Original Article

Documentation Of Various Pharmaceutical Dosage Forms According To Ich Guidelines

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Abstract

This study describes the documentation required for various dosage forms according to ICH Guidelines. The main aim of the documentation to increase the productivity and profits of pharmaceutical products and minimize the loss of investments. The document is help in planning, controlling, and co-coordinating of the material and production management in any firm. They are also help to increase the planning. The various dosage form included are tablet, capsule, creams, ointments and ophthalmic preparations. The various documentation involved according to ICH guidelines are Quality control test, BFR, MFR etc... By viewing this study, the documentation procedure is clear, ambiguous according to ICH guidelines.

Key words: Documentation, ICH guidelines, tablet, capsule, creams, ointments and ophthalmic preparations.

DOCUMENTATION

Documentation is a vital component of successful processes of production. It creates an information and control structure to minimise the risk of misunderstanding and/or misunderstanding in oral communication. As a consequence, the quality and coherence of all products and services is enhanced by clear and explicit instructions to be followed, including legally necessary active pharmacological substances by persons responsible for particular tasks.[1]

PRINCIPLE

Documentation is an important component and should be applied in all parts of GMP in the quality assurance system. Its aim is to define all the manufacturing and control materials and methods specifications and processes, ensure that all manufacturing staff know what to do and when to do so, ensure that all the information necessary to decide whether to produce a drug batch for sale is available to authorised persons and ensure that there are documented evidence; traceability; It ensures that the information necessary to validate, examine and analyse the data is available. The design and usage of the document is based on the information and control system of the manufacturer, which lowers the risk of misinterpretation and/or error in spoken communication. The consequence of this is to increase the quality and consistency of all goods and services by providing clear, unequivocal instructions for those involved in specific activities, including active pharmacological substances, which are legally necessary.[2]

OBJECTIVE

1.The construction and the premises All the components of pharmaceutical production that need proper documentationneed to be installed, validated, cleaned and upkeep.
2. Staff: training, sanitation, etc.
3. Installed, calibrated, validated, maintained and cleaned equipment[3]

D represents design, development, differences, dossiers, Drug Master Files, and distribution records for both regulated markets.
O= Operational and non-specific operating procedures, techniques and methodologies (OOSs) (OOT)
Cleaning, calibration, checks, complaints and containers, contamination and the control of changes are all letters for cleaning, calibration, checks, complaints, contamination and the control of change.
U= user needs, water systems, hydrocarbons, hydrocarbons and so on.
M stands for human beings, equipment, machinery, processes, maintenance, production and monitoring activities, master formulas, handbooks (quality, safety and environment) and health records.
E Engineering controls, environmental controls and qualifying documents for equipment are all abbreviated as E.

N stands for non-standard activities, new goods, and substances.
T stands for technology transfer, training, and testing, as well as trend analysis and technical dossiers.
S SOPs, safety practices, hygienic, larder, self-inspection, standardization, supplier qualification, specifications and standard test methods, and the site master file are all acronyms for standard operating procedures. (Quality Control) [4]

MASTER FORMULA RECORD

A master formula record is a yield -specific credentials that has been compiled, checked, authorised, and permitted by qualified technical professionals from several organisations. But, as necessary and appropriate, functions like as research, production, packaging, and quality control are intertwined.
The master formula record, like any other piece of paperwork, should be open to scrutiny. Any changes, if any, must be approved by the designated personnel in charge of manufacturing and quality control.[5]

BATCH MANUFACTURING RECORD

A bunch of production record is a result and collection –unique document that provides a complete and reliable picture of each product's manufacturing history.
Batch manufacturing records must be unite, examined, legalized, and authorised by a competent technical person in charge of production and quality control, and must be based primarily on the master formula record. To avoid transcribing errors, photo reproduction or another system (e.g. computer printouts) should be used, provided that suitable protections are in place to prevent unauthorised re-production.

