INTERNATIONAL STANDARD

ISO 8871-2

Second edition
2020-05

Elastomeric parts for parenterals and for devices for pharmaceutical use —

Part 2: Identification and characterization

Éléments en élastomère pour administration parentérale et dispositifs à usage pharmaceutique —
Partie 2: Identification et caractérisation

Reference number
ISO 8871-2:2020(E)

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Published in Switzerland

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Foreword

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The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular, the different approval criteria needed for the different types of ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

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. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT) see www.iso.org/iso/foreword.html.

This document was prepared by Technical Committee ISO/TC 76, *Transfusion, infusion and injection, and blood processing equipment for medical and pharmaceutical use*, in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/TC 205, *Non-active medical devices*, in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

This second edition cancels and replaces the first edition (ISO 8871-2:2003), which has been technically revised. It also incorporates the Amendment ISO 8871-2:2003/Amd.1:2005. The main changes compared to the previous edition are as follows:

— expansion of the scope to include coated stoppers;

— addition of terms and definitions;

— addition of H.6 on the interpretation of results for ATR.

A list of all parts in the ISO 8871 series can be found on the ISO website.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

The elastomeric parts specified in the ISO 8871 series are produced from rubber. However, rubber is not a unique entity, since the composition of rubber materials can 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 might have a significant effect on the overall properties. Polymer coatings or films are often applied to either entire or partial surface(s) of a rubber component to impart certain physical or chemical properties. The effectiveness, purity, stability and safe handling of a drug preparation can 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 2:
Identification and characterization

1 Scope

This document specifies identification and characterization procedures applicable to elastomeric parts including coated stoppers used for drug containers and medical devices.

The physical and chemical test procedures specified in this document permit the determination of the typical characteristics of elastomeric parts including coatings and surface treatments and can serve as a basis for agreements between manufacturer and user regarding the product consistency in subsequent supplies. Depending upon the type of elastomer and its application, an appropriate set of tests is selected.

2 Normative references

The following documents are referred to in the text in such a way that some or all of their content constitutes requirements 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 48-4, *Rubber, vulcanized or thermoplastic — Determination of hardness — Part 4: Indentation hardness by durometer method (Shore hardness)*

ISO 247-1:2018, *Rubber — Determination of ash — Part 1: Combustion method*

ISO 2781:2018, *Rubber, vulcanized or thermoplastic — Determination of density*

ISO 8871-1, *Elastomeric parts for parenterals and for devices for pharmaceutical use — Part 1: Extractables in aqueous autoclavates*

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at http://www.electropedia.org/

3.1
barrier coating
layer of a different polymer completely or partly covering the elastomeric part to reduce migration, permeation and/or interactions of substances of rubber component to drug product and vice versa

Note 1 to entry: The coating can be applied by different techniques, such as spraying, tumbling or vapour-depositing a liquid or vapour onto the rubber component or laminating a film onto the elastomeric surface during the moulding process.

Note 2 to entry: The presence of the coating can be verified by using the test method described in Annex H.

3.2
elastomer
base polymer that is converted into rubber by vulcanization

3.3
lubrication coating
layer of a different polymer completely or partly covering the elastomeric part to support functionality in the final container closure system

Note 1 to entry: Certain lubrication coatings can also be used to eliminate the need for silicone oil in the container closure system and/or enhancing other functionalities, such as gliding force, break loose force or removal force.

Note 2 to entry: The coating can be applied by different techniques, such as spraying, tumbling or vapour-depositing a liquid or vapour onto the rubber component or laminating a film onto the elastomeric surface.

3.4
rubber
vulcanized material obtained by crosslinking of elastomer

[SOURCE: ISO 11999-1:2015 3.75, modified]

3.5
surface treatment
treatment of the surface of rubber by physical or chemical means to get desired properties

EXAMPLE Siliconization, chlorination.

Note 1 to entry: Surface treatments are applied to avoid sticking together and enhance machinability on processing lines.

4 Tests

4.1 General

Rubber is a complex material and it is not generally definable. The only property which all elastomeric materials have in common is a special type of resilience or elasticity. When a strip of rubber is stretched, it will extend by up to many times its original length without breaking. On release of the stretching force, it snaps back to its original size and shape virtually unaltered. Similarly, one can squeeze it, twist it or distort it in any direction comparatively easily, and it will virtually spring back again to its original shape unchanged.

Owing to its three-dimensional network, achieved by chemical cross-linking of the elastomer during vulcanization, rubber is practically insoluble in solvents such as tetrahydrofuran, although considerable reversible swelling may occur; this characteristic differentiates rubber from pseudo-elastic materials, such as poly(vinyl chloride) and certain thermoplastic elastomers.

