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Draft Indian Standard

**POLYETHYLENE CONTAINERS FOR PHARMACEUTICAL USE —
SPECIFICATION**

PART 1 OTHER THAN PARENTERAL AND OPHTHALMIC PREPARATIONS

(*Second Revision* of IS 7803 (Part 1))

(ICS 83.080.01)

Plastics packaging Sectional Committee,
PCD 21

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FOREWORD

(Formal clause will be added later)

This Indian Standard was originally published in 1975. This revision has been undertaken to update the cross referred standards and incorporate the amendments issued.

With the growth of indigenous packaging industry, polyethylene containers are replacing conventional containers made of materials, such as glass, metal, etc. Polyethylene containers are also being increasingly used for pharmaceutical trade.

The package requirements for pharmaceutical preparations can broadly be classified into following two categories, depending upon their use and requirements:

- a) Parenteral and ophthalmic preparations, and
- b) Other than parenteral and ophthalmic preparations.

Since the containers for parenteral and ophthalmic preparations have to meet some extra requirements, it was felt necessary to cover the containers for above purposes in two parts of this standard.

A scheme of labelling environment friendly products with the ECO logo has been introduced at the instance of the Ministry of Environment and Forests (MEF), Government of India. The ECO-Mark is being administered by the Bureau of Indian Standards (BIS) under the BIS Act, 1986 as per the Resolutions No. 71 dated 21 February 1991 and No. 425 dated 28 October 1992 published in the Gazette of the Government of India. For a product to be eligible for marking with the ECO logo, it shall also carry the ISI Mark of the BIS besides meeting additional environment friendly requirements. For this purpose, the Standard Mark would be a single mark being a combination of the ISI Mark and the ECO logo.

For the purpose of deciding whether a particular requirement of this standard is complied with, the final value, observed or calculated, expressing the result of a test or analysis shall be rounded off in accordance with IS 2 : 2022 'Rules for rounding off numerical values (*second revision*)'. The number of significant places retained in the rounded off value should be the same as that of the specified value in this standard.

1 SCOPE

This standard (Part 1) prescribes requirements for polyethylene containers for pharmaceutical use excluding parenteral and ophthalmic preparations.

2 REFERENCE

The following standards contain provisions which through reference in this text constitute provisions of this standard. At the time of publication, the editions indicated were valid. All standards are subject to revisions, and parties to agreements based on this standard are encouraged to investigate the possibility of applying the most recent editions of the standard indicated below.

<i>IS No.</i>	<i>Title</i>
IS 4905 : 2015 / ISO 24153 : 2009	Random Sampling and Randomization Procedures (<i>first revision</i>)
IS 7019 : 1998	Glossary of terms in plastics and flexible packaging, excluding paper (<i>second revision</i>)
IS 7328 : 2020	Specification for polyethylene material for moulding and extrusion (<i>second revision</i>)
IS 9833 : 2018	List of colourants for use in plastics in contact with foodstuffs and pharmaceuticals (<i>second revision</i>)

3 TERMINOLOGY

3.1 For the purpose of this standard, definitions given in IS 7019 shall apply.

4 REQUIREMENTS

4.1 Material

Only virgin polyethylene material conforming to the requirements of IS 7328 which is practically odourless, shall be used in the manufacture of the containers or any accessory product. Pigments used, if any, shall conform to IS 9833.

4.2 Size and Design

The size, shape and design of the container shall be as agreed to between the purchaser and the supplier.

5 PERFORMANCE TESTS

5.1 Leakage Test

There shall be no signs of leakage when the container filled with water and fitted with all the prescribed closures is kept inverted at ambient temperature for a period of 24 h.

5.2 Collapsibility Test

A container shall, by collapsing inwards during use, yield at least 90 percent of its nominal contents at the required rate of flow at ambient temperature.

NOTE — This test is applicable when the containers used are of squeeze-bottle type.

5.3 Container Material Tests — These tests shall be performed only on material obtained from containers before filling.

5.3.1 Clarity of Aqueous Extract — An aqueous extract prepared in accordance with A-2.2 shall be colourless and free from turbidity.

Note — Applicable only when the containers are used for liquid orals.

5.3.2 Water-Soluble Impurities Content — The impurities in an aqueous extract prepared in accordance with A-2.2 shall not exceed the appropriate limits given in Table 1.

5.3.3 Non-volatile Residue — The non-volatile residue of the aqueous extract when tested in accordance with Annex B shall not exceed 12.5 mg.

