International Journal of Pharmacy Teaching & Practices 2012, Vol.3, Issue 2, 261-265.

A Comparative Study of In-Process and Finished Products Quality Control Tests for Ophthalmic Products in Different Pharmacopoeias

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Research Article

Please cite this paper as: N. Srujana, Pooja M. Balachandra*, M.P. Venkatesh, Balamuralidhara V, T.M. Pramod Kumar. A Comparative Study of In-Process and Finished Products Quality Control Tests for Ophthalmic Products in Different Pharmacopoeias. IJPTP, 2012,3(2),261-265.

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Abstract

The present study deals with the transitory overview of comparative study of in-process and finished product quality control tests for ophthalmic products taking compendia specifications of IP, BP, USP, JP and Ph. Eur into consideration. When it comes to most sensitive part of body i.e.; Eye, a high degree of precautions should be taken during and after production of product for it to avoid any hitches. The sterility of these products, as well as accuracy in the calculation and preparation of doses is of great importance. There are many preparations available in the global market depending on the ease of use for consumer; but in the global field, each regulatory body obeys their own specifications of their country's pharmacopoeia. The high graded quality product always refers to a product which is within the compendia limits. This article focuses on different dosage form under ophthalmic preparations, the procedures that are employed to maintain the quality and sterility of these ophthalmic products. This includes specifications and limits of different dosage forms according to different pharmacopoeia (like IP, BP, USP, JP, Ph. Eur etc.) which helps in comparative study of specifications provided in different pharmacopoeia. Different regulatory requirements of the respective countries demand products with different specific limits, so this comparative study will help in meeting all the requirements of the pharmacopoeias and later the regulatory requirements of that particular country.

Keywords: *Indian Pharmacopoeia, British, Pharmacopoeia, United States Pharmacopoeia, European Pharmacopoeia, Japan Pharmacopoeia and Ophthalmic products.*

Introduction

In today's emerging pharmaceutical industry, Total quality management is the primary criteria demanded to ensure the orderliness of quality assurance to prevent substandard product which does not fall under compendia specifications. Quality is suitability of drugs for their intended use determined by their efficiency weighed against safety, according to label claim, or as promoted or publicized their conformity to specifications regarding identity, purity and other characteristics. The ISO definition states that quality control is "the operational techniques and activities that are used to fulfill requirements for quality". This definition could imply that any activity whether serving the improvement, control, management or assurance of quality could be a quality control activity. Quality control of Pharmaceutical products is a concept that covers all measures taken, including the setting of specifications, sampling, testing and analytical clearance, to ensure that the raw materials, intermediates, packaging materials and finished pharmaceutical products conform with established specifications for identity, strength, purity and other characteristics.

The In-Process Quality Control system lays emphasis on the responsibility of manufacturer's processors in ensuring consistency in quality during all stages of production by adopting quality control drills and exercising control on raw materials and bought-out components, manufacturing process, packing and final testing. Finished product is product which has undergone all stages of production including packaging. Quality control test is done for finished product to check the integrity of these products. Different pharmacopoeia gives specific limits according to the regulatory requirements of that particular region.

The comparative study helps in harmonizing the specifications so that the expectations of all the regulatory bodies can be satisfied giving a quality ophthalmic product with no errors.

IN-PROCESS AND FINISHED PRODUCT QUALITY CONTROL TEST FOR OPHTHALMIC PRODUCTS

Ophthalmic preparations are sterile liquid, semi-solid or solid preparations intended for administration upon the eyeball and/or to the conjunctiva or for insertion in the conjunctive sac.

Several categories of eye preparations may be distinguished:

i. Eye drops,
ii. Eye lotions,
iii. Powders for eye drops and eye lotions,
iv. Semi-solid eye preparations,
v. Ophthalmic inserts.

Specific tests for ophthalmic preparations are discussed in Table 1. Test for sterility, pyrogen test, particulate matter test, uniformity of weight, deliverable mass or volume tests are similar to that of parenteral preparations.

