4226 Determination of ExtractableTungsten for Prefilled Syringes

Glass prefilled syringes are typically produced from glass tubing via a hot-forming process. One important step of this process is the cone formation and more importantly its opening with a pin that has the form of a filament and that is made of material resistant to high temperatures such as a tungsten pin. In the case of tungsten pins, tungsten residuals may form on the inner surface of the glass barrel. This method applies to the determination of extractable tungsten of glass prefilled syringes.

Carry out the method for inductively coupled plasma optical emission spectrometry *<0411>* or the method for inductively coupled plasma mass spectrometry *<0412>*.

Instruments

Inductively coupled plasma optical emission spectrometer (ICP-OES), in accordance with the requirements of inductively coupled plasma optical emission spectrometry *<0411>*.

Inductively coupled plasma mass spectrometer (ICP-MS), in accordance with the requirements of inductively coupled plasma mass spectrometry *<0412>*.

Ultrasonic bath.

Preparation of test solution

Method 1

It is used to determine the water-soluble amount of tungsten from glass prefilled syringes.

Filling: Take 1 prefilled syringe and assemble the matching plunger stopper and plunger rod as a reference. Measure accurately the exact volume (labelled quantity) of water into a suitable container and aspirate the complete volume through the needle or the Luer channel into the syringe without capturing any air. Remove accidentally captured air bubbles by turning the syringe tip upwards and pushing the plunger rod carefully. Close the syringe with a tip cap or a needle shield, which is filled with water. Mark the resulting filling level (position of the stopper) with a permanent marker. Then transfer this filling level from the reference syringe to the syringes to be tested by suitable means, e.g. by a ruler, see Figure 1.

In addition, take 60 prefilled syringes, and assemble the matching plunger stoppers and plunger rods. Aspirate the water to tightly beneath the mark without capturing any air bubbles. Fill the tip cap/needle shield with water and close the syringe with it. The excessive liquid shall be removed with a paper towel.

Extraction: Put the syringes vertically (tip down) in a rack and then put it into the ultrasonic bath preheated to 75°C± 5°C, start the sonication process for 60 min at 45 kHz specific power of at least 16 W/l. When the extraction is finished, take out the rack from the ultrasonic bath, gently dry every syringe outside with paper towel. Take the syringe, turn it tip cap facing up. Tap the tip cap to move the bubble towards the flow channel, screw the plunger rod on the stopper, pull the plunger stopper to remove the water from the tip channel and then take off the tip cap. Flush the extraction solution into the sample tubes. Rinse the syringes twice by aspirating water into each syringe to the marked position and flush it into the same sample tube which contains the extraction

solution. A second extraction shall be done with the same test syringes by reproducing the same process from “aspirating the purified water to tightly beneath the mark”. The second extraction solution is flushed into the same tube that contains the first extraction, which will be the test solution.

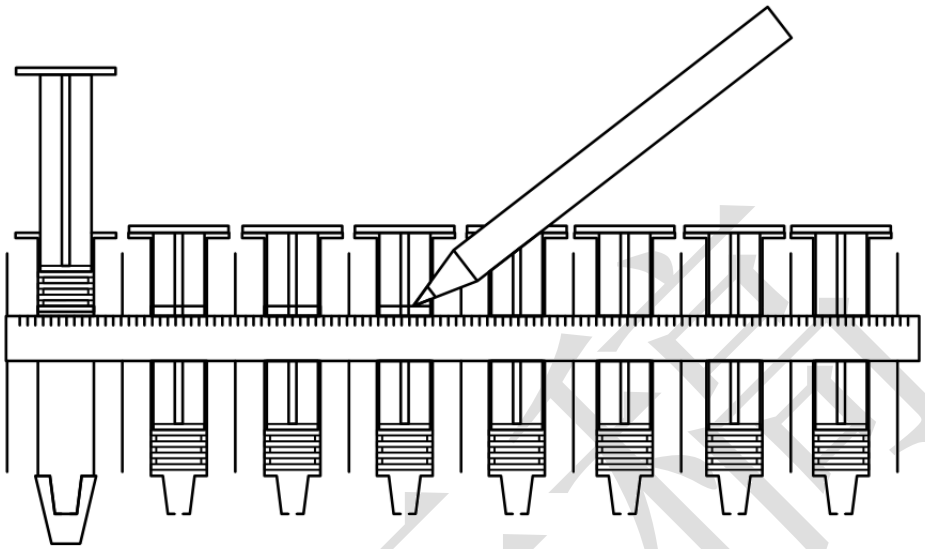

Fig.1 Transfer of the filling level marks to the syringes to be tested

Method 2

It is used for the determination of the extractable amount of tungsten in different forms from glass prefilled syringes.

“0.01mol/L sodium hydroxide solution” is used as the extraction medium and rinsing solution, and two extractions are carried out according to the first method to prepare the test solution.

Preparation of standard solutions: Prepare a series of calibration solutions by dilution of standard solution with suitable medium, which includes a minimum of 5 concentrations.

Determination: The instrument shall meet the usage requirements, and the working parameters can be optimized according to the specific situation. Determine the series of calibration solutions and test solution, draw calibration curve, and calculate the regression equation by using the concentration of calibration solutions as the abscissa and the respond correspondingly as the ordinate (if the internal standard method is used for determination, using the ratio of the peak response value of the element to be measured in the calibration solution to that of the internal standard element as the ordinate). The linear coefficient r is not less than 0.99. Calculate the concentration of tungsten in the test solution according to the regression equation. Perform a blank determination under the same analysis conditions and make any necessary correction according to the instrument manual. If necessary, dilute the test solution for analysis.

Result representation: The absolute amount of extractable tungsten per prefilled syringe is calculated based on the measured concentration of extractable tungsten

(ng/ml), and the result is expressed as the absolute amount of extractable tungsten in ng per prefilled syringe.

Note: It is recommended to use rigid plastic containers, such as PTFE containers, during the experimental process, and if glass containers are used, it shall be noted that the containers used shall not affect the test results.

起草单位：山东省医疗器械和药品包装检验研究院　　联系电话：0531-82682912

参与单位：上海市食品药品包装材料测试所、山东威高普瑞医药包装有限公司、山东省药用玻璃有限公司、宁波正力药品包装有限公司、山东永聚医药科技有限公司、肖特玻璃科技（浙江）有限公司、碧迪医疗器械（上海）有限公司