5.3.4 pH Value — The pH value of an aqueous extract prepared in accordance with A-2.2 shall be within the range of 4.0 to 7.75, and when 5 percent of a 0.9 percent (m × v) aqueous solution of sodium chloride is added to the extract the change in pH value shall not exceed 1 unit.

NOTE — Applicable only when the containers are used for liquid preparations.

Table 1
(Clause 5.3.2)
Limits for Water-Soluble Impurities

Sl No. (1)	Impurity (2)	Maximum limit (3)	Method of Test, Ref to Appendix (4)
i)	Oxidizable matter	25 ml of 0.01 N potassium permanganate solution for total test solution	C
ii)	Sulphate ions (SO ₄)	Should pass the test	D
iii)	Ammonium ions (NH ₄)	Should pass the test	E

iv)	Heavy metals (as Pb)	0.25 mg for total test solution or should pass the test	F
v)	Chloride ions (Cl)	1.5 mg for total test solution	G

NOTE — Not applicable to containers used for tablets, capsules, granules and powder, other than for dental preparations.

5.4 Compatibility Test — The compatibility tests shall be carried out in order to establish the compatibility of the container with the contents so that the quality, purity and strength of the active ingredients of pharmaceuticals when packed in polyethylene containers are ensured. The test shall be carried out as given in Annex H.

6 ADDITIONAL REQUIREMENTS FOR ECO-MARK

6.1 General Requirements

6.1.1 The product shall conform to the requirements for quality, safety and performance prescribed.

6.1.2 The manufacturer shall produce to BIS the consent clearance as per the provisions of Water (*Prevention and Control of Pollution*) Act, 1974 and Air (*Prevention and Control of Pollution*) Act, 1981 along with the authorization, if required under Environment (Protection) Act, 1986 and the Rules made thereunder while applying for the ECO-Mark. The manufacturer shall produce documentary evidence with respect to the compliance of regulation under Prevention of Food Adulteration Act, 1954 and Drugs and Cosmetic Act, 1940 and Rules made thereunder, wherever necessary.

6.1.3 The product must display a list of critical ingredients in descending order of quantity present expressed as percent of the total. The list of such ingredients shall be identified by Bureau of Indian Standards.

6.1.4 The product packaging shall display in brief the criteria based on which the product has been labelled as 'Environment Friendly'.

6.1.5 The material used for product packaging shall be recyclable or biodegradable.

6.1.6 It shall also suitably mention that ECO-Mark label is applicable only to the packaging material/package, if content is not separately covered under ECO-Mark. It may be stated that ECO-Mark is applicable to the product or packaging material or both.

6.2 Product Specific Requirements

For the manufacture of this product, virgin material covered in following Indian Standard shall be used:

<i>IS No.</i>	<i>Title</i>
10146 : 1982	Specification for polyethylene for its safe use in contact with foodstuffs, pharmaceuticals and drinking water

7 PACKING AND MARKING

7.1 Packing

The containers shall be delivered packed in acceptable outer packages. Only containers of the same nominal capacity and bearing the same batch identification shall be packed together in one package.

7.2 Marking

7.2.1 The following information shall appear in legible and indelible marking on each container:

- a) The name or trade name or trade-mark of the manufacturer, and
- b) The batch identification.

7.2.2 *BIS Certification Marking*

The containers may also be marked with the BIS Certification Mark.

7.2.2.1 The use of the Standard Mark is governed by the provisions of Bureau of Indian Standards. Act, 2016 and the Rules and Regulations made thereunder. The details of conditions under which the license for the use of Standard Mark may be granted to manufacturers or producers may be obtained from the Bureau of Indian Standards.

8 SAMPLING AND CRITERIA FOR CONFORMITY

8.1 Lot — All the containers of the same size, shape and design manufactured from the same raw materials under similar conditions of production, in a consignment, shall constitute a lot.

8.1.1 Samples shall be selected and tested for each lot separately to determine its conformity to the requirements of the specification.

8.2 Number of Samples — The number of containers to be selected in the sample from a lot shall depend upon the size of the lot and shall be in accordance with col 1, 2 and 4 of Table 2.

Table 2
(Clauses 8.2, 8.4 and 8.5)

Scale of Sampling and Criteria for Conformity

Lot Size (Number of Containers in the Lot)	Performance Tests		Container Material Test	
	Sample Size	Permissible, Number of Defective Containers	Sample Size	Permissible Number of Defective Containers
(1)	(2)	(3)	(4)	(5)
501 to 1000	13	0	5	0
1001 to 3000	20	0	8	0
3001 to 10000	32	1	13	0
10001 to 35000	50	2	20	0

8.3 Selection of Sample — The samples shall be selected at random from the lot and, in order to ensure the randomness of selection, methods as given in IS 4905 may be adopted.

