2.4.5. Fluorides

Figure 2.4.5.-1. – Apparatus for limit test for fluorides
Dimensions in millimetres

Introduce into the inner tube of the apparatus (see Figure 2.4.5.-1) the prescribed quantity of the substance to be examined, 0.1 g of acid-washed sand R and 20 mL of a mixture of equal volumes of sulfuric acid R and water R. Heat the jacket containing tetrachloroethane R maintained at its boiling point (146 °C). Heat the steam generator and distill, collecting the distillate in a 100 mL volumetric flask containing 0.3 mL of 0.1 M sodium hydroxide of the distillate in a 100 mL volumetric flask containing 0.3 mL of a 1 g/L solution of hydroxyquinoline in chloroform R, for 1 min each time. Allow to stand. Separate and discard the organic layer. To the aqueous solution add 0.4 mL of butylamine R and 0.1 mL of triethanolamine R. Adjust the solution, if necessary, to pH 10.5 to pH 11.5. Add 4 mL of the solution of hydroxyquinoline in chloroform, shake for 1 min, allow to stand and separate. Use the lower layer for comparison. Prepare a standard in the same manner using a mixture of 1 mL of magnesium standard solution (10 ppm Mg) R and 9 mL of water R.

Any colour in the solution obtained from the substance to be examined is not more intense than that in the standard.

2.4.6. Magnesium

To 10 mL of the prescribed solution add 0.1 g of disodium tetraborate R. Adjust the solution, if necessary, to pH 8.8 to pH 9.2 using dilute hydrochloric acid R or dilute sodium hydroxide solution R. Shake with 2 quantities, each of 5 mL, of a 1 g/L solution of hydroxyquinoline in chloroform R, for 1 min each time. Allow to stand. Separate and discard the organic layer. To the aqueous solution add 0.4 mL of butylamine R and 0.1 mL of triethanolamine R. Adjust the solution, if necessary, to pH 10.5 to pH 11.5. Add 4 mL of the solution of hydroxyquinoline in chloroform, shake for 1 min, allow to stand and separate. Use the lower layer for comparison. Prepare a standard in the same manner using a mixture of 1 mL of magnesium standard solution (10 ppm Mg) R and 9 mL of water R.

Any colour in the solution obtained from the substance to be examined is not more intense than that in the standard.
If the result is difficult to judge, filter the solutions through a suitable membrane filter (nominal pore size 0.45 μm). Carry out the filtration slowly and uniformly, applying moderate and constant pressure to the piston. Compare the spots on the filters obtained with the different solutions.

METHOD B

**Test solution.** 12 mL of the prescribed solution of the substance to be examined prepared using an organic solvent containing a minimum percentage of water (for example, dioxan containing 15 per cent of water or acetone containing 15 per cent of water).

**Reference solution (standard).** A mixture of 10 mL of lead standard solution (1 or 2 ppm Pb), as prescribed, and 2 mL of the prescribed solution of the substance to be examined in an organic solvent. Prepare the lead standard solution (1 or 2 ppm Pb) by dilution of lead standard solution (100 ppm Pb) R with the solvent used for the substance to be examined.

**Blank solution.** A mixture of 10 mL of the solvent used for the substance to be examined and 2 mL of the prescribed solution of the substance to be examined in an organic solvent.

To each solution, add 2 mL of buffer solution pH 3.5 R. Mix and add to 1.2 mL of thioacetamide reagent R. Mix immediately. Examine the solutions after 2 min.

**System suitability:** the reference solution shows a slight brown colour compared to the blank solution.

**Result:** any brown colour in the test solution is not more intense than that in the reference solution.

If the result is difficult to judge, filter the solutions through a suitable membrane filter (nominal pore size 0.45 μm). Carry out the filtration slowly and uniformly, applying moderate and constant pressure to the piston. Compare the spots on the filters obtained with the different solutions.

METHOD C

**Test solution.** Place the prescribed quantity (not more than 2 g) of the substance to be examined in a silica crucible with 4 mL of a 250 g/L solution of magnesium sulphate R in dilute sulphuric acid R. Mix using a fine glass rod. Heat cautiously. If the mixture is liquid, evaporate gently to dryness on a water-bath. Progressively heat to ignition and continue heating until an almost white or at most greyish residue is obtained. Carry out the ignition at a temperature not exceeding 800 °C. Allow to cool. Moisten the residue with a few drops of dilute sulphuric acid R. Evaporate, ignite again and allow to cool. The total period of ignition must not exceed 2 h. Take up the residue in 2 quantities, each of 5 mL, of dilute hydrochloric acid R and then concentrated ammonia R until a pink colour is obtained. Cool, add glacial acetic acid R until the solution is decolourised and add 0.5 mL in excess. Filter if necessary and wash the filter. Dilute to 20 mL with water R.

