

BS ISO 4802-1:2016



BSI Standards Publication

Glassware — Hydrolytic resistance of the interior surfaces of glass containers

Part 1: Determination by titration method
and classification

National foreword

This British Standard is the UK implementation of ISO 4802-1:2016. It supersedes BS ISO 4802-1:2010 which is withdrawn.

The UK participation in its preparation was entrusted to Technical Committee CH/212, IVDs.

A list of organizations represented on this committee can be obtained on request to its secretary.

This publication does not purport to include all the necessary provisions of a contract. Users are responsible for its correct application.

© The British Standards Institution 2016. Published by BSI Standards Limited 2016

ISBN 978 0 580 88545 7

ICS 71.040.20

Compliance with a British Standard cannot confer immunity from legal obligations.

This British Standard was published under the authority of the Standards Policy and Strategy Committee on 30 June 2016.

Amendments issued since publication

Date	Text affected
------	---------------

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

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

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

Partie 1: Détermination par analyse titrimétrique et classification





COPYRIGHT PROTECTED DOCUMENT

© ISO 2016, Published in Switzerland

All rights reserved. Unless otherwise specified, no part of this publication may be reproduced or utilized otherwise in any form or by any means, electronic or mechanical, including photocopying, or posting on the internet or an intranet, without prior written permission. Permission can be requested from either ISO at the address below or ISO's member body in the country of the requester.

ISO copyright office
Ch. de Blandonnet 8 • CP 401
CH-1214 Vernier, Geneva, Switzerland
Tel. +41 22 749 01 11
Fax +41 22 749 09 47
copyright@iso.org
www.iso.org

Contents

Page

Foreword	iv
Introduction	v
1 Scope	1
2 Normative references	1
3 Terms and definitions	1
4 Principle	4
5 Reagents	4
6 Apparatus	5
7 Sample preparation	6
7.1 Sample size.....	6
7.2 Determination of the filling volume.....	6
7.2.1 Flat-bottomed containers ≤20 mm outer flange diameter (except ampoules, syringes and cartridges).....	6
7.2.2 Flat-bottomed containers >20 mm outer flange diameter.....	6
7.2.3 Round-bottomed containers.....	7
7.2.4 Lipped containers.....	7
7.2.5 Ampoules.....	7
7.2.6 Syringes and cartridges.....	7
8 Procedure	8
8.1 General.....	8
8.2 Cleaning of samples.....	8
8.3 Filling and heating.....	8
8.4 Analysis of the extraction solutions.....	9
8.5 Test to determine whether the containers have been surface treated.....	10
9 Expression of results	10
9.1 Determination.....	10
9.2 Classification.....	10
9.3 Distinction between containers of hydrolytic resistance container class HC _T 1 and hydrolytic resistance container class HC _T 2.....	10
9.4 Designation.....	11
10 Test report	11
11 Reproducibility	12
Bibliography	13

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.

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).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

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 4802-1:2010), 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.

The European Pharmacopoeia Commission has adopted the principle of the determination by titration and has set up a classification for glass containers for injectable preparations which is now included in this part of ISO 4802. In addition, this part of ISO 4802 contains a classification of containers other than for injectable preparations.

According to many results of international interlaboratory tests, this part of ISO 4802 specifies the test conditions in more detail than the European Pharmacopoeia in order to increase the reproducibility of the test results. In particular, the autoclaving cycle is described in detail.

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

Part 1: Determination by titration method and classification

1 Scope

This part of ISO 4802 specifies:

- a) a method for determining the hydrolytic resistance of the interior surfaces of glass containers when subjected to attack by water at $121\text{ °C} \pm 1\text{ °C}$ for $60\text{ min} \pm 1\text{ min}$. The resistance is measured by titration of a known aliquot portion of the extraction solution produced with hydrochloric acid solution, in which case the resistance is inversely proportional to the volume of acid required;
- 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.

