INTERNATIONAL STANDARD

ISO 4802-2

Second 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
ISO 4802-2:2010(E)

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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 4802-2 was prepared by Technical Committee ISO/TC 76, *Transfusion, infusion and injection equipment for medical and pharmaceutical use*.

This second edition cancels and replaces the first edition (ISO 4802-2:1988), which has been technically revised.

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 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 385, *Laboratory glassware — Burettes*

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

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

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

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

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 Ampoules are 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 Bottles are normally thick-walled and have a capacity usually of more than 50 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 These containers are made from borosilicate or soda-lime-silica glass.

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

NOTE 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.

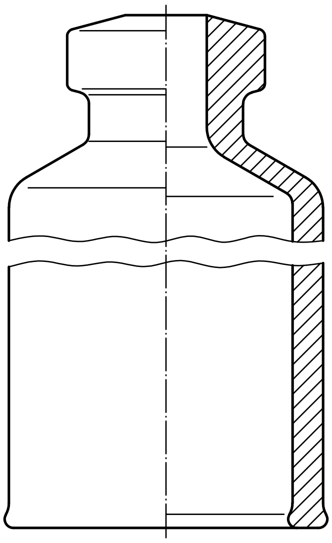
3.6
borosilicate glass
silicate glass having a very high hydrolytic resistance due to its composition containing significant amounts of boric oxide

NOTE 1 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.

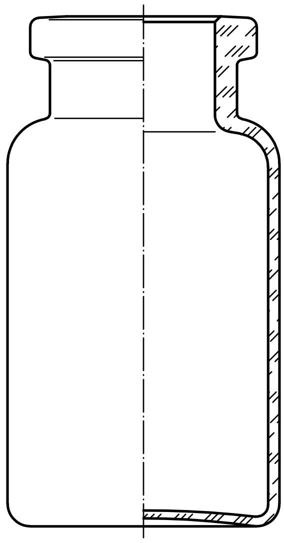
NOTE 2 Neutral glass is a borosilicate glass having a very high hydrolytic resistance and a high thermal shock resistance. When tested according to ISO 720, it meets the requirements of class HGA 1. Containers properly made from this glass comply with hydrolytic resistance container class HC_F 1 of this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

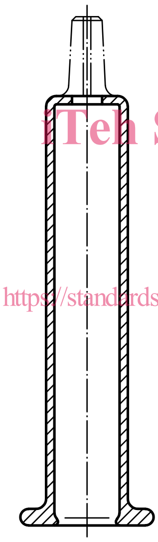
NOTE Containers made from this glass will have a moderate hydrolytic resistance due to the chemical composition of the glass, and comply with hydrolytic resistance container class HC_F 3.



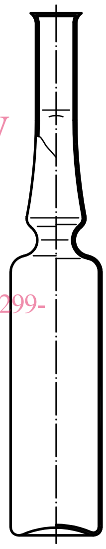
a) Example of a glass cylinder for pen-injectors (see ISO 13926-1)



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 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 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, complying with the requirements specified in ISO 3696 for grade 2 water or better.

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

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

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

5.5 Distilled water or **water of equivalent purity** (grade 3 water complying with the requirements specified in ISO 3696).

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.

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 should normally 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 % of the spectrochemical buffer solution (5.6).

6 Apparatus

Ordinary laboratory apparatus, and those specified in 6.1 to 6.6.

6.1 Autoclave or **steam sterilizer**, capable of withstanding a pressure of at least 250 kPa (2,5 bar) and of carrying out the heating cycle specified in 8.3. It shall be capable of maintaining a temperature of (121 ± 1) °C, equipped with a calibrated thermometer or a calibrated thermocouple recorder, a pressure gauge and a vent-cock.

When necessary and appropriate, the autoclave vessel and ancillary equipment shall be thoroughly cleaned before use using the test water (5.1) in order to avoid contamination that can influence the test results.

6.2 Burettes, having a suitable capacity according to the analytical procedure to be used and complying with the requirements specified for class A burettes in ISO 385 and made of glass of hydrolytic resistance grain class HGA 1 as specified in ISO 720[1)] or ISO 719.

6.3 One-mark volumetric flasks, having a capacity of 1 000 ml and complying with the requirements specified for class A one-mark volumetric flasks in ISO 1042.

6.4 Water bath, capable of being heated to approximately 80 °C.

6.5 Flame atomic absorption (FAAS) or **flame atomic emission (FAES) instrument**.

FAAS instruments shall be equipped with line sources for sodium, potassium and calcium; they shall be equipped with air/propane or air/acetylene gas supplies and burners for measuring sodium and potassium, and with a nitrous oxide/acetylene gas supply and burner for measuring calcium.

FAES instruments shall be equipped with air/propane or air/acetylene gas supplies and burners for measuring sodium and potassium.

6.6 Beakers, having a suitable capacity and complying with the requirements specified in ISO 3819.

Before use, each new beaker shall be pretreated by subjecting it to the autoclaving conditions described in 8.3.

1) Glass of hydrolytic resistance grain class ISO 719-HGB 1 adequately meets the requirements of class HGA 1 specified in ISO 720.