INTERNATIONAL STANDARD

ISO 4802-2

Third edition
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Glassware — Hydrolytic resistance of the interior surfaces of glass containers —

Part 2:
Determination by flame spectrometry and classification

Verrerie — Résistance hydrolytique des surfaces internes des récipients en verre —

Partie 2: Détermination par spectrométrie de flamme et classification

Reference number
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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).

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For an explanation on 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 the following URL: www.iso.org/iso/foreword.html.

The committee responsible for this document is ISO/TC 76, *Transfusion, infusion and injection, and blood processing equipment for medical and pharmaceutical use*.

This third edition cancels and replaces the second edition (ISO 4802-2:2010), which has been technically revised in particular by amending

— the subclauses on water (test water and purified water),

— the test procedure, and

— the subclause on autoclave and steam sterilizer respectively.

ISO 4802 consists of the following parts, under the general title *Glassware — Hydrolytic resistance of the interior surfaces of glass containers*:

— *Part 1: Determination by titration method and classification*

— *Part 2: Determination by flame spectrometry and classification*

Introduction

This part of ISO 4802 is largely based on a method of test approved by the International Commission on Glass (ICG), Technical Committee 2, *Chemical Durability and Analysis,* for measuring the hydrolytic resistance of the interior surfaces of glass containers.

This part of ISO 4802 contains a classification which is related to but not equivalent to the classification set up in ISO 4802-1 for the titration method.

Glassware — Hydrolytic resistance of the interior surfaces of glass containers —

Part 2:
Determination by flame spectrometry and classification

1 Scope

This part of ISO 4802 specifies:

a) methods for determining the hydrolytic resistance of the interior surfaces of glass containers when subjected to attack by water at (121 ± 1) °C for (60 ± 1) min. The resistance is measured by determining the amount of sodium and other alkali metal or alkaline earth oxides in the extraction solution using flame atomic emission or absorption spectrometry (flame spectrometry);

b) a classification of glass containers according to the hydrolytic resistance of the interior surfaces determined by the methods specified in this part of ISO 4802.

The test method specified in this part of ISO 4802 might not be applicable to containers whose surfaces have been treated with silicon (e.g. containers that are ready for direct filling).

2 Normative references

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

ISO 385, *Laboratory glassware — Burettes*

ISO 719, *Glass — Hydrolytic resistance of glass grains at 98 degrees C — Method of test and classification*

ISO 720, *Glass — Hydrolytic resistance of glass grains at 121 degrees C — Method of test and classification*

ISO 1042, *Laboratory glassware — One-mark volumetric flasks*

ISO 3819, *Laboratory glassware — Beakers*

ISO 9187-1, *Injection equipment for medical use — Part 1: Ampoules for injectables*

3 Terms and definitions

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

3.1
ampoule
small, normally flat-bottomed container having stems in many different forms

Note 1 to entry: Ampoules are usually thin-walled and have a capacity normally up to 30 ml. They are intended to be closed, after filling, by flame sealing.

3.2
bottle
flat-bottomed container, made from moulded glass

Note 1 to entry: Bottles are normally thick-walled and have a capacity usually of more than 5 ml. They may be of circular or other geometric cross-section. Bottles are sealed with a closure made from a material other than glass, and not by flame-sealing.

3.3
brimful capacity
volume of water required to fill a container, placed on a flat, horizontal surface

3.4
container
article made from glass to be used as primary packaging material intended to come into direct contact with the pharmaceutical preparations

EXAMPLE Bottles, vials, syringes, ampoules and cartridges. See also Figure 1.

Note 1 to entry: These containers are made from borosilicate or soda-lime-silica glass.

3.5
filling volume
defined volume of water to fill the test specimen

Note 1 to entry: For the determination of the filling volume, see 7.2. The filling volume is a test specific quantity that is used to compare container sets from different sources or lots. It has no relation to the nominal product volume.

