

# International Standard



# 4802

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## Glass — Hydrolytic resistance of the interior surfaces of glass containers — Methods of test

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## Foreword

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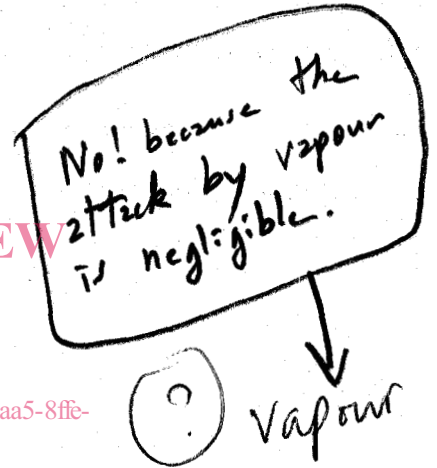
Draft International Standards adopted by the technical committees are circulated to the member bodies for approval before their acceptance as International Standards by the ISO Council.

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It has been approved by the member bodies of the following countries:

Australia	Hungary	Spain
Brazil	Italy	United Kingdom
Canada	Korea, Rep. of	USA
Czechoslovakia	Poland	USSR
France	Romania	
Germany, F. R.	South Africa, Rep. of	

No member body expressed disapproval of the document.



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# Glass — Hydrolytic resistance of the interior surfaces of glass containers — Methods of test

## 0 Introduction

This International Standard is based largely on methods of test approved by the International Commission on Glass, Subcommittee A 2, *Chemical Durability*, for measuring the hydrolytic resistance of the interior surfaces of glass containers. The European Pharmacopoeia Commission has adopted the determination by titration and set up a classification for glass containers for injectable preparations.

## 1 Scope

This International Standard specifies methods for determining the hydrolytic resistance of the interior surfaces of glass containers when subjected to attack by water at  $121 \pm 1$  °C for  $60 \pm 1$  min.

The resistance is measured either by titration of a known aliquot of the extract produced under the conditions of test (in which case the resistance is inversely proportional to the volume of acid required) or, and particularly for smaller containers, by the determination of the amount of sodium and other alkali or alkaline earth oxides in the extraction solution, using the flame emission or the atomic absorption spectrometric method (flame spectrometric methods).

NOTE — It should be noted that the values obtained by titration and those obtained using the flame emission or atomic absorption spectrometer are not directly comparable.

Details of a dithizone limit test for heavy metals are given in the annex.

## 2 Field of application

The methods are applicable to all containers for laboratory and pharmaceutical use which are capable of being subjected to the conditions of the tests.

They are applicable to articles made from soda-lime-silicate glass or borosilicate glass (including neutral glass), either in the original or in the surface-treated condition.

## 3 References

ISO 385/2, *Laboratory glassware — Burettes — Part 2: Burettes for which no waiting time is specified.*<sup>1)</sup>

ISO 648, *Laboratory glassware — One-mark pipettes.*

ISO 1773, *Laboratory glassware — Boiling flasks (narrow-necked).*

ISO 3819, *Laboratory glassware — Beakers.*<sup>2)</sup>

ISO 6955, *Analytical flame emission, atomic absorption and atomic fluorescence spectroscopy — Vocabulary.*<sup>2)</sup>

## 4 Principle

The methods of test are surface tests normally applied on glass containers as delivered.

The containers to be tested are filled with specially pure water to a specified capacity and heated under specified conditions. The degree of the hydrolytic attack is measured by analysis of the extraction solutions.

## 5 Reagents

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

### 5.1 Specially pure water.

Water which is free from heavy metals, particularly copper, as shown by a dithizone test (see the annex)<sup>3)</sup>, having a specific

1) At present at the stage of draft. (Revision, in part, of ISO/R 385.)

2) At present at the stage of draft.

3) For testing heavy metals with dithizone see Iwantscheff, G. : *Das Dithizon und seine Anwendung in der Mikro- und Spurenanalyse* [Dithizone and its application in micro- and trace analysis]. Weinheim : Verlag Chemie 1972.

conductivity less than  $1,0 \times 10^{-4} \text{ S/m}^{(1)(2)}$  at 20 °C, and which has been freed from dissolved gases such as carbon dioxide, by boiling for at least 15 min in a flask of silica or borosilicate glass previously treated as specified in 6.3.