Table 1: TEST PROCEDURE FOR OPHTHALMIC PREPARATIONS

Reference code	Test Procedure
OQC-1	**UNIFORMITY OF VOLUME** Pour completely the contents of each container into calibrated volume measures of the appropriate size and determine the volume of contents of 10 containers. The average net volume of the contents of the 10 containers is not less than the labeled amount, and the net volume of the contents of any single container is not less than 91% and not more than 109 % of the labeled amount where the labeled amount is 50 ml or less or not less than 95.5% and not more than 104.5% of the labeled amount where the labeled amount is more than 50 ml but not more than 200 ml, or not less than 97% and not more than 103% of the labeled amount where the labeled amount is more than 200 ml but not more than 300 ml. If these requirements are not met, determine the net volume of the contents of 10 additional containers. The average net volume of the contents of the 20 containers is not less than the labeled amount, and the net volume of the contents of not more than 1 of the 20 containers is less than 91 % or more than 109% of the labeled amount where the labeled amount is 50 ml or less or not less than 95.5% and not more than 104.5% of the labeled amount where the labeled amount is more than 50 ml but not more than 200 ml, or not less than 97% and not more than 103% of the labeled amount where the labeled amount is more than 200 ml but not more than 300 ml.
OQC-2	**TEST FOR METAL PARTICLES IN OPHTHALMIC OINTMENTS** Take 10 ophthalmic ointments to be tested, and extrude the contents into a Petri dish. Cover the dish and heat between 85°C to 110°C for 2 h to dissolve the bases. Allow the sample to room temperature without agitation to solidify the contents. Invert each dish on the stage of suitable microscope previously adjusted to provide more than 40 times magnifications and equipped with eye piece micrometer disk. Each dish is illuminated from above 45° relative to the plane dish. Examine the entire bottom of each dish for metal particles and record the total number of particles, measuring 50 µm or more in dimensions. No particles should be present.
OQC-3	**INSOLUBLE PARTICULATE MATTER TEST FOR OPHTHALMIC SOLUTIONS** Fit the membrane filter on to the membrane filter holder. Filter under reduced pressure 200 ml of the purified water for particulate matter test at the rate of 20 to 30 ml / min. Apply vacuum until the surface of the membrane is free from water and remove the membrane and dry it carefully below 50°C. After the filter is dried, place it under the microscope. Adjust the microscope to get the best view of the particles that are equal to or greater than 150 µm. Ascertain that the number is not more than 1. Fit another membrane filter and wet it with purified water for particulate matter test. Pour the sample solution into the filter. For viscous solutions, dilute suitably with purified water for particulate matter test and filter. When the amount of solution on the filter becomes small, add 30 ml of water. Repeat the process 3 times with 30 ml of the water. Apply the vacuum gently until the surface of membrane filter is free from water. Dry it and observe under microscope. Count the number of particles which are equal to or larger than 300 µm
OQC-4	**PARTICLE SIZE** Introduce a suitable quantity of the preparation into a counting cell or with a micropipette onto a slide, as appropriate and scan under microscope an area corresponding to 10 µg of the solid phase. For practical reasons, it is recommended that the whole sample is first scanned at low magnification (e.g. 50X) and particles greater than 25 µm are identified. These larger particles can then be measured at a larger magnification (e.g. 200X to 500X). For each 10 µg of solid active substance, particle size and number of particles are given in the Table 4.1.

Table 4.1: Limits for particle number as per IP, USP, BP, JP, Ph. Eur

Pharmacopoeia	Particle size	No. of particles allowed
IP	25 µm 50 µm 100 µm	Not more than 20 Not more than 2 Nil
BP, JP, Ph. Eur	25 µm 50 µm 90 µm	Not more than 20 Not more than 10 Nil

SPQC-5

UNIFORMITY OF CONTENT

Determine the content of the active ingredient of each of 10 containers taken at random. The preparation under examination complies with the test if the individual values thus obtained are all between 85 and 115 percent of the average value. The preparation under the examination fails to comply with the test if more than one individual value is outside the limits 85 to 115 percent of the average value or if any one individual value is outside the limits 75 to 125 percent of the average value. If one individual value is outside the limits 85 to 115 percent but within the limits 75 to 125 percent of the average value, repeat the determination using another 20 containers taken at random. The preparation under examination complies with the test if in the total sample of 30 containers not more than one individual value is outside the limits 85 to 115 percent and none is outside the limits 75 to 125 percent of the average value.