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 648, *Laboratory glassware — Single-volume pipettes*

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 1773, *Laboratory glassware — Narrow-necked boiling 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

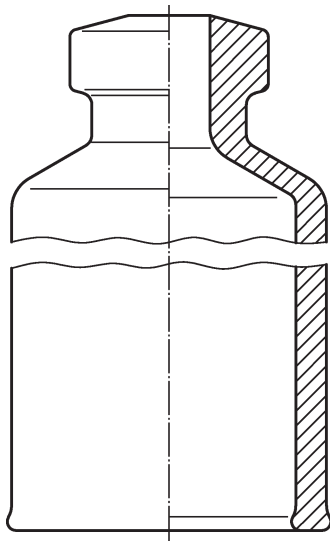
Note 1 to entry: Borosilicate glass contains a mass fraction of boric oxide usually between 5 % and 13 %. This glass type can also contain aluminium oxide and/or alkaline earth oxides.

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

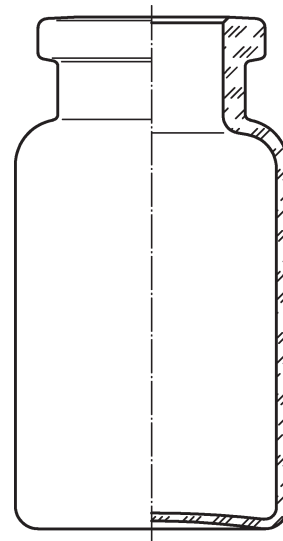
3.7 soda-lime-silica glass

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

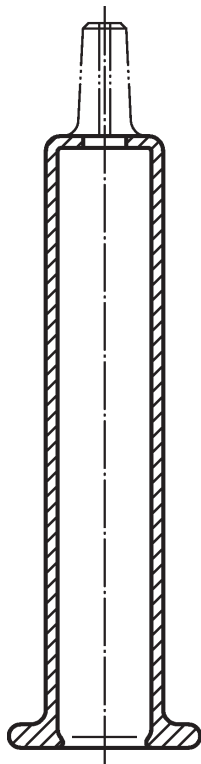
Note 1 to entry: Containers made from this glass have a moderate hydrolytic resistance due to the chemical composition of the glass, and comply with hydrolytic resistance container class HC_T 3.



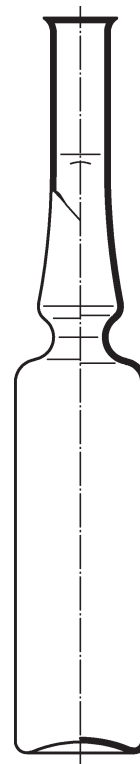
a) Example of a glass cylinder for pen-injectors
(see ISO 13926-1)



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_T 3 to a container of hydrolytic resistance class HC_T 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 titration of the extraction solutions.

5 Reagents

During the test, unless otherwise stated, use only reagents of recognized 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 $5,5 \pm 0,1$ 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 $\mu\text{S}/\text{cm}$, 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, standard volumetric solution, $c(\text{HCl}) = 0,01 \text{ mol/l}$.

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

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

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

5.5 Methyl red, indicator solution.

Dissolve 25 mg of the sodium salt of methyl red ($C_{15}H_{14}N_3NaO_2$) in 100 ml of the test water (5.1).

5.6 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[2] is suitable.

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

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.

Most recent autoclave models are not provided with a vent cock that can be operated manually. The operator is referred to the user instructions and/or technical description provided by the manufacturer of the autoclave with regard to the functioning of the venting operations. A time/temperature printout can be used as evidence of a proper venting stage.

For autoclaves using a steam generator, it is not necessary to hold the temperature at 100 °C for 10 min.

6.2 Burettes, having a suitable capacity of 50 ml, 25 ml, 10 ml or 2 ml, 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 719 or ISO 720¹⁾.

The capacity of the burettes shall be chosen according to the expected consumption of hydrochloric acid (5.2).

6.3 Conical flasks, having a capacity of 100 ml and 250 ml and complying with the requirements of ISO 1773.

Before its first use, each flask shall be pretreated by filling with purified water (5.6) and autoclaving at 121 °C for at least 1 h (see 8.3).

IMPORTANT — If it is intended to use these flasks for other purposes, before being re-used in accordance with this part of ISO 4802, the flasks shall be properly cleaned (e.g. by treatment with hydrochloric acid and/or by autoclave cleaning).

6.4 Pipettes, having a suitable capacity and complying with the requirements specified for class A pipettes described in ISO 648.

