**Atomic absorption spectrometry (2.2.23, Method I).**

**Test solution.** Add 5 ml of nitric acid R per litre of the water to be examined. In a 50 ml borosilicate glass flask, with a ground-glass-stopper, place 20 ml of the water to be examined and add 1 ml of *dilute nitric acid R* and shake. Add 0.3 ml of *bromine water R1*. Stopper the flask, shake and heat the stopped flask at 45 °C for 4 h. Allow to cool. If the solution does not become yellow, add 0.5 ml of *bromine water R1* and re-heat at 45 °C for 4 h. Add 0.5 ml of a freshly prepared 10 g/l solution of *hydroxyamine hydrochloride R*. Shake. Allow to stand for 20 min.

**Reference solutions.** Use freshly prepared reference solutions (0.0005 ppm to 0.002 ppm) obtained by diluting *mercury standard solution (1000 ppm Hg) R* with a 5 per cent V/V solution of *dilute nitric acid R* and treat as described for the test solution.

To a volume of solution suitable for the instrument to be used, add *stannous chloride solution R2* equal to 1/5 of this volume. Fit immediately the device for the entrainment of the mercury vapour. Wait 20 s and pass through the device a stream of *nitrogen R* as the carrier gas.

**Source:** mercury hollow-cathode tube or a discharge lamp.

**Wavelength:** 253.7 nm.

**Atomisation device:** flameless system whereby the mercury can be entrained in the form of cold vapour.

**Potassium:** maximum 2 ppm.

Atomic emission spectrometry (2.2.22, Method I).

**Test solution (a).** Dilute 50.0 ml of the water to be examined to 100 ml with *distilled water R*. Carry out a determination using this solution. If the potassium content is more than 0.75 mg/l, further dilute the water to be examined with *distilled water R*.

**Test solution (b).** Take 50.0 ml of the water to be examined or, if necessary, the water to be examined diluted as described in the preparation of test solution (a). Add 1.25 ml of *potassium standard solution (20 ppm K) R* and dilute to 100.0 ml with *distilled water R*.

**Reference solutions.** Prepare reference solutions (0 ppm; 0.25 ppm; 0.50 ppm; 0.75 ppm; 1 ppm) using *potassium standard solution (20 ppm K) R*.

**Wavelength:** 766.5 nm.

Calculate the potassium content of the water to be examined in parts per million from the expression:

\[
p \times \frac{n_1}{n_2} \times 0.5
\]

- **p** = dilution factor used for the preparation of test solution (a),
- **n₁** = measured value of test solution (a),
- **n₂** = measured value of test solution (b).

**Sodium:** maximum 50 ppm.

Atomic emission spectrometry (2.2.22, Method I).

**Test solution.** The water to be examined. If the sodium content is more than 10 mg/l, dilute with *distilled water R* to obtain a concentration suitable for the apparatus used.

**Reference solutions.** Prepare reference solutions (0 ppm; 2.5 ppm; 5.0 ppm; 7.5 ppm; 10 ppm) using *sodium standard solution (200 ppm Na) R*.

**Wavelength:** 589 nm.

**Zinc:** maximum 0.1 ppm.

Atomic absorption spectrometry (2.2.23, Method I): use sampling and analytical equipment free from zinc or not liable to yield zinc under the conditions of use.

**Test solution.** The water to be examined.

**Reference solutions.** Prepare reference solutions (0.05 ppm to 0.15 ppm) using *zinc standard solution (100 ppm Zn) R*.

**Source:** zinc hollow-cathode lamp.

**Wavelength:** 213.9 nm.

**Atomisation device:** oxidising air-acetylene flame.

**HAEMODIALYSIS, SOLUTIONS FOR**

**Solutiones ad haemodialysim**

**DEFINITION**

Solutions for haemodialysis are solutions of electrolytes with a concentration close to the electrolytic composition of plasma. Glucose may be included in the formulation.

Because of the large volumes used, haemodialysis solutions are usually prepared by diluting a concentrated solution with water of suitable quality (see the monograph on *Haemodialysis solutions concentrated, water for diluting* (1167)), using for example an automatic dosing device.

**Concentrated solutions for haemodialysis**

Concentrated haemodialysis solutions are prepared and stored using materials and methods designed to produce solutions having as low a degree of microbial contamination as possible. In certain circumstances, it may be necessary to use sterile solutions.

During dilution and use, precautions are taken to avoid microbial contamination. Diluted solutions are to be used immediately after preparation.

Concentrated solutions for haemodialysis are supplied in:
- rigid, semi-rigid or flexible plastic containers,
- glass containers.

