

(2) After filtration of sample solution into the apparatus to which the membrane filters are fitted, 100 mL of each medium is added to the apparatus itself.

I-6. Culture and observation

Incubate thioglycollate medium I for sterility test at between 30°C and 35°C and soybean-casein digest medium at between 20°C and 25°C for not less than 14 days. Observe the test containers for growth of microorganisms at least once between the fifth and ninth day, two times in total. If the sample makes the medium turbid so that the presence or absence of microbial growth can not be determined readily or in other case of need, transfer suitable portions of the medium to fresh containers of the same medium, incubate the transfer containers at the same temperature for not less than 7 days and examine the medium for growth.

I-7. Interpretation

If no evidence of microbial growth is found as a result of the above-mentioned test, the product tested meets the requirement of the Sterility Test. If microbial growth is found, the product tested fails to meet the requirement of the Sterility Test. However, provided that various factors and/or properties of the contaminant(s) suggest that the sterility test itself was inadequate, the test is repeated. If no evidence of microbial growth is found in the repeat test the product complies with the Sterility Test. If microbial growth is found in the repeat test the product does not comply with the Sterility Test.

II. Direct transfer method

This is the method by which the entire content or a portion of the content of a sample container is transferred directly to the culture medium and incubated. Usually, this method is applied for medicines to which the membrane filtration method can not be applied or for which the application of the direct transfer method, rather than the Membrane filtration method, is rational.

II-1. Opening of containers

Usually, proceed as directed for the Membrane filtration method.

II-2. Preparation of sample solution

Usually, proceed as directed for the Membrane filtration method. In the case of an insoluble medicine, the product is suspended or crushed in a suitable manner and used as a sample.

II-3. Quantities of sample solution to be transferred

For a liquid medicine and for a solid medicine to be administered after dissolving or suspending, unless otherwise specified, take a quantity of the product specified in Table 3. The volume of the sample should be not more than 10% of the volume of the medium. For a hydrophobic medicine, transfer the quantity prescribed in Table 4 according to the amount stated on the label into 200 mL each of thioglycollate medium I for sterility test and soybean-casein digest medium.

II-4. Culture and observation

Proceed as directed for the Membrane filtration method.

II-5. Interpretation

Proceed as directed for the Membrane filtration method.

55. Sulfate Limit Test

The Sulfate Limit Test is a limit test for sulfate contained in drugs.

In each monograph, the permissible limit for sulfate (as SO_4) is described in terms of percentage (%) in parentheses.

Procedure

Unless otherwise specified, transfer the quantity of the sample, directed in the monograph, to a Nessler tube, dissolve it in sufficient water, and add water to make 40 mL. Add 1 mL of dilute hydrochloric acid and water to make 50 mL, and use this solution as the test solution. Transfer the volume of 0.005 mol/L sulfuric acid VS, directed in the monograph, to another Nessler tube, add 1 mL of dilute hydrochloric acid and water to make 50 mL, and use this solution as the control solution. When the test solution is not clear, filter both solutions according to the same procedure.

Add 2 mL of barium chloride TS to the test solution and to the control solution, mix well, and allow to stand for 10 minutes. Compare the white turbidity produced in both solutions against a black background by viewing downward or transversely.

The turbidity produced in the test solution is not thicker than that of the control solution.

56. Test for Acid-neutralizing Capacity of Gastrointestinal Medicines

The Test for Acid-neutralizing Capacity of Gastrointestinal Medicines is a test to determine the acid-neutralizing capacity of a medicine, as a crude material or preparation, which reacts with the stomach acid and exercises an acid control action in the stomach. When performing the test according to the following procedure, the acid-neutralizing capacity of a crude material is expressed in terms of the amount (mL) of 0.1 mol/L hydrochloric acid VS consumed per g of the material, and that of a preparation is expressed by the amount (mL) of 0.1 mol/L hydrochloric acid VS consumed per dose per day (when the daily dose varies, the minimum dose is used).

Preparation of sample

A crude material and a solid preparation which conforms to Powders in the General Rules for Preparations: may be used, without any treatment, as the sample. Preparations in dose-unit packages: weigh accurately the content of not less than 20 packages, calculate the average mass of the content for a daily dose, mix uniformly, and use the mixture as the sample. Granules in dose-unit packages and other solid preparations which do not conform to Powders in the General Rules for Preparations: weigh accurately the content of not less than 20 packages, calculate the average mass of the content for a daily dose, powder it, and use as the sample. Granules not in dose-unit packages and other solid preparations which do not conform to Powders in the General Rules for Preparations: take not less than 20 doses, powder it, and use as the sample. Capsules and tablets: take not less