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

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

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

Before its first use, each beaker shall be pretreated by filling with purified water (5.6) and autoclaving at 121 °C for at least 1 h (see 8.3).

6.7 Metal foil, e.g. made from aluminium or stainless steel.

7 Sample preparation

7.1 Sample size

The number of containers to be tested depends on the capacity of the container, the volume of extraction solution necessary for one titration and the number of titration results required. It shall be calculated according to the requirements given in Table 1.

Table 1 — Capacity of containers, volume of extraction solution and number of titrations/containers

Capacity of container [volume corresponding to filling volume (see 7.2)] ml	Volume of extraction solution for one titration ml	Number of titrations/ containers
≤3	25,0	1
>3 ≤ 30	50,0	2
>30 ≤ 100	100,0	2
>100	100,0	3

7.2 Determination of the filling volume

7.2.1 Flat-bottomed containers ≤20 mm outer flange diameter (except ampoules, syringes and cartridges)

Select six containers (having a capacity ≤100 ml) or three containers (having a capacity > 100 ml) at random from the sample lot and remove any debris or dust by shaking the containers. Allow the dry containers to reach room temperature. Weigh each of the empty containers to the nearest 0,01 g for containers having a nominal volume ≤30 ml, and to the nearest 0,1 g for containers having a nominal volume >30 ml. Place the containers on a horizontal surface and fill them nearly to the top with purified water (5.6), avoiding overflow and introduction of air bubbles. Adjust the liquid levels to the brimful line using purified water (5.6). The meniscus shall be equal to the upper edge of the bore.

Weigh the filled container to the nearest 0,01 g for containers having a nominal volume ≤30 ml, and to the nearest 0,1 g for containers having a nominal volume >30 ml. Calculate the mass of water, in grams, contained within the container.

Determine the mean value of the results from six containers and express the result in millilitres of water; this value is the mean brimful capacity of the containers.

Determine 90 % of this mean brimful capacity to one decimal place. This volume is the filling volume for the particular sample lot.

7.2.2 Flat-bottomed containers >20 mm outer flange diameter

Proceed as described in 7.2.1 but cover each container with a strike-plate (for measuring the brimful capacity of small and other bottles). The strike-plate shall be made of rigid, inert, transparent material of any convenient shape, but with a central hole approximately 5 mm in diameter. The strike-plate shall

be large enough to fit snugly on and completely cover the sealing surface of the container for which the brimful capacity is to be measured.

Determine 90 % of this mean brimful capacity to one decimal place. This volume is the filling volume for the particular sample lot.

7.2.3 Round-bottomed containers

Select six containers (having a capacity ≤ 100 ml) or three containers (having a capacity > 100 ml) at random from the sample lot and remove any debris or dust by shaking the containers. Allow the dry containers to reach room temperature. Fix each container vertically in an appropriate device and determine the brimful capacity in accordance with [7.2.1](#).

Then determine 90 % of the mean brimful capacity to one decimal place. This volume is the filling volume for the particular sample lot.

7.2.4 Lipped containers

Wrap adhesive plastic tape around the rim of the containers such that the tape around the lip is level with the rim. Weigh the container, then fill and reweigh as described in [7.2.1](#).

7.2.5 Ampoules

Place at least six dry ampoules on a flat, horizontal surface and fill them with purified water ([5.6](#)), at room temperature, from a burette ([6.2](#)), until the water level (meniscus) reaches h_6 of ISO 9187-1, where the body of the ampoules declines to the shoulder (see [Figure 2](#)). Read the capacities to two decimal places and calculate the mean value.

This volume, expressed to one decimal place, is the filling volume and shall be filled in all ampoules of the same lot.

NOTE The filling volume can also be determined by weighing.

7.2.6 Syringes and cartridges

Select six syringes or cartridges. Close the small opening (mouth of cartridges and needle and/or Luer cone of syringes) using an inert material (e.g. tip cap). Determine the mean brimful volume in accordance with [7.2.1](#).

Then determine 90 % of the mean brimful capacity to one decimal place. This volume is the filling volume.