OQC-6

TEST FOR STERILITY

Culture Media

1. Fluid thioglycollate medium: It is used for anaerobic bacteria. Use fluid thioglycollate medium by incubating it at 30° - 35°C.

2. Soyabean-casein digest medium: It is used for fungi and aerobic bacteria. Use soybean- casein digest medium by incubating it at 20°C - 25°C under aerobic conditions.

3. Alternative thioglycollate medium: For use with turbid and viscid products and for devices having tubes with small Lumina.

Table 6.1 : Strains of the microorganisms used for the test as per IP, USP, BP, JP, Ph. Eur

Medium	Test micro organism	Incubation		
		Temp. (°C)	Duration (Days)	Type of micro organism
Fluid thioglycollate	Bacillus subtilis Staphylococcus aureus Pseudomonas aeruginosa	30-35 30-35 30-35	3 days 3 days 3 days	Anaerobic Anaerobic Anaerobic
Alternate thioglycollate	Bacteroides vulgates Clostridium sporogenes	30-35 30-35	3 days 3 days	Anaerobic Anaerobic
Soya bean casein digest	Asperigillus niger Candida albicans	20-25 20-25	5 days 5 days	Aerobic Aerobic

Test procedure: Method A (membrane filtration) is to be preferred where the substance under examination is

An oil

An ointment that can be put into solution

A non-bacteriostatic solid not readily soluble in the culture medium and

A soluble powder or a liquid that have bacteriostatic and /or fungistatic properties.

For liquid products where the volume in a container is 100 ml or more, method A should be used.

Method A – Membrane filtration

The method calls for the routine use of positive and negative controls.

Apparatus: Cellulose nitrate filters are used for aqueous, oily and weakly alcoholic solutions and cellulose acetate filters are recommended for strongly alcoholic solutions.

Diluting Fluids (IP, BP)

Fluid A: Dissolve 1 g of peptic digest of animal tissue (such as bacteriological peptone) or its equivalent in water to make 1 L, filter or centrifuge to clarify, adjust to pH 7.1 ± 0.2, dispense into flasks in 100 ml quantities and sterilize at 121°C for 20 min.

Fluid B: If the test sample contains lecithin or oil, use fluid A to each liter of which has been added 1 ml of polysorbate 80, adjust to pH 7.1± 0.2, dispense into flasks and sterilize at 121°C for 20 min.

Quantities of sample to be used

For ophthalmic preparations: Take an amount within the range prescribed in column (A) of table 6.3, if necessary, using the contents of more than one container, and mix thoroughly. For each medium use the amount specified in column (B) of Table 6.3, taken from the mixed sample.

Test method

For aqueous solutions: Aseptically transfer a small quantity of fluid A on to the membrane and filter it. Transfer aseptically the combined quantities of the preparation under examination prescribed in the two media onto one membrane. If the solution under examination has antimicrobial properties, wash the membrane(s) by filtering through it (them) not less than three successive quantities, each of 100 ml, of sterile fluid A. Do not exceed a washing cycle of 5 times or 200 ml, even if it has been demonstrated during validation that such a cycle does not fully eliminate the antimicrobial activity. The quantities of fluid used should be sufficient to allow growth of a small inoculum of organisms (approximately 50 CFU) sensitive to the antimicrobial substance in the presence of the residual inhibitory material on the membrane.

After filtration, aseptically remove the membrane(s) from the holder, transfer the whole membrane or cut it aseptically into 2 equal parts. Transfer one half to each of two suitable media.

Incubate the media for not less than 14 days.

Observe the containers of media periodically during the 14 days of incubation. If the test specimen is positive before 14 days of incubation, further incubation is not necessary. For products terminally sterilized by a validated moist heat process, incubate the test specimen for not less than 7 days.

For liquids immiscible with aqueous vehicles, and suspensions: Carry out the test described under for aqueous solutions but add a sufficient quantity of fluid A to the pooled sample to achieve rapid filtration. Sterile enzyme preparations such as penicillinase or cellulase may be added to fluid A to aid in dissolving insoluble substances. If the substance being examined contains lecithin, use fluid B for diluting.

