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Plastics collapsible containers for human blood and blood components

Poches en plastique souple pour le sang et les produits du sang

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Contents

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Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

International Standard ISO 3826 was prepared by Technical Committee ISO/TC 76, *Transfusion, infusion and injection equipment for medical use*.

Annexes A and B form an integral part of this International Standard. Annex C is for information only.

Introduction

In some countries national pharmacopoeia or other government regulations are legally binding and these requirements may take precedence over this International Standard.

The manufacturers of the plastics container or the suppliers are expected to disclose in confidence to the national control authority, if requested by them, full details of the plastics material(s) and the components of the materials and their methods of manufacture, details of manufacture of the plastics containers including the chemical names and quantities of any additives, whether incorporated by the manufacturer of the containers or present in the raw material, as well as full details of any additives that have been used.

Plastics collapsible containers for human blood and blood components

1 Scope

1.1 This International Standard specifies requirements, including performance requirements, for di-(2-ethylhexyl)phthalate (DEHP) plasticized poly(vinyl chloride) (PVC) for plastics collapsible, non-vented, sterile containers complete with collecting tube outlet port(s), integral needle and with optional transfer tube(s), for the collection, storage, processing, transport, separation and administration of blood and blood components. The containers may contain anticoagulant and/or preservative solutions, depending on the application envisaged. These requirements are intended to

a) ensure that the quality of blood and blood components is maintained as high as possible;

b) make possible efficient and safe collection, identification, storage, separation and transfusion of the contents, with special attention to reducing to a minimum the risks resulting from

— contamination, in particular microbiological contamination,

— air embolism,

— errors in identification of containers and any representative samples of contents,

— interaction between the container and its contents;

c) ensure functional compatibility when used in combination with transfusion sets as specified in ISO 1135-4;

d) provide maximum resistance to breakage and deterioration in a package of minimal mass and volume.

1.2 The requirements specified in this International Standard also apply to multiple units of plastics containers, e.g. to double, triple or quadruple units.

1.3 The term "plastics containers" is used throughout this International Standard to mean the container complete with collecting tube and needle, port(s), anticoagulant and/or preservative solutions and transfer tube(s) and associated container(s), where applicable.

1.4 Unless otherwise specified, all tests specified in this International Standard apply to the plastics container as prepared ready for use.

2 Normative references

The following standards contain provisions which, through reference in this text, constitute provisions of this International Standard. At the time of publication, the editions indicated were valid. All standards are subject to revision, and parties to agreements based on this international Standard are encouraged to investigate the possibility of applying the most recent editions of the standards indicated below. Members of IEC and ISO maintain registers of currently valid International Standards.

ISO 247:1990, *Rubber — Determination of ash.*

ISO 1135-3:1986, *Transfusion equipment for medical use — Part 3: Blood-taking set.*

ISO 1135-4:1987, *Transfusion equipment for medical use — Part 4: Transfusion sets for single use.*

3 Dimensions and designation

3.1 Dimensions

See figure 1 and table 1. Only the dimensional values shown in figure 1 are binding; the dimensions given in table 1 are for guidance purposes only.

NOTES

1 The figure illustrates the components of a plastics container and, apart from the dimensions shown, does not form part of the requirements of this International Standard.

2 For guidance, additional dimensions are given in table 1. These dimensions are optional and are not requirements of this International Standard.

