Stability Studies of Parenteral Products

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Abstract

The stability studies of parenteral products are one of the very significant criteria for the new drugs' formulation. Stability studies confirm that the quality, safety, and effectiveness of drug products are preserved all through the shelf life as an essential requirement. The stability tests must be performed subsequently according to the regulations given by the International Council for Harmonization, the World Health Organization, and/or other agencies. This chapter discusses the importance of stability studies, stability testing techniques, and specifications on stability studies with other factors. It provides a summary of the various stability study types that validate the stages of drug development. Furthermore, the chapter will discuss the framework of the ICH guidelines and also the importance of analytical techniques in the stability of parenteral products.

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15.1 What Are Parenteral Products?

Parenteral products are generally described as sterilized solutions, suspensions, emulsions, and powders for injections; these formulations are given directly into the tissue of the human body, skin, and mucous membranes by primary protection systems [1]. The word "parenteral," which is used for the preparation given through injection or infusion into one or additional skin tissue layers, is taken from the Greek term "para" and "enteron," which mean outside the gut and used for the dosage forms given by routes besides the oral route. Some drugs can only be given parenterally, specifically peptides, proteins, and several chemotherapy drugs because when given orally, they are denatured in the gastrointestinal tract. Parenteral preparation must be purified and exempt from any physical, chemical, and biological contaminations. They must be compliant with intravenous diluents, administration process, as well as additional co-administered drugs [2]. The parenteral preparations are administrated into the body by injecting, e. g., directly, bolus intravenous, intramuscular, or subcutaneous, or by infusion with a controlled rate or by direct implantation through intramuscular or subcutaneous. The different routes of administration for parenteral formulations are:

Intradermal: These are incorporated into the skin between both the dermal and the epidermal layer.
Subcutaneous: The drug is injected into the tissues between the skin and the muscles.
Intramuscular: The drug is injected deep into the muscles.
Intravenous: Drug is injected directly through the veins into the bloodstream.
Intra-arterial: Drug is injected into the artery for an immediate peripheral effect.
Intra-cardiac: The injection places the drug directly into the left ventricle.
Intrathecal: Drug is administered into the subarachnoid space of the spinal cord.
Peri-dural: Drug is injected between the dura matter and the inner aspects of the spine.
Intra-articular: Drug is injected into the synovial fluid in a joint [3, 4].

15.2 Why We Formulate These Products and What Are the Limitations?

Parenteral products are developed to avoid the most guarding barriers of the body skin and the mucosa; hence, these must be "essentially" contamination-free. Most of these are injected into body tissues and enter the bloodstream without passing through the liver. This may include injections and topical and inhalation routes [5]. Several drug products can only be administered directly via injection because

when taken orally, they become denatured in the gastrointestinal tract. Parenteral drugs are generally unstable and extremely strong, requiring strict monitoring of patient administration [6]. Parenteral formulation is used to cause localized effect, administer drugs to an insentient patient, and assure that the drug is delivered to the targeted tissues.

Parenteral preparations are distinct from other dosage forms because they are directly entered into the bloodstream. They must be aseptic and free from all kinds of contamination. Such standards put a greater responsibility on the pharmaceutical industry to follow current good manufacturing practice (cGMP) in parenteral product preparation and to pharmacists as well as other healthcare professionals to perform good aseptic practice in the administration of parenteral products to patients [7]. Although parenteral drug delivery can often be confusing and associated with concerns including a small number of suitable excipients, strict standards for aseptic manufacturing, safety concerns, and patient non-compliance, this route retains its importance due to various benefits such as the rapid onset of action in emergencies [5, 8].

15.3 Types of Parenteral Products

Parenteral products can be listed as small-volume, large-volume, and lyophilized products [9]. These are sterilized products which are delivered into the body through multiple routes, through injections, infusions, and implantations. Several types of parenteral products can be distinguished [28].

15.3.1 Injections

Injections are aseptic solution, emulsion, or suspension. Injections are formulated by disintegrating and emulsifying the active material and additional excipients either in water for injections, in a compatible clean nonaqueous solvent, or a combination of such components. The solution to be injected can contain sediments that can be readily distributed by shaking the container. Suspension should stay stable to give a homogeneous dosage when extracted from the bottle.

15.3.2 Infusions

These are aseptic aqueous solution or emulsion; typically, they are isotonic with blood and mainly designed for large-volume dispensing. Infusion does not carry added antimicrobic preservatives.