LABORATORY CONTROL RECORDS

To ensure compliance with set specifications and standards, laboratory control records should incorporate complete data produced from all tests completed, including examinations and assays, as follows:

- A presentation of or reference to each test technique used
- A Characterization of samples obtained for examining, including the object label or source, batch number in turn farther distinguishing code, date sample was taken, and, where appropriate, the quantity and date the sample was received for testing;
- A statement of the sample weight or measure used for each test as indicated in the method; data on or cross-reference to the fabrication and testing of reference standards, reagents, and standard solutions;
- A comprehensive transcript of all raw measurements generated during each test, as well as graphs, charts, and spectra from laboratory apparatus, all of which are appropriately labelled to reflect the precise item and batch tested.[6]

ICH GUIDELINES USED IN PHARMA INDUSTRY

The International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) is solitary in that it brings regulatory agencies and the pharmaceutical industry together to debate scientific and technical aspects of pharmaceuticals and establish ICH standards.
Q1E – Stability Data Evaluation Q1 (R2) – New Drug Substances and Product Stability Testing
Stability Testing (Q1 B) Q1A: New Drug Substances and Product Photo Stability Testing
Q1C – New Dosage Forms Stability Testing
Q1D – Bracketing and Matrixing Designs for Stability Testing of New Drug Substances and Product
Q1F – Stability Data Package for Registration Application in Climatic Zones III and IV
Q2 (R1) Validation of Analytical Procedures: Text and Methodology
Q3A (R2) – Impurities in New Drug Substances
Q3B (R2) Impurities in New Drug Products
Q3C (R5) Impurities: Guideline for Residual Solvent
Q3D – Impurities: Guideline for Elemental Impurities
Q4A – Pharmacopeial Harmonisation

The pharmacopeial esteem , working well-balanced through the Pharmacopeial Discussion Group (PDG), have been firmly involved with the work of ICH since the outset and harmonisation between the extensive pharmacopoeias, which started before ICH, has proceeded in parallel.

Q4B – Evaluation and Recommendation of pharmacopeial Text for use in the ICH Regions
Q4B Annex 1(R1) – Residue on Ignition /Sulphated Ash General Chapter
Q4B Annex 2(R1) – Test for Extractable Volume of Parenteral Preparation General Chapter
Q5A(R1) – Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin
Q5B – Quality of Biotechnology Products
Q5C – Quality of Biotechnology Products: Quality of Biotechnological
Q5D – Derivation and Characterisation of Cell Substrates used for Production of Biotechnological/Biological Product
Q5E – Comparability of Biotechnological/Biological Products Subject to Changes in their Manufacturing Process
Q6A – Specifications: Test Procedure and Acceptance Criteria for New Drug Substances and New Drug Products
Q6B – Specifications: Test Procedure The pharmacopeial authorities, working together through the Pharmacopeial

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Q5E – Comparability of Biotechnological/Biological Products Subject to Changes in their Manufacturing Process [7]
Q6A – Specifications: Test Procedure and Acceptance Criteria for New Drug Substances and New Drug Products
Q6B – Specifications: Test Procedure

METHODOLOGY

The documentation's major goal is to maximise pharmaceutical product production and revenues while minimising investment losses. The document is useful for material and production management planning, control, and coordination in any company. They also aid in the improvement of planning.

DOCUMENTAL OBJECTIVES:

To specify the requirements and processes for all materials, manufacturing methods, and quality assurance.
To ensure that everyone involved in the manufacturing process knows what to do and when to do it.
To ensure that authorised individuals have all of the information they need to decide whether or not to proceed.[8]

AS PER THE ICH GUIDELINE, A DOCUMENT IS REQUIRED FOR A SOLID DOSAGE FORM.

Documentation System And Specifications:

Written procedures should be followed to produce, examine, approve, and distribute all documentation relevant to the creation of intermediates or APIS. These materials can be printed or stored electronically.
All documents should be regulated through the use of revision history to track their issue, revision superseding, and withdrawal.
A procedure for archiving all relevant papers should be devised. These papers should have their retention durations defined.

