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COUNCIL OF EUROPE
CONSEIL DE L'EUROPE

European Pharmacopoeia Commission Secretariat

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Strasbourg, 23/04/2018

Subject: Revision of the general chapter on Arsenic
Difficulty to comply with the suitability test of reagent *silver diethyldithiocarbamate solution R* (1110401)

Dear Users,

The revised Arsenic general method was published in supplement 9.4 of the European Pharmacopoeia and entered into force on 1st April 2018.

The EDQM has been made aware of a problem with the revised detection method (method A, 2.4.2). Indeed, while trying to perform the updated analytical procedure and in particular the suitability tests of the newly introduced reagent *silver diethyldithiocarbamate solution R* (1110401), many laboratories reported UV-visible absorbance values above the prescribed limits, thus invalidating the whole analytical procedure.

The EDQM has already started investigations to find an appropriate solution to this issue.

In the meantime, considering that this issue would block the release of materials under test, the EDQM proposes to temporarily revert back to the previous version of the general method for control of Arsenic, as available in Edition 9.0 and which is reproduced in the Annex for your convenience.

Please be assured that the EDQM is putting every effort to rapidly identify appropriate measures and a long-term solution.

Yours sincerely,

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ANNEX

ARSENIC, METHOD A

The apparatus (see Figure 1) consists of a 100 mL conical flask closed with a ground-glass stopper through which passes a glass tube about 200 mm long and of internal diameter 5 mm. The lower part of the tube is drawn to an internal diameter of 1.0 mm, and 15 mm from its tip is a lateral orifice 2 mm to 3 mm in diameter. When the tube is in position in the stopper, the lateral orifice should be at least 3 mm below the lower surface of the stopper. The upper end of the tube has a perfectly flat, ground surface at right angles to the axis of the tube. A second glass tube of the same internal diameter and 30 mm long, with a similar flat ground surface, is placed in contact with the first, and is held in position by two spiral springs. Into the lower tube insert 50 mg to 60 mg of lead acetate cotton R, loosely packed, or a small plug of cotton and a rolled piece of lead acetate paper R weighing 50 mg to 60 mg. Between the flat surfaces of the tubes place a disc or a small square of mercuric bromide paper (see description below) large enough to cover the orifice of the tube (15 mm × 15 mm).

In the conical flask dissolve the prescribed quantity of the substance to be examined in 25 mL of water R, or in the case of a solution adjust the prescribed volume to 25 mL with water R. Add 15 mL of hydrochloric acid R, 0.1 mL of stannous chloride solution R and 5 mL of potassium iodide solution R, allow to stand for 15 min and introduce 5 g of activated zinc (see description below). Assemble the two parts of the apparatus immediately and immerse the flask in a bath of water at a temperature such that a uniform evolution of gas is maintained. Prepare a standard in the same manner, using 1 mL of arsenic standard solution (1 ppm As) R, diluted to 25 mL with water R.

After not less than 2 h the stain produced on the mercuric bromide paper in the test is not more intense than that in the standard.

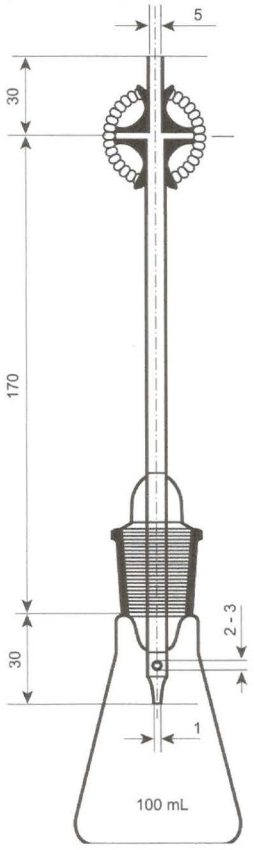

Figure 1. - *Apparatus for limit test A for arsenic*
Dimensions in millimetres

List of specific reagents

Mercuric bromide paper.
In a rectangular dish place a 50 g/L solution of mercuric bromide in anhydrous ethanolR and immerse in it pieces of white filter paper weighing 80 g per square metre (speed of filtration = filtration time expressed in seconds for 100 mL of water at 20 °C with a filter surface of 10 cm^2 and constant pressure of 6.7 kPa: 40 s to 60 s), each measuring 1.5 cm by 20 cm and folded in two. Allow the excess liquid to drain and allow the paper to dry, protected from light, suspended over a non-metallic thread. Discard 1 cm from each end of each strip and cut the remainder into 1.5 cm squares or discs of 1.5 cm diameter.
Storage: in a glass-stoppered container wrapped with black paper.

Activated zinc.
Place the zinc cylinders or pellets to be activated in a conical flask and add a sufficient quantity of a 50 ppm solution of chloroplatinic acidR to cover the metal. Allow the metal to remain in contact with the solution for 10 min, wash, drain and dry immediately.
Arsenic (MethodA). To 5 g of the activated zinc add 15 mL of hydrochloric acidR, 25 mL of waterR, 0.1 mL of stannous chloride solutionR and 5 mL of potassium iodide solutionR. No stain is produced on the mercuric bromide paperR.
Activity. Repeat the test for arsenic using the same reagents and adding a solution containing 1 µg of arsenic. An appreciable stain appears on the mercuric bromide paperR.