Three types of concentrated solutions are used:

1. **Concentrated solutions with acetate or lactate**

Several formulations of concentrated solutions are used. The concentrations of the components in the solutions are such that after dilution to the stated volume the concentrations of the components per litre are usually in the following ranges:
Concentrated solutions with acetate or lactate are diluted before use.

2. Concentrated acidic solutions

Several formulations of concentrated solutions are used. The concentrations of the components in the solutions are such that after dilution to the stated volume and before neutralisation with sodium hydrogen carbonate the concentrations of the components per litre are usually in the following ranges:

<table>
<thead>
<tr>
<th>Component</th>
<th>Expression in mmol</th>
<th>Expression in mEq</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>130 - 145</td>
<td>130 - 145</td>
</tr>
<tr>
<td>Potassium</td>
<td>0 - 3.0</td>
<td>0 - 3.0</td>
</tr>
<tr>
<td>Calcium</td>
<td>0 - 2.0</td>
<td>0 - 4.0</td>
</tr>
<tr>
<td>Magnesium</td>
<td>0 - 1.2</td>
<td>0 - 2.4</td>
</tr>
<tr>
<td>Acetate or lactate</td>
<td>32 - 45</td>
<td>32 - 45</td>
</tr>
<tr>
<td>Chloride</td>
<td>90 - 120</td>
<td>90 - 120</td>
</tr>
<tr>
<td>Glucose</td>
<td>0 - 12.0</td>
<td></td>
</tr>
</tbody>
</table>

Sodium hydrogen carbonate must be added immediately before use. Inject 10 ml of the solution per kilogram of the rabbit’s body weight. If the labelled amount is greater than 0.5 ml/kg, adjust to 0.5 ml/kg.

3. Concentrated solutions without buffer

Several formulations of concentrated solutions without buffer are used. The concentrations of the components in the solutions are such that after dilution to the stated volume, the concentrations of the components per litre are usually in the following ranges:

<table>
<thead>
<tr>
<th>Component</th>
<th>Expression in mmol</th>
<th>Expression in mEq</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>80 - 110</td>
<td>80 - 110</td>
</tr>
<tr>
<td>Potassium</td>
<td>0 - 3.0</td>
<td>0 - 3.0</td>
</tr>
<tr>
<td>Calcium</td>
<td>0 - 2.0</td>
<td>0 - 4.0</td>
</tr>
<tr>
<td>Magnesium</td>
<td>0 - 1.2</td>
<td>0 - 2.4</td>
</tr>
<tr>
<td>Acetic acid</td>
<td>2.5 - 10</td>
<td>2.5 - 10</td>
</tr>
<tr>
<td>Chloride</td>
<td>90 - 120</td>
<td>90 - 120</td>
</tr>
<tr>
<td>Glucose</td>
<td>0 - 12.0</td>
<td></td>
</tr>
</tbody>
</table>

Concentrated solutions without buffer are used together with parenteral administration of suitable hydrogen carbonate solutions.

### Tests

#### Appearance of solution
The solution to be examined is clear (2.2.1). If it does not contain glucose, it is colourless (2.2.2, Method D). If it contains glucose, it is not more intensely coloured than reference solution Y7 (2.2.2, Method I).

#### Prescribed solution
Take 20 ml of the solution to be examined, adjust to pH 6.0 and add 10 ml of acetate buffer solution pH 6.0 R.

#### Reference solution
Mix 1 ml of aluminium standard solution (2 ppm Al) R, 10 ml of acetate buffer solution pH 6.0 R and 9 ml of water R.

#### Blank solution
Mix 10 ml of acetate buffer solution pH 6.0 R and 10 ml of water R.

#### Extractable volume
The volume measured is not less than the nominal volume stated on the label.

#### Sterility
If the label states that the concentrated haemodialysis solution is sterile, it complies with the test for sterility.

#### Bacterial endotoxins
Less than 0.5 IU/ml in the solution diluted for use.

#### Pyrogens
Solutions for which a validated test for bacterial endotoxins cannot be carried out comply with the test for pyrogens. Dilute the solution to be examined with water for injections R to the concentration prescribed for use. Inject 10 ml of the solution per kilogram of the rabbit’s mass.

### Assay

#### Density
Determine the density (2.2.5) of the concentrated solution and calculate the content in grams per litre and in millimoles per litre.

#### Sodium
97.5 per cent to 102.5 per cent of the content of sodium (Na) stated on the label.

Atomic emission spectrometry (2.2.22, Method I).
Test solution. Dilute 5.0 ml of the solution to be examined to 100.0 ml with water R. Dilute 2.0 ml of this solution to 50.0 ml with water R. To 1.0 ml of this solution add 10 ml of lanthanum chloride solution R and dilute to 100.0 ml with water R.