Cleaning And Use Records For Major Equipment:

Records of significant equipment utilisation. Cleaning, sanitization, and/or sterilisation and maintenance records should include the date, time (if applicable), product, and batch member of each batch processed in the equipment, as well as the name of the person who cleaned and maintained the equipment.[9]

Master Production Instruction:

The following are the master production instructions (also known as the master production and control records):
To achieve batch-to-batch consistency, master production instructions for each intermediate ad API should be created, dated, and signed by one person and checked, doted, and signed by a person in the quality units.
The name of the intermediate or API being created, as well as an identifying document reference code, if appropriate, should be included in the master production instructions. A comprehensive inventory of raw materials and intermediates, each with a name or code that is specific enough to identify any unique quality attributes.[10]

Batch Production Records (Also Known As Batch Production And Control Records) Include The Following:

For each intermediate and API, batch production records should be created, which should include all relevant information about the batch's production and control. Before issuing the batch production record, double-check that it is the correct version and a legible precise reproduction of the suitable master production instruction. If a distinct component of the master document is used to create the batch production record. A reference to the current master production instruction should be included in that document.
When issued, these records should be numbered, dated, and signed with a unique batch or identification number. Until the final number is assigned, the product code, along with the date and time, can function as a unique identification in continuous manufacturing.[11]

TABLET DEFINITION:

Tablets are solid drug delivery systems made by compressing one or more active therapeutic substance(s) with some additives/pharmaceutical excipients into a single dose. They can be circular, oblong, oval, triangular, or cylindrical in shape, and their faces can be flat, round, concave, or convex, with straight or bevelled edges.

TABLET EVALUATION TESTS:

Weight fluctuation, disintegration, dissolution, and drug content are all official tests.
Hardness and Friability are two non-official tests.

Weight variation test is an official test (uniformity of weight) [14]
Weigh 20 tablets at random. Each one should be weighed separately. X1, X2, X3, X4, X5, X6, X7, X8, X9, X10,
Calculate the average weight using the formula X=(X1+X2 +X3+...+ Xz)/20.
Formula: Average Tablet Weight - Individual Tablet Weight / Average Tablet Weight * 100
Upper limit: average weight + (average weight * percent error), lower limit: average weight − (average weight * percent error). Individual weights are compared to upper and lower limits, and NMT two tablets depart from the average table weight. Tables No. 1 and 2 show the results of the weight variation test using USP XX-NF STANDARDS and IPSTANDARDS.

TEST FOR CONTENT UNIFORMITY:

Choose 30 pills at random. NLT 85 percent and NMT 115 percent of the listed drug content were found in 10 of these tablets, with the 10th tablet containing no less than 75 percent and no more than 125 percent of the labelled content. If these parameters aren't met, the remaining 20 tablets will be tested individually, and none of them will fall beyond the 85 to 115 percent range. [15]

Test For Disintegration (U.S.P.)

It is the time it takes for the tablet to disintegrate into particles; the disintegration test only measures the time it takes for a batch of tablets to disintegrate into particles under a certain set of conditions. It is used to determine the disintegration of a tablet over a specific time period.
The controlled and sustained release pills are not subjected to a disintegration test. The tablet must crumble and all particles must pass through the 10-mesh screen in the time allotted, according to the test. If any residue remains, it must be delicate in texture. The disintegration test was carried out using a disintegration equipment (Figure No.2).

Media Of Disintegration:

The disintegration test was carried out in a variety of media, including water, simulated gastric fluid (pH = 1.2 HCl), and simulated intestinal fluid (pH = 7.5, KH2PO4 (phosphate buffer) + pancreatic enzyme + NaOH). Conditions and Interpretation of Disintegration Testing were presented. Table No. 3:
Disintegration Test for Uncoated, Coated and Enteric Coated Tablets U.S.P. method for uncoated tablets
Uncoated, coated, and enteric coated tablets undergo a disintegration test. For uncoated tablets, use the USP procedure.
Six pills were disintegrated in a test. Repeat the test on another 12 pills if one or two of the six tablets fail to decompose fully after 30 minutes. (In other words, the entire test will take 18 pills). NLT 16 tablets dissolve perfectly in a short period of time. The batch must be rejected if more than two pills (out of the 18) fail to dissolve.

Tablets With A Coating:

For 5 minutes, soak the tablet in purified water. Place the tablet in the device and soak it in water or HCL for 30 minutes at 37 degrees Celsius (according to the U.S.P). Put in intestinal fluid if it hasn't decomposed.