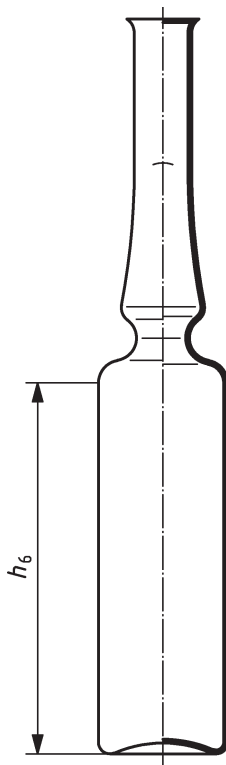


Figure 2 — Filling volume of ampoules (up to h_6)

8 Procedure

8.1 General

This procedure shall be completed within one working day.

8.2 Cleaning of samples

The following cleaning process for each container shall be completed within 20 min to 30 min.

Remove from all open samples any debris or dust which has collected during storage and transport. Shortly before the test, rinse each sample thoroughly at least twice with the purified water (5.6) at ambient temperature, then allow to stand, filled with the purified water (5.6). Immediately before testing, empty the samples, rinse once with purified water (5.6), and then once with the test water (5.1) and allow to drain.

Closed ampoules shall not be rinsed before testing.

NOTE For opening by flame, closed ampoules can be warmed, e.g. in a water bath or air-oven at about 40 °C for approximately 2 min before opening, to avoid under pressure when opening, or cut and broken at the height of the sealing point.

8.3 Filling and heating

Fill each container, selected for the sample size in accordance with 7.1 and cleaned in accordance with 8.2, to the filling volume with the test water (5.1) by means of suitable volumetric measuring devices.

Cap each container, including ampoules, loosely with an inert material, for example with inverted beakers (6.6) of such a size that the bottoms of the beakers fit snugly down on the rims of the sample.

Cap ampoules with a clean metal foil (6.7). Place syringes and cartridges in a beaker and cover the beaker with a clean metal foil (6.7).

Ensure that the metal foil does not release measurable ions into the test water.

Place the samples, gathered in groups in glass dishes or in the beaker, on the rack in the autoclave (6.1), containing purified water (5.6) at ambient temperature, and ensure that they are held above the level of the water in the vessel.

Insert the end of a calibrated thermal device in a filled container through a hole of approximately the diameter of the thermocouple and connect it to an external measuring device. If the container is too small to insert a thermocouple, apply a thermocouple in a suitable, similar container. Close the autoclave door or lid securely but leave the vent-cock open. Start automatic recording of the temperature versus time and heat the autoclave at a regular rate such that steam issues vigorously from the vent-cock after 20 min to 30 min, and maintain a vigorous evolution of steam for a further 10 min. Close the vent-cock and raise the temperature from 100 °C to 121 °C at a rate of 1 °C/min within 20 min to 22 min. Maintain the temperature at (121 ± 1) °C for (60 ± 1) min from the time when the holding temperature is reached. Cool down to 100 °C at a rate of 0,5 °C/min, venting to prevent formation of a vacuum, within 40 min to 44 min.

NOTE 1 For autoclaves using a steam generator it is not necessary to maintain the temperature for 10 min at 100 °C.

CAUTION — For security reasons (boiling retardation) do not open the autoclave before the water in the containers has reached a temperature of 95 °C. Consider the safety instructions of the user manual!

NOTE 2 Experience has shown that the rate of heating to 121 °C, the holding temperature of (121 ± 1) °C and the rate of cooling to 100 °C are critical. Deviations from the specified conditions can produce variable results to the extent of invalidating them.

Remove the hot samples from the autoclave and cool to room temperature within 30 min. Start the titration after cooling. Special care shall be taken in cooling down large capacity containers as thermal drops larger than 40 °C can cause the fracture of the glass by thermal shock.

8.4 Analysis of the extraction solutions

Carry out the titration within 1 h of removal of the containers from the autoclave. Combine the extraction solutions obtained from the containers to be tested (see Table 1) and mix. Introduce the volume according to column 2 of Table 1 into a conical flask. When emptying small stemmed ampoules the extraction solution can be partly neutralized by absorbing carbon dioxide (CO₂) from the atmosphere. To obviate this, invert the ampoules and heat the base gently with a flame. Ensure that no flame gases contaminate the test solution. In the case of combined extraction solutions from containers having a capacity ≤3 ml, pipette a volume of 25,0 ml (see column 2 of Table 1) into a conical flask (6.3) having a capacity of 100 ml. In the case of combined extraction solutions from containers having larger capacities, pipette the required volumes (see column 2 of Table 1) into separate conical flasks (6.3) of suitable capacity.