In view of the complexity of rubber, a set of tests is needed for reliable identification.

The manufacturer shall guarantee that all elastomeric parts of current supplies have been produced from the same formulation and that they exhibit the same characteristics as the initially supplied samples.

4.2 Hardness

Hardness shall be determined in accordance with ISO 48-4.

4.3 Density

Density shall be determined in accordance with the procedure described in ISO 2781:2018, Clause 4, method A.

4.4 Ash

The inorganic residue after combustion shall be determined as described in ISO 247-1:2018, 4.1, method A.

4.5 Infrared spectrum

4.5.1 Material

One method to create a fingerprint of a rubber material is to record an infrared (IR) spectrum. The two common methods for obtaining an IR spectrum of a rubber material are pyrolysis IR and surface IR/ATR (attenuated total reflectance)-technique.

The pyrolysis IR can be obtained as described in Annex A. Alternatively, an aliquot of the pyrolysate can be brought on an ATR crystal of an FTIR-spectrometer as described in Annex H. The surface IR/ATR can be obtained as described in Annex H. The spectra should be compared with a spectrum obtained by the same IR method on a reference sample of the material.

In practice, pyrolysis IR requires a time-consuming sample preparation. In addition, it needs the cautious handling of hazardous vapours and oils.

In contrast to this, the surface IR/ATR offers the possibility to obtain a fingerprint from an elastomeric part with minimum or no sample preparation.

4.5.2 Coating

The presence of a coating (barrier and lubrication coating) can be verified by comparing FTIR spectra of the surface and of the core material of the product (see Annex H). For measuring the coating, the samples do not need to be cut.

4.6 Compression set

The compression set indicates the degree of permanent deformation remaining after compression at a constant deformation and defined temperature for a defined time. The compression set can be determined in accordance with Annex B.

4.7 Swelling

Elastomeric materials are subject to varying degrees of swelling when exposed to organic solvents. The degree of volume and/or mass increase is primarily influenced by the type of elastomer. Swelling requires special care when the rubber components are in contact with emulsions or oily vehicles.

The relevant procedure is specified in Annex C.

4.8 Development of a fingerprint by gas chromatography

The elastomeric materials under examination are extracted in a solvent which does not dissolve but might swell the rubber. The extract is injected into a gas chromatograph. The chromatogram obtained exhibits a typical profile and can be used as a fingerprint for identification purposes. Furthermore, GC-coupling techniques, for example gas chromatography – mass spectrometry (GC-MS), may provide additional information about the composition of the extract.

The relevant procedure is specified in Annex D.

4.9 Detection of volatile substances by gas chromatography

Elastomeric materials may release volatile substances. These may originate from one of the following categories of material:

— oligomers or process aids present in the base polymer;

— stabilizers or antioxidants;

— softeners.

The relevant procedure is specified in Annex E.

4.10 Determination of residual moisture

While undergoing treatments which are typical in the pharmaceutical industry, elastomeric parts can absorb moisture in considerable quantities. During storage of the pharmaceutical product, the trapped moisture may be released and absorbed by the pharmaceutical product, thus reducing its effectiveness (critical case: lyophilized drugs). The nature of the absorption and desorption processes is affected by the composition of the rubber, the type of treatment (e.g. steam autoclaving) and the efficiency of any subsequent drying process.

The relevant procedure is specified in Annex F.

4.11 Determination of fingerprint by thermogravimetric analysis (TGA)

Elastomeric parts are composed of components which can be classified relative to their performance under thermal treatment, as follows:

— base polymers;

— inorganic fillers;

— substances volatile at elevated temperatures;

— carbon black.

The relevant procedure is specified in Annex G.

4.12 Determination of extractables in aqueous autoclavates

Elastomeric materials may release substances of undetermined nature in water. For the general assessment of the chemical cleanliness of closures ISO 8871-1 applies.

5 Preparation of samples for testing

5.1 Treatment before testing

The various test procedures may require different pretreatments, see Annexes A to H.

It is generally assumed that samples of rubber parts will be provided in a clean state in accordance with the state of the art. In order to avoid contamination, they shall be contained in a suitable packaging. Any particular treatment or method of packaging to be carried out by the manufacturer shall be subject to agreement between the manufacturer and the customer.

5.2 Number of samples needed for the tests

Due to the large number of tests in this document and their complexity, usually not all of the tests are performed in each investigation. For this reason, the number of samples needed shall be agreed on

between the manufacturer and the test laboratory. Each annex specifies the number of samples that are needed to perform that specific test.

6 Reagents and materials

6.1 Use only reagents of recognized analytical grade, for example water Grade 1 or 2 of ISO 3696 or any comparable water quality according to current USP and Ph Eur.

6.2 All glass equipment shall be made from borosilicate glass.