U.S.P. And B.P Method For Enteric Coated Tablets:

For one hour, the tablet was immersed in simulated stomach fluid (0.1M HCL). Then, for two hours, inject synthetic intestinal fluid. Repeat the test on another 12 tablets if one or two pills fail to dissolve. As a result, 16 of the 18 tablets should be totally disintegrated. The Batch must be rejected if more than two fail to dissolve.

TEST OF DISSOLUTION:

The purpose of dissolution was to determine the percentage amount of release dosage forms. Tablet, for example. In the dissolving media, small tablet particles with the most surface area are used. The disintegration research did not show that the particle would release the medicine into solution at the acceptable pace, which is why dissolution tests were performed for all tablet products, as well as its characteristics. The process of dissolution is one of mass transfer. Dissolution is mostly determined by the drug's water solubility. It is a procedure that involves the transfer of solid material into a liquid medium.[12]

Dissolution Is Based On Four Different Processes, Including:

Solubility In Water
Diffusion
Swelling

The size, shape, and surface area of the particles are all key factors that influence the rate of drug dissolution. As aqueous solubility rises, so does the rate of medication dissolution. The dissolution test was carried out in a dissolution device (Figure No.3). [16]
The word "dissolution test" is used in a variety of ways.

Dissolution

Process of transferring solid mass to a liquid medium.

Diffusion
Diffusion is the mass transfer process of individual molecules of atoms that are contained in a concentration gradient and have a continuous random molecular motion.

Dialysis
Through a semipermeable membrane, easily diffusible particles are separated from weakly diffusible particles.

Ultra-Filtration
Colloidal and sub-colloid particles are separated using a semi-permeable membrane.

Osmosis
Solvent molecules flow through a semipermeable membrane into solution.semi

Semi Permeable Membrane
A thin layer capable of separating two phases.

Consistent Sate
Per unit time, the mass transfer process remains constant.

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Per unit time, the mass transfer process remains constant.

Osmotic Pressure
Through a concentration gradient, pressure is applied to the walls of a semipermeable membrane.
The amount of material transported in a semipermeable membrane is called diffusant (penetrant).

Con. Gradient
Material transit concentration in a high-congested area. To a low-con area.[13]

DOCUMENT FOR CAPSULES ACCORDING TO ICH GUIDELINES
DEFINITION OF CAPSULES:
Capsules are solid dosage forms with either hard or soft shells. They come in a variety of shapes and sizes, and each one contains one or more active substances in a single dose. They're designed to be taken by mouth.

Gelatin or other substances are used to make capsule shells, and the consistency of these shells can be changed by adding glycerol or sorbitol.

When excipients are included, they must not have an unfavourable effect on the active ingredient (stability,)'s dissolving rate, bioavailability, safety, or efficacy; there must be no incompatibility between any of the dosage form's components.[14]

The following are the different types of capsules:
– hard capsules
– soft capsules
-- Capsules with a modified release

TEST FOR DISINTEGRATION
The Disintegration Test for Tablets and Capsules is met by hard capsules. Unless the individual monograph specifies hydrochloric acid (0.1 mol/l) VS, use water as the immersion fluid. Examine the status of the capsules after 30 minutes of operation using the device. If the capsules float, use a disc as specified in the Suppositories Disintegration Test.

SOFT CAPSULES
Definition
Antimicrobial preservatives are generally added to soft capsules, which have thicker shells than hard capsules. The shells are one-piece and come in a variety of forms. Soft capsules usually contain non-aqueous liquid solutions or suspensions of the active ingredient(s).[15]

MODIFIED-RELEASE CAPSULES
Definition
Modified-release capsules are hard or soft capsules in which the contents, shell, or both contain additives, excipients, or are prepared by special procedures such as microencapsulation, which are designed to modify the rate, place, or time of release of the active ingredient(s) in the gastrointestinal tract, either separately or together.