8.4 The containers selected in accordance with **8.2** (Table 2, col 2) shall be tested for leakage and collapsibility (*see 5.1, 5.2 and 5.4*). A container failing in any of the two tests will be considered as defective. A lot shall be considered as having satisfied the requirements of the standard only if the number of containers found defective in the sample does not exceed the number of permissible defectives given in col 3 of Table 2.

8.5 The containers selected in the sample according to **8.2** (Table 2, col 4) shall be individually tested for all the requirements of material (*see 5.3.1, 5.3.2, 5.3.3, 5.3.4*). A container failing in anyone or more of the tests shall be considered as defective. A lot shall be considered as having satisfied the requirements of material only if all the containers tested in the sample pass all the tests individually.

ANNEX A
(Clauses 5.3.1, 5.3.2 and 5.3.4)

METHOD OF PREPARATION OF SAMPLES AND EXTRACTS

A-1 APPARATUS AND REAGENTS

A-1.1 Unless otherwise stated, use only borosilicate glassware, analytical grade reagents and double distilled water from an all-glass distilling apparatus.

A-1.2 Clean all glassware with chromosulphuric acid and rinse thoroughly with water. Clean other apparatus thoroughly using suitable detergents.

A-2 PROCEDURE

A-2.1 Preparation of Sample — Select unlabeled, unmarked and non-laminated portions from suitable containers, taken at random, sufficient to yield a total area of sample required, taking into account the surface area of both sides. Cut these portions into strips, none of which have a total area of more than 20 cm². Wash the strips, free from extraneous matter by shaking them in a flask with at least two separate portions of water for about 30 s in each case, then draining off the water thoroughly.

NOTE — Do not wipe the sample or wash it with detergents.

A-2.2 Preparation of Extract — Select, cut up and wash as prescribed in **A-2.1** portions of the samples with a total surface area of 1250 cm². Transfer to a 500 ml flask, add 250 ml of water, and cover the neck with an inverted glass beaker and autoclave at 121 °C for 30 min (preferably in autoclave that enables the charge to be cooled rapidly, after autoclaving, to a room temperature).

A-2.2.1 Autoclave simultaneously a blank consisting of 250 ml of water.

ANNEX B
(Clause 5.3.3)

METHOD OF DETERMINATION OF NON-VOLATILE RESIDUE OF AQUEOUS EXTRACTS

B-1 PROCEDURE

B-1.1 Pipette 100 ml of the aqueous extract prepared in accordance with **A-2.2** into a dried and tared evaporating dish; evaporate to dryness on a water-bath and dry the residue to constant weight at 105 °C.

ANNEX C
[Table 1, Item (i)]

METHOD OF LIMIT TEST FOR OXIDIZABLE MATTER IN AQUEOUS EXTRACT

C-1 REAGENTS

C-1.1 Potassium Permanganate Solution — 0.01 N, accurately standardized.

C-1.2 Dilute Sulphuric Acid — approximately 16 percent (v/v), aqueous dilution of concentrated sulphuric acid.

C-1.3 Potassium Iodide (KI)

C-1.4 Starch Indicator — 1 percent, aqueous.

C-1.5 Sodium Thiosulphate Solution — 0.01 N, standardized against the potassium permanganate solution.

C-2 PROCEDURE

C- 2.1 Pipette into the first of two 250 ml conical flasks (marked 1), 20 ml of the aqueous extract of the sample (*see A-2.2*) and into the second (marked 2), 20 ml of the blank (*see A-2.2.1*). Pipette into each flask 20 ml of the potassium permanganate solution, add 1.0 ml of the dilute sulphuric acid and boil for exactly 3 min. Cool the flask rapidly and add to each approximately 0.10 g of the potassium iodide and 5 drops of the starch indicator. Back titrate the liberated iodine in flasks 1 and 2 with the Sodium Thiosulphate solution and call the 2 volumes of Sodium Thiosulphate solution used A and B respectively.

C-3 TEST RESULT

C-3.1 Result of 'B' minus result of 'A' is the quantity of potassium permanganate reduced. Total quantity of potassium permanganate solution used for 10 ml of aqueous extract should not be more than 1 ml.

ANNEX D
[Table 1, Item (ii)]

METHOD OF LIMIT TEST FOR SULPHATE IONS IN AQUEOUS EXTRACT

D-1 REAGENTS

D-1.1 Ethanolic Potassium Sulphate Solution — A freshly prepared solution of 0.018 1 g of potassium sulphate in a mixture of 69 ml of water and 31 ml of 95 percent (v/v) ethanol.