Dimensions in millimetres

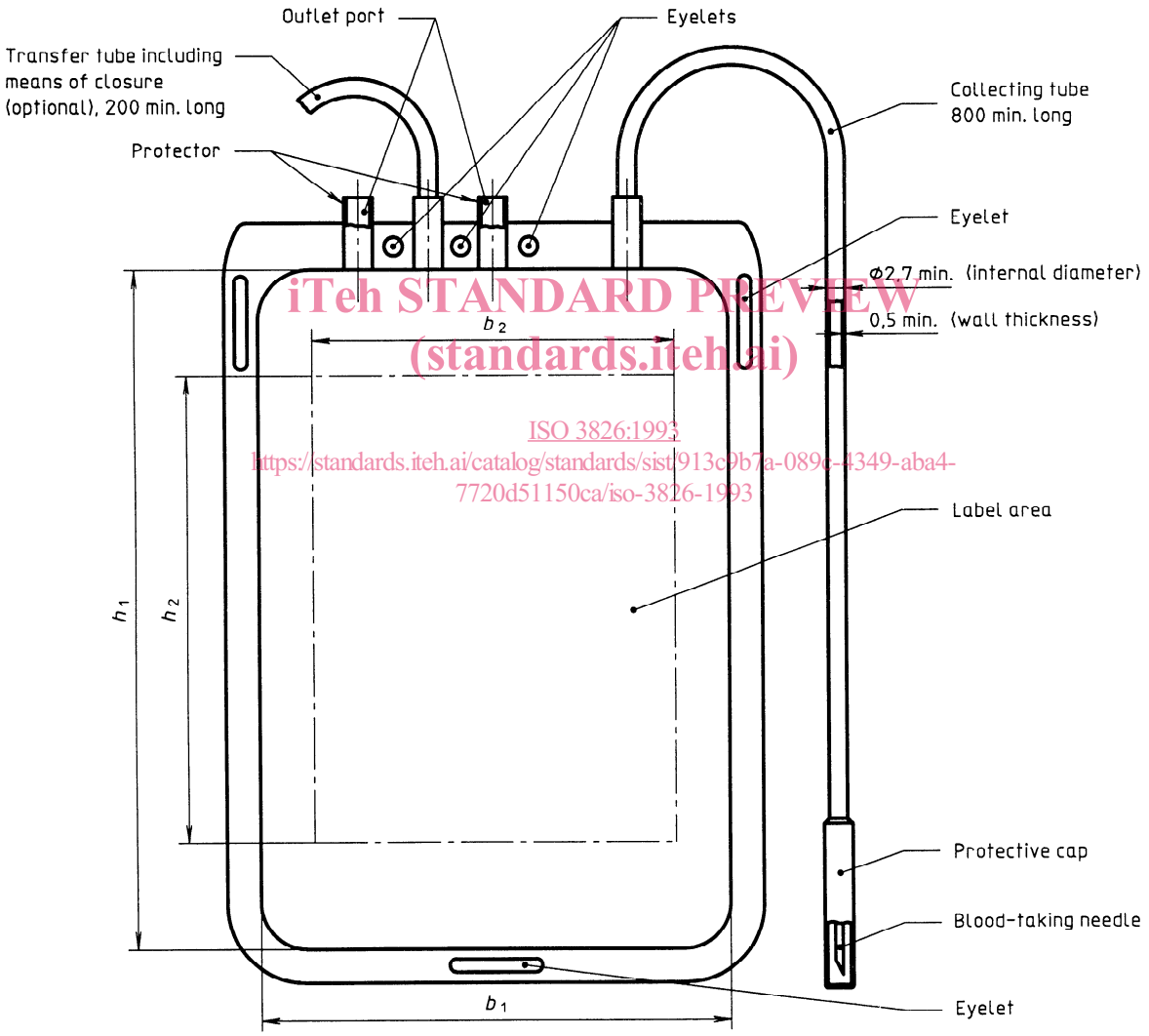

Figure 1 — Schematic representation of plastics container

Table 1 — Dimensions for plastics containers, label areas and nominal capacity (for guidance purposes only)

Dimensions in millimetres

Nominal capacity ml	Inside width b_1	Inside height h_1	Size of label area	
			$b_2 \pm 5$	$h_2 \pm 5$
100	75	120	60	85
250	120	130	90	85
400	120	170	100	100
500	120	185	100	100

3.2 Designation example

Designation example of a plastics collapsible container with a nominal capacity of 500 ml complying with the requirements specified in this International Standard:

Plastics container ISO 3826 - 500

4 Design

4.1 General

The design of the plastics container shall provide for the safe and convenient collection, storage, processing, transport, separation and administration of whole blood and blood components. The design and manufacture shall not adversely affect the preservation of blood and blood components. The container shall permit the preparation of plasma or centrifuged or resuspended cellular components with a minimal hazard of contamination by microorganisms. The container shall be functionally compatible with the transfusion set specified in ISO 1135-4. Its design shall also ensure that it can be used in a centrifuge cup.

4.2 Air content

4.2.1 The total volume of air contained in the blood collection pathway and the container used for the collection of blood and for each transfer container and its associated tubing shall not exceed 10 ml. The volume of air contained in each additional transfer container and associated tubing shall not exceed 10 ml.

4.2.2 When used in accordance with the manufacturer's instructions, the plastics container shall be capable of being filled with blood without air being introduced.

4.3 Emptying under pressure

The plastics container filled with a volume of water at a temperature of 23 °C ± 2 °C equal to its nominal capacity and connected to a transfusion set as specified in ISO 1135-4 inserted in an outlet port (see 4.8) shall empty without leakage within 2 min when gradually squeezed between two plates to an internal pressure of 40 kPa above atmospheric pressure.

4.4 Pilot samples

The plastics container shall be designed so that pilot samples of unmistakable identity can be collected for the performance of appropriate laboratory tests without the closed system of the container being penetrated.