Sustained Release Capsules

Definition of sustained-release capsules (also known as extended- or prolonged-release capsules).
The active ingredient(s) in sustained-release capsules are released at a slower pace in the gastrointestinal tract.
Individual monographs detail the requirements for these unique dosage formulations.
Delayed release capsules (gastro-resistant/enteric capsules)

Definition

Delayed-release capsules are hard or soft capsules designed to resist the action of gastric fluid while releasing the active ingredient(s) in the presence of intestinal fluid.[16]

Manufacture

The same assertions that apply to hard or soft capsules also apply to delayed release capsules.
Test for disintegration
When using hydrochloric acid (0.1 mol/l) VS as the immersion fluid, delayed-release capsules pass the 5.3 Disintegration test for tablets and capsules. Unless specifically mentioned in the individual monograph (but in any instance, operate the device for 2 hours), and look at the capsules to see how they're doing. Any capsule that shows evidence of disintegration or rupture, allowing the contents to escape, should be avoided. Where indicated in the individual monograph, replace the acid with phosphate buffer solution, pH 6.8, TS with additional pancreatin R. Examine the status of the capsules after 60 minutes of operation.

NON-OFFICIAL TESTS

Hardness

Tablets with a certain hardness or strength and resistance to friability that can survive mechanical shocks during manufacturing, packaging, and delivery. The strength of crushing a tablet is measured by its hardness (Figure No.7).
Importance Determine whether or not the tableting machine's pressure has to be adjusted. Hardness can effect disintegration, and if the tablet is excessively soft, it will break during further processing, such as coating or packaging. In general, we undertake a disintegration analysis before rejecting a batch because of its maximal hardness. Accept the batch if the disintegration is within acceptable limits.

Friability

Take a sample of whole tablet corresponding to 6.5 gm in a friability study of tablet with unit mass equal to or less than 650 mg, according to the US Pharmacopeia. Take a sample of 10 tablets with a unit mass greater than 650 mg. Friability of a tablet can be determined in a laboratory by spinning a friability test device at 25 rpm for 4 minutes and dropping the tablets into a friabilator at a distance of six inches.[17]

EVALUATION OF PRECOMPRESSIONAL CHARACTERISTICS OF TABLETSOR RHEOLOGICAL CHARACTERISTICS OF GRANULES PARTICLE SIZE AND SHAPE DETERMINATION

Surface Area

If required, particle size is determined, and surface area is calculated from this. Gas absorption and air permeability are the most commonly utilised methods.
A. Gas is absorbed as a monolayer on particles in the gas absorption method, which is computed and converted to surface area.
The rate at which air permeates a bed of powder is used to compute the surface area of the powder sample in the air permeability method. [18]
Angle of Repose
It is calculated using two methods: static angle of repose and dynamic angle of repose. Figure 9 shows various methods for determining angle of repose, as well as acceptance limits for angle of repose stated in Table No.5. tan = h/r is the equation.
Were, an is the angle of repose, h is the height of the pile, and r is the radius of the pile.

Hausners Ratio

The Hausner's ratio is useful for detecting particle interparticulate friction and powder flow properties. If a powder with low specific friction, such as coarse spherical, has a Hausner's ratio of about 1.2, but powders with higher ascohesiveness and less free flow, such as flaks, have a Hausner's ratio of more than 1.6.

Hausner's Ratio Formula.

Bulk density / tapped density

Moisture Level

The granules usually have a moisture content of 2%. It is essential for the binding of powder or granules in the die cavity during compression. Moisture Balance or IR Balance are used to calculate the percentage of moisture. The moisture content of a tiny sample taken from the oven and placed in the moisture balance.

After the IR lamp is turned on, the moisture in the granules is evaporated via heating, and the reading is recorded. percent of moisture is calculated by, percent of moisture is calculated by, percent of moisture is calculated by, percent of Initial weight - Final weight / initial weight X 100 = Moisture content[19]

Compressibility Index

It is proportional to the relative flow rate, particle size, and cohesiveness. It is a simple, quick, and widely used method of determining powder flow characteristics. The percent Compressibility index can be calculated using bulk density measurements. Acceptance threshold In Table No.6, the compressibility index was presented.
% Compressibility index = Tapped density - Bulk density / Tapped density X 100.