Prepare reference solutions (blank) by pipetting volumes of the test water (5.1), equivalent to those taken from the extraction solutions, into conical flasks (6.3) having a capacity commensurate with the size of the containers being tested. Add two drops of methyl red indicator solution (5.5) for each 25 ml of test water (5.1) and titrate the blank solution with hydrochloric acid (5.2) until a clearly visible colour change occurs.

Add two drops of methyl red indicator solution (5.5) to each flask for each 25 ml of extraction solution and titrate with hydrochloric acid (5.2) until the colour matches exactly that of the coloured reference solution.

Titration values of less than 1,0 ml shall be expressed to two decimal places, titration values greater than or equal to 1,0 ml to one decimal place.

NOTE Properly calibrated automatic titration equipment giving results with the same or better accuracy can also be used.

8.5 Test to determine whether the containers have been surface treated

NOTE The hydrolytic resistance of the interior surface of vials and bottles made from soda-lime-silica glass can be considerably increased by treating these surfaces during the course of production. Ampoules made from borosilicate glass tubing are not normally subjected to an internal surface treatment because their high chemical resistance is dependent upon the chemical composition of the glass as a material (see [Clause 3](#)).

If there are doubts whether or not a container has been surface-treated and/or to distinguish between type I and type II glass containers, unused glass containers or the container samples previously tested shall be used.

Fill the samples with a mixture of one volume of hydrofluoric acid ([5.4](#)) and nine volumes of hydrochloric acid ([5.3](#)) to the brimful point. Allow the filled samples to stand at ambient temperature for 10 min, then empty the solution very carefully. Rinse the samples five times with purified water ([5.6](#)), then at least once again with purified water ([5.6](#)). Then test the samples as specified in [8.3](#) and [8.4](#).

CAUTION — Hydrofluoric acid is extremely aggressive. Even tiny quantities can cause life-threatening injuries. Consider material safety data sheet!

If the results are considerably higher than those obtained from the original surfaces (about five to ten times), the samples shall be considered to have been surface-treated.

9 Expression of results

9.1 Determination

Determine the mean value of the titration results and express it in millilitres of hydrochloric acid solution ([5.2](#)) per 100 ml of the extraction solution. The blank value (see [8.4](#)) shall be considered.

9.2 Classification

The containers shall be classified as shown in [Table 2](#), according to the consumption of hydrochloric acid solution ([5.2](#)), when tested as specified in [8.4](#) and determined according to [9.1](#).

9.3 Distinction between containers of hydrolytic resistance container class HC_T 1 and hydrolytic resistance container class HC_T 2

After etching and re-testing in accordance with [8.5](#), containers of hydrolytic resistance container class HC_T 1 shall satisfy the requirements for hydrolytic resistance container classes HC_T 1 and HC_T 2 in [Table 2](#).

After etching and re-testing in accordance with [8.5](#), containers of hydrolytic resistance container class HC_T 2 shall produce values that are significantly greater than those given in column 2 of [Table 2](#) and which are much closer to those values for hydrolytic resistance container class HC_T 3 in [Table 2](#).

Table 2 — Maximum values in the hydrolytic resistance container surface test (titration method)

Capacity of container [volume corresponding to the filling volume (see 7.2)] ml	Maximum values for the consumption of hydrochloric acid solution [$c(\text{HCL}) = 0,01 \text{ mol/l}$] (5.2) per 100 ml of the extraction solution, ml			
	Classes HC _T 1 and HC _T 2	Class HC _T 3	Class HC _T B	Class HC _T D
≤1	2,0	20,0	4,0	32,0
>1 ≤ 2	1,8	17,6	3,6	28,0
>2 ≤ 3	1,6	16,1	3,2	25,7
>3 ≤ 5	1,3	13,2	2,6	21,0
>5 ≤ 10	1,0	10,2	2,0	17,0
>10 ≤ 20	0,80	8,1	1,6	13,5
>20 ≤ 50	0,60	6,1	1,2	9,8
>50 ≤ 100	0,50	4,8	1,0	7,8
>100 ≤ 200	0,40	3,8	0,80	6,2
>200 ≤ 500	0,30	2,9	0,60	4,6
>500	0,20	2,2	0,40	3,6