Such water can normally be stored for 24 h in a stoppered flask without change of the pH value.

When tested immediately before use, the water shall be neutral to methyl red, i.e. it shall produce an orange-red (not a violet-red or yellow) colour corresponding to pH  $5,5 \pm 0,1$  when 2 drops of the methyl red indicator solution (5.5) are added to 25 ml of the water.

NOTE — The water, so coloured, may also be used as the reference solution (see 8.2.1).

**5.2 Hydrochloric acid 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 (HF)**, 400 g/l solution.

**5.5 Methyl red indicator solution**.

Dissolve 25 mg of the sodium salt of methyl red ( $\text{C}_{15}\text{H}_{14}\text{N}_3\text{NaO}_2$ ) in 100 ml of the specially pure water (5.1).

**5.6 Distilled water or water of equivalent purity**.

## 6 Apparatus

Ordinary laboratory apparatus and

**6.1 Autoclave or steam sterilizer**, capable of withstanding a pressure of at least  $2,5 \times 10^5 \text{ N/m}^2$  \* and of carrying out the heating cycle specified in 8.1. It should preferably be equipped with a constant-pressure regulator or other means for maintaining the temperature at  $121 \pm 1$  °C. The vessel shall be capable of containing at least six containers of about 90 mm diameter, and shall be equipped with a heating device, a thermometer, a pressure gauge, a vent-cock, and a rack for supporting the samples.

The autoclave vessel and ancillary equipment shall be thoroughly cleaned before use.

**6.2 Burettes**, of suitable capacity, as follows :

- 25 ml, complying with the requirements of class A of ISO 385/2;
- 10 ml, graduated in 0,02 ml;
- 2 ml, graduated in 0,01 ml.

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

**6.3 Conical flasks**, of capacity 100 and 250 ml, complying with the requirements of ISO 1773. New flasks shall be suitably aged by heating in steam at 121 °C for 30 min in the autoclave (6.1).

**6.4 Pipettes**, of suitable capacity, complying with the requirements of class A of ISO 648.

**6.5 Water bath**, capable of being controlled at about 80 °C.

**6.6 Flame emission or atomic absorption spectrometer**.

**6.7 Beakers**, of suitable capacity, complying with the requirements of ISO 3819.

## 7 Preparation of samples

### 7.1 For the determination of the hydrolytic resistance by titration

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 titrations required. It can be calculated according to the requirements given in table 1.

Table 1 — Number of containers for the determination of the hydrolytic resistance by titration

Capacity (volume corresponding to 90 % of overflow volume) ml	Number of containers for one titration	Volume of extraction solutions for one titration ml	Number of titrations
up to 3	at least 10	25,0	1
above 3 up to 30	at least 5	50,0	2
above 30 up to 100	at least 3	100,0	2
above 100	1	100,0	3

1) Water of this quality can be prepared by passing the water source through a mixed ion-exchange resin column, distilling the eluant from an all-quartz or all-borosilicate glass still and finally boiling the distillate.

2) Water of even lower conductivity and of equally acceptable quality can be prepared by distilling the source water, and passing the distillate through a deionizer cartridge packed with a nuclear-grade resin mixture. The resin mixture should contain a strong acid-cation exchanger in the hydrogen form and a strong base-anion exchanger in the hydroxide form with a one-to-one cation-anion equivalence ratio. The eluant should then be passed through a cellulose-ester membrane having openings not exceeding 0,45 µm and then through an in-line conductivity cell to verify the conductivity. After flushing all discharge lines, the water should be dispensed directly into the test vessel.

\*  $1 \times 10^5 \text{ N/m}^2 = 0,1 \text{ MPa} = 1 \text{ bar}$

## 7.2 For the determination of the hydrolytic resistance using flame spectrometric methods

For each container type to be tested by flame spectrometric methods, the number of containers which are to be measured separately are indicated in table 2.

