INTERNATIONAL STANDARD

**ISO 4802-2**

Fourth edition

# 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*



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Reference number
ISO 4802-2:2023(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 document 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).

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This document was prepared by Technical Committee ISO/TC 76, *Transfusion, infusion and injection, and blood processing equipment for medical and pharmaceutical use*.



This fourth edition cancels and replaces the third edition (ISO 4802-2:2016), which has been technically revised.

The main changes are as follows:

— the explanation of the hydrolytic classes $HC_F1$, $HC_F$ 2, $HC_F$ 3, $HC_FB$, $HC_F$ D for different glass types;

— clarification of needed properties of purified water and test water;

— harmonization of the samples cleaning and the autoclavation process with Ph.Eur.;

— including containers up to 0,5 ml filling volume.

A list of all parts in the ISO 4802 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.

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# Introduction

This document is largely based on a test method 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 document contains a classification which is related to but not equivalent to the classification set up in ISO 4802-1 for the titration method.

The hydrolytic resistance of the inner glass surface is evaluated by determination of the released alkali reacting ions. According to their hydrolytic resistance, glass containers are classified in defined categories.

$HC_F1$ glass containers are suitable for most preparations whether or not for parenteral administration.

$HC_F2$ glass containers are suitable for most acidic and neutral, aqueous preparations whether or not for parenteral administration.

$HC_F3$ glass containers are in general suitable for non-aqueous preparations for parenteral administration, for powders for parenteral administration (except for freeze-dried preparations) and for preparations not for parenteral administration.

$HC_FB$ glass containers are in general suitable for drinking ampoules (Container Class HGB 2 according to ISO 719).

$HC_FD$ glass containers are in general suitable for lower demands on hydrolytic resistance (Container Class HGB 4 and HGB 5 according to ISO 719).

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

# Part 2: Determination by flame spectrometry and classification

## 1 Scope

This document specifies:

a) a method 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 document.

The test method specified in this document might not be applicable to containers whose surfaces have been treated for functional modifications, e.g. silicone (e.g. containers that are ready for direct filling).



## 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 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 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.

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

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

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

**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 a pharmaceutical preparation

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 conform with hydrolytic resistance container class $HC_F$ 1 of this document.

**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 conform with hydrolytic resistance container class $HC_F$ 3.

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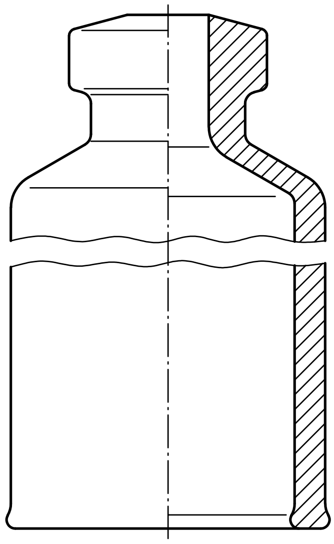
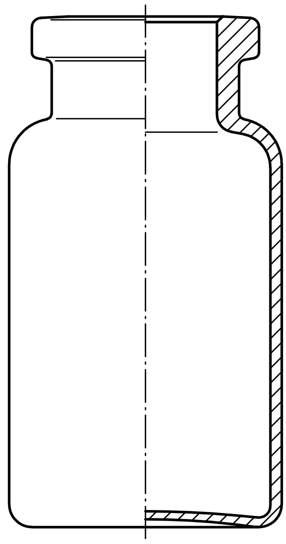
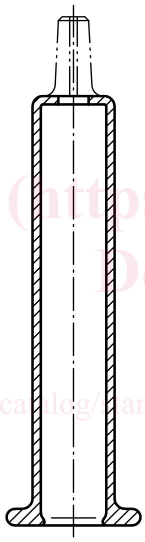
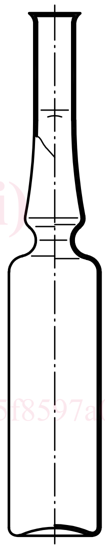




**a) Example of a glass cylinder for a pen-injector/cartridge (see ISO 13926-1)**

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







**c) Example of a syringe 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 test method 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. The measurement data shall be classified in accordance with the limits defined in appropriate container specific limit values in accordance with Table 2.

Dependent on different glass types, specific limit values are defined in the following:

The hydrolytic resistance is evaluated by determination of the released alkali reacting ions. According to their hydrolytic resistance, glass containers are classified as follows:

— $HC_F$ 1 glass containers: neutral glass, borosilicate glass with a high hydrolytic resistance due to the chemical composition of the glass itself;

NOTE 1 In the Ph.Eur. 3.2.1[12] and the USP <660>[15] the hydrolytic resistance classification are designated Type I.

— $HC_F$ 2 glass containers: usually of soda-lime-silica glass with a high hydrolytic resistance resulting from suitable treatment of the inner surface;

NOTE 2 In the Ph.Eur. 3.2.1[12] and the USP <660>[15] the hydrolytic resistance classification are designated Type II.



— $HC_F$ 3 glass containers: usually of soda-lime-silica glass with only moderate hydrolytic resistance;



NOTE 3 In the Ph.Eur. 3.2.1[12] and the USP <660>[15] the hydrolytic resistance classification are designated Type III.



— $HC_F$ B glass containers: usually made of borosilicate or soda-lime-silica glass composition with higher hydrolytic resistance (container class: HGB 2 according to ISO 719);



— $HC_F$D glass containers: usually made of soda-lime-silica glass with low hydrolytic resistance (container class: HGB 4 or HGB 5 according to ISO 719).

The index “F” indicates that the measures for the classification is based on Flame Spectrometry.

## 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 purified water (5.5) 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, e.g. preparation of carbon dioxide-free water according to Ph.Eur. 3.2.1[12], USP 660[15].

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.

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