4.5 Rate of collection

4.5.1 The plastics container shall be flexible enough to offer minimum resistance to filling under normal conditions of use.

4.5.2 The plastics container shall be designed so that it is capable of being filled to its nominal capacity in less than 8 min when tested in accordance with B.2.

4.6 Collecting and transfer tube(s)

4.6.1 The plastics container may be provided with one or more collecting or transfer tube(s) to allow the collection and separation of blood and blood components.

The transfer tube shall be fitted with a device, which acts first as a seal and, when broken, permits the free flow of blood components in either direction.

4.6.2 The tubes shall be such that they can be sealed hermetically and do not collapse under normal use.

4.6.3 The plastics container, filled with water (see note 4 under 5.2.8) to its nominal capacity and sealed, and the tubes connected to the plastics container, shall form a hermetic seal and a tight leakproof joint which will withstand, without leakage occurring, a tensile force of 20 N, applied to the tubing for 15 s. The tensile force shall be applied at right angles to the edge of the joint and in the longitudinal axis of the plane of the container at a temperature of 23 °C ± 2 °C.

There shall be no leakage at the junctions and the container shall also conform to the requirements specified in 5.2.8.

4.6.4 Under visual inspection, the tubing shall not display any cracks, blisters, kinks or other defects.

4.7 Blood-taking needle

The needle shall be integral with the collecting tube and covered by a protective cap. The protective cap shall prevent leakage of anticoagulant and/or preservative solution from the plastics container during storage, shall maintain the sterility of the fluid path and shall be readily removable. The protective cap shall be tamper-evident and manufactured so that either it is impossible to replace or any attempt at manipulating it is blatantly obvious.

The blood-taking needle, as specified in ISO 1135-3, shall withstand, without working loose from the assembly, a tensile force of 20 N applied along the longitudinal axis of the tubing for 15 s.

4.8 Outlet port(s)

4.8.1 The plastics container shall be provided with one or more outlet ports for the administration of blood and blood components through a transfusion set. The port(s), which shall have a puncturable, non-resealable closure, shall allow connection of a transfusion set without leakage on insertion or during conditions of use, including emptying under pressure (see 4.3). To ensure functional interchangeability, the port(s) shall be of such size and design to allow insertion of a transfusion set having a closure-piercing device in accordance with ISO 1135-4. Before the closure is pierced by the point of the closure-piercing device, the outlet port(s) shall be tightly occluded by the closure-piercing device.

4.8.2 Each outlet port shall be fitted with a hermetically sealed, tamper-evident protector to maintain the sterility of the internal surface.

4.9 Suspension

The plastics container shall have adequate means of suspension or positioning, which do not interfere with use of the container during collection, storage, processing, transport and administration. The means of suspension or positioning shall be capable of withstanding a tensile force of 20 N applied along the longitudinal axis of the outlet port(s) for 60 min at a temperature of 23 °C ± 2 °C without breaking.

5 Requirements

5.1 General

The plastics container shall be transparent, virtually colourless (see 5.3.2), flexible, sterile, non-pyrogenic, free from toxicity (see 5.4) and non-frangible under conditions of use (see 5.2.5). It shall be compatible with the contents under normal conditions of storage. The container shall be sterilized in the final stage of manufacture, and the container shall not be tacky or become tacky during sterilization or, subsequently, during storage for its shelf-life at temperatures not exceeding 40 °C.

The plastics container shall be stable biologically, chemically and physically with respect to its contents during its shelf-life and shall not permit penetration of microorganisms. Any substances leached from the container by the anticoagulant and/or preservative solution, blood and blood components by either chemical interaction or physical dissolution, shall be within the limits specified.

In many countries there are national pharmacopoeias, government regulations or standards detailing suitable tests for assessing such chemical or physical interactions. However, if no such regulations are provided, the test methods indicated in table 2 shall be used.

5.2 Physical requirements

5.2.1 Conditions of manufacture

All processes involved in the manufacture, assembly and storage of the plastics container shall be carried out under clean and hygienic conditions in compliance with the appropriate national authorities in accordance with the relevant legislation and international agreements. Every practicable precaution shall be taken at all stages to reduce the risk of adventitious contamination by microorganisms or foreign matter.

5.2.2 Sterilization

5.2.2.1 The plastics container shall have been sterilized by autoclaving or any other method approved by the national control authority.

5.2.2.2 The method of sterilization used shall not adversely affect the materials or contents nor cause any loosening of joints and deterioration of welds in the plastics material nor any major alteration in the shape of the plastics container.