For oils and oily solutions: Filter oils or oily solutions of sufficiently low viscosity without dilution through a dry membrane. Dilute viscous oils as necessary with a suitable sterile diluent such as isopropyl myristate that has been shown not to have antimicrobial properties under the conditions of the test. Allow the oil to penetrate the membrane and filter by applying pressure or by suction, gradually. Wash the membrane by filtering through it at least three successive quantities, each of approximately 100 ml of sterile fluid B or any other suitable sterile diluent.

After filtration, aseptically remove the membrane(s) from the holder, transfer the whole membrane or cut it aseptically into 2 equal parts. Transfer one half to each of two suitable media**.** Incubate the media for not less than 14 days.

Observe the containers of media periodically during the 14 days of incubation. If the test specimen is positive before 14 days of incubation, further incubation is not necessary. For products terminally sterilized by a validated moist heat process, incubate the test specimen for not less than 7 days.

For ointments and creams: Dilute ointments in a fatty base and emulsions of the water-in-oil type to give a fluid concentration of 1 % w/v, by heating, if necessary, to not more than 40°C with a suitable sterile diluent such as isopropyl myristate previously rendered sterile by filtration through a 0.221 µm membrane filter that has been shown not to have antimicrobial properties under the conditions of the test. Filter as rapidly as possible and complete the test as described under for oils and oily solutions. In exceptional cases, it may be necessary to heat the substance to not more than 44°C and to use warm solutions for washing the membrane.

For soluble solids: For each medium, dissolve not less than the quantity of the substance under examination, as prescribed in Table 6.3, in a suitable sterile solvent such as fluid A and carry out the test described under for aqueous solutions using a membrane appropriate to the chosen solvents.

For solids for injection other than antibiotics: Constitute the test articles as directed on the label, and carry out the test as described under for aqueous solutions or for oils and oily solutions, as applicable.

Table 6.2: Quantities of samples to be used for ophthalmic preparations.

Type of preparation	Quantity to be mixed (A)	Quantity to be used for each culture medium (B)
Ophthalmic solution other than non-parenteral liquid preparations	10 to 100 ml	5 to 10 ml
Other preparations soluble on water or appropriate solvents; insoluble preparations to be suspended or emulsified.	1 to 10 g	0.5 to 1 g
Absorbent cotton	1 to 10 g	Not less than 1 g.

Method B: Direct inoculation method

The quantity of the substance or preparation under examination to be used for inoculation in the culture media varies according to the quantity in each container.

Test method

For aqueous solutions and suspensions: Remove the liquid from the test containers with a sterile pipette or with a sterile syringe or a needle. Transfer the quantity of the preparation under examination prescribed in Table 6.2 directly into the culture medium so that the volume of the preparation under examination is not more than 10 % of the volume of the medium, unless otherwise prescribed. When the quantity in a single container is insufficient to carry out the tests, the combined contents of two or more containers are to be used to inoculate the media.

If the preparation under examination has antimicrobial activity, carry out the test after neutralizing this with a suitable neutralizing substance or by dilution in a sufficient quantity of culture medium. When it is necessary to use a large volume of the product it may be preferable to use a concentrated culture medium prepared in such a way that it takes account of the subsequent dilution. Where appropriate, the concentrated medium may be added directly to the product in its container.

Incubate the inoculated media for not less than 14 days. Observe the cultures several times during the incubation period. Observe the containers of media periodically during the 14 days of incubation. If the test specimen is positive before 14 days of incubation, further incubation is not necessary. For products terminally sterilized by a validated moist heat process, incubate the

