, impurity profile, physicochemical qualities, process capacity, and stability of the drug substance synthesizing process are all affected by the starting materials' attributes. To define robustness parameters, it is necessary to evaluate various operating circumstances, scales, and equipment to get an understanding of the process**.[14]**

7. MODR (Method Operable Design Region)

A multidimensional space based on method factors and settings is created using the MODR method operable design region (MODR). It may also be utilised to develop relevant method

controls like system appropriateness, RRT, and RRF. In order to confirm ATP conformity and, eventually, to define the MODR, further method verification activities might be used**.[15]**

8. Control Strategy and Risk Assessment

Analyte nature and MODR comprehension serve as the basis for the development of a control approach**.[10–13]** Data obtained during the DoE and MODR phases, as described above, may be used to develop a method control plan. Correlations between technique and analyte properties may be established for the capacity to fulfil ATP requirements from this statistical data set The contradiction in the method parameters will be resolved by a control approach (e.g., reagent grade, instrument brand or type, and column type). Under the AQbD technique, the method control strategy does not seem to be much different from the old approach. In order to assure a tighter connection between the method's goal and performance, method controls are built based on experimental data from CQA, DoE, and MODR.**[16]**

9. AQbD Method Validation

It is possible to validate an analytical technique using a variety of API batches using the AQbD method validation methodology. In order to build method validation for all types of API manufacturing modifications without revalidation, it makes use of both DoE and MODR expertise. Additionally, it offers information on the interactions, measurement uncertainty and control technique that are necessary for ICH validation. This method uses less resources than the standard validation methodology while maintaining the same level of quality**.[17]**

10. Continuous Method Monitoring (CMM) and Continual Improvement

In the commercial stage, life cycle management is employed as a control approach. In the last phase of the AQbD life cycle, CMM is a continual process of sharing knowledge gathered throughout the creation and deployment of design spaces. Assumptions based on past information and statistical design considerations are part of this. For routine purposes, the technique may be utilised after validation, and the method's performance can be tracked on an ongoing basis. Control charts or monitoring data on system appropriateness, method-related research, and so on may be used to do this. Any out-of-trend behaviour in the data may be quickly identified and remedied using CMM**.[18]**

Benefits and Suggestions AQbD is a method that focuses on preventing failures rather to just fixing them when they occur. The scope of the risk assessment relies on the project's position in the timetable. Right strategy, planning, use of tools, and timely completion of work are all critical to AQbD's success rate. Preventing technique failures and gaining a better grasp of the design space and control approach may both be facilitated by timely use of suitable risk assessment tools**.[19]**

11. Quantitative Impurity Assays

An impurity-quantification technique must be validated at least to the reporting level of the impurity and up to a maximum of 120 percent of the specification limit, according to ICH Q2 (L_{imp}). In accordance with ICH Q3A, the analytical procedure's quantification limit shall not exceed the reporting threshold. In this way, the range of concentrations across which the technique must be verified is defined. A quantitative impurity assay's ultimate goal is to accurately declare a drug substance or product compliant, hence the validation acceptability limits should not be bilateral throughout all concentration ranges. An effective way to prevent overestimation is to specify method validation acceptability limits for concentration levels less than the impurity specification (L_{imp}). Overestimation of impurity concentrations in this concentration range has the potential to misclassify otherwise conforming substances and products as non-compliant. Thus, the producer bears the brunt of this**.[20]** However, this producer risk is only discussed inside the pharmaceutical sector since it primarily concerns manufacturability, and would not be made public to other parties. However, it is crucial for the sector to be aware of this risk and to ultimately minimize it if it is deemed undesirable. This region of the concentration range does not suffer from underestimation. The issue arises when the concentration is higher than what is specified in the specification (L_{imp}). In fact, the analytical technique must not underestimate the impurity content at these concentration levels. This might lead to a chemical or product being labelled as compliant when it really isn't, putting patients at danger in the process**.[21]** Patient safety is of paramount importance, and as such, it should be addressed in the proposed treatment protocol. Therefore, the validation acceptability limit and validation decision process should be established to control underestimate for this region of the concentration range.**[22]** Figure 4 illustrates this point. Quantitative impurity test acceptability limits may be specified in concentration values to account for these factors: L_{imp} 1 is the impurity specification under study, and its value is 14.

