INTERNATIONAL STANDARD

ISO 8871-1

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Elastomeric parts for parenterals and for devices for pharmaceutical use —

Part 1: Extractables in aqueous autoclavates

Éléments en élastomère pour administration parentérale et dispositifs à usage pharmaceutique —

Partie 1: Substances extractibles par autoclavage en milieu aqueux

Reference number
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ISO copyright office
Case postale 56 • CH-1211 Geneva 20
Tel. + 41 22 749 01 11
Fax + 41 22 749 09 47
E-mail copyright@iso.org
Web www.iso.org

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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.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. 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.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

ISO 8871-1 was prepared by Technical Committee ISO/TC 76, *Transfusion, infusion and injection equipment for medical and pharmaceutical use*.

Together with the other parts (see below), this part of ISO 8871 cancels and replaces ISO 8871:1990, which has been technically revised.

ISO 8871 consists of the following parts, under the general title *Elastomeric parts for parenterals and for devices for pharmaceutical use*:

— *Part 1: Extractables in aqueous autoclavates*

— *Part 2: Identification and characterization*

— *Part 3: Determination of released-particle count*

— *Part 4: Biological requirements and test methods*

— *Part 5: Functional requirements and testing*

Introduction

The elastomeric parts specified in the various parts of this International Standard are produced from a material which is usually called “rubber”. However, rubber is not a unique entity, since the composition of rubber materials may vary considerably. The base elastomer and the type of vulcanization have a major influence on the principle characteristics of an individual rubber material, as do additives such as fillers, softeners and pigments. These may have a significant effect on the overall properties. The effectiveness, purity, stability and safe handling of a drug preparation may be affected adversely during manufacture, storage and administration if the rubber part used has not been properly selected and validated (approved).

Elastomeric parts for parenterals and for devices for pharmaceutical use —

Part 1:
Extractables in aqueous autoclavates

1 Scope

1.1 This part of ISO 8871 defines procedures for classifying elastomeric parts for primary packs and medical devices used in direct contact with preparations for parenteral use, including both aqueous preparations and dry preparations which have to be dissolved before use.

It specifies a series of comparative test methods for chemical evaluation by the determination of extractables in aqueous autoclavates (see Clause 4) and describes the various fields of application for elastomeric parts. Dimensions and functional characteristics are specified in the relevant International Standards. Required properties as specified in this part of ISO 8871 are regarded as minimum requirements.

1.2 This part of ISO 8871 is applicable for the categories of elastomeric parts given in Clause 3; specific requirements, however, are laid down in the relevant International Standards dealing with the items or devices listed in Clause 3.

Elastomeric parts for empty syringes for single use are excluded from the scope of this part of ISO 8871 as they are not in contact with the injected preparation for a significant length of time.

1.3 Compatibility studies with the intended preparation have to be performed before the approval for final use can be given; however, this part of ISO 8871 does not specify procedures for carrying out compatibility studies.

2 Normative references

The following referenced documents are indispensable for the application of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 8362-2:1988, *Injection containers for injectables and accessories — Part 2: Closures for injection vials*

ISO 8362-5:1995, *Injection containers for injectables and accessories — Part 5: Freeze drying closures for injection vials*

ISO 8536-2:2001, *Infusion equipment for medical use — Part 2: Closures for infusion bottles*

ISO 8536-6:1995, *Infusion equipment for medical use — Part 6: Freeze drying closures for infusion bottles*

ISO 11040-2:1994, *Prefilled syringes — Part 2: Plungers and discs for dental local anaesthetic cartridges*

ISO 11040-5:2001, *Prefilled syringes — Part 5: Plungers for injectables*

3 Classification

Elastomeric parts exist in various designs and sizes depending on the intended end-use. These parts serve different purposes depending on the item or device in which they are incorporated. Elastomeric parts have, therefore, been classified into the following categories:

— elastomeric parts for injection vials (see ISO 8362-2);

— elastomeric parts for infusion bottles (see ISO 8536-2);

— elastomeric parts for prefilled syringes (see ISO 11040-2 and ISO 11040-5);

— elastomeric parts for medical devices for pharmaceutical use (excluding gloves and probes);

— elastomeric parts for freeze-dried products (see ISO 8362-5 and ISO 8536-6).

4 Requirements

4.1 Resistance to steam sterilization

Elastomeric parts shall not lose their required biological, chemical and physical properties after being sterilized twice in saturated steam at (121 ± 2) °C for 30 min each time.

4.2 Chemical requirements

Elastomeric parts shall comply with the chemical requirements specified in Table 1.

Elastomers are divided into the following types:

— Type I elastomer: this meets the strictest requirements and is the preferred type.

— Type II elastomer: this does not meet these severe requirements as a result of its different chemical composition which is necessary to give the mechanical properties required for special applications (e.g. multiple piercing).

The methods to be used to determine the chemical characteristics of the elastomeric parts are specified in Annex A to Annex J.