15.3.3 Concentrates for Injections or Infusions

These are aseptic solutions designed for injection and infusion upon dilution. The concentrates are diluted to a prescribed volume with the prescribed liquid before dispensing. They meet the criteria for injection and infusion when diluted.

15.3.4 Powders for Injections or Infusions

Powders for injections or infusions are solid, aseptic substances that are dispersed in their final bottles and which, upon shaking with the prescribed volume of the sterile solvent, quickly form either a transparent and particle-free solution or a homogenous suspension.

15.3.5 Implants

They are sterilized solid formulations of a size and form ideal for parenteral insertion, which release the drug for a more extended period. Each dosage is given in an aseptic bottle [10, 11].

15.4 Stability Issues

Stability is determined as the period in a certain storage environment in a particular container-closure system where the substance maintains all its original characteristics within predetermined limits. The stability is defined in US Pharmacopeia (USP, 2016) [12] as the degree to which the drug stays in defined limits and through the storage and time of utilization, with similar characteristics and qualities which it had at the time of its production [13]. The stability of parenteral products must be maintained so that the desired dosage is given to patients. Hydrolytic and oxidative drug decay is the most common form of instability, but it rarely shows as cloudiness, precipitates, or color changes. The hydrolysis rate may be altered by the storage temperature or solution's pH. Oxidation is affected by temperature, pH, light, oxygen concentration in solution, impurity, and concentration of the oxidizing substance. Other degradation types can also happen in the solution. The selected stability method should have the ability to view the breakdown products as well as the original entity. Attempts should be made to force degradation and assess the changes to the original entity. To determine stability, it must be known what instability looks like [14]. Since drug stability is affected by several factors, pharmacists should use a short beyond-use date (BUD) to compound parenteral from bulk chemicals or know from the literature that more extended stability exists. The packaging selection is also important for parenteral drug stability [15].

15.5 Stability Evaluation

Stability studies aim to set up at least three batches of drug products based on testing and analyze the stability data (comprising, where applicable, physical, chemical, biological, and microbiological study results) and a retesting time relevant to the entire later drug product batches developed within the same conditions. The variability extent of individual batches influences the assurance that the later production batch should follow the guidelines through the allocated retest time (ICH Guideline, 2003) [16, 17]. The layout of the drug product stability study should focus on the analysis of all determinants, which can lead to physical, chemical, or biological changes over the suggested storage time. Tests for the drugs and the degeneration products and assessment of pH alteration, color, and appearance should be included. The drug stability evaluation facilitates the production of safer and more effective formulation, suitable packaging selection, setting up proper storing conditions, and the allocation of shelf life [17].

15.6 Stability Testing

Stability testing is a significant element of the drug development procedure and a prerequisite for the approval of drug products. The International Council for Harmonization (ICH 2003), the World Health Organization (WHO 2009), and the Food and Drug Administration (FDA 1998, 2014) have issued the stability testing guidelines for new drug products, including long-term, medium-term, and rapid stability tests. Stability tests aim to show how the quality of drug products changes over time due to several environmental factors, e. g., temperature, moisture, and light, and to set a reset timeframe for drug products or shelf life of drugs also prescribed during storing condition [16, 17].

15.7 Chemical Kinetics Involved in the Stability Issues

Chemical kinetics analyzes the rates and factors that affect chemical reactions. The stability studies of drug products involve the analysis of drug chemical deterioration reaction kinetics in a dosage form. The shelf life of a product should be determined in specified storing conditions. Drug product has different chemical structures and under different conditions with different orders of reaction follows one or more mechanisms of degradation. The most common drug degradation reactions involve oxidation, hydrolysis, and also photolysis. Such reactions can take place when the drug product is manufactured, stored, and used. To ensure the safety of the patient, the pharmacist must be conscious of the impacts of such reactions on efficacy loss and of product toxicity development. The stability-indicating assay method (SIAM) can evaluate the degradation compounds that can also give a precise efficacy loss assessment of drug products. To assess the shelf life of a drug product and determine the expiry date, SIAM data are then put through kinetic treatment. A reassessment of

the packaging and storage condition may be required if the formulation specifications are altered to increase product stability. A clear understanding of the basic principles of chemical kinetics is required to determine the degradation reaction rate of the drug product and predict the shelf life and expiry date. The kinetic parameter can help elucidate the degradation reaction mechanism and, therefore, allow proper measures to stabilize the product [17].