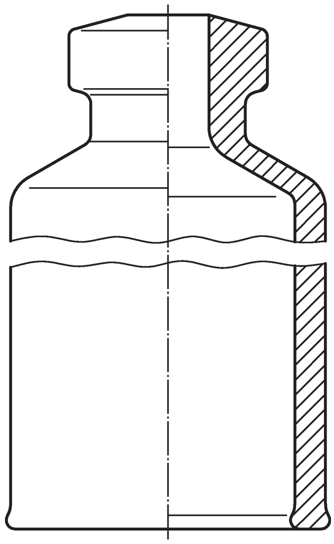
3.6
borosilicate glass
silicate glass having a very high hydrolytic resistance due to its composition containing significant amounts of boric oxide

Note 1 to entry: Borosilicate glass contains a mass fraction of boric oxide between 5 % and 13 %. This glass type may also contain aluminium oxide and/or alkaline earth oxides.

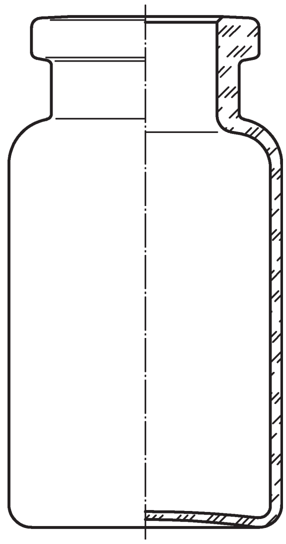
Note 2 to entry: Neutral glass is a borosilicate glass having a very high hydrolytic resistance and a high thermal shock resistance. When tested according to ISO 720, it meets the requirements of class HGA 1. Containers properly made from this glass comply with hydrolytic resistance container class HC_F 1 of this part of ISO 4802.

3.7
soda-lime-silica glass
silicate glass containing a mass fraction up to approximately 15 % of alkali metal oxides, mainly sodium oxide, and a mass fraction up to about 15 % of alkaline earth oxides, mainly calcium oxide

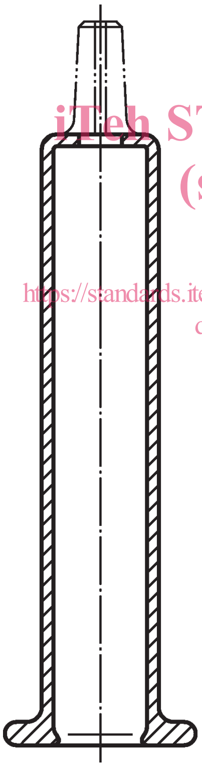
Note 1 to entry: Containers made from this glass will have a moderate hydrolytic resistance due to the chemical composition of the glass, and comply with hydrolytic resistance container class HC_F 3.



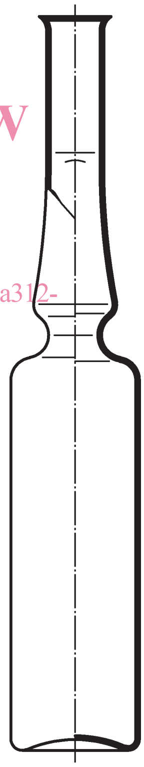
a) Example of a glass cylinder for pen-injectors (see ISO 13926-1)



b) Example of an injection vial made of glass tubing (see ISO 8362-1)



c) Example of a glass barrel (see ISO 11040-4)



d) Example of a stem cut ampoule with constriction (see ISO 9187-1)

Figure 1 — Examples of containers

3.8
surface treatment
treatment of the internal surface of glass containers with reagents in order to achieve a de-alkalized surface and to produce a significantly lower release of alkali metal ions (and alkali earth metal ions)

Note 1 to entry: Surface treatment is used, for example, in order to change a soda-lime-silica glass container of hydrolytic resistance class HC_F 3 to a container of hydrolytic resistance class HC_F 2 container. Treated containers are rinsed before use.

3.9
vial
small, flat-bottomed container, made from tubing or from moulded glass

Note 1 to entry: Vials are normally thick-walled and have a capacity up to 100 ml. They are normally sealed with a closure made from a material other than glass, and not by flame-sealing.

4 Principle

This method of test is a surface test applied to glass containers as produced and/or as delivered.

The containers to be tested are filled with specified water to a specified capacity. They are loosely capped and then heated under specified conditions. The degree of the hydrolytic attack is measured by flame spectrometric analysis of the extraction solutions.

5 Reagents

During the test, unless otherwise stated, use only reagents of recognised analytical grade.