5 Sampling

Take a random sample of the elastomeric parts which is representative of each delivery, with the parts in their original state. The number of elastomeric parts taken shall be as specified in the relevant International Standards (see Clause 3).

Table 1 — Chemical requirements for testing aqueous autoclavates

Characteristic	Requirements	Test as described in Clause/Annex
Turbidity	Type I: Not more turbid than reference suspension II	A.1
	Type II: Not more turbid than reference suspension III	
Colour	Type I and II: Not more intensely coloured than reference solution GY_5	A.2
Acidity/alkalinity	Type I and II: $\leqslant$ 0,3 ml sodium hydroxide solution, c(NaOH) = 0,01 mol/l or $\leqslant$ 0,8 ml hydrochloric acid, c(HCl) = 0,01 mol/l	B
Absorbance	Type I: $\leqslant$ 0,2 AU across the whole range from 220 nm to 360 nm	C
	Type II: $\leqslant$ 4,0 AU across the whole range from 220 nm to 360 nm	
Reducing substances	Type I: $\leqslant$ 3,0 ml sodium thiosulfate solution, $c(Na_2S_2O_3)$ = 0,01 mol/l	D
	Type II: $\leqslant$ 7,0 ml sodium thiosulfate solution, $c(Na_2S_2O_3)$ = 0,01 mol/l	
Extractable heavy metals	Type I and II: $\leqslant$ 2,0 mg/l	E
Extractable zinc	Type I and II: $\leqslant$ 5,0 mg/l	F
Extractable ammonia	Type I and II: $\leqslant$ 2,0 mg/l	G
Residue on evaporation	Type I: $\leqslant$ 2,0 mg/50 ml	H
	Type II: $\leqslant$ 4,0 mg/50 ml	
Volatile sulfides	Type I and II: Black stain on acetate paper shall not be larger or darker than reference (0,154 mg Na_2S for every 20 cm^2 of stopper surface area.)	I
Conductivity (optional)	Type I: $\leqslant$ 15 µS/cm	J
	Type II: $\leqslant$ 30 µS/cm	
A blank may be prepared where appropriate for system control, but correction of the result using the blank result is only allowed if mentioned in the corresponding annex.		

6 Apparatus and reagents

6.1 Use only reagents of recognized analytical grade. For the preparation of standard solutions, see the relevant annex.

6.2 Use purified water prepared by distillation or by any other suitable means.

Its conductivity shall be less than 3,0 µS/cm.

NOTE Purified water as specified in various national pharmacopoeias corresponds to grade 1 and grade 2 water as specified in ISO 3696.

6.3 Glassware shall be made from borosilicate glass.

7 Preparation of test solutions

7.1 Closures shall be processed in the as-delivered condition.

7.2 Place a suitable number of complete elastomeric parts in a wide-necked flask and add 300 ml of purified water for every 150 cm^2 of surface area of the elastomeric parts. Cover the mouth of the flask, e.g. with aluminium foil or an inverted borosilicate glass beaker. Weigh the flask plus contents. Heat in an autoclave so that a temperature of (121 ± 2) °C is reached within 20 min to 30 min and maintain this temperature for 30 min. Cool to room temperature over about 30 min. Make up to the original mass with purified water if necessary (if tightly closed containers are not used).

Shake this solution (solution S_1) and immediately separate it from the elastomeric parts. Shake solution S_1 before each test.

7.3 Prepare a blank solution (solution S_0) in the same way as for solution S_1 except that 300 ml of purified water are used without the elastomeric parts.

7.4 Use solutions S_1 and S_0 obtained as described to carry out the chemical tests.

Annex A
(normative)

Appearance of solution

A.1 Turbidity of solution S_1

A.1.1 General

The determination may be carried out instrumentally using a turbidimeter or by visual comparison.

A.1.2 Visual comparison with standards

A.1.2.1 Reagents

A.1.2.1.1 Hydrazine sulfate solution

Dissolve 1,0 g of hydrazine sulfate in water and dilute to 100 ml with water. Allow to stand for 4 h to 6 h.

A.1.2.1.2 Hexamethylenetetramine solution

Dissolve 2,5 g of hexamethylenetetramine in 25,0 ml of water in a glass-stoppered 100 ml flask.

A.1.2.1.3 Stock suspension

To the solution of hexamethylenetetramine in the flask add 25,0 ml of hydrazine sulfate solution. Mix and allow to stand for 24 h. This suspension is stable for 2 months, provided it is stored in a glass container free from surface defects. Discard if the suspension adheres to the glass. Mix well before use.

A.1.2.1.4 Standard suspension

Dilute 15,0 ml of the stock suspension to 1 000 ml with water. This suspension shall be freshly prepared and may not be stored for longer than 24 h.

A.1.2.1.5 Reference suspensions

Prepare reference suspensions in accordance with Table A.1. Mix well before use.

Table A.1

	I	II	III
Standard suspension	5,0 ml	10,0 ml	30,0 ml
Water	95,0 ml	90,0 ml	70,0 ml