15.7.1 Factors Affecting the Stability of the Parenteral Products

The drug products' physical and chemical properties are affected by multiple factors. These factors affect the stability of various dosage forms while manufacturing and storing and are defined as the external and internal factors.

15.7.2 External Factors

External factors contain temperature, sun, humidity, oxygen, carbon dioxide, as well as microbiological contamination. The use of suitable packing material and storage conditions can accommodate external factors.

15.7.3 Internal Factors

Internal factors involve pH, solvent, buffer type, particle size, and drug-drug, drug-excipient, and drug-bottle interaction. By choosing optimal formulation parameters to maintain an appropriate degree of stability, the effect of internal factors can be reduced [17].

15.7.4 Standards and Guidelines for Stability Study of Parenteral Products

In 1992 ICH Stability Testing Guidelines (Q1A) were issued, which were accepted across the ICH area, that is, the European Union, the USA, and also Japan. Other regions, such as Australia, Canada, and Switzerland, accepted the guidelines in principle. This guideline aims to demonstrate the key stability data plan for the new drug product; however, it allows ample flexibility to cover a range of empirical situations which can occur as a result of certain scientific consideration and material characteristics to be tested.

15.7.5 ICH Q1A: Stability Testing of New Drug Substances and Products

The selection of testing conditions set out in the guideline is established on a study of atmoshpheric condition effect in the three regions of EC, Japan, and the USA. The climate data can be used for calculating the average kinetic temperature in any region of the globe and dividing it into four I–IV climate zones. This guideline discusses the climate zones I and II. The concept has been developed to ensure that the stability data given to any of the three EC regions, Japan, and the USA should also apply to other two areas, mutually, given that the data is following the guideline and that the labeling conforms to national and regional criteria [16].

15.7.6 Q1B: Photostability Testing

Before ICH guidelines, protocols and instruments were not systemized or generally utilized to measure the photosensitivity of a drug product. Therefore, experts from Japan were necessary to address optimum photo sources that stimulate sunlight as well as techniques to calculate the light intensity. As a response, in November 1996, the tripartite harmonized ICH guideline (Q1B), photostability testing of new drug substances and products, was annexed to a parent stability guideline [18]. This ICH guideline has helped in strategy standardization. An overview of ICH guidelines describing specific terms in photochemistry, examining photostability analysis and photo source characterization, and also calculating the results from the source of photolysis used for photostability testing in pharmaceutical industries is given by Thatcher et al. [19]. Table 15.1 outlines the ICH guideline codes and descriptions.

Table 15.1 Codes and titles covered under ICH guidelines. (Adopted from Ref "Saranjit. S, Monika. B, 2000")

ICH codes	Guidelines
Q1A	Stability testing of new drug substances and products (second revision)
Q1B	Photostability testing of new drug substances and products
Q1C	Stability testing of new dosage form
Q1D	Bracketing and matrixing designs for the stability testing of drug substances and products
Q1E	Evaluation of stability data
Q1F	Stability data package for registration applications in climatic zones III and IV
Q5C	Stability testing of biotechnological/biological products
Q6A	Specifications: test procedures and acceptance criteria for new drug substances and new drug products – chemical substances
Q6B	Specifications: test procedures and acceptance criteria for new drug substances and new drug products – biotechnological/biological products

15.7.7 Q1C: Stability Testing for New Dosage Forms

The TH-ICH Q1C guideline was adopted during 1996. This broadens the fundamental stability guidelines for a new formulation of previously authorized drugs and specifies the conditions in which decreased stability data may be approved. This the most concise of all other ICH guidelines to date. It is because ICH authorities could not decide on the level of supporting data of identical drugs and products or the same dosage forms, which can enable producers to minimize the new formulation stability testing [16].

15.7.8 Q1D: Bracketing and Matrixing

Q1D guideline outlines the concept of decreased stability testing and gives bracketing and matrixing design description. The adoption of this strategy by authorities saves producers a large number of needless stability testing. Limited data, on the contrary, indicates a higher chance that the outcomes produced might not be large enough to maintain the anticipated shelf life [20].

15.7.9 Q1E: Evaluation of Stability Data

In February 2003, TH-ICH Q1E guideline was concluded. Q1E guide broadens the fundamental guideline by describing possible scenarios in which retest period/shelf life extrapolation over real-time data can be acceptable. It also gives an example of analytical techniques for stability data studies [21, 22].