5.2.2.3 The manufacturer shall be able to produce evidence acceptable to the national control authority of the effectiveness of the sterilization process actually used. If required by the national control authority, positive controls to check the effectiveness of sterilization shall be included in each sterilization lot.

5.2.3 Transparency

When tested with the suspension as specified in B.1, the opalescence of the suspension shall be perceptible when viewed through the plastics container as compared with a similar container filled with water.

5.2.4 Coloration

The material of the plastics container shall not be coloured to such an extent that assessment of the colour of the blood is adversely affected.

5.2.5 Thermal stability

The plastics container, filled to half of its nominal capacity with purified water, shall withstand storage at −80 °C for 24 h, subsequent immersion in water at 50 °C ± 2 °C for 20 min, and returning to room temperature. The plastics container shall meet the requirements of 4.6.3, 4.9, 5.2.7 and 5.2.8.

NOTE 3 If a refrigerant solution is used, the plastics container may be enclosed in a protective bag to avoid direct contact between the refrigerant solution and the plastics container.

5.2.6 Vapour transmission

The plastics container, without an over-package, shall be filled with the labelled volume of anticoagulant and/or preservative solution, if any, and with a volume of sodium chloride solution [ρ(NaCl) = 9 g/l] equal to the nominal capacity, sealed and labelled ready for use. The plastics container shall then be capable of being stored in still air conditions for six weeks at a temperature of 5 °C ± 1 °C and a maximum relative humidity of 55 % without loss of more than 2 % (*m/m*) of water from the solution.

5.2.7 Resistance to distortion

When centrifuged, the plastics container filled with water to its nominal capacity shall withstand an acceleration of 5 000*g* for 30 min at temperatures of 4 °C and 37 °C without becoming permanently distorted.

5.2.8 Resistance to leakage[1)]

When filled to nominal capacity with purified water and sealed, the plastics container shall not develop leaks under conditions of centrifugation at 5 000*g* for 30 min at 4 °C followed by 30 min at 37°C. In addition, the container, similarly filled to nominal capacity and sealed, shall show no leakage on being gradually squeezed between two plates, lined with indicator paper, to an internal pressure equivalent to 100 kPa above atmospheric pressure at 23 °C ± 2 °C, reached within 1 min and maintained for 10 min.

NOTE 4 When the plastics container is filled with anticoagulant solution, such as an ACD solution or other solutions with similar pH, leakage may be detected by pressing the container against sheets of blue litmus paper and observing the development of pink spots on the paper. For solutions of other pH, the same method with an appropriate indicator may be used. Alternative methods affording at least the same degree of sensitivity may be used.

5.2.9 Permanence of marking and labelling

Any attempt to peel the label off shall result in the label being destroyed.

When tested in accordance with B.3, the label(s) shall not separate from the containers after removal from water. Printing on the label or on the container shall remain legible.

5.3 Chemical requirements

5.3.1 Requirements for extract

The limits specified in table 2 shall not be exceeded when the appropriate tests are carried out on the extract obtained in accordance with A.2 and A.3.9.

5.3.2 Requirements for plastics material

When plastics materials are tested by the methods given in column 3 of table 3, the limits shown in column 2 of the table shall not be exceeded.

1) The test using centrifugation specified in 5.2.8 can be carried out in a single operation with the test specified in 5.2.7.

Table 2 — Chemical limits on extracts

Characteristics	Limit	Test method in
Oxidizable matter	⩽ 2 ml of $c(0{,}5\ Na_2S_2O_3) = 0{,}01$ mol/l	A.3.1
Ammonia (NH_3)	⩽ 2 mg/l	A.3.2
Chloride ions (Cl^-)	⩽ 4 mg/l	A.3.3
Acidity or **alkalinity**	⩽ 0,4 ml of $c(NaOH) = 0{,}01$ mol/l , or ⩽ 0,8 ml of $c(HCl) = 0{,}01$ mol/l	A.3.4
Residue on evaporation	⩽ 3 mg/100 ml	A.3.5
Opalescence	Slightly opalescent, but not more pronounced than that of reference suspension 2	A.3.6
Coloration	No coloration	A.3.7
Ultraviolet (UV) absorption	Extinction ⩽ 0,2 in the range of 230 nm to 360 nm	A.3.8
Extractable di(2-ethylhexyl) phthalate (DEHP)	⩽ 10 mg/100 ml	A.3.9

Table 3 — Chemical limits on plastics material

Characteristics		Limit	Test method in
Ash		⩽ 1 mg/g	A.4.1
Elements	Ba, Pb	⩽ 1 mg/kg	A.4.2.1
	Cd, Sn	⩽ 0,6 mg/kg	A.4.2.2
Vinyl chloride monomer		⩽ 1 µg/g	A.4.3

5.4 Biological requirements

The plastics container shall not release any substances which may adversely affect the therapeutic effectiveness of blood and blood components, including those substances which may exhibit toxic, cytotoxic, bacteriostatic, bactericidal, pyrogenic or haemolytic reactions.

