INTERNATIONAL STANDARD

ISO 8871

Second edition
1990-08-01

AMENDMENT 1
1995-10-01

Elastomeric parts for aqueous parenteral preparations

AMENDMENT 1

Éléments en élastomère pour préparations aqueuses parentérales

AMENDEMENT 1

Reference number
ISO 8871:1990/Amd.1:1995(E)

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.

Amendment 1 to International Standard ISO 8871:1990 was prepared by Technical Committee ISO/TC 76, *Transfusion, infusion and injection equipment for medical use.*

Annexes N and P form an integral part of ISO 8871.

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Printed in Switzerland

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Page iv

Add the following to the list of contents:

Annex N Determination of visible particles on elastomeric parts

Annex P Determination of subvisible particles on elastomeric parts

Page v

Amend the last paragraph of the foreword to include annexes N and P as forming an integral part of this International Standard.

Page vi

Beneath the existing introduction, add the following text:

The pharmaceutical industry requires to an increasing extent concrete details from the rubber manufacturer about the presence of particles the closures may release to the injectable where elastomeric closures are used as primary packaging materials in direct contact with pharmaceutical preparations. This request has been taken into account by preparing annexes N and P.

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After this page, insert the following two new annexes.

Annex N
(normative)

Determination of visible particles on elastomeric parts

N.1 Principle

Elastomeric closures may be superficially contaminated with particles visible to the naked eye.

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

This method serves to evaluate contamination of this kind by collecting and counting the particles, detached from the elastomeric parts by rinsing.

N.2 Classification

For the purposes of this method, particles are divided in categories as follows, using the longest visible dimension as the classifying parameter:

Class I: larger than 25 µm and smaller than or equal to 50 µm

Class II: larger than 50 µm and smaller than or equal to 100 µm

Class III: larger than 100 µm

N.3 Apparatus and reagents

N.3.1 Shaking machine, moving in a horizontal circle of 12 mm ± 1 mm diameter at 300 min^{-1} to 350 min^{-1}.

N.3.2 Membrane filters, with maximum pore size of 0,8 µm, provided with grid lines at 3 mm × 3 mm.

NOTE 6 The colour of the filter may significantly affect the test results.

In case no specific agreements have been made between parties, the colour should be medium grey, and meet the following coordinate ranges in the CIE system:

L* between 60 % and 70 %

a* between −4,7 % and −3,7 %

b* between −4,7 % and −3,7 %

These specifications are valid for measurements on the grid-imprinted face of the filter, assuming a 3 mm square grid in green colour.

N.3.3 Clean, wide-mouth Erlenmeyer flasks, of capacity 300 ml.

N.3.4 Rinse fluid, prepared by dissolving 3 g of commercially available highly concentrated sodium *N*-methyl-*N*-oleyltaurate powder[1] in 10 l of purified water as specified in ISO 3696, grade 1 or grade 2.

N.3.5 Equipment to supply the rinse fluid under adequate pressure, using a final filter with maximum pore size of 1,2 µm.

N.3.6 Microscope, magnification about × 50, with appropriate object illumination, incident angle with the object stage between 0° and 10°.

N.4 Preparations

N.4.1 Provide the apparatus and reagents as specified in N.3.

N.4.2 Ensure such an environment for carrying out all operations that no extraneous particles can interfere. This involves wearing suitable garments and gloves, and using a suitable clean air workstation, for example providing laminar airflow to Class 100[2] as well as suitably decontaminated tools and handling means.

N.4.3 Carry out a blank preparation, as follows.

N.4.3.1 In an Erlenmeyer flask, place 50 ml of prefiltered rinse fluid

1) Sodium salt of *N*-methyl-*N*-oleylmethylaminoethanesulfonic acid.

2) As specified in USA Federal Standard 209E.

N.4.3.2 Shake for 20 s.

N.4.3.3 Immediately filter the fluid over a membrane filter.

N.4.3.4 Add another 50 ml portion of rinse fluid to the flask, shake, and filter in the same way.

N.4.3.5 Store the filter suitably.

N.4.3.6 Count the particles on the filter by means of the microscope.

N.4.3.7 No more than five particles of Class I nor more than one particle of Class II shall be found; no particle of Class III shall be present.