15.7.10 Q5C: Stability Testing of Biotech Products

Since the majority of proteins and polypeptides are unstable compared with micromolecules and since assay protocols and deterioration products are distinctive, the ICH committee decided at an early stage to encourage biotech experts to establish specific guidelines for such product types. The tripartite harmonized ICH guidelines on (QC5) stability testing of biotechnological/biological products was published in November 1995 [23].

15.8 Guidelines

15.8.1 Drug Substance

Stability drug product data is an essential element of the formal stability analysis method.

15.8.2 Stress Testing

Stress testing is essential to analyze the drug substances and products in different circumstances of higher temperatures and moisture. Stress testing data can help to understand the stability profile in production, storage, distribution, and patient usage. Such testing gives insight into possible deterioration products and helps to identify the pathways for deterioration [16, 24].

15.8.3 Batch Selection

Stability test data should be given not less than three batches of drug products. The production of batches should be along the same synthetic course at a minimum pilot scale utilizing manufacturing procedure, and a technique simulating the terminal procedure can be used for manufacturing batches. The general standard of product batches used in the validated stability tests should be indicative of material quality manufactured on the production scale [16].

15.8.4 Container-Closure System

Stability tests should be performed on drug products packed into a container-closure system, which is similar to or replicates the suggested package for storage and supply.

15.8.5 Specifications

Specifications are explained in ICH Q6A and Q6B as a series of tests relating to analytical methods and the proposed terms of approval. In Q3A, the product degradation specifications for a drug substance are also addressed. Stability studies should also contain an analysis of those drug product characteristics subjected to alter amidst storage period and are anticipated to have an impact on quality and effectiveness. The tests should involve, as needed, physical, chemical, biological, and microbiological properties. The outcomes of the validation studies rely on whether and to what extent replication is to be done [16, 25].

15.8.6 Testing Frequency

The guideline suggests testing every 3 months of the first year, every 6 months of the second year, and yearly afterward. This means a total of three time points (together with starting and ending time points) are needed for accelerated and four time points for the moderate condition. Minimal three time points, with starting and ending points (0, 3, 6 months), from a 6 months' study, are suggested for accelerated

storage. Where an assumption (derived from developmental experience) which outcomes from rapid studies are potentially approach substantial change thresholds, additional testing should be done by increasing sample at the last point time or by point four in study design. A total of four time points (0, 6, 9, 12 months), with the starting and ending times points from a 12-month study, is suggested. At the same time, testing at moderate storage conditions is required due to substantial changes in accelerated storage.

15.8.7 Storage Conditions

In the ICH cycle, a number of suitable storage requirements are harmonized in zones I and II. To assess the stability of drug products, an amalgamation of temperature and moisture is essential. Besides, the guideline describes the scope of temperature and moisture parameters for storage chamber control: The temperature of the compartment should be managed within ±2 C and moisture should be within ±5% of the relative humidity. The drug products are stored at room temperature, and the guideline specifies a median temperature of 30 C/65% RH testing in this median state is required if there is a substantial change in samples that are stored for 6 months in rapid RH 40/75% condition. Significant changes are noticed for the drug product when any evaluation of rapid samples does not comply with room temperature requirements. This analysis must be done promptly in order to pull the stored samples from the chamber and to be examined immediately.

15.8.8 Stability Commitment

ICH guideline commends that stability commitment should be included in the registration application. It requires the candidate to carry out stability tests for three commercial batches following the current protocol via projected shelf life. The guideline also states that the stability method used for long-term stability commitment studies for primary batches should be constant. Thus, when there is a considerable variation in the accelerated condition of primary batches, samples of intermediate condition should be checked, and samples from three production batches of intermediate condition should be tested as well.

15.8.9 Data Evaluation

The ICH guideline suggests that the data assessment should be conducted for the submission of batches. It also explains that no systematic statistical analysis is important if data indicate any no deterioration or variation. A reason for exclusion is requisite to prove that the data set stays under the range of the method and does not indicate any specific trend over time.

15.8.10 Labeling

A storage document for labeling should be implemented following the applicable national or regional criteria. The emphasis should be on evaluating the stability of drug substances. Clear instruction should be given, where applicable, especially for drugs that cannot tolerate freezing. The time for a retest should be determined from stability data, and where applicable, the container label should have a retest date on it [16, 21].

15.8.11 Other ICH Guidelines

15.8.11.1 Drug Product

The layout of structured stability studies of a pharmaceutical product should build on the understanding of actions and characteristics of drug substances, stability studies, as well as expertise of clinical formulation study. The possible changes in storage and reasoning for the selection of properties to be evaluated in structured stability studies should be mentioned.