D-1.2 Barium Chloride Solution — A 25 percent (m/v) aqueous solution of barium chloride ($\text{BaCl}_2 \cdot 2\text{H}_2\text{O}$).

D-1.3 Dilute Hydrochloric Acid Solution — An approximately 30 percent (v/v) aqueous dilution of concentrated hydrochloric acid.

D-1.4 Blue Litmus Paper

D-1.5 Aqueous Potassium Sulphate Solution — A 0.0171 percent (m/v) aqueous solution of potassium sulphate (K_2SO_4).

D-2 PROCEDURE

D-2.1 Pipette 0.25 ml of the Ethanolic Potassium Sulphate solution and 1.0 ml of barium chloride solution into each of 2 matched test tubes. Shake well, wait for 1 min and pipette 10 ml of the aqueous extract (*see A-2.2*) of the sample into the first tube and 9 ml of the blank (*see A-2.2.1*) and 1 ml of aqueous potassium sulphate solution into the second tube. Test the mixture in the 2 tubes with the litmus paper and, if necessary, neutralize the mixtures with dilute hydrochloric acid. Then add an additional 0.5 ml of dilute hydrochloric acid to each tube and shake. Compare the turbidity in the tubes after 5 min.

D-3 TEST RESULT

D-3.1 The sample is deemed to have passed the test if the turbidity in the first tube does not exceed that in the second tube.

ANNEX E

(Table 1, Item (iii))

METHOD OF LIMIT TEST FOR AMMONIUM IONS IN AQUEOUS EXTRACT

E-1 REAGENTS

E-1.1 Ammonia-Free Water — Water that shows no colour when a 20 ml portion is tested with 2 ml of the alkaline potassium mercuric iodide solution.

E-1.2 Alkaline Potassium Mercuric Iodide Solution — Dissolve 3.5 g of potassium iodide in about 40 ml of water and 1.25 g of mercuric chloride in about 40 ml of water. Mix the solutions and add, with constant stirring, a saturated aqueous solution of mercuric chloride until a slight red precipitate remains. Dissolve 12 g of sodium hydroxide in the solution and add a little more of saturated mercuric chloride solution and enough of the ammonia free water to yield 100 ml. Allow to stand and decant the clear liquid for use.

E-1.3 Ammonium Chloride Solution — 0.015 percent (m/v) aqueous solution of ammonium chloride (NH_4Cl).

E-2 PROCEDURE

E-2.1 Pipette 1 ml of ammonium chloride solution into the first of two matched Nessler tubes and fill the tube up to the 50 ml mark with the blank solution (*see A-2.2.1*). Fill the second tube up to the 50 ml mark with the aqueous sample extract (*see A-2.2*). Place both tubes on a white tile, add 1 ml of the alkaline potassium mercuric iodide solution to each tube and compare the intensity of the colour developed in each after 2 min.

E-3 TEST RESULT

E-3.1 The sample is deemed to have passed the test if the intensity of colour in the second tube does not exceed that in the first tube.

ANNEX F

(Table 1, Item (iv))

METHOD OF LIMIT TEST FOR HEAVY METALS IN AQUEOUS EXTRACT

F-1 REAGENTS

F-1.1 Diluted Acetic Acid — Dilute 60 ml of glacial acetic acid with water to make 1 000 ml.

F-1.2 Hydrogen Sulphide Solution — Saturated solution of hydrogen sulphide made by passing hydrogen sulphide gas (H₂S) into cold water. Store in small, dark amber bottle.

F-1.3 Lead Nitrate Stock Solution — Dissolve 159.8 mg of lead nitrate in 100 ml of water to which has been added 1 ml of nitric acid, then dilute with water to 1 000 ml. Prepare and store this solution in glass containers free from soluble lead salts,

F-1.4 Lead Nitrate Solution — Dilute 10 ml of lead nitrate stock solution with water to 100 ml. This solution shall be freshly prepared. Each millilitre of this solution contains the equivalent of 0.01 mg of lead.

F-2 PROCEDURE

F-2.1 Pipette 25 ml of the aqueous extract into one of two matched 50 ml Nessler tubes and add 2 ml of dilute acetic acid. Into the second Nessler tube, pipette 22.5 ml of blank (*see A-2.2.1*), 2 ml of dilute acetic acid and 2.5 ml of lead nitrate solution. Place the tubes on a white tile and 10 ml of hydrogen sulphide solution. Mix well and allow to stand for 10 min. View downward and compare the colour.