9.4 Designation

The hydrolytic resistance of the interior surface of glass containers measured in accordance with this part of ISO 4802 shall be designated as follows:

EXAMPLE The designation for a 9 ml capacity container with a consumption of 1,6 ml of hydrochloric solution [$c(\text{HCL}) = 0,01 \text{ mol/l}$] per 100 ml extraction solution shall be:

Glass, hydrolytic resistance container class ISO 4802-HC_T B

10 Test report

The test report shall include the following information:

- a) a reference to this part of ISO 4802, i.e. ISO 4802-1;
- b) an identification of the samples;
- c) mean brimful capacity of samples (except ampoules);
- d) the filling volume of the samples;
- e) the number of samples used for one titration;
- f) the mean value of the titrations;
- g) hydrolytic resistance container class HC_T (designation of the container tested);
- h) for hydrolytic resistance container class HC_T 2, a statement whether the test has been repeated after etching of the surface (see 8.5) and the results obtained;
- i) a statement whether closed ampoules were tested;
- j) any unusual features noted during the determination.

11 Reproducibility

Extensive research was carried out by Technical Committee 2 of the International Commission on Glass in order to identify the uncertainty sources that can affect the reproducibility of the method. It was found that changes to the rinsing procedure and/or to the opening temperature of the autoclave can slightly affect the within-laboratory variance. By far, the largest variation occurring between laboratories is the autoclaving cycle and this was shown to be a major factor. Proper calibration of the autoclave and of the temperature control devices are of great help in improving the reproducibility.

To standardize the test procedure, the certified reference material IRMM 435^[13] is available at the Institute for Reference Materials and Measurements at the European Commission Joint Research Centre in Geel, Belgium.

For this material, the volume of 0,01 mol/l HCl solution necessary to the titration of 50 ml of extraction solution from containers of 18,9 ml brimful capacity was quoted as 0,38 ml ± 0,04 ml, where the uncertainty is an expanded uncertainty with a coverage factor $k = 2$, corresponding to a level of confidence of 95 %. Further intercomparison work is requested to investigate the method of reproducibility at different concentration levels when different types of glass containers are tested.

For more details see References ^[14] and ^[15].

Bibliography

- [1] ISO 3585, *Borosilicate glass 3.3 — Properties*
- [2] ISO 3696, *Water for analytical laboratory use — Specification and test methods*
- [3] ISO 8362-1, *Injection containers and accessories — Part 1: Injection vials made of glass tubing*
- [4] ISO 8362-4, *Injection containers and accessories — Part 4: Injection vials made of moulded glass*
- [5] ISO 8536-1, *Infusion equipment for medical use — Part 1: Infusion glass bottles*
- [6] ISO 13926-1, *Pen systems — Part 1: Glass cylinders for pen-injectors for medical use*
- [7] ISO 11040-1, *Prefilled syringes — Part 1: Glass cylinders for dental local anaesthetic cartridges*
- [8] ISO 11040-4, *Prefilled syringes — Part 4: Glass barrels for injectables and sterilized subassembled syringes ready for filling*
- [9] ISO 11418-1, *Containers and accessories for pharmaceutical preparations — Part 1: Drop-dispensing glass bottles*
- [10] ISO 11418-4, *Containers and accessories for pharmaceutical preparations — Part 4: Tablet glass bottles*
- [11] ISO 11418-7, *Containers and accessories for pharmaceutical preparations — Part 7: Screw-neck vials made of glass tubing for liquid dosage forms*
- [12] EUROPEAN PHARMACOPOEIA. 3.2.1 Glass containers for pharmaceutical use <http://www.edqm.eu/>
- [13] CERTIFIED REFERENCE MATERIAL I.R.M.M. 435, Institute for Reference Materials and Measurements, Retieseweg 111, B-2440 Geel, Belgium, <http://www.irmm.jrc.be/>
- [14] ICG/TC2. Influence of some parameters on the approximation of European Pharmacopoeia and ISO Standard 4802: Reasons for harmonisation. *Glass Technol.* 2000, **41** (8)
- [15] http://www.irmm.jrc.be/html/reference_materials_catalogue/catalogue/attachements/IRMM-435_cert.pdf

British Standards Institution (BSI)

BSI is the national body responsible for preparing British Standards and other standards-related publications, information and services.

