INTERNATIONAL STANDARD

ISO 8871-3

First edition
2003-08-01

Elastomeric parts for parenterals and for devices for pharmaceutical use —

Part 3: Determination of released-particle count

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

Partie 3: Dénombrement des particules libérées

Reference number
ISO 8871-3:2003(E)

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Published in Switzerland

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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 8871-3 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

When elastomeric closures are used as primary packaging materials in direct contact with pharmaceutical preparations, the pharmaceutical industry requires, to an increasing extent, definite details from the rubber manufacturer about the presence of particles the closures may release into an injectable. The test methods specified in Clauses 3 and 4 make it possible to meet this request.

Elastomeric parts for parenterals and for devices for pharmaceutical use —

Part 3: Determination of released-particle count

1 Scope

Elastomeric closures may be superficially contaminated with visible and subvisible particles, and fragments can also be produced when the closure is pierced by a needle.

Such particles may be transferred to pharmaceutical preparations in contact with the elastomeric parts and affect the quality of such preparations.

This part of ISO 8871 specifies methods for the determination of the number of visible and subvisible particles, respectively, detached from elastomeric parts by rinsing.

It does not specify particle contamination limits. These will have to be agreed upon between manufacturer and user.

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 3696:1997, *Water for analytical laboratory use — Specification and test methods*

3 Determination of visible-particle count

3.1 Principle

This method evaluates the potential for contamination by collecting and counting the particles detached from elastomeric parts on rinsing with water.

3.2 Classification

For the purposes of this method, particles are divided into size classes as follows, using the longest dimension as the classifying parameter:

Class I: > 25 µm but $\leqslant 50$ µm;

Class II: > 50 µm but $\leqslant 100$ µm;

Class III: > 100 µm.

3.3 Apparatus and materials

3.3.1 Shaking machine, moving in a horizontal circle of 12 mm ± 1 mm diameter at 300 min^{-1} to 350 min^{-1}.

3.3.2 Membrane filters, with a maximum pore size of 0,8 µm, provided with grid lines dividing the surface into 3 mm × 3 mm squares.

NOTE The colour of the filter may significantly affect the test results.

If no specific agreement has been made between the interested parties, the basic colour shall be medium grey and lie within the following coordinate ranges in the CIE (International Commission on Illumination) system:

L^* between 60 % and 70 %;

a^* between – 4,7 % and – 3,7 %;

b^* between – 4,7 % and – 3,7 %.

These specifications apply to the grid-imprinted surface of the filter, and assume this surface has a 3-mm-square grid made up of green lines.

3.3.3 Clean, wide-mouthed conical flasks, of capacity 300 ml.

3.3.4 Rinse fluid, prepared by dissolving 3 g of commercially available highly concentrated polysorbate 80 (Tween 80) in 10 l of purified water (grade 1 or grade 2 as specified in ISO 3696).

3.3.5 Equipment for supplying the rinse fluid under a suitable pressure, including a terminal filter with a maximum pore size of 1,2 µm.

3.3.6 Microscope, magnification about × 50, with suitable direct illumination at an angle of 0° to 10° with the microscope stage.

3.4 Preparation for the test

3.4.1 Ensure that the environment in which the test is to be carried out is free from extraneous particles which could cause interference. This involves wearing suitable garments and gloves and using a suitable clean-air work station, for example a laminar-flow cabinet meeting the requirements of Class 8 of ISO 14644-1 (Class 100,000 of US Federal Standard 209E), as well as suitably decontaminated tools and sample-handling equipment.

3.4.2 Carry out a blank test, as follows:

- Place 50 ml of filtered rinse fluid in a conical flask.
- Shake for 20 s.
- Immediately filter the fluid through a membrane filter.
- Add another 50 ml portion of rinse fluid to the flask, shake, and filter in the same way.
- Transfer the filter to the microscope, taking care not to contaminate it.
- Count the particles on the filter.

No more than five particles of Class I and no more than one particle of Class II shall be found. No particles of Class III shall be present.

If these requirements are not met, investigate the possible causes of failure, rectify, and repeat the blank test until satisfactory results are obtained.

Carry out a blank test both before and after each series of tests. Only when satisfactory values are obtained both before and after the series of tests can the results of the tests be considered valid.

3.5 Test

— Place a number of complete elastomeric parts with a total surface area of approximately 100 cm^2 into a conical flask.

— Add 50 ml of filtered rinse fluid.

— Shake for 20 s.

— Immediately filter the fluid through a membrane filter.

— Add another 50 ml portion of rinse fluid to the flask, shake and filter in the same way.

— Transfer the filter to the microscope, taking care not to contaminate it.

— Count the particles on the filter.

3.6 Test report

For each test, report the following:

a) the total surface area of the elastomeric parts tested, and the number of complete parts tested;

b) the total particle count in each of the three particle-size classes;

c) the particle counts in each of the three classes for the blank tests performed;

d) the average particle count in each class per 10 cm^2 of surface, rounded to one place of decimals.

4 Determination of subvisible-particle count

4.1 Principle

In contact with liquid pharmaceutical preparations, elastomeric parts may release particles having dimensions of 25 µm or smaller, and hence not visible to the naked eye. Their presence can be detected by means of electrical or optical instruments.

This method evaluates the potential of elastomeric parts to release such particles by bringing the parts in contact with water and examining the contact fluid with a suitable particle counter operating on the light extinction principle.