In many countries there are national pharmacopoeias, government regulations or standards detailing suitable tests for assessing biological safety and sterility. However, if no such regulations are provided, the test method specified in table C.1 should be used.

5.4.1 Requirements for type test

The type test shall be established and assessed by an expert(s) in the transfusion field and on toxicology of plastics material. It shall cover the elements in 5.4.1.1 to 5.4.1.4.

5.4.1.1 General biological safety of plastics container

Materials shall be assessed for biocompatibility by carrying out suitable tests for those properties detailed in table C.1 and the results of the tests shall indicate freedom from toxicity.

5.4.1.2 Compatibility of plastics container with process of manufacture and sterilization

The process of manufacture and sterilization and the prolonged contact with the anticoagulant solution, blood and blood components shall not alter properties of the plastics material and of the plastics container itself.

5.4.1.3 Compatibility of material of plastics container with anticoagulant and/or preservative solution, blood and blood components

Migration after sterilization and prolonged contact of the constituents or additives of the plastics material shall not alter the properties of the anticoagulant and/or preservative solution, of blood and blood components or cause any toxicological risk for the patient.

5.4.1.4 Biological safety of plastics container with cellular elements of blood and blood components

The type test shall cover this aspect.

5.4.2 Requirements for lot test

5.4.2.1 Sterility

The plastics container and its contents shall be supplied sterile; guidance on testing for sterility is given in C.3.1.

5.4.2.2 Pyrogens

The plastics container supplied shall be assessed for freedom from pyrogens using a suitable test (guidance on testing for pyrogens is given in C.3.2) and the result shall indicate that the plastics container is pyrogen-free.

6 Packaging

The plastics container shall be placed inside a sealed over-package to meet the requirements specified below.

6.1 The plastics container shall not lose more than 2,5 % (*m/m*) of water from the anticoagulant and/or preservative solution during storage for 1 year at 55 % humidity, 23 °C ± 2 °C and atmospheric pressure.

6.2 The shelf-life of a plastics container shall be established by the manufacturer on the basis of stability data. When containing anticoagulant and/or preservative solution, the shelf-life shall not be greater than the time during which the water loss equals 5 % (*m/m*), but in any case shall not be less than 2 years.

NOTE 5 For the purposes of this International Standard, the term "shelf-life" refers to the period between the date of sterilization and the date after which the plastics containers should not be used for the collection of blood.

6.3 The interior surface of the over-package should not interact with any of its contents and shall be treated to prevent growth of mould or fungus inside the package. If chemical fungicides are used, evidence shall be provided to show there has been no harmful penetration of, or deleterious effect on, the plastics container and its contents.

6.4 The over-package shall be sealed in such a manner as to be tamper-evident and to prevent opening or reclosing without displaying signs that the seal has been destroyed.

6.5 The over-package shall be strong enough to resist damage under conditions of normal handling and use.

6.6 The over-package shall be adequately pest-proof, account being taken of the hazards of the region in which it is to be used.

6.7 The plastics container and components shall be arranged in the over-package in a manner which will prevent the collecting tube and connecting tube(s) [transfer tube(s)] from kinking and acquiring a permanent set.

7 Marking and labelling

Marking and labelling of a plastics container shall conform to applicable national regulations and shall include the requirements specified in 7.1 to 7.4.

7.1 Marking on plastics container

The label shall contain the following information:

a) description of the contents;

b) nature and volume, in millilitres, or mass, in grams, of anticoagulant and/or preservative solution and any other material introduced, and the volume, in millilitres, or mass, in grams, of blood and blood components to be collected;

c) statement: "STERILE AND PYROGEN-FREE";

d) instruction: "DO NOT USE IF THERE IS ANY VISIBLE SIGN OF DETERIORATION", or precise alternative wording;

e) instruction: "CONTAINER NOT TO BE RE-USED", or precise alternative wording;

f) instruction: "DO NOT VENT";

g) instructions for use of the plastics container, including conditions of storage of the plastics container when filled with blood and blood components;

h) manufacturer's name and address and/or the name and address of the supplier responsible;

i) lot designation;

j) expiry date for the unused plastics container indicated by the instruction: "DO NOT FILL WITH BLOOD AFTER ...".