**4202 Determination of Hydrolytic Resistance of the Inner Surfaces for Glass Containers**

Hydrolytic resistance of the inner surface of glass containers is a method that can evaluate the resistance of glass containers’ inner surface to water erosion. The test is to pour test water into containers to the specified capacity, and heat~~ed~~ under specified conditions. The degree of water resistance of glass containers’ inner surface is determined by titrating the extraction solution.

**Instruments:** Autoclave, electronic balance, burette, pipette, beaker, and conical flask (Note: The glass container must be made of borosilicate glass or quartz glass. The average linear thermal expansion coefficient is about 3.3×10-6K-1 for borosilicate glass. New glass containers must undergo repeated aging treatment according to the specified conditions in the test procedure until the water is neutral to 0.025% methyl red sodium aqueous solution).

The test water should comply with the following requirements:

(1) The conductivity of test water shall not exceed 0.1 mS/m at 25℃±1℃.

(2) To remove carbon dioxide and other dissolved gas, the test water should be boiled vigorously for more than 15 min in aging-treated conical flask.

(3) The test water shall be neutral to the 0.025% methyl red sodium aqueous solution. The color of the water turns to orange-red (pH5.4-5.6) when added 4 drops of 0.025% methyl red sodium aqueous solution to 50ml water. The water can be used for blank test.

**Determination of filling volume:** In accordance with Method I of Determination of Capacity for Glass Containers (General Chapter 4024), for injection vials made of glass, infusion glass bottles, pharmaceutical glass bottles, glass components for pen-injector, and glass barrel for prefilled syringes, the filling volume should be 90% of the brimful capacity. Brimful capacity is the average of three containers if their capacity exceeds 100 ml. Brimful capacity is the average of six containers if their capacity is less than or equal to 100 ml. Calculate to one decimal place. Among them, the glass barrels for pen-type injectors and glass syringes for prefilled syringes shall be sealed with inert materials at the small mouth, and then carry out the follow-up test.

For glass ampoules, the filling volume shall reach the bottle shoulder (Figure), and the filling volume should be the average value of at least 6 samples with one decimal place.



**Sample preparation:** The number of the test sample depends on the capacity of the container, the volume of extraction solution for one titration and the time of titration required, which can be calculated according to Table 1.

Table 1. The number of containers required of hydrolytic resistance determination by titration

|  |  |  |  |
| --- | --- | --- | --- |
| Filling volume(ml) | The minimum number of containers for one titration | Volume of test liquid for one titration(ml) | Time of titrations |
| ≤3 | 10 | 25.0 | 1 |
| >3-30 | 5 | 50.0 | 2 |
| >30-100 | 3 | 100.0 | 2 |
| >100 | 1 | 100.0 | 3 |

Complete the cleaning procedure within 20-25 min and remove debris or dust inside. Rinse each container thoroughly at least twice with purified water at environment temperature. Refill the containers with purified water for later use. Empty the containers before use, and rinse once with purified water and test water respectively. Allow the containers to drain completely.

**Determination:** Take the cleaned containers and fill test water to the filling volume. Cover the containers with inverted beakers (after aging treatment) or other suitable material. Place all the samples into the autoclave. Leave the vent-cock open and heat the autoclave at a regular rate for 20-30 min. The steam is released vigorously from the vent-cock for 10 min after heating.Close the vent-cock, and raise the temperature to 121℃±1℃ at a rate of 1℃/min within 20-22 min, the timer starts when this temperature is reached. Maintain the temperature at 121℃±1℃ for 60 min±1 min. Cool down and decompress slowly to 100℃ within 40-44min (to prevent the formation of ~~a~~ vacuum). Take out the samples when the temperature is lower than 95℃, combine the extraction solution and cool to room temperature. The titration should be completed within 1 hour after removing from the autoclave.

According to Table 1, for the glass containers with a filling volume that less than or equal to 100 ml, combine all the extraction solution obtained from the containers and into a dry beaker**.** Transfer the extraction solutions into a conical flask with a pipette. Prepare the prescribed number of samples in the same manner.

According to Table 1, for the glass containers with a filling volume that more than 100 ml, transfer 100 ml extraction solutions from containers into a conical flask with a pipette. Prepare 3 samples in the same manner.

Use test water for blank correction.

Add 2 drops of 0.025% methyl red sodium aqueous solution to each 25 ml extraction solution. Titrate the extraction solutions with hydrochloric acid (0.01 mol/L) VS, until the color is the same as the blank determination.

**Result representation:** Calculate the average of the titration results. Express the results in ml of hydrochloric acid (0.01mol/L) VS per 100 ml of test solution. Express titration values of less than 1.0 ml to two decimal places; express titration values of greater than or equal to 1.0 ml to one decimal place.

**Grade:** The hydrolytic resistance of the inner surfaces of glass containersshall be classified with the results (ml) of hydrochloric acid (0.01mol/L) VS in Table 2.

Table 2. Classification of Hydrolytic Resistance for the Surface Class Test

|  |  |
| --- | --- |
| Filling Volume(ml) | Maximum Volume of hydrochloric acid (0.01mol/L) VS per 100 ml of Test Solution |
| HC1 or HC2 | HC3 | HCB |
| ≤1 | 2.0 | 20.0 | 4.0 |
| >1-2 | 1.8 | 17.6 | 3.6 |
| >2-3 | 1.6 | 16.1 | 3.2 |
| >3-5 | 1.3 | 13.2 | 2.6 |
| >5-10 | 1.0 | 10.2 | 2.0 |
| >10-20 | 0.80 | 8.1 | 1.6 |
| >20-50 | 0.60 | 6.1 | 1.2 |
| >50-100 | 0.50 | 4.8 | 1.0 |
| >100-200 | 0.40 | 3.8 | 0.80 |
| >200-500 | 0.30 | 2.9 | 0.60 |
| >500 | 0.20 | 2.2 | 0.40 |

NOTE: HC2 is suitable for glass containers with inner surface treatment. The surface etching test is used when it is necessary to determine whether a container has been surface treated. The surface etching test method: fill to the brimful point with a mixture of 40% hydrofluoric acid and 2 mol/L hydrochloric acid (volume ratio: 9:1), and allow to stand for 10 min at room temperature. Empty the containers carefully, and rinse with purified water for three times, and with test water for two or more times. Submit these containers to the same autoclaving and determination procedure as described above. If the test results are more than 5 times higher than the result of the original inner surface, it is considered that these containers have undergone surface treatment. (NOTE: Hydrofluoric acid is extremely corrosive, even a very small amount may cause life-threatening injuries.)

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