SEMI SOLID DOSADE FORM DOCUMENT ACCORDING TO ICH GUIDELINES

Creams: -

Creams are easily absorbed into the skin due to their high water content. This makes them appropriate for treatment locations with a large number of patients. At the same time, if you have dry skin, rashes, or skin lesions, the oil content is beneficial because the cream stays on the surface of your skin to protect against moisture loss. Creams are often sold in jars as daily moisturisers. Hydrocortisone for bug bites and rashes, for example, may come in tubes for more accurate application.[20]

Ointments

Ointments have the highest oil concentration of any skin product. They're designed to have an occlusive effect, meaning they stay on top of the skin rather than being absorbed immediately away. This provides additional protection against moisture loss as well as factors such as dry air. Mineral oil and lanolin are common constituents in ointments. Topical drugs, such as antibiotics for infections or corticosteroids for psoriasis, may be better absorbed in ointment form since they don't evaporate off the skin. Due to the same benefits, moisturisers in ointment form may assist extremely dry skin.

Creams are classified as follows: -
Creams are divided into groups based on their purpose. They are as follows:
1. Creams for cleansing and cooling.
2. Vanishing Creams and Foundations
3. Message and Night Creams
4. Creams for the hands and body.
5. Cleansing and Cold Creams are all-purpose creams.

Ointments are classified as follows:-
1.hydrocarbon bases
2.absorption bases
3.emulsion or water removable
4.water soluble bases[21]

QC TESTS FOR OINTMENTS AND CREAMS INCLUDE THE FOLLOWING:

1. Physical Appearance: -

For the physical appearance of ointments and creams, the following characteristics must be evaluated: •Emulsion cracking (separation of oil and water phase) •Development of granular or lumpy appearance •Marked changes in viscosity •Crystal growth •Gross microbial contamination

2. Determination Of Particle Size:

Using an equivalent amount of glycerol or liquid paraffin, dilute a reasonable amount of the preparation (as specified in monograph). Place the mixture on a slide and view it under a microscope with a high resolving power. Count the number of particles with a diameter more than or less than the monograph's set limit.

3. Weight Variation Test:

Remove any labels that may cause weight fluctuation. Clean the outer surface well, dry it, and weigh each unit separately. Cut the lateral section of the containers, remove the contents by washing them, dry them, and weigh each unit and its parts. Calculate the contents' average weight.

4. Solubility Test:

The contents should have Alcohol, ether, and chloroform should all be miscible with the contents.

5. Viscosity Determination:

Viscosity must be determined according to the specific monograph's instructions

6. Active Content Assay: -

Active content assay should be done according to the official monograph, and the percentage should be within the official limits.

7.Ophthalmic Ointments Containing Metal Particles: -

Melt the contents of 10 tubes in 60mm Petri dishes one at a time. Cover the plates and bake for 2 hours at 85°C. Allow each to cool and solidify at room temperature. Invert the Petri dish onto a microscope stage that has a 30x magnification and a calibrated eye piece micrometre. Direct an illuminator from above at a 45-degree angle in addition to the typical light source. Look for metal particles at the bottom of the Petri dish.[22]

OPTHAMALIC PREPARTION DOCUMENTATION IN ACCORDANCE WITH ICH GUIDELINES

Ophthalmic preparations (eye preparations) are sterile liquid, semi-solid, or solid preparations with one or more active medicinal ingredient(s) for use on the conjunctiva, conjunctival sac, or eyelids.

STERILIZATION TECHNIQUES

Visual Examination

Examine any ointments, watery or oily solutions, suspensions, or emulsions you have. Changes in hue and odour can indicate physical and/or chemical instability.

VERIFY STERILITY

Size Of The Particles

The following test is performed on ophthalmic preparations that contain dispersed solid particles.
Place a quantity of the preparation in a counting cell or distribute thinly on a slide that corresponds to at least 10g of solid active ingredient (shake the container slightly if necessary). Cover the sample with a cover-glass and scan the entire area under a microscope. 1

Containers

The materials used to make containers and closures should not degrade the quality of the preparation or enable any form of diffusion into or across the container's material into the preparation. The container should be equipped with a microbial-resistant closure and a mechanism that indicates whether the container has ever been opened.