**Reference solution (standard).** Prepare as described for the test solution, using the prescribed volume of lead standard solution (10 ppm Pb) R instead of the substance to be examined and drying in an oven at 100-105 °C. To 10 mL of the solution obtained add 2 mL of the test solution.

**Monitor solution.** Prepare as described for the test solution, adding to the substance to be examined the volume of lead standard solution (10 ppm Pb) R prescribed for preparation of the reference solution and drying in an oven at 100-105 °C. To 10 mL of the solution obtained add 2 mL of the test solution.

**Blank solution.** A mixture of 10 mL of water R and 2 mL of the test solution.

To 12 mL of each solution, add 2 mL of buffer solution pH 3.5 R. Mix and add to 1.2 mL of thioacetamide reagent R. Mix immediately. Examine the solutions after 2 min.

**System suitability:**
- the reference solution shows a slight brown colour compared to the blank solution,
- the monitor solution is at least as intense as the reference solution.

**Result:** any brown colour in the test solution is not more intense than that in the reference solution.

If the result is difficult to judge, filter the solutions through a suitable membrane filter (nominal pore size 0.45 μm). Carry out the filtration slowly and uniformly, applying moderate and constant pressure to the piston. Compare the spots on the filters obtained with the different solutions.

METHOD D

**Test solution.** In a silica crucible, mix thoroughly the prescribed quantity of the substance to be examined with 0.5 g of magnesium oxide R. Ignite to dull redness until a homogeneous white or greyish-white mass is obtained. If after 30 min of ignition the mixture remains coloured, allow to cool, mix using a fine glass rod and repeat the ignition. If necessary repeat the operation. Heat at 800 °C for about 1 h. Take up the residue in 2 quantities, each of 5 mL, of a mixture of equal volumes of hydrochloric acid R1 and water R. Add 0.1 mL of phenolphthalein solution R and then concentrated ammonia R until a pink colour is obtained. Cool, add glacial acetic acid R until the solution is decolourised and add 0.5 mL in excess. Filter if necessary and wash the filter. Dilute to 20 mL with water R.

**Reference solution (standard).** Prepare as described for the test solution using the prescribed volume of lead standard solution (10 ppm Pb) R instead of the substance to be examined and drying in an oven at 100-105 °C. To 10 mL of the solution obtained add 2 mL of the test solution.

**Monitor solution.** Prepare as described for the test solution, adding to the substance to be examined the volume of lead standard solution (10 ppm Pb) R prescribed for preparation of the reference solution and drying in an oven at 100-105 °C. To 10 mL of the solution obtained add 2 mL of the test solution.

**Blank solution.** A mixture of 10 mL of water R and 2 mL of the test solution.

To 12 mL of each solution, add 2 mL of buffer solution pH 3.5 R. Mix and add to 1.2 mL of thioacetamide reagent R. Mix immediately. Examine the solutions after 2 min.

**System suitability:**
- the reference solution shows a slight brown colour compared to the blank solution,
- the monitor solution is at least as intense as the reference solution.

**Result:** any brown colour in the test solution is not more intense than that in the reference solution.

If the result is difficult to judge, filter the solutions through a suitable membrane filter (nominal pore size 0.45 μm). Carry out the filtration slowly and uniformly, applying moderate and constant pressure to the piston. Compare the spots on the filters obtained with the different solutions.

METHOD E

**Test solution.** Dissolve the prescribed quantity of the substance to be examined in 30 mL of water R or the prescribed volume.

**Reference solution (standard).** Unless otherwise prescribed, dilute the prescribed volume of lead standard solution (1 ppm Pb) R to the same volume as the test solution.

Prepare the filtration apparatus by adapting the barrel of a 50 mL syringe without its piston to a support containing, on the plate, a membrane filter (nominal pore size 3 μm) and above it a prefILTER (Figure 2.4.8-1).

Transfer the test solution into the syringe barrel, put the piston in place and then apply an even pressure on it until the whole of the liquid has been filtered. In opening the support and removing the prefiltter, check that the membrane filter remains uncontaminated with impurities. If this is not the case replace it with another membrane filter and repeat the operation under the same conditions.