**Table 2 — Number of containers for the determination of the hydrolytic resistance using flame spectrometric methods**

Capacity (volume corresponding to 90 % of overflow volume) ml	Number of containers to be measured separately
up to 2	20
above 2 up to 5	15
above 5 up to 30	10
above 30 up to 100	5
above 100	3

**7.3** Any packaging debris, or dirt which has been collected during storage and transport, shall be removed from all of the samples. Rinse each sample thoroughly at least twice with the distilled water (5.6) at ambient temperature, then allow to stand filled with the distilled water for at least 30 min. Immediately before testing, rinse twice with the distilled water, and then once with the specially pure water (5.1). Closed ampoules ("Marzocchi" ampoules, for instance) shall be opened but not rinsed.

## 8 Procedure

### 8.1 Filling and heating

Fill each container selected for the sample in accordance with 7.1 and 7.2 to within 90 % of the overflow capacity with the specially pure water (5.1). Fill ampoules to 90 % of the capacity measured up to the sealing point.

Ampoules shall be sealed by fusion in the normal manner, i.e. with a flame just hot enough for sealing. Bottles and other containers shall be loosely capped with an inert material, for example with the inverted beakers (6.7), which have been suitably aged (see 6.3) and of such a size that the bottoms of the beakers fit snugly down on the rims of the samples. Place the samples on the rack in the autoclave (6.1), containing distilled water (5.6) at ambient temperature, and ensure that they are held above the level of the water in the chamber. Close the autoclave lid or door securely but leave the vent-cock open. Heat at a regular rate such that steam issues vigorously from the vent-cock after 20 to 30 min, and maintain a vigorous evolution of steam for a further 10 min. Close the vent-cock and increase the temperature at a rate of 1 °C/min to 121 °C. Maintain the temperature at 121 ± 1 °C for a period of 60 ± 1 min from the time when the holding temperature is reached, then cool at a rate of 0,5 °C/min to 100 °C, venting to prevent formation of a vacuum.

Remove the hot samples from the autoclave, place in the water bath (6.5), controlled at about 80 °C, and run cold water into and out of the bath at a rate which will cool the samples to ambient temperature as quickly as possible, commensurate with

the size and wall thickness of the samples and the type of glass from which the samples are made. The cooling time shall not exceed 30 min. Carry out the determination after cooling.

## 8.2 Analysis of the extraction solutions

### 8.2.1 By titration

For samples with a capacity up to 100 ml (see column 1 of table 1), combine the extraction solutions from the containers referred to in column 2 and mix thoroughly. Pipette the corresponding volume of solution (see column 3 of table 1) into a conical flask; the capacity of the conical flask shall be 100 ml for a 25 ml portion and shall be 250 ml for 50 and 100 ml portions.

For samples with a capacity above 100 ml (column 1 of table 1), pipette 100,0 ml from each container into separate conical flasks (6.3) of 250 ml capacity.

Pipette the same volumes of 25,0, 50,0 or 100,0 ml (as taken from the extraction solutions) of the specially pure water (5.1) into conical flasks (6.3) of equal capacity.

Add to each flask two drops of the methyl red indicator solution (5.5) for each 25 ml of extraction solution and titrate the extraction solutions with the hydrochloric acid (5.2) until the colour matches exactly that of the coloured specially pure water (5.1).

NOTE — Values of consumption < 1,0 ml should be expressed to two decimal places, values > 1,0 ml to one decimal place.

### 8.2.2 By flame spectrometric methods

Spray the extraction solutions from the samples required in table 2 directly into the flame emission or atomic absorption spectrometer (6.6) and determine the concentrations of Na<sub>2</sub>O (and K<sub>2</sub>O and CaO, if present) by reference to calibration graphs produced from aqueous solutions of the corresponding chlorides of suitable concentration.

Carry out a preliminary measurement of the potassium and calcium oxide concentration on one of the extraction solutions. When (for one container type) the concentration of K<sub>2</sub>O is less than 0,2 µg/ml, and when the concentration of CaO is less than 0,1 µg/ml, the remaining extraction solutions of this container type need not be analysed for these constituents.