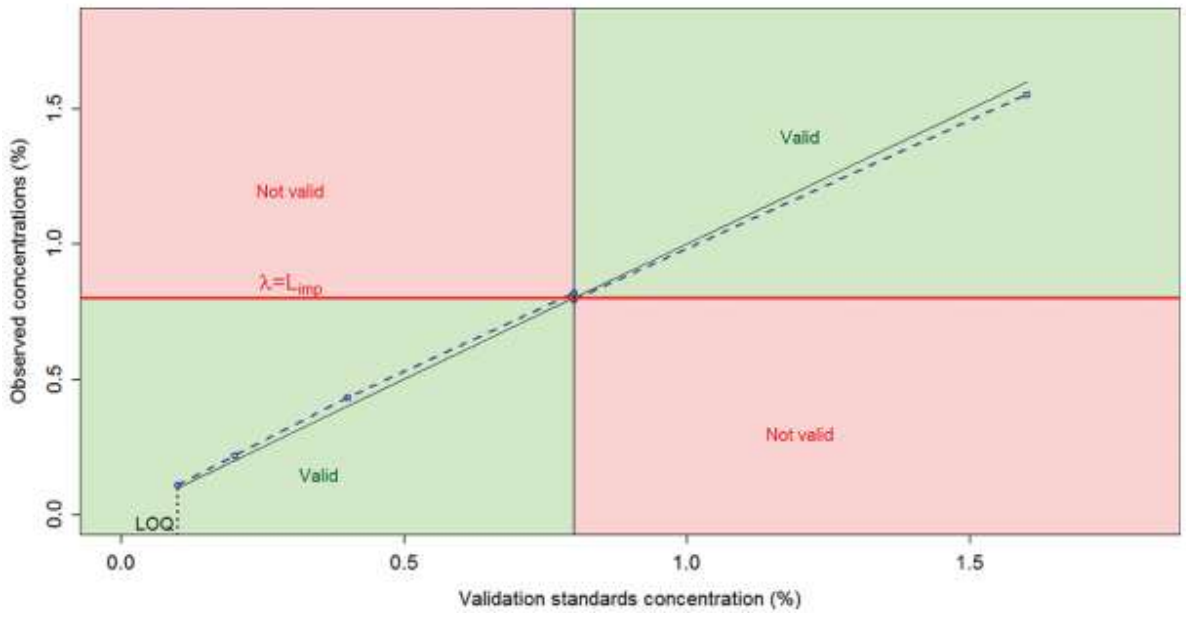

Figure 4: Decision profile for assessing the validity of an HPLC-UV method for quantification of (R)-timolol impurity in (S)-timolol drug substance