To the prefiltter or to the prescribed volume of the prefiltter add 2 mL of buffer solution pH 3.5 R. Mix and add to 1.2 mL of thioacetamide reagent R. Mix immediately and allow to
stand for 10 min and again filter as described above, but
inverting the order of the filters, the liquid passing first through
the membrane filter before passing through the pref ilter
(Figure 2.4.8.-1). The filtration must be carried out slowly and
uniformly by applying moderate and constant pressure to
the piston of the syringe. After complete filtration, open the
support, remove the membrane filter, and dry using filter paper.
In parallel, treat the reference solution in the same manner as
the test solution.
Result: the colour of the spot obtained with the test solution
is not more intense than that obtained with the reference solution.

METHOD F
Test solution. Place the prescribed quantity or volume of the
substance to be examined in a clean, dry, 100 mL long-necked
combustion flask (a 300 mL flask may be used if the reaction
foams excessively). Clamp the flask at an angle of 45°. If the
substance to be examined is a solid, add a sufficient volume of a
mixture of 8 mL of sulfuric acid R and 10 mL of nitric acid R
to moisten the substance thoroughly; if the substance to be
examined is a liquid, add a few millilitres of a mixture of 8 mL
of sulfuric acid R and 10 mL of nitric acid R. Warm gently
until the reaction commences, allow the reaction to subside
and add additional portions of the same acid mixture, heating
after each addition, until a total of 18 mL of the acid mixture
has been added. Increase the amount of heat and boil gently
until the solution darkens. Cool, add 2 mL of nitric acid R and
heat again until the solution darkens. Continue the heating,
followed by the addition of nitric acid R until no further
darkening occurs, then heat strongly until dense, white fumes
are produced. Cool, cautiously add 5 mL of water R, boil gently
until dense, white fumes are produced and continue heating to
reduce to 2–3 mL. Cool, cautiously add 5 mL of water R and
examine the colour of the solution. If the colour is yellow,
cautiously add 1 mL of strong hydrogen peroxide solution R
and again evaporate until dense, white fumes are produced
and reduce to a volume of 2–3 mL. If the solution is still yellow
in colour, repeat the addition of 5 mL of water R and 1 mL
of strong hydrogen peroxide solution R until the solution is
colourless. Cool, dilute cautiously with water R and rinse into a
50 mL colour comparison tube, ensuring that the total volume
does not exceed 25 mL. Adjust the solution to pH 3.0–4.0,
using short range pH indicator paper as external indicator,
with concentrated ammonia R1 (dilute ammonia R1 may be
used, if desired, as the specified range is approached), dilute
with water R to 40 mL and mix. Add 2 mL of buffer solution
pH 3.5 R. Mix and add to 1.2 mL of thiocetamide reagent R.
Mix immediately. Dilute to 50 mL with water R and mix.

Reference solution (standard). Prepare at the same time and
in the same manner as the test solution, using the prescribed
volume of lead standard solution (10 ppm Pb) R.

Monitor solution. Prepare as described for the test solution,
adding to the substance to be examined the volume of lead
standard solution (10 ppm Pb) R prescribed for the preparation
of the reference solution.

Blank solution. Prepare as described for the test solution,
omitting the substance to be examined.

Examine the solutions vertically against a white background
after 2 min.

System suitability:
– the reference solution shows a brown colour compared to
the blank solution,
– the monitor solution is at least as intense as the reference
solution.

Result: any brown colour in the test solution is not more intense
than that in the reference solution.

If the result is difficult to judge, filter the solutions through a
suitable membrane filter (nominal pore size 0.45 μm). Carry
out the filtration slowly and uniformly, applying moderate and
constant pressure to the piston. Compare the spots on the
filters obtained with the different solutions.

METHOD G
CAUTION: when using high-pressure digestion vessels the
safety precautions and operating instructions given by the
manufacturer must be followed. The digestion cycles have to
be elaborated depending on the type of microwave oven to
be used (for example, energy-controlled microwave ovens,
temperature-controlled microwave ovens or high-pressure
ovens). The cycle must conform to the manufacturer’s
instructions. The digestion cycle is suitable if a clear solution
is obtained.

Test solution. Place the prescribed amount of the substance to
be examined (not more than 0.5 g) in a suitable, clean beaker.
Add successively 2.7 mL of sulfuric acid R, 3.3 mL of nitric
acid R and 2.0 mL of strong hydrogen peroxide solution R
using a magnetic stirrer. Allow the substance to react with a
reagent before adding the next one. Transfer the mixture to a dry high-pressure-resistant digestion vessel (fluoropolymer or quartz glass).

*Reference solution (standard).* Prepare as described for the test solution, using the prescribed volume of lead standard solution (10 ppm Pb) R instead of the substance to be examined.

