add 25 ml of the test solution containing a quantity of the substance being examined as specified in the individual monographs. To cylinder C add 25 ml of another solution containing the same quantity of the substance being examined as cylinder B dissolved in the solvent as specified in the individual monographs, the same volume of lead standard solution as cylinder A, and 2 ml of acetate BS (pH 3.5).

If the original test solution is colured, it may be matched by the addition of a few drops of dilute caramel solution or other suitable solution to cylinder A.

To each cylinder add 2 ml of thioacetamide TS and mix well, allow to stand for 2 minutes, compare the colour produced by viewing down the vertical axis of the three cylinders against a white background. The colour produced in cylinder B is not more intense than that produced in cylinder A and the colour produced in cylinder C is equal to or more intense than that produced in cylinder A. If the colour produced in cylinder C is lighter than that produced in cylinder A, use Method 2 instead of Method 1 for the substance being examined.

If the colour cannot be matched by the addition of caramel solution or other suitable solution, use Method 2 instead of Method 1 for the substance being examined.

If the substance being examined contains a ferric salt which interferes with the test, the same quantity of 0.5-1.0 g of ascorbic acid should be added to each cylinder.

Unless otherwise specified, evaporate the same quantity of the same reagents to dryness in a porcelain dish. Dissolve the residue in 2 ml of acetate BS (pH 3.5) and 15 ml of water. Transfer the solution to a Nessler cylinder, add the specified quantity of lead standard solution and water or other solvent as specified under individual monographs to 25 ml. The solution is used as the reference solution for the test solution which is prepared by using more than 1 ml of hydrochloric acid, 2 ml of ammonia TS or by treating with other reagents.

Method 2

Unless otherwise specified, use Method 2 instead of Method 1 for a quantity of the substance being examined or use immediately Method 2, using the residue obtained in the test for Residue on ignition 〈*0841*〉. If the substance being examined is a liquid, evaporate a volume of the substance being examined as specified in the individual monographs to dryness, using the residue obtained in the test for Residue on ignition, add 0.5 ml of nitric acid, evaporate to dryness, heat until nitrous oxide fumes are no longer evolved (or alternatively, ignite a quantity of the substance being examined in a crucible until thoroughly charred, cool, moisten the residue with 0.5-1 ml of sulfuric acid, ignite at a low temperature until sulfurous acid fumes are no longer evolved, add 0.5 ml of nitric acid, evaporate to dryness, heat until nitrous oxide fumes are no longer evolved and ignite at 500-600℃ until the incineration is complete). Cool, add 2 ml of hydrochloric acid, evaporate to dryness on a water bath, add 15 ml of water, followed by ammonia TS dropwise until the solution is slight pink to phenolphthalein IS, then add 2 ml of acetate BS (pH 3.5) and warm to effect dissolution. Transfer the resulting solution to Nessler cylinder B, dilute with water to 25 ml. Place the same quantity of the same reagents used for the preparation of test solution in a porcelain dish and evaporate to dryness, heat gently to dissolve in 2 ml of acetate BS (pH 3.5) and 15 ml of water, transfer to the Nessler cylinder A and add the specified volume of lead standard solution, dilute with water to 25 ml. To each cylinder add 2 ml of thioacetamide TS and mix well, allow to stand for 2 minutes, compare the colour produced by viewing down the vertical axis of the two cylinders against a white background. The colour produced in cylinder B is not more intense than that produced in cylinder A.

Method 3

Unless otherwise specified, dissolve a quantity of the substance being examined in 5 ml of sodium hydroxide TS and 20 ml of water. Transfer the solution to a Nessler cylinder, add 5 drops of sodium sulfide TS and mix well, the colour produced is not more intense than that of a reference preparation containing the specified volume of lead standard solution and treated in the same manner.

0822 Limit Test for Arsenic

Arsenic standard solution Dissolve 0.132 g of arsenic trioxide in 5 ml of 20% sodium hydroxide solution in a 1000 ml volumetric flask, neutralize with dilute sulfuric acid and add 10 ml in excess. Dilute with water to volume and mix well, as a stock solution.