12. Decision Methodology

For this class of quantitative procedures, the two most important criteria for validation are method accuracy (bias, commonly referred to as trueness) and precision. A technique with poor accuracy could nevertheless be suitable for its intended application if it has high enough precision, therefore applying an acceptability limit to each of these characteristics individually isn't essential. As stated by Hoffman and Kringle& Hubert and coworkers, the validity of quantitative impurity tests should be judged by the simultaneous combination of both criteria. The term "total error" or "results accuracy" may refer to either one or the other of these two concepts when (by opposition to the method accuracy). Using the total error technique, biases such as concentration biases may be dealt with. A QbD strategy may be more suitable if an overall method bias is identified and can be eliminated or corrected for. When it comes to accurately measuring this, the statistical approach of tolerance intervals is the best option. Based on how one defines "tolerance," it may be an interval that encompasses, for example, 10% of the distribution, or an interval that each future result has the user-defined chance of falling inside. It is possible to argue that a tolerance interval contains an anticipated 90% of future analytical outcomes. It's important not to mistake tolerance intervals with confidence intervals, which only provide information on a statistical parameter's sample distribution, such as its mean. As a result, Hubert and coworkers or Hoffman and Kringle's decision-making approach should be used, which compares the tolerance intervals generated from the validation data with the previously specified acceptance limits. Using the quantitative impurity assay, Hoffman and Kringle employed -content -confidence tolerance intervals, which apply a probability or confidence level to the range, to calculate the -expectation tolerance intervals, as shown in the Supporting Information. For further in-depth information on tolerance intervals, interested readers might consult the following publications. It is important to note that only one side of the impurity specification level should be evaluated when using a tolerance interval here. It is expected that the procedure will be flawless when the impurity concentration is precisely at the impurity specification (L_{imp}). In reality, this is a non-starter. Because of this, the technique is no longer able to provide accurate findings at concentrations close to the limit of the specification. If the routine findings are still giving accurate information regarding a product's compliance with appropriate guarantee at values around the specified limit(L_{imp}), then this is an essential step to take. Since the specification limit (L_{imp})is the maximum unreliable area [U_{low}; U_{up}] surrounding the limit, the ATP definition should include a maximum likelihood of making a bad choice, which is the maximum false compliance risk [U_{low}; U_{up}]. False noncompliance is a possible additional danger. It is not necessary to include the risk of incorrect noncompliance judgments in the ATP definition, as this is entirely a manufacturer risk. However, the risk of noncompliance might still be reflected in the internal method approval criteria of the organisation (in the remainder of this paper, both risks will be included in the ATP for this last reason)**.[23]**

13. Decision Graph.

Two things must be checked to see whether the analytical approach is appropriate for the task at hand. The first step is to determine whether or not the technique can provide accurate findings across the whole concentration range being investigated, excluding the unreliable area around the impurity specification**.[24]** The decision graph is used to accomplish this. -expectation tolerance intervals are calculated using the analytical data acquired at each concentration level of the validation standards in order to build the decision graph. For concentration levels below the validation acceptance limit, the upper and lower tolerance limits are linearly linked; for concentration levels beyond the validation acceptance limit, the lower and higher tolerance limits are linearly connected. This graph can be used to determine a decision rule, for example, if (1) all of the upper -expectation tolerance intervals, computed at the concentration levels of validation standards that are lower than U_{low}, are under $=L_{imp}$, and (2) if all ofthe lower -expectation tolerance intervals, computed at the concentration levels that are lower than U_{low}, are under $=L_{imp}$. It's not enough, however, since the analytical method's unreliability range may be bigger than the ATP's maximum unreliability range.**[25]**

14. Unreliability Graph.

Two things must be checked to see whether the analytical approach is appropriate for the task at hand. The first step is to determine whether or not the technique can provide accurate findings across the whole concentration range being investigated, excluding the unreliable area around the impurity specification. The decision graph is used to accomplish this. -expectation tolerance intervals are calculated using the analytical data acquired at each concentration level of the validation standards in order to build the decision graph. For concentration levels below the validation acceptance limit, the upper and lower tolerance limits are linearly linked; for concentration levels beyond the validation acceptance limit, the lower and higher tolerance limits are linearly connected. This graph can be used to determine a decision rule, for example, if (1) all of the upper -expectation tolerance intervals, computed at the concentration levels of validation standards that are lower than U_{low}, are under $=(L_{imp})$, and (2) if all ofthe lower -expectation tolerance intervals, computed at the concentration levels that are lower than U_{low}, are under $=(L_{imp})$. It's not enough, however, since the analytical method's unreliability range may be bigger than the ATP's maximum unreliability range**.[26]**

15. Content Assays

To measure the amount of active ingredients in drug substances or drug products, you may use the quantitative impurity assay approach mentioned above. The primary distinction is that product specifications in the United States are often bilateral. When it comes to specifications, there's an upper and lower limit (L_{up} = 105% or 101% of the production goal, for example, and L_{low} = 95%

or 90% of the label claim). The decision profile for an active ingredient content test in a pharmaceutical formulation is shown in Figure 5.