	test specimen for not less than 7 days. **For oils and oily solutions**: Use media to which has been added a suitable emulsifying agent at a concentration shown to be appropriate in the validation of the test, for example, polysorbate 80 at a concentration of 10g/L and which has been shown not to have any antimicrobial properties under the conditions of the test. Carry out the test as described under for aqueous solutions and suspensions. During the incubation period shake the cultures gently each day. However, when thioglycollate medium or other similar medium is used for the detection of anaerobic micro-organisms, keep shaking or mixing to a minimum in order to maintain anaerobic conditions. **For ointments and creams**: Prepare by diluting to about 1 in 10 by emulsifying with the chosen emulsifying agent in a suitable sterile diluent such as fluid A. Transfer the diluted product to a medium not containing an emulsifying agent. (Before use, test the emulsifying agent to ascertain that in the concentration used it has no significant antimicrobial effects during the time interval for all transfers). Mix 10 ml of the fluid mixture so obtained with 80 ml of the medium and proceeds as directed under for aqueous solutions and suspensions. **For solids:** Transfer the quantity of the preparation under examination to the quantity of medium specified in Table 6.3 and mix. Proceed as directed under for aqueous solutions and suspensions. **Observation and Interpretation of Results** At intervals during the incubation period and at its conclusion, examine the media for macroscopic evidence of microbial growth. If the material being tested renders the medium turbid so that the presence or absence of microbial growth cannot be easily determined by visual examination, 14 days after the beginning of incubation, transfer portions (each not less than 1 ml) of the medium to fresh vessels of the same medium and then incubate the original and transfer vessels for not less than 4 days. If no evidence of microbial growth is found, the preparation under examination complies with the test for sterility. If evidence of microbial growth is found, the preparation under examination does not comply with the test for sterility. Do not repeat the test unless it can be clearly shown that the test was invalid for causes unrelated to the preparation under examination. The test may be considered invalid only when one or more of the following conditions are fulfilled: Microbial growth is found in negative controls. Data on microbial monitoring of the sterility testing facility show a fault. A review of the testing procedure used for the test in question reveals a fault. After identifying the micro organisms isolated from the containers showing microbial growth may be as scribed without any doubt to faults with respect to the materials and/or technique

	used in conducting the test procedure. If the test is declared to be invalid, repeat with the same number of units as in the original test. If no evidence of microbial growth is found in the repeat test, the preparation under examination complies with the test for sterility. If microbial growth is found in the repeat test and confirmed microscopically, the preparation under examination does not comply with the test for sterility. Table 6.3 gives guidance on the minimum no. of items recommended to be tested. **Table 6.3 : Minimum No. of items to be tested** **Number of items in the batch** / **Minimum number of items recommended to be tested** **Ophthalmic and other non-Parenteral preparations.** Not more than 200 containers — 5% or containers whichever is greater. More than 200 containers — 10 containers.
OQC-7	**TEST FOR DELIVERABLE MASS OR VOLUME OF LIQUID AND SEMI-SOLID PREPARATIONS** The test applies to liquid (solutions, emulsions and suspensions) and semi-solid preparations supplied in single-dose containers where only part of the contents is used. **LIQUID PREPARATIONS** Empty as completely as possible the contents of one container and determine the mass or volume of the contents as appropriate. In the case of emulsions and suspensions, shake the container before the determination. The mass or volume is not less than the amount stated on the label. **SEMI-SOLID PREPARATIONS** Empty as completely as possible the contents of one container. The mass of the contents is not less than that which is stated on the label.
OQC-8	**UNIFORMITY OF WEIGHT** Remove labels and wash the container and dry. Weigh the container along with its contents. Empty the containers as completely as possible. Rinse with water and with ethanol and dry at 100°C to a constant weight. Allow to cool in desiccators and weigh. The difference between the weights represents the weight of the contents. Repeat the procedure with further 19 containers and determine the average weight. Not more than two of the individual weights deviate from the average weight by more than 10% and none deviates by more than 20%. **Table 8.1: Limits for uniformity of weight**

Pharmaceutical formulation	Average mass	Percentage deviation (%)
Powders for eye drops Powders for eye lotions	Less than 300 mg 300 mg or more	10 7.5

OQC-9

TEST FOR PYROGEN

The test involves measurement of the rise in body temperature of rabbits following the intravenous injection of a sterile solution of the substance under examination. Do not use animals for pyrogen tests more frequently than once every 48 h. After a pyrogen test in the course of which a rabbit's temperature has risen by 0.6°C or more, or after a rabbit has been given a test substance that was adjudged pyrogenic, at least 2 weeks must be allowed to elapse before the animals is used again.