15.8.11.2 Photostability Testing

Photostability tests should be performed with minimum one primary drug product batch, as needed. The basic criteria for photostability tests are set out in ICH Q1B [26].

15.8.11.3 Selection of Batches

Formal stability test data should be given for a minimum of three primary batches of the drug product. The batches should be produced at a small pilot scale along the same synthetic route as the production batches by a manufacturing and processing system which replicates the final procedure, which is used for production batches. The general quality of drug product batches used in the formal stability testing should indicate the quality of the material manufactured next at commercial scale. Additional data support may be given.

15.8.11.4 Container-Closure System

Stability tests should be performed on a drug product packed into a container closure system, which is similar to or replicates the suggested package for storage and supply.

15.8.11.5 Specification

Specifications are explained in ICH Q6A and Q6B as a series of tests relating to analytical methods and the proposed terms of approval: test procedures and acceptance criteria for new drug substances and new drug products, chemical substances (Q6A), and drug products, biotechnology/biological products (Q6B). In Q3A, the product degradation specifications for a drug substance are also addressed. Stability studies should also contain an analysis of those drug product characteristics which

are subject to alter amidst the warehouse period and are anticipated to have an impact on quality and effectiveness. The tests should include, as needed, physical, chemical, biological, and microbiological characteristics. The outcomes of validation studies rely on whether and to what extent replication is to be done [25].

15.8.11.6 Testing Frequency

The test frequency should suffice to evaluate the stability profile of the drug product in long-term studies. For drugs with a recommended retest minimum period of 12 months, testing should usually be every 3 months of the first year, every 6 months of the second year, and yearly afterward. This means a total of three time points (together with starting and ending time points) is needed for accelerated and four time points for the moderate condition. Minimal three time points, with starting and ending points (0, 3, 6 months), from a 6 months' study, is recommended for accelerated storage. Where an assumption (derived from developmental experience) which outcomes from rapid studies are potentially approach substantial change thresholds, additional testing should be done by increasing sample at last point time or by point four in study design. A total of four time points, with the starting and ending time points (0, 6, 9, 12 months), from a 12-month study, is suggested. At the same time, testing at moderate storage conditions is required due to substantial changes in accelerated storage.

15.8.11.7 Storage Conditions

The drug product should generally be assessed within storage condition (with suitable tolerance) that evaluates its thermal stability and also moisture sensitivity, where necessary. Long-term testing should comprise at least 12 months for a minimum of three primary batches at the time of submission and should be extended for some time sufficient to cover the planned retest period. If required, supplemental data obtained through the evaluation of application registration can be given to the authorities.

15.8.11.8 Stability Commitment

If long-term stability data for primary batches do no incorporate the suggested retest timeframe upon approval, to develop a firm retest period commitment shall be made to pursue post-approval stability studies. A commitment after approval is deemed needless when the submission requires long-term stability data for three production batches comprising the suggested retesting duration. Therefore, one of these obligations should be met:

If data from stability studies for a minimum of three production batches are included in this submission, a commitment to perform these studies during the recommended retest period should be made. If the submission contains stability study data from less than three batches, a commitment to continue these studies during the recommended retest period should be made, and add supplementary production batches to a total of three batches to a total of at least three batches, on long-term stability studies during recommended retest period.

15.8.11.9 Evaluation

The approach for interpreting the quantitative attribute data expected to alter over a period is to measure the time at which a 95% unilateral dependence limit for the average curve crosses the acceptance criteria. If the data show a high batch-to-batch variation, the data should be merged into a cumulative estimate, and it is desirable to merge the data into a total estimate. It can be undertaken by implementing suitable statistical tests first, such as p values with a significance level higher than 0.25 at regression line slope and zero time intercept for each batch. If combining the data of several batches is not appropriate, the average retest cycle should be based upon the least time that the batch can anticipate to stay under the acceptance criteria. The type of any deterioration association would decide if the data should be converted to linear regression analysis. In general, the association can be expressed by a linear, quadratic, or cubic form on a + 6 arithmetic scale. Statistical methods should be used to check the data quality of all batches and mixed batches (if applicable) of the expected deterioration curve. Restricted real-time data observation from a long-term storage condition above the range identified to broaden the retest duration may be performed at the time of approval if appropriate. For example, the reasoning should build on what has been known regarding the deterioration process, test result within the accelerated condition, quality of the mathematical model, batch size, or supporting stability data. Nevertheless, such observation implies that the same deterioration relation would be applied further than identified data. The analysis should comprise not just the test but also the extent of the deterioration product and other relevant parameters.