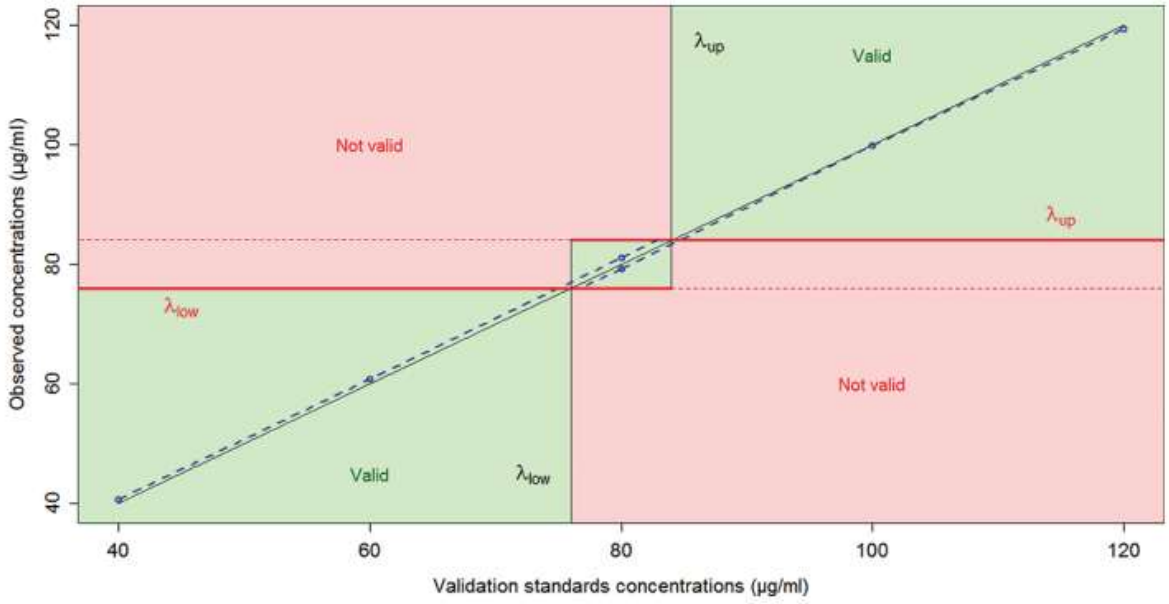

Fig 5: Decision profiles for assessing the validity of an HPLCUV method for quantification of fenofibrate in a drug product. Dashed lines are the 95% β-expectation tolerance intervals (either one-sided or bilateral); the diagonal solid line is the identity line y = x; and λL$_{imp}$ and λ$_{up}$ are the lower and upper specifications of the active substances in the product, respectively. Open circles represent the concentration levels of the validation standards analyzed to assess the validity of the method

An HPLC UV test is used to measure the amount of fenofibrate in a pharmaceutical product. For this approach to work, it must be able to measure fenofibrate API in the presence of any possible impurity or degradation product, as well as in the presence of any of the excipients contained in the medicinal product, throughout a concentration range of 40 to 120 g/mL fenofibrate. In order to arrive at this conclusion, the analytical approach should be able to show that the probability of incorrect compliance and noncompliance judgments are at most 5% outside of the unreliability zones of maximum 1.5 percent around the API standards. (5% around goal) relates to low and high limits of g/mL of fenofibrate that were set for the drug. U_{low} is 74.9 g/mL; U_{up} is 78.2; the two greatest unreliability zones surrounding product requirements are [U_{low} + = 82.7 g/mL, and U_{up} + = 85.3; respectively]. To meet the criteria outlined in the technique ATP, a quality level probability of = 95% was chosen. Overestimation is a problem when dealing with concentrations that go below a lower specification (low). As a result, it is only necessary to compare the top one-sided -expectation tolerance intervals to this specification. For concentrations over the upper specified limit (up), underestimation should be managed. It is important to compare one-sided -expectation intervals to this specification. However, at concentration levels within the criteria [low up],