*Monitor solution.* Prepare as described for the test solution, adding to the substance to be examined the volume of lead standard solution (10 ppm Pb) R prescribed for the preparation of the reference solution.

*Blank solution.* Prepare as described for the test solution, omitting the substance to be examined.

Close the vessels and place in a laboratory microwave oven. Digest using a sequence of 2 separate suitable programmes. Design the programmes in several steps in order to control the reaction, monitoring pressure, temperature or energy depending on the type of microwave oven available. After the first programme allow the digestion vessels to cool before opening. Add to each vessel 2.0 mL of strong hydrogen peroxide solution R and digest using the second programme. After the second programme allow the digestion vessels to cool before opening. If necessary to obtain a clear solution, repeat the addition of strong hydrogen peroxide solution R and the second digestion programme.

Cool, dilute cautiously with water R and rinse into a flask, ensuring that the total volume does not exceed 25 mL.

Using short-range pH indicator paper as external indicator, adjust the solutions to pH 3.0-4.0 with concentrated ammonia R1 (dilute ammonia R1 may be used as the specified range is approached). To avoid heating of the solutions use an ice-bath and a magnetic stirrer. Dilute to 40 mL with water R and mix. Add 2 mL of buffer solution pH 3.5 R. Mix and add to 1.2 mL of thioacetamide reagent R. Mix immediately. Dilute to 50 mL with water R, mix and allow to stand for 2 min.

Filter the solutions through a suitable membrane filter (nominal pore size 0.45 μm). Carry out the filtration slowly and uniformly, applying moderate and constant pressure to the piston. Compare the spots on the filters obtained with the different solutions.

*System suitability:*

- the spot obtained with the reference solution shows a brown colour compared to the spot obtained with the blank solution,
- the spot obtained with the monitor solution is at least as intense as the spot obtained with the reference solution.

*Result:* the brownish-black colour of the spot obtained with the test solution is not more intense than that of the spot obtained with the reference solution.

01/2008:20409

### 2.4.9. IRON

Dissolve the prescribed quantity of the substance to be examined in water R and dilute to 10 mL with the same solvent or use 10 mL of the prescribed solution. Add 2 mL of a 200 g/L solution of citric acid R and 0.1 mL of thioglycollic acid R. Mix, make alkaline with ammonia R and dilute to 20 mL with water R. Prepare a standard in the same manner, using 10 mL of iron standard solution (1 ppm Fe) R.

After 5 min, any pink colour in the test solution is not more intense than that in the standard.

01/2008:20410

### 2.4.10. LEAD IN SUGARS

Determine the lead by atomic absorption spectrometry (2.2.23, *Method I*).

*Test solution.* Dissolve 20.0 g of the substance to be examined in a mixture of equal volumes of dilute acetic acid R and water R and dilute to 100.0 mL with the same mixture of solvents. Add 2.0 mL of a clear 10 g/L solution of ammonium pyrrolidinedithiocarbamate R and 10.0 mL of methyl isobutyl ketone R and then shake for 30 s protected from bright light. Allow the layers to separate and use the methyl isobutyl ketone layer.

*Reference solutions.* Prepare 3 reference solutions in the same manner as the test solution but adding 0.5 mL, 1.0 mL and 1.5 mL respectively of lead standard solution (10 ppm Pb) R in addition to the 20.0 g of the substance to be examined.

Set the zero of the instrument using methyl isobutyl ketone R treated as described for the test solution without the substance to be examined. Measure the absorbance at 283.3 nm using a lead hollow-cathode lamp as source of radiation and an air-acetylene flame.

The substance to be examined contains not more than 0.5 ppm of lead, unless otherwise prescribed.

01/2008:20411

### 2.4.11. PHOSPHATES

To 100 mL of the solution prepared and, if necessary, neutralised as prescribed add 4 mL of sulfololybic reagent R3. Shake and add 0.1 mL of stannous chloride solution R1. Prepare a standard in the same manner using 2 mL of phosphate standard solution (5 ppm PO4) R and 98 mL of water R. After 10 min, compare the colours using 20 mL of each solution.

Any colour in the test solution is not more intense than that in the standard.

01/2008:20412

### 2.4.12. POTASSIUM

To 10 mL of the prescribed solution add 2 mL of a freshly prepared 10 g/L solution of sodium tetraphenylborate R. Prepare a standard in the same manner using a mixture of 5 mL of potassium standard solution (20 ppm K) R and 5 mL of water R.

After 5 min, any opalescence in the test solution is not more intense than that in the standard.