F-3 TEST RESULT

F-3.1 The same is deemed to have passed the test, if the intensity of colour produced in the first tube does not exceed that produced in the second tube.

ANNEX G
(Table 1, Item (v))

METHOD OF LIMIT TEST FOR CHLORIDE IONS IN AQUEOUS EXTRACT

G-1 REAGENTS

G-1.1 Nitric Acid (HNO₃) — 6 N, accurately standardized.

G-1.2 Silver Nitrate Solution — 0.1 N, accurately standardized.

G-1.3 Sodium Chloride Solution — Dissolve 170 mg of sodium chloride in water and make up to 1 000 ml. Each millimeter of this solution is equivalent to 0.103 1 mg of chloride.

G-2 PROCEDURE

G-2.1 Pipette 25 ml of aqueous extract (*see A-2.2*) into one of the two matched Nessler tubes and to the other pipette 1.5 ml of sodium chloride solution and 8.5 ml of blank (*see A-2.2.1*). Pipette 1 ml 6 N nitric acid and 1 ml of 0.1 N silver nitrate solution to both the tubes. Mix and observe after 5 min, the turbidity in both the tubes.

G-3 TEST RESULT

G-3.1 The sample is deemed to have passed the test if the turbidity in the first tube does not exceed that in the second tube.

ANNEX H
(Clause 5.4)

METHOD OF TEST FOR COMPATIBILITY OF POLYETHYLENE CONTAINERS

H-1 PRINCIPLE

H-1.1 Pieces of polyethylene material with which the container is made are treated at an elevated temperature with the liquid which the container is intended to contain. The compatibility tests shall be carried out in accordance with **H-3.1** and **H-3.2** if the contents to be packed are liquid preparations. In case of dry powdered pharmaceuticals, the method given in **H-3.2** only shall be applicable.

H-2 TEST SPECIMEN

H-2.1 Material — Three test pieces of approximately equal size and having an area of not less than 15 cm² shall be cut from any convenient part of the container. Each test piece shall be cleaned, wiped and dried. It shall be measured for length, width and thickness to the nearest 0.05 mm and weighed to the nearest milligram.

H-3.2 Container — Six samples of specific container intended for packing of particular product shall be tested in accordance with the procedure given in **H-3.2**.

H-3 PROCEDURE

H-3.1 Testing of Material — The liquid which is intended to be filled in the container shall be introduced into a glass vessel and test piece; completely immersed, avoiding unnecessary contact with the other pieces or the walls of the glass vessel. Where the density of plastics material is less than that of the liquid, small weights inert to the liquid, may be used to prevent the test pieces from either floating or curling. The test shall be carried out continuously over 28 days at a temperature of 50 ± 2 °C. The liquid and the test pieces shall be thoroughly agitated every 24 h. After the required test period has elapsed, the test pieces shall be removed from the liquid, suitably cleaned, dried, weighed and measured.

H-3.2 Testing of Container — In order to assess the compatibility of the container, the container shall be filled with the product to the nominal capacity, sealed and capped in the manner intended and tested at anyone of the following conditions, depending upon the thermolabile characteristic of the product being tested:

- a) 50 ± 2 °C for a period of 28 days;
- b) 37 ± 2 °C for a period of 3 months;
- c) 27 ± 2 °C for 1/3 of the anticipated shelf life period; and
- d) 37 ± 2 °C and 75 ± 5 percent relative humidity for 3 months (for preparations other than liquids).

H-3.2.1 The above test conditions are intended to serve as a guideline for usage of the container. However, a shelf life storage test at 27 ± 2 °C or at ambient temperature should be carried out till the anticipated shelf life period of the product in order to confirm the suitability of the container.

H-4 TEST RESULTS AND INTERPRETATION

H-4.1 Material — At the end of the test period, any change in weight, dimension or alterations in other characteristics, such as colour, blooming, etc. shall be used for determining the suitability of the container for the intended purpose.

H-4.2 Containers — At the end of the test period, containers shall be examined for the following:

- a) Visible cracks, if any;
- b) Change in colour;
- c) Change in weight; and
- d) Change in shape.

H-4.2.1 In the event of any sign of crack, the container shall be deemed to be unsuitable for use for the particular product. Any change in weight or shape or both shall be used by the manufacturer and purchaser to determine the suitability of the container. A very slight change in colour shall be considered insignificant.

H-4.2.2 In addition, the contents shall be tested to ensure that it meets the house specification of the pharmaceutical manufacturer and shall be substantially free from foreign odour and taste.