Reference solutions. Into 4 identical volumetric flasks each containing 30 ml of lanthanum chloride solution R, introduce respectively 1.0 ml, 2.0 ml, 4.0 ml and 5.0 ml of sodium standard solution (10 ppm Na) R and dilute to 100.0 ml with water R.

Wavelength: 589.0 nm.

Potassium: 95.0 per cent to 105.0 per cent of the content of potassium (K) stated on the label.

Atomic absorption spectrometry (2.2.23, Method I).

Test solution. Dilute with water R an accurately weighed quantity of the solution to be examined to a concentration suitable for the instrument to be used. To 100 ml of this solution add 10 ml of a 22 g/l solution of sodium chloride R.

Reference solutions. Prepare the reference solutions using potassium standard solution (100 ppm K) R. To 100 ml of each reference solution add 10 ml of a 22 g/l solution of sodium chloride R.

Source: potassium hollow-cathode lamp.

Wavelength: 766.5 nm.

Atomisation device: air-acetylene flame.

Calcium: 95.0 per cent to 105.0 per cent of the content of calcium (Ca) stated on the label.

Atomic absorption spectrometry (2.2.23, Method I).

Test solution. Dilute 5.0 ml of the solution to be examined to 100.0 ml with water R. To 3.0 ml of this solution add 5 ml of lanthanum chloride solution R and dilute to 50.0 ml with water R.

Reference solutions. Into 4 keep volumetric flasks each containing 5 ml of lanthanum chloride solution R, introduce respectively 2.5 ml, 5.0 ml, 7.0 ml and 10.0 ml of calcium standard solution (10 ppm Ca) R and dilute to 50.0 ml with water R.

Source: calcium hollow-cathode lamp.

Wavelength: 422.7 nm.

Atomisation device: air-acetylene flame.

Magnesium: 95.0 per cent to 105.0 per cent of the content of magnesium (Mg) stated on the label.

Atomic absorption spectrometry (2.2.23, Method I).

Test solution. Dilute 5.0 ml of the solution to be examined to 100.0 ml with water R. To 2.0 ml of this solution add 5 ml of lanthanum chloride solution R and dilute to 50.0 ml with water R.

Reference solutions. Into 4 identical volumetric flasks each containing 5 ml of lanthanum chloride solution R, introduce respectively 1.0 ml, 2.0 ml, 3.0 ml and 4.0 ml of magnesium standard solution (10 ppm Mg) R and dilute to 50.0 ml with water R.

Source: magnesium hollow-cathode lamp.

Wavelength: 285.2 nm.

Atomisation device: air-acetylene flame.

Total chloride: 95.0 per cent to 105.0 per cent of the content of chloride (Cl) stated on the label.

Dilute to 50 ml with water R an accurately measured volume of the solution to be examined containing the equivalent of about 60 mg of chloride. Add 5 ml of dilute nitric acid R, 25.0 ml of 0.1 M silver nitrate and 2 ml of dibutyl phthalate R. Shake. Using 2 ml of ferric ammonium sulphate solution R2 as indicator, titrate with 0.1 M ammonium thiocyanate until a reddish-yellow colour is obtained.

1 ml of 0.1 M silver nitrate is equivalent to 3.545 mg of Cl.

Acetate: 95.0 per cent to 105.0 per cent of the content of acetate stated on the label.

To a volume of the solution to be examined, corresponding to about 0.7 mmol of acetate, add 10.0 ml of 0.1 M hydrochloric acid. Carry out a potentiometric titration (2.2.20), using 0.1 M sodium hydroxide. Read the volume added between the 2 points of inflexion.

1 ml of 0.1 M sodium hydroxide is equivalent to 0.1 mmol of acetate.

Lactate: 95.0 per cent to 105.0 per cent of the content of lactate stated on the label.

To a volume of the solution to be examined, corresponding to about 0.7 mmol of lactate, add 10.0 ml of 0.1 M hydrochloric acid. Then add 50 ml of acetonitrile R. Carry out a potentiometric titration (2.2.20), using 0.1 M sodium hydroxide. Read the volume added between the 2 points of inflexion.

1 ml of 0.1 M sodium hydroxide is equivalent to 8.40 mg of NaHCO₃.

Reducing sugars (expressed as anhydrous glucose): 95.0 per cent to 105.0 per cent of the content of glucose stated on the label.

Transfer a volume of the solution to be examined containing the equivalent of 25 mg of glucose to a 250 ml conical flask with a ground-glass neck and add 25.0 ml of cupri-citric solution R. Add a few grains of pumice, fit a reflux condenser, heat so that boiling