management of both over- and underestimation should be done simultaneously. Calculation of tolerance intervals on both sides and comparison to bilateral specification limits is required for this. This HPLC UV method's decision profile is shown in Figure 5. It's clear from Figure 5 that except for concentrations very near to the specification limits, -expectation tolerance intervals don't go beyond those limits. However, when concentrations approaching those specified by the requirements are approached, the technique ceases to yield outcomes within those parameters with the desired probability**.[27]** This content assay's unreliability areas are established by the range of routine findings across which the technique is no longer trustworthy, which must be compared to the maximum unreliability regions described in the ATP. As with the quantitative impurity assays, this is done by looking at the dependability profile in the same manner. For the reliability profiles, the lower one-sided -expectation tolerance intervals for concentration levels below the lower specification limit (low), the upper one-sided -expectation tolerance intervals for concentration levels above the upper specification limit (up), and the two-sided -expectation tolerance intervals for concentrations within these specification limits must be calculated**.[28]**

16. QbD approach in HPLC

Velusamy B. Subramanian et.al (2020) Impurities in the tablet dosage form of apixaban (APX) may be detected using a high-resolution HPLC approach based on quality by design (QbD). With a simple and stable HPLC approach, nine known contaminants were measured with a high degree of peak resolution. Acetonitrile and buffer were mixed 90:10 in MP-A, whereas acetonitrile and water were used 10:90 in MP-B. MP-A 75 percent for the first minute, B 25 percent for the next 20, MP-A 65 percent for the next 30, MP-A 40 percent for the next 40 minutes, MP-A 40 percent for the next 60 minutes, MP-A 40 percent for the next 60 minutes, MP-A 75 percent for the next 50 minutes, and so on. A Zorbax RX C18 250 4.6 mm column, 5 m (1.0 ml min^{-1}, 280 nm) and a column temperature of 40°C were used to perform the chromatographic separation. Experiments were conducted utilising design of experiments to find the most efficient way of separation. Validation findings show that the proposed approach may be used to analyse regular product quality and stability in the production stream**.[29]**

Lalit kumar et.al(2021) The goal of this work was to create a robust, easy, inexpensive, and sensitive HPLC-UV technique for the determination of irinotecan (IRI) in marketed formulations utilising the "quality by design" approach. HyperClone (Phenomenex®) C18 column (249 mm id, particle size 5 m, ODS 130) with Box-Behnken design was used as the stationary phase in the development of RP-HPLC. As a mobile phase, 45:55 percent (V/V) acetonitrile and 20 mmol L–1 potassium phosphate buffer (pH 2.5) containing 0.1 percent triethylamine were utilised. A volume of 20 L was used to inject the sample into the HPLC apparatus. The IRI was estimated and quantified using a 254 nm UV detector. With a flow rate of 0.75 mL min–1, Isocratic elution was used. IRI had a retention time of 4.09 minutes. A coefficient of determination of 0.9993 was discovered for the concentration range of 0.5 to 18.0 g mL–1. Between 0.1 to 0.4 percent, the percent relative standard deviation for intraday and interday accuracy was determined. There was

a LOD of 4.87 ng mL–1 and LQ of 14.75 ng mL–1. In robustness tests, the developed approach had an RSD of less than 0.1 percent. IRI may be estimated in an injectable formulation using this approach since it is easy, accurate, sensitive, robust, and inexpensive**.[30]**