15.8.11.10 Labeling

A storage document for labeling should be implemented following the applicable national or regional criteria. The statement should focus on evaluating the stability of drug substances. Specific instruction should be given, where applicable, especially for drugs which cannot tolerate freezing. The time for a retest should be determined from stability data, and where applicable, the container label should have a retest date on it [16, 21].

15.8.12 Analytical Techniques for Stability Studies of Parenteral Products

Analytical techniques, from drug development to marketing and post-marketing, play an essential role to determine the drug's physical and chemical stability, evaluating the stability of drug molecules, indicating the drug's stability in the formulation and thus the shelf life particularly, and signaling the presence of the substance in its pure form or the existence of any contaminants (either as a drug precursor or degradation product as a result of chemical/photochemical effects). This can be done by using the stability-indicating assay method like high-performance liquid chromatography (HPLC), for the evaluation of preserved substance but also its degradation product. To achieve the required specification of a specific system,

the process should be validated. The stability of drug products produced in many dosage forms and kept in distinct packing can also be assessed with variable strengths [17, 27]. When presenting and evaluating the stability data, a structured approach should be followed that should include physical, chemical, biological, and microbiological test characteristics if required. All product characteristics, for example, assay value or effectiveness, the decomposition product material, and physicochemical properties, probably influenced by storage, should be determined. To determine if these additives stay active and stable across their anticipated shelf life, test methods for demonstrating the effectiveness of additives, for instance, antimicrobial agents, should be used. Analytical methods should be verified, and both accuracy and precision should be noted (standard variations). The test methods selected should be indicative of stability. The tests should be checked for related compounds or degradation products to indicate their specificity and their sufficient sensitivity to the product being tested [17]. The following chemical and microbiological tests are typically performed for the final products to ensure that each of the following criteria for a parenteral product is properly met.

Chemical testing involves:

(i) Identification test for the pharmaceutically active ingredient
(ii) Potency assay
(iii) Calculation of deteriorating product or impurities relating to the process
(iv) pH
(v) Osmolality
(vi) Appearance (color testing)
(vii) Assay for the contents of essential excipients and their main degradation products (e.g., dextrose and 5-hydroxymethylfurfural and ethanol)
(viii) Suspension and emulsion particle size distribution
(ix) Water content for lyophilized dosage forms

Microbiological testing includes:

(i) Sterility test
(ii) Microbial endotoxin test
(iii) Particulate matter test
(iv) Bioburden analysis (bulk)
(v) Container/closure solidity [9]

15.8.13 Advantages of Analytical Techniques

Modern analytical techniques provide the following advantages:

(i) Proper identification of drugs in bulk form or as a manufactured product
(ii) Indicate the proportion of the specified material of drug in formulation within a specified limit

(iii) Determine the drug's stability in the formulation and thus the shelf life particularly, the presence of the drug in its preserved form, or the presence of any contamination (as drug precursor or decomposition product because of chemical/photochemical factors)
(iv) Usage in the study of dissolution rates, i.e., at what speed the drug is released from its formulation for absorption into bloodstream (bioavailability studies)
(v) Confirm that the specification and sterility of drug (bulk form) fulfill official standards and monographs
(vi) Confirm that the specification and sterility of excipients used in formulation fulfill official standard criteria
(vii) Indicate the concentration of identified contaminants in the pure drug substance [28].

15.8.14 Disadvantages of Analytical Techniques

(i) Instrumental techniques are expensive due to cost and maintenance, and trained staff is needed for handling.
(ii) Sensitivity and precision rely on the instrument type.
(iii) The outcomes must often be checked using other techniques.
(iv) The instrumental approach might not be accurate in a particular situation.

15.9 Conclusion

Parenteral products are sterile products that are designed for direct administration into the systemic circulation of humans or animals. This chapter gives an understanding of stability studies and issues involved in instability testing and its importance. The stability studies have made the critical methodological contribution to the new drugs as well as new formulation development program, and it became easy to predict the shelf life and the effect of environmental factors for the product degradation. Any variation in the defined stability profile can affect its quality, safety, and efficacy. Stability tests are performed to add suggested storage and shelf life conditions to the label, and it is safe and efficient during its shelf life. They should comply with the pharmaceutical quality standards depicted in different pharmacopeias and ICH guidelines, assure clinical tolerance, and be safe for the desired use.

Conflicts of Interest The authors declare no conflict of interest.

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