5.1 Test water, to be prepared as follows:

Prepare the test water from distilled water (5.6) by multiple distillations. Remove the carbon dioxide by boiling for at least 15 min before use in a boiling flask (6.3) of fused silica or borosilicate glass and cool.

NOTE 1 Any other suitable method can be used.

When tested immediately before use, water prepared as described above shall produce an orange-red (not violet-red or yellow) colour corresponding to the neutral point of methyl red indicator of pH 5,5 ± 0,1 when 0,05 ml of methyl red indicator solution (5.5) is added to 50 ml of the water to be examined.

This water may also be used as the reference solution (see 8.4).

The conductivity of the water shall not exceed 1 µS/cm, determined at 25 °C by an in-line conductivity meter.

NOTE 2 This description is based on the European Pharmacopoeia 3.2.1[12]. In the European Pharmacopoeia, water prepared as described above is designated water R1.

NOTE 3 Water of Grade 2 according to ISO 3696[2] is suitable for this test.

5.2 Hydrochloric acid, solution, $c(HCl) \approx 2$ mol/l.

5.3 Hydrochloric acid, solution, $c(HCl) \approx 6$ mol/l (≈ 1 + 1).

5.4 Hydrofluoric acid, $c(HF) \approx 22$ mol/l (i.e. ≈400 g HF/l solution).

CAUTION — Hydrofluoric acid is very toxic and highly corrosive. Consider material safety data sheet!

5.5 Purified water prepared by distillation, by ion exchange, by reverse osmosis or by any other suitable method from water having drinking water quality.

NOTE 1 See national or regional regulation on water intended for human consumption.

NOTE 2 Water that corresponds to Grade 3 according to ISO 3696 is suitable.

NOTE 3 In the European Pharmacopoeia 3.2.1[12], water as described above is designated water R.

5.6 Spectrochemical buffer solution (caesium chloride solution, CsCl).

Dissolve 80 g of caesium chloride in approximately 300 ml of test water (5.1), add 10 ml of hydrochloric acid (5.3) and transfer to a 1 000 ml volumetric flask (6.3). Dilute to the mark with the test water (5.1) and mix.

5.7 Stock solutions.

5.7.1 Dry sodium chloride, potassium chloride and calcium carbonate at (110 ± 5) °C for 2 h. Prepare aqueous stock solutions, using the test water (5.1), directly from the chlorides and from the calcium carbonate, after dissolving in the minimum amount of hydrochloric acid so that all solutions have concentrations of 1 mg/ml, calculated as sodium oxide, potassium oxide and calcium oxide.

5.7.2 Commercially available standard solutions may also be used.

5.8 Standard solutions.

5.8.1 Prepare standard solutions by diluting the stock solutions (5.7) with the test water (5.1) to obtain concentrations suitable for establishing the reference solutions in an appropriate manner, e.g. with concentrations of 20 µg/ml of sodium oxide, potassium oxide and calcium oxide respectively.

5.8.2 Commercially available standard solutions may also be used.

5.9 Reference solutions.

The reference solutions for establishing the calibration graph (set of calibration solutions) shall be prepared by diluting suitable concentrated standard solutions (5.8) with the test water (5.1). They shall cover the optimum working ranges of the specific elements according to the instrument used for the measurement. Typical concentration ranges of the reference solutions are:

— for determination by flame atomic emission spectroscopy (FAES) of sodium oxide and potassium oxide: up to 10 µg/ml;

— for determination by flame atomic absorption spectrometry (FAAS) of sodium oxide and potassium oxide: up to 3 µg/ml;

— for determination by flame atomic absorption spectrometry (FAAS) of calcium oxide: up to 7 µg/ml.

For the measurement of containers of hydrolytic resistance container classes HC_F 1, HC_F 2 or HC_F B (borosilicate or highly resistant glasses), the reference solutions shall be used without addition of the spectrochemical buffer solution (5.6).

Nevertheless, when the test is run for arbitration purposes it is recommended that the spectrochemical buffer solution also be added to these container classes.

For the measurement of containers of hydrolytic resistance container classes HC_F 3 or HC_F D (soda-lime-silica glasses), the reference solutions shall contain a volume fraction of 5 % *(V/V)* of the spectrochemical buffer solution (5.6).