Test animals: Healthy adult rabbit of either sex (1.5 Kg)

Recording of temperature: Use temperature-sensing device such as a clinical thermometer or thermistor or other suitable probes (accuracy of 0.10°C). Insert the thermometer or temperature-sensing probe into the rectum of the test rabbit to a depth of about 5 cm. (IP, BP) **{7.5 cm –USP, Ph. Eur and JP}**

Preliminary Test (Sham Test)

Injecting intravenously 10 ml/ kg body weight of a pyrogen-free saline solution warmed to about 38.5°C. Record the temperatures of the animals, beginning at least 90 min before injection and continuing for 3 h after injection of the test solution. Any animal showing a temperature variation of 0.6°C or more must not be used in the main test.

Main Test: Carry out the test using a group of three rabbits.

Preparation of the sample: Dissolve the substance with pyrogen-free saline solution. Warm the liquid under examination to approximately 38.5°C before injection.

Procedure: Record the temperature of each animal 90 min before the injection and continue for 3 h after the injection for every 30 min. Record the "initial temperature" of each rabbit and temperature after 30 min. Rabbits showing a temperature variation greater than 0.2°C between two successive readings in the determination of "initial temperature" should not be used for the test. Do not use any rabbit having a temperature higher than 39.8°C and lower than 38°C.

Inject the solution slowly into the marginal vein of the ear of each rabbit over a period not exceeding 4 min. The volume of injection is not less than 0.5 ml/kg and not more than 10 ml/kg of body weight. The difference between the "initial temperature" and the "maximum temperature" which is the highest temperature recorded for a rabbit is taken as its response. When this difference is negative, the result is counted as a zero response.

Interpretation of results: Having carried out the test, first on a group of three rabbits, repeat if necessary on further groups of rabbits given in the Table 9.1, depending on the results obtained. If the summed response of the first group does not exceed the figure given in the third column of the Table 9.1, the substance passes the test. If the response exceeds the figure given in the third column of the table but does not exceed the figure given in the fourth column of the table, repeat the test as indicated above. If the summed response exceeds the figure given in the fourth column of the table, the product fails the test.

Table 9.1: Results according to IP, BP, USP, JP, Ph. Eur.

Pharmacopeia	No. of rabbits in a group	Passes if temp. is not more than (°C)	Fails if temp is more than (°C)
IP	3 8	1.4 3.7	Each rabbit temp raise should not be more than 0.6°C
USP	3 8	---- 3.3	Each rabbit temp raise should not be more than 0.6°C
BP, Ph. Eur	3 6 9 12	1.15 2.80 4.45 6.6	2.65 4.30 5.95 6.6
JP	3 6 9	1.3 3 5	2.5 4.2 5

Following are the specifications for each test for ophthalmic preparations according to IP, BP, USP, JP and Ph. Eur for each dosage forms.

Table 2: Specifications for eye drops and eye lotions according to IP, BP, USP, Ph. Eur. & JP

Tests	Reference code.	IP	BP	USP	Ph. Eur	JP
Uniformity of volume	OQC-1	50 ml or less ±9% 50 to 200 ml ±4.5% 200 to 300 ml ±3%	×	×	×	×
Sterility	OQC-6	No growth in 14 days	No growth in 14 days	No growth in 14 days	No growth in 14 days	No growth in 14 days
Particulate matter	OQC-3	×	×	≥ 25µm -2 can be present	×	≥ 25 µm -2 can be present
Particle size	OQC-4	×	No particle should be ≥ 90µm.	×	No particle should be ≥ 90 µm	No particle should be ≥ 90 µm
Deliverable mass or volume	OQC-7	×	×	×	Not less than 100%	×

Table 3: Specifications for powders for eye drops according to BP, USP & Ph. Eur

Tests	Reference code	BP	USP	Ph. Eur
Sterility	OQC-6	No growth in 14 days	No growth in 14 days	No growth in 14 days
Uniformity of content	OQC-5	85-115%	85-115%	85-115%
Uniformity of mass	OQC-8	90-110%	90-110%	90-110%

Table 4: Specifications for semisolid eye preparations according to IP, BP, Ph. Eur & JP