Transfer 10 ml of the stock solution, accurately measured, to a 1000 ml volumetric flask immediately before use, add 10 ml of dilute sulfuric acid, dilute with water to volume and mix well (each ml is equivalent to 1 μg of arsenic).

Method 1 (Gutzeit's method)

Apparatus (as Fig. 1). A is a 100 ml conical flask with standard ground joint; B is a standard hollow ground glass stopper connected to glass conduit C (external diametre 8.0 mm, internal diametre 6.0 mm), the total length of B and C is about 180 mm; D is a plastic screw, the upper part of which has an aperture 6.0 mm in diametre and the lower part of which has an aperture 8.0 mm in diametre; E is a plastic screw cap which has an aperture 6.0 mm in diametre. A wad of lead acetate cotton weighing about 60 mg is packed into tube C to a depth of about 60-80 mm. A disc of mercuric bromide paper is placed between the contacting surfaces of D and E.

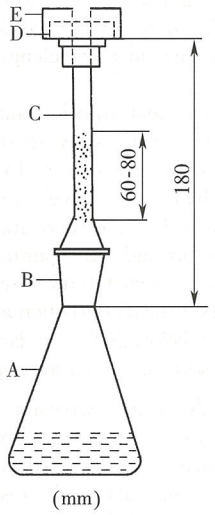

Fig. 1 Apparatus of method 1

Arsenic standard stain Place 2 ml of standard arsenic solution, accurately measured, in flask A. Add 5 ml of hydrochloric acid and 21 ml of water. Then add 5 ml of potassium iodide TS and 5 drops of acid stannous chloride TS, allow to stand at room temperature for 10 minutes and add 2 g of granulated zinc. Insert the stopper B and conduit C into the mouth of flask A and immerse the flask in a water bath at 25-40℃ for 45 minutes. Remove the mercuric bromide paper. Use arsenic standard solution instead of the substance being

examined and treat it in the same manner described in the individual monographs. Then prepare the arsenic standard stain as described above, if the substance being examined needs to be destroyed organically before carrying out the limit test for arsenic.

Procedure Transfer the test solution prepared as described in the individual monographs to flask A and proceed as described under arsenic standard stain, beginning with the words "Then add 5 ml of potassium iodide TS...". Any stain produced is not more intense than the standard stain.

Method 2 (Silver diethyldithiocarbamate method)

Apparatus (as Fig. 2) A is a 100 ml conical flask with standard ground joint; B is a standard hollow ground glass stopper connected to glass conduit C (at one end, the external diametre is 8.0 mm and the internal diametre is 6.0 mm; the other end is in length of 180 mm, in external diameter of 4 mm and in internal diametre of 1.6 mm, the internal diametre of sharp end is 1 mm). D is a glass tube with flat bottom (length 180 mm, internal diametre 10 mm, and with a graduation at 5.0 ml). A wad of lead acetate cotton weighing about 60 mg is packed into conduit C to a depth of about 80 mm, and measure accurately 5 ml of silver diethyldithio-car-bamate TS in tube D.