N.4.3.8 If these requirements are not met, investigate the possible causes for the failure, improve, and repeat the test until satisfactory results are obtained.

NOTE 7 Only when satisfactory blank values have been obtained, both before and after a test series on parts, are the results of the part tests considered valid.

N.5 Test

N.5.1 Place the number of intact elastomeric parts to be tested, with a total surface of approximately 100 cm², in an Erlenmeyer flask.

N.5.2 Add 50 ml of prefiltered rinse fluid.

N.5.3 Shake for 20 s.

N.5.4 Immediately filter the fluid over a membrane filter.

N.5.5 Add another 50 ml portion of rinse fluid to the flask, shake and filter in the same way.

N.5.6 Store the filter suitably.

N.5.7 Count the particles on the filter by means of the microscope.

N.6 Expression of results

For each test, report the following:

a) total surface tested, and number of whole parts tested;

b) total count of particles in each of the three classes;

c) counts in each of the three classes for at least one of the blank tests performed;

d) average count of particles in each class per 10 cm² of tested surface, rounded to one decimal.

Annex P
(normative)

Determination of subvisual particles on elastomeric parts

P.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 serves to evaluate the potential of elastomeric parts to release such particles by bringing the parts in contact with water and scanning the contact fluid with a suitable instrument based on the light blockage principle.

P.2 Classification

For the purposes of this method, particles are divided in categories as follows, using the equivalent sphere diameter as the classifying parameter:

- ⩾ 2 µm and < 5 µm;
- ⩾ 5 µm and < 10 µm;
- ⩾ 10 µm and < 25 µm;
- ⩾ 25 µm.

P.3 Apparatus and reagents

P.3.1 Shaking machine, moving in a horizontal circle of 12 mm ± 1 mm diameter at 300 min^{-1} to 350 min^{-1}.

P.3.2 Clean, wide-mouth Erlenmeyer flasks, of capacity 300 ml.

P.3.3 Water, containing not more than 100 particles larger than 2 µm per 5 ml.

P.3.4 Scanning instrument, fitted with a light blockage, capable of classifying particles in a fluid into the classes as defined.

P.4 Preparations

P.4.1 Provide the apparatus and reagents as specified in P.3.

P.4.2 Ensure such an environment for carrying out all operations that no extraneous particles can interfere. This involves using a suitable clean air workstation, for example providing laminar airflow to Class 100[1], as well as suitably decontaminated tools and handling means.

P.4.3 Carry out a blank preparation, as follows.

P.4.3.1 In an Erlenmeyer flask place 100 ml of particle-free water (P.3.3).

P.4.3.2 Shake for 20 s.

P.4.3.3 Examine the obtained fluid in the counting instrument in the time interval starting 15 min and ending 30 min after preparation, and record the results.

P.4.3.4 Repeat the entire operation twice.

P.4.3.5 In no case shall more than 100 particles larger than 2 µm per 5 ml be found.

P.4.3.6 If this requirement is not met, investigate the possible causes for the failure, improve, and repeat the test until a satisfactory result is obtained.

NOTE 8 Only when satisfactory blank values have been obtained before a test series on parts are the results of the part tests considered valid.

P.5 Test

P.5.1 Place the number of intact parts to be tested, with a total surface of approximately 100 cm^2, in an Erlenmeyer flask.

P.5.2 Add 100 ml of particle-free water (P.3.3).

1) As specified in USA Federal Standard 209E.

P.5.3 Shake for 20 s.

P.5.4 Examine the obtained fluid in the counting instrument in the time interval starting 15 min and ending 30 min after preparation, and record the results.

P.5.5 Repeat the entire operation twice.

P.6 Expression of results

For each test, report the following:

a) total surface tested, and number of whole parts tested;

b) the three individual count values in each of the four classes;

c) the average values in each of the four classes, calculated from the individual values and expressed per 10 cm^2 of tested surface, rounded to the nearest integer;

d) total count of particles in each of the four classes;

e) counts in each of the four classes for at least one of the performed blank tests;

f) average count of particles in each class per 10 cm^2 of tested surface, rounded to one decimal.

ICS 11.040.20

Descriptors: medical equipment, parenteral infusion equipment, components, rubber products, specifications, tests, packaging, marking, storage.

Price based on 5 pages