NOTE — Values of concentration < 1,0 µg/ml should be expressed to two decimal places, values > 1,0 µg/ml to one decimal place.

### 8.3 Testing, if the containers are internally surface-treated

The hydrolytic resistance of the interior surfaces of soda-lime-silicate glass containers can be considerably increased by treating those surfaces during the course of production. For testing whether or not the containers are made of surface-treated soda-lime-silicate glass, use the samples previously tested in accordance with 8.2.

In such cases, fill the samples with an acidic solution comprising 1 volume of the hydrofluoric acid (5.4) and 9 volumes of the hydrochloric acid (5.3) to the overflow point. Allow the filled

samples to stand at ambient temperature for 10 min, then empty the acidic solution very carefully. Rinse the samples 3 times with the distilled water (5.6), then at least twice with the specially pure water (5.1). Then test the samples as specified in 8.1 and 8.2.

If the results are considerably higher than those obtained from the original surfaces, the samples shall be considered to be surface-treated.

## 9 Expression of results

### 9.1 Titration method

Calculate the mean value of the titration results and express it as millilitres of hydrochloric acid solution,  $c(\text{HCl}) = 0,01 \text{ mol/l}$ , per 100 ml of the extraction solution. The results can additionally be calculated and expressed as micrograms of sodium oxide ( $\text{Na}_2\text{O}$ ) per 100 ml of the extraction solution.

1 ml of hydrochloric acid solution,  $c(\text{HCl}) = 0,01 \text{ mol/l} \cong 310 \mu\text{g}$  of sodium oxide.

### 9.2 Flame spectrometric methods

Calculate the mean value of the concentration of individual oxides (8.2.2) found in each of the samples tested and express it in micrograms of the individual oxides per millilitre of the extraction solution and the sum of the individual oxides calculated as mass concentration of sodium oxide expressed as micrograms of  $\text{Na}_2\text{O}$  per millilitre of the extraction solution.

## 10 Test report

The test report shall include the following particulars :

- a) a reference to this International Standard;
- b) an identification of the samples;
- c) the capacity of the samples (volume corresponding to 90 % of overflow volume);
- d) the reference of the method used (titration or flame spectrometric methods);
- e) in case of titration :
  - the number of samples used for one titration  $\lambda$   $\lambda$
  - mean value of the titrations;
- f) in case of flame spectrometric methods :
  - the specific ions determined  $\lambda$   $\lambda$
  - single values and mean value calculated as  $\text{Na}_2\text{O}$ ;
- g) a declaration whether or not the test has been repeated after etching of the surface (see 8.3) and the results;
- h) a declaration whether or not closed ampoules were tested;
- i) any usual features noted during the determination.

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## Annex

## Dithizone limit test for heavy metals

## A.1 Scope and field of application

This annex specifies a dithizone limit test for heavy metals corresponding to the following limits :

Copper :	0,02 mg/l
Lead :	0,05 mg/l
Iron :	0,05 mg/l
Cobalt :	0,5 mg/l
Manganese :	0,4 mg/l
Nickel :	0,2 mg/l
Zinc :	0,2 mg/l

## A.2 Reagents

During the analysis, use only reagents of recognized analytical grade, free from the heavy metals mentioned in clause A.1.

A.2.1 Ammonia ~~approximately 5 M solution~~

solution,  $\rho(\text{NH}_3) \approx 5 \text{ mol/l}$ .

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## A.2.2 Dithizone, 4 mg/l solution in chloroform.

## A.3 Apparatus

## A.3.1 Glass vessel, of borosilicate glass, fitted with a ground glass stopper.

## A.4 Procedure

Shake vigorously, in the ground glass stoppered borosilicate glass vessel (A.3.1), 25 ml of the sample with 0,05 ml of the ammonia solution (A.2.1) and 5 ml of the dithizone solution (A.2.2) and allow to stand for 5 min.

Examine the colour of the lower layer.

The sample shall give a lower layer coloured green.

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