Labelling

The labelling criteria established by Good Manufacturing Practices must be followed by all pharmaceutical preparation
The label should provide the following information:
Wherever possible, International Nonproprietary Names (INN) should be used; the name of the pharmaceutical product; the name(s) of the active ingredient(s);the active ingredient(s) concentration(s) and the amount or volume of preparation in the container the manufacturer's batch (lot) number; the expiry date, the utilisation period, and, if applicable, the date of manufacture; any special storage conditions or handling precautions that may be required; the period of use after opening the container; directions for use, warnings, and precautions that may be required;

Storage:

When maintained at the temperature specified on the label, ophthalmic medicines should preserve their integrity throughout their shelf life. Individual monographs may provide special storage advice or constraints.[23]
Specifications for several types of ophthalmic preparations

OPHTHALMIC DROPS

Ophthalmic drops (eye drops) are sterile aqueous or oily solutions, suspensions, or emulsions that are applied to the conjunctival sac.
When inspected under ideal conditions of visibility, ophthalmic drops should be clear and practically devoid of particles.
In the production of aqueous ophthalmic drops, "water for injections" should be utilised.
The necessity for isotonicity, a certain buffering capacity, the required pH, the addition of antibacterial agents and/or antioxidants, and other factors must all be carefully considered while making aqueous ophthalmic drops. Ophthalmic drops are considered isotonic when the tonicity is equal to that of a 0.9 percent solution of sodium chloride. The eye can usually tolerate solutions equivalent to 0.5-1.8 percent of sodium chloride.[24]

Visual Examination

Evidence of physical instability is demonstrated by the formation of agglomerates or precipitates in aqueous solutions (suspensions) that do not disperse when the solution is shaken gently.
Ophthalmic ointments
Ophthalmic ointments are sterile, homogeneous, semi-solid preparations intended for application to the conjunctiva or the eyelids.

Inspection of organoleptic properties
The following are examples of physical instability:
A significant change in consistency, such as excessive "bleeding" (liquid separation) or the production of agglomerates or grittiness;

- discolouration;
- emulsion disintegration;
- crystal formation;
- shrinking as a result of water evaporation; or
- evidence of microbial development
- uniform consistency

The consistency of ophthalmic ointments should be consistent. There should be no solid components visible while rubbing a sample on the back of the hand.

Containers

Ophthalmic ointments are usually packaged in tiny, sterile tubes with a tamper-evident applicator. The tubes' containers or nozzles are shaped in such a way that the ointment can be applied without polluting the contents of the tube. The amount of preparation in such a container is limited to no more than 5 g. Single-dose containers that are suitable for this purpose can also be utilised.

OPHTHALMIC PHARMACEUTICAL UNIVERSAL TESTS

Description

This test, sometimes known as appearance on a specification, is a qualitative assessment of ophthalmic medicines. A specification might say, for example, that ophthalmic preparations are described as follows: Preparation of transparent/opaque materials, correct labelling, and imprinting with the word ‘‘Rx"

Identification

The goal of an identification or identity test in ophthalmic pharmaceuticals is to confirm the identity of the active pharmaceutical ingredient (API). This test should be able to distinguish between chemicals with similar structures that are likely to be found together.

Assay

This test, often known as a content test, determines the strength or content of the API in ophthalmic medications.
Impurities
This test detects the presence of any component that isn't an ophthalmic pharmaceutical's API or excipient. Related compounds, which are processed impurities from novel drug substance manufacturing, API degradation products, or both, are the most common type of impurities tested.

PHARMACEUTICAL OPHTHALMIC PREPARATIONS QUALITY CONTROL PARAMETERS

QC testing of ophthalmic medications is a necessary step in ensuring their safety and effectiveness. The following are QC tests for ophthalmic medications based on pharmacopeial standards and specifications:

PH

The pH of ophthalmic medicines has a crucial role. The pH of normal tears is around 7.4 and they have some buffering capacity. Many ophthalmic medications, such as alkaloidal salts, have a low buffer capacity and are weakly acidic. When only 1 or 2 drops of a solution containing them are injected into the eye, the tears' buffering activity is usually sufficient to elevate the pH and protect the eye.