Tests	Reference Code	IP	BP	Ph. Eur	JP
Particle size	OQC-4	No particle should be ≥ 100µm	No particle should be ≥ 90µm	No particle should be ≥ 90µm	×
Sterility	OQC-6	No growth in 14 days	No growth in 14 days	No growth in 14 days	No growth in 14 days
Uniformity of weight	OQC-8	90-110 %	×	×	×
Deliverable mass/volume	OQC-7	×	×	Not less than stated amount	×
Test of metal particles	OQC-2	×	×	×	Metal particles should be absent

Table 5: Specifications for ophthalmic inserts according to IP, BP, USP, Ph. Eur & JP

Tests	Reference Code	IP	BP	USP	Ph. Eur	JP
Uniformity of content	OQC-5	85-115%	85-115%	×	85-115%	85-115%
Sterility	OQC-6	No growth in 14 days	No growth in 14 days	No growth in 14 days	No growth in 14 days	No growth in 14 days

Summary

The objective of the present work was to compare various in process and finished product QC tests as per IP, BP, USP, JP and EP for sterile products. The comparison is made among different ophthalmic formulations. The available QC tests from various pharmacopoeias supplement each other and one pharmacopoeia gives more details on a special issue than the other. Each pharmacopoeia has its own specifications for each test. Table (a) gives summary of the dosage forms included in IP, BP, USP, JP and EP.

IPC and FPC tests for eye drops are official in all the five Pharmacopoeias. Uniformity of volume is official only in IP whereas particulate matter test for eye drops is available only in USP, particle size test is available in BP, EP and JP. Deliverable volume test is available only in EP.

Table: (a) Summary of dosage forms available in Pharmacopoeias

Dosage form	IP	BP	USP	EP	JP
Eye preparations					
Eye drops	✓	✓	✓	✓	✓
Eye lotions	✓	✓	✓	✓	✓
Powders for eye drops &eye lotions	**NM**	✓	✓	✓	**NM**
Semi solid eye preparations	✓	✓	✓	✓	✓
Ophthalmic inserts	✓	✓	✓	✓	✓

NM --- Not mentioned

Table (b): In process and finished product quality control tests for eye drops.

Tests	IP	BP	USP	EP	JP
Uniformity of volume	✓	×	×	×	×
Sterility	✓	✓	✓	✓	✓
Particulate matter	×	×	✓	×	✓
Particle size	×	✓	×	✓	✓
Deliverable mass or volume	×	×	×	✓	×

Table (c): In process and finished product quality control tests for Powders for eye drops.

Tests	IP	BP	USP	EP	JP
Sterility	----	✓	✓	✓	----
Uniformity of content	----	✓	✓	✓	----
Uniformity of mass	----	✓	✓	✓	----

IPC and FPC tests for powders for injections are available in only BP, USP and JP

Table (d): In process and finished product quality control tests for Semi solid eye preparations

Tests	IP	BP	USP	EP	JP
Particle size	✓	✓	×	✓	×
Sterility	✓	✓	✓	✓	✓
Uniformity of weight	✓	×	×	×	×
Deliverable mass/volume	×	×	×	✓	×
Test of metal particles	×	×	✓	×	✓

IPC and FPC tests for semi solid eye preparations are official in all the five pharmacopoeias. Particle size testing is done according to IP, BP, EP and Test of metal particles is done according to USP and EP.

Table (e): In process and finished product quality control tests for ophthalmic inserts.

Tests	IP	BP	USP	EP	JP
Uniformity of content	✓	✓	×	✓	✓
sterility	✓	✓	✓	✓	✓

Conclusion

From the above review it can be concluded that though IP, BP, EP, JP and USP included most of the in process and finished products QC tests for various ophthalmic dosage forms, there were some significant difference observed. Some of the tests are available only in some Pharmacopoeias. The differences in the tests and their limits as specified in the different pharmacopoeias needs to be harmonized and streamlined in such a way that if the test meets the specified limit as per harmonized one, it meets all the requirements of all the pharmacopoeias and later the regulatory requirements of that particular country. This is important for the products which are marketed globally and can also save lot of time, money and man power.

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AUTHORS' CONTRIBUTIONS

Authors contributed equally to all aspects of the study.

PEER REVIEW

Not commissioned; externally peer reviewed

CONFLICTS OF INTEREST

The authors declare that they have no competing interests