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APPROCHES OF ANALYTICAL METHOD DEVELOPMENT AND VALIDATION: A REVIEW

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ABSTRACT

The development and validation of analytical method requires estimation of active pharmaceutical ingredients (API), degraded products and selection of solvents for reducing the bias errors and significantly improve the precision. It plays a critical part in risk assessment and develops a precise way of acceptance criteria regarding drug consent by regulatory authorities. During drug development there is a demand for new sensitive and accurate method development procedure for rapid analysis by quality assurance as well as quality control department. Advanced analytical instruments reduced the cost, time of study and increase accuracy, precision. The most sensitive method for qualitative and quantitative estimation for drugs is spectroscopic and chromatographic techniques. It is involved in drug discovery, production and identification of toxicity and purity of drugs. The guidelines of ICH provide the validation parameters in terms of precision, linearity and accuracy, detection limit (LOD), limit of quantification (LOQ), suitability of system and robustness. The review focused on to explain systematic approaches to develop a sensitive, accurate and specific method for analysis pharmaceutical substances and pharmaceutical products.

Keywords: Validation, ICH guidelines, chromatography, Accuracy and Method development.

INTRODUCTION

Excellent quality and purity of drug and dosage form are required for human use that can be achieved by qualitative and quantitative estimation. Chemical structure, composition and behaviour of matter study under qualitative parameter which involved in drug discovery, safety, formulation, quality control, storage etc. The development of validated new method for determining quality, efficacy, purity of drugs and their composition by the use of spectrophotometer, chromatography, and hyphenated technology of chromatography and spectroscopy[1-2] has been frequently used. Every year large numbers of drugs and drugs combinations introduced into the market. These may be partially modified of existing one, either new moiety. Most frequently there is a time space from the date of marketing of a product to its inclusion date in the pharmacopoeias. Under these conditions' pharmacopoeias do not have available criteria and analytical protocols for these pharmaceuticals. It is therefore necessary to develop analytical methods for such drugs. The Analytical methods should be developed within GMP and GLP conditions with protocols and acceptance criteria mentioned in guidelines of ICH Q2 (R1). While developing a novel analytical procedure, the selection of analytical instrumentation and methodology should be based on the proposed objective and scope of the analytical method[3].

METHOD DEVELOPMENT

The method developments are complex and expensive procedure for routine analysis of quality parameters of drug, and it may include sample preparation, preparation of reagents and standards, instrument selection, generation of calibration curve and calculations, the standard and protocols

corresponding to the reference for granting approval, authentication and registration have been set by different regulatory agencies. If any improvements are made to the validated non-standard methods, the impact of such modifications should be reported, and new validation should be carried out.[1,4]

Conditions for method development

1. The drugs and their combinations are not official in any pharmacopoeia.
2. A proper analytical procedure for drugs and their combinations may not be available in the literature.
3. Analytical procedure may not be available for the drugs in the form of formulations.
4. The existing analytical procedure may be costlier.
5. Analytical method for the quantitation of the drugs present in biological matrices may not be available.

VALIDATION

The word validation originated from Latin word *Validus*, meaning strong and indicate the approval of something which is proved to be true, useful[5].

METHOD VALIDATION

Analytical method validation is "A Documented evidence which provides a high level of assurance for fulfilling the requirement for the intended analytical applications[6].

Criteria for method validation

Following reasons for having method validation[7-8]

1. For the registration of any pharmaceutical dosage form or pesticide formulation.
2. For accreditation as per ISO 17025 guidelines.
3. For assuring the quality product.
4. For achieving the acceptance of the products by the international authorities.

For the manufacturer validation is important in the following aspects[8]

1. Understanding the process which ultimately reduces the chances of risk.
2. Decrease the risk of defect cost.
3. Decrease the risk of regulatory compliance.

PARAMETERS FOR METHOD VALIDATION AS PER GUIDELINES OF ICH[9-10]

1. Accuracy
2. Precision
3. Linearity
4. Limit of detection (LOD)
5. Limit of quantification (LOQ)
6. Specificity
7. Range
8. Robustness
9. Ruggedness

Accuracy[10-11]

Accuracy is a measurement of immediacy between the observed and standard value. It is calculated by the percentage recovery of the spiked analyte. The reported limit for accuracy for drug substance and products are respectively 98.0%-102% and 97.0%-103%.

Precision[10,12]

It represents the agreement between replicate analysis of a consistent sample, and measured in the form of relative standard deviation (RSD) of set of replicates and that should be 2% for major analytes. It is subdivided into three subcategories: repeatability, intermediate precision and reproducibility[13].

Linearity[14-15]

It is defined as the ability to obtain test results which are directly proportional to the analyte concentration present in the sample. Acceptability of the linearity data is evaluated by correlation coefficient and intercept of the linear regression line. The correlation of coefficient is considered to be>0.999.

Limit of detection (LOD)[6,8]

It is the minimum concentration of a drug which is generally detected but not necessarily quantitated. It is determined visually by signal to noise ratio, the estimation of signal to noise ratio is between 2:1 is acceptable, and limit of detection is also calculated mathematically by the using of formula of LOD=3.3x σ/s, Where, σ is standard deviation of intercepts of calibration curve and s is the slop of linearity plot.

Limit of quantification (LOQ)[6,16-17]

It is the minimum amount of drug which can be quantitated with acceptable precision and accuracy. It is determined visually by signal to noise ratio of 10:1 and mathematically expressed as LOQ=10x σ/s, Where σ is standard deviation of intercepts of calibration curve and s, is the slop of linearity plot.

Specificity[16,18]

The ability to identify the desired drug components, in the occurrence of components that may be likely to be present in the form of degradation products, impurity and excipients is termed as specificity. It measures the desired drug components are present without any interference might be present.

Range[11,19]

The range of analytical procedure is defined as the interval among the higher and lower concentration of drug, for which it has been demonstrated with sufficient degree of precision, accuracy and linearity.

Robustness[8,20]

The robustness is the ability to remain unchanged by small, but deliberate variations of the method parameters and provide an indication of its reliability, during its uses, such as changes in pH and mobile phase composition, sample temperature etc.

Ruggedness[21-22]

Ruggedness is a measure of reproducibility of result under normal, expected operational condition from laboratory to laboratory and analyst to analyst.

The ruggedness is the reproducibility of test result achieved by the analysis of the same sample under a variety of conditions.

CONCLUSION

Various drug products are launching day by day in the market for customer requirement with market race, but all of them are not having reproducible testing method so they required a precise validated and reproducible method. A reproducible, precise and economical method development, validation is the vital part of the drug discovery and pharmaceutical industry. This review provides the details parameters, which helps in developing a reproducible method regarding analysis of new drug moiety including stability studies and in addition to those having some structural changes in pre-existing drug moiety.

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