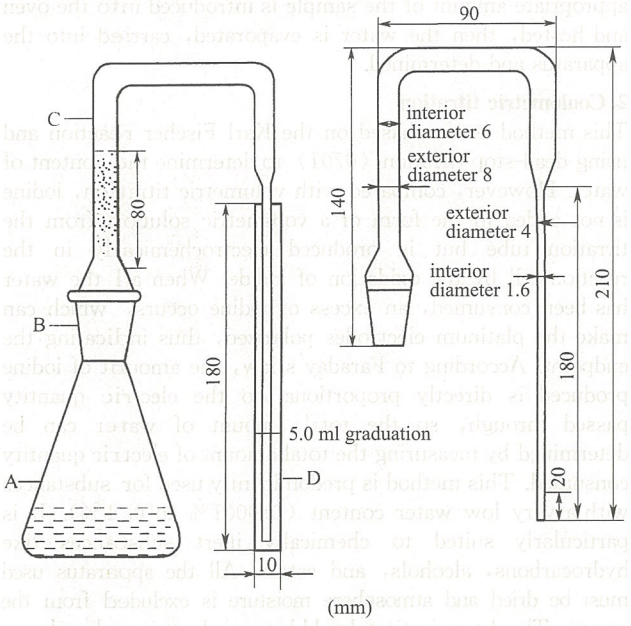

Fig. 2 Apparatus of Method 2

Arsenic reference solution Transfer 2 ml of arsenic standard solution as described under Method 1 to flask A, accurately measured. Add 5 ml of hydrochloric acid and 21 ml of water. Then add 5 ml of potassium iodide TS and 5 drops of acid stannous chloride TS, allow to stand at room temperature for 10 minutes and add 2 g of granulated zinc. Connect conduit C into flask A immediately, and allow the evolved arsine to enter tube D. Immerse the flask A in a water bath at 25-40℃ for 45 minutes. Remove tube D, add chloroform to the graduation, mix well.

Use arsenic standard solution instead of the substance being examined and treat in the same manner in the individual monographs. Then prepare the arsenic reference solution as described above, if the substance being examined needs to be destroyed organically before carrying out the limit test for arsenic.

Procedure Transfer the test solution prepared as described in the individual monographs to flask A and proceed as described under arsenic reference solution, beginning with the words "Then add 5 ml of potassium iodide TS...". Compare the above two solutions against a white background. Any colour produced by the test preparation is not more intense than that produced by the standard arsenic reference solution. If necessary, determine the absorbance at the wavelength of 510 nm, using silver diethyldi-thiocarbamate TS as the blank 〈*0401*〉.

Notes (1) Make sure that a blank test produces no arsenic stain or only a barely visible stain.

(2) The preparation of standard stain and test stain must be carried out simultaneously.

(3) The granulated zinc should be arsenic free and the size is such that they will pass through a No. 1 sieve. The quantity used should be increased and the reaction time should be extended up to 1 hour, if the granules are of larger size.

(4) Lead acetate cotton is prepared by immersing 1.0 g of absorbent cotton in 12 ml of a mixture of equal volumes of lead acetate TS and water. Drain off excess liquid and make the cotton fluffy, allow it to dry at a temperature below 100℃ and preserve in a well closed glass container.

0831 Determination of Loss on Drying

Mix the substance being examined thoroughly. If it is in the form of large crystals, reduce them to a size of about 2 mm by quickly crushing. Place about 1 g or the amount specified in the individual monographs of the substance being examined in a tared, shallow weighing bottle, previously dried to constant weight at 105℃, unless otherwise specified. The substance being examined should be evenly distributed to form a layer of not more than 5 mm in the thickness, or not more than 10 mm in the case of bulky material. When the loaded bottle is placed in the drying chamber or desiccator, remove the stopper and put it beside the bottle, or leave it on the bottle in half open position. Upon the opening of the drying chamber or desiccator, the bottle should be closed promptly. If the substance is dried by heating, allow it to cool to room temperature in a desiccator before weighing.

If the substance melts at a lower temperature than the specified drying temperature, unless otherwise specified, maintain the bottle with its content at about 5-10℃ below the melting point until most of the water is removed, and then dry it under the specified conditions. For biological products, dry it under the specified conditions after most of the water of the substance being examined was removed at a lower temperature.

If a vacuum desiccator or constant temperature vacuum desiccator is to be used (Set the temperature as specified in the monograph. For biological products, set the temperature at 60℃ unless otherwise specified.) a pressure of 2.67 kPa (20 mmHg) or less should be maintained unless otherwise directed. The desiccants used in a desiccator are usually phosphorus pentoxide, anhydrous calcium chloride or silica gel. Phosphorus pentoxide is often used in a constant temperature vacuum desiccator. The desiccants should be replaced in time.

0832 Determination of Water

Method 1 (Karl Fischer's method)

1. Volumetric titration

This method is based on the quantitative reaction of water