BSI is incorporated by Royal Charter. British Standards and other standardization products are published by BSI Standards Limited.

About us

We bring together business, industry, government, consumers, innovators and others to shape their combined experience and expertise into standards-based solutions.

The knowledge embodied in our standards has been carefully assembled in a dependable format and refined through our open consultation process. Organizations of all sizes and across all sectors choose standards to help them achieve their goals.

Information on standards

We can provide you with the knowledge that your organization needs to succeed. Find out more about British Standards by visiting our website at bsigroup.com/standards or contacting our Customer Services team or Knowledge Centre.

Buying standards

You can buy and download PDF versions of BSI publications, including British and adopted European and international standards, through our website at bsigroup.com/shop, where hard copies can also be purchased.

If you need international and foreign standards from other Standards Development Organizations, hard copies can be ordered from our Customer Services team.

Copyright in BSI publications

All the content in BSI publications, including British Standards, is the property of and copyrighted by BSI or some person or entity that owns copyright in the information used (such as the international standardization bodies) and has formally licensed such information to BSI for commercial publication and use.

Save for the provisions below, you may not transfer, share or disseminate any portion of the standard to any other person. You may not adapt, distribute, commercially exploit, or publicly display the standard or any portion thereof in any manner whatsoever without BSI's prior written consent.

Storing and using standards

Standards purchased in soft copy format:

- A British Standard purchased in soft copy format is licensed to a sole named user for personal or internal company use only.
- The standard may be stored on more than 1 device provided that it is accessible by the sole named user only and that only 1 copy is accessed at any one time.
- A single paper copy may be printed for personal or internal company use only.

Standards purchased in hard copy format:

- A British Standard purchased in hard copy format is for personal or internal company use only.
- It may not be further reproduced – in any format – to create an additional copy. This includes scanning of the document.

If you need more than 1 copy of the document, or if you wish to share the document on an internal network, you can save money by choosing a subscription product (see 'Subscriptions').

Reproducing extracts

For permission to reproduce content from BSI publications contact the BSI Copyright & Licensing team.

Subscriptions

Our range of subscription services are designed to make using standards easier for you. For further information on our subscription products go to bsigroup.com/subscriptions.

With **British Standards Online (BSOL)** you'll have instant access to over 55,000 British and adopted European and international standards from your desktop. It's available 24/7 and is refreshed daily so you'll always be up to date.

You can keep in touch with standards developments and receive substantial discounts on the purchase price of standards, both in single copy and subscription format, by becoming a **BSI Subscribing Member**.

PLUS is an updating service exclusive to BSI Subscribing Members. You will automatically receive the latest hard copy of your standards when they're revised or replaced.

To find out more about becoming a BSI Subscribing Member and the benefits of membership, please visit bsigroup.com/shop.

With a **Multi-User Network Licence (MUNL)** you are able to host standards publications on your intranet. Licences can cover as few or as many users as you wish. With updates supplied as soon as they're available, you can be sure your documentation is current. For further information, email subscriptions@bsigroup.com.

Revisions

Our British Standards and other publications are updated by amendment or revision.

We continually improve the quality of our products and services to benefit your business. If you find an inaccuracy or ambiguity within a British Standard or other BSI publication please inform the Knowledge Centre.

Useful Contacts

Customer Services

Tel: +44 345 086 9001

Email (orders): orders@bsigroup.com

Email (enquiries): cservices@bsigroup.com

Subscriptions

Tel: +44 345 086 9001

Email: subscriptions@bsigroup.com

Knowledge Centre

Tel: +44 20 8996 7004

Email: knowledgecentre@bsigroup.com

Copyright & Licensing

Tel: +44 20 8996 7070

Email: copyright@bsigroup.com

BSI Group Headquarters

389 Chiswick High Road London W4 4AL UK