Sagar Suman Panda et.al(2015) It is the goal of the Quality by Design (QbD) method to ensure and forecast the quality of the final product. To measure the medicinal dose form of telaprevir (TEL), a QbD-based reversed phase ultrafast liquid chromatographic technique was developed. The robustness of the method was assessed by selecting organic phase composition (percent), mobile phase flow rate (mL/min), and pH of the borate buffer as the factors, and their effect on responses such as retention time, theoretical plate count, and tailing factor was studied using a Box-Behnken experimental design. This was done. Enable-C18G (250 4.6 mm i.d., 5 m) column was used for chromatographic separation using methanol: borate buffer of pH 9.0 (90:10 v/v) as the mobile phase and PDA detection at 270 nm. Accuracy and precision were within acceptable limits for mean percent recoveries between 98.9 and 100.7 percent once the calibration curve was established. The detection and quantitation limits were 1.60 and 4.75 g/mL, respectively. a high degree of method repeatability and robustness was found via a system appropriateness analysis In tests including forced deterioration, the new approach was shown to be very specific for TEL and the degradation products that result from it. Routine TEL analysis in bulk drugs and medicinal dosage forms was successfully accomplished using the newly devised approach**.[31]**

HishamHashem et.al (2018) For the determination of levetiracetam and pyridoxine HCl, a novel simple, quick and sensitive RP-HPLC technique was developed by applying the Quality by Design (QbD) methodology. Treatment with the antiepileptic levetiracetam leads to a shortfall in pyridoxine HCl, hence the two are given together. Flow rate, injection volume, and the percent of organic modifier were all tested separately using FFD to determine their effects on the pH of the mobile phase's aqueous portion. According to an ANOVA, all four variables were statistically significant. The chromatographic conditions were optimised using a central composite design (CCD) (CCD). An isocratic mobile phase of MeOH and 25 mM KH2PO4 buffer pH 3 (38.4:61.6, v/v) was used to perform the analysis on the BDS Hypersil C8 (250 4.6 mm, 5 m) column at 0.8 mL/min flow rate with UV detection at 214 nm and a 5 L injection volume. Validation of the suggested procedure was carried out in accordance with ICH standards. As a result of the adjusted circumstances, the linear ranges for levetiracetam and pyridoxine were 0.39–100 g/mL and 0.999, respectively. There was a wide range of recoveries, ranging from 95.46% to 101.14%. The precisions were less than one percent, both within and between days. In terms of predictability and robustness, the suggested approach performed well**.[32]**

17. Conclusion

Analytical Quality by Design (AQbD) plays a key role in the pharmaceutical industry for ensuring the product quality. The result of AQbD is the knowledge from product development to commercial manufacturing. Scientist can readily recognise the danger first so that quality can be enhanced. AQbD tools are ATP, CQA, Method Optimization and Development with DoE, MODR,

and Control Strategy with Risk Assessment, Method validation and Continuous Method Monitoring (CMM), and continuous improvement. AQbD involves the correct ATP and Risk Assessment and employment of relevant tools and doing the required amount of work within reasonable timescales. Validation of analytical procedures ensures that the findings provided by them are trustworthy and reliable when they are used on a regular basis. These findings are used to make critical choices, such as batch compliance and patient health monitoring. This study has shown how technique validation may be used to ensure that analytical methods offer daily data that can be effectively utilised to make appropriate judgments. To put it another way, method validation is intimately tied to the efficient use of various analytical techniques. Method validation in the context of quality-by-design (QbD) for pharmaceutical product development should be possible using the technique provided here. Use of a decision profile and unreliability region graph allows for an accurate assessment of the method's validity by reducing the possibility of false compliance. According to this concept, analytical methods for quantifying contaminants and active ingredients in pharmaceuticals or pharmaceutical products have been addressed. This method can be used with any quantitative analysis method, however. While still adhering to the present regulatory framework for method validation, this study has shown how a QbD compliant approach to validation may replace the regretfully too often checklist technique used in the past.

Acknowledgement

I am thankful to the management of School of Pharmacy, LNCT University for providing best lab facilities necessary for completion of my research. All authors listed have significantly contributed to the development and the writing of this article.

Conflict of interest

The authors declare no conflict of interest.

Funding
No Funding Required

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