Isotonicity

The phrase isotonic refers to a tone that is equal in volume. When the effective osmole concentration of one solution matches that of another, the solution is said to be isotonic. When the concentration of solutes outside the cell equals the concentration of solutes inside the cell, the solutions on either side of the cell membrane are said to be isotonic. Because there is no concentration to prevent noticeable discomfort, the cell does not expand or shrink in this circumstance. pH levels can range from 3.5 to 8.5. Some medicines, such as pilocarpine hydrochloride and epinephrine bitartrate, are more acidic and put the lacrimal fluid's buffer capacity to the test. An ophthalmic solution should ideally have the same pH, At this pH, most alkaloidal salts precipitate as free alkaloids. Furthermore, several medications are chemically unstable at certain pH levels. At the high temperatures used in heat sterilisation, this instability is particularly pronounced. As a result, the buffer system that is closest to the physiological pH of 7.4 gradient should be used to promote significant volumes of water diffusion across the cell membrane. It's best to use solutions that are isotonic with tears.[25]

VISCOSITY

The resistance of a solution to flow when a stress is applied is measured by viscosity. A solution's viscosity is measured in poise units. The centipoise (cp or cps) is a unit of measure that equals 0.01 poise and is most commonly used in

pharmaceutical applications. Compounds used to increase viscosity come in a variety of grades, such as 15 cps, 100 cps, and so on.

Efficacy Of Treatment

The highest therapeutically effective form of the active ingredient(s) should be present. For reasons of solubility or stability of the active ingredient of patient comfort, this goal is frequently compromised. Many medications, for example, are most active in their undissociated form, yet this form is also the least soluble. Clarifying agents allowed for use in ophthalmic preparations are listed

Concentration of clarifying agent (percent)

- 20 1.0 Polysorbate
- 80 1.0 Polysorbate

Particles Of Matter

Other than gas bubbles that are accidentally present on the product, particulate matter consists of particles that will not dissolve in solution. In the processing, particulate matter can arise from a variety of places. The pharmacopoeias have limits for ophthalmic medicines.

Counting of microscopic particles

This approach uses a 0.8 m grey gridded filter to filter the products. The number of particles in the filter is then counted microscopically at 100. Light obscuration cannot be used to test some articles in a meaningful way. Individual monographs are used in such circumstances.[26]

Size of the Particles

This test, according to BP, is suitable for eye drops. Eye drops in the form of a suspension must pass the following test unless differently justified and authorised: Introduce a reasonable amount of the suspension into a counting cell or onto a slide with a micropipette, as appropriate, and scan an area corresponding to 10 g of the solid phase under a microscope. For practical reasons, the entire sample is first scanned at a low magnification (e.g. 50) to identify particles larger than 25 m. These larger particles can then be examined under a higher magnification (e.g. 200 to 500). There should be no more than 20 particles per 10 g of solid active ingredient.

UNIFORMITY OF VOLUME

In accordance with IP This test is suitable for the use of eye drops. Pour the contents of each container's ophthalmic preparation entirely into calibrated volume measures of the proper size for this test, and ascertain the volume of the contents of 10 containers.

The net volume of the contents of the 20 containers is not less than the labelled amount, and the net volume of the contents of not more than 1 of the 20 containers is less than 91 percent or more than 109 percent of the labelled amount where the labelled amount is 50 ml or less, or not less than 95.5 percent and not more than 104.5 percent of the labelled amount where the labelled amount is 50 ml or less.

Bacterial Endotoxins

Toxins that are unable to pass through the bacterial cell wall and are therefore kept within the bacteria are known as endotoxins. They are only released when the cells die and begin to decompose. Using a lysate generated from the hemolymph cells or amoebocytes of the horseshoe crab, Limulus polyphemus, the test for bacterial endotoxins (BET) evaluates the concentration of bacterial endotoxins that may be present in the sample or on the product to which the test is applied. Tachypneas gigas, Tachypneas tridentate, and Carcinoscropius rotundicauda are other horseshoe crab species that produce amoebocyte lysate with similar activity.

Membrane Filtration

Membrane filtration is used when the nature of the product allows it, such as for filterable aqueous preparations, alcoholic or oily preparations, and preparations miscible with or soluble in aqueous or oily solvents, as long as the solvents do not have an antimicrobial effect in the test conditions. Use membrane filters with a nominal pore size of less than 0.45 m that have been proven to effectively retain microorganisms, according to BP. Filters made of cellulose nitrate are used for aqueous, oily, and weakly alcoholic solutions, whereas cellulose acetate filters are used for aqueous, oily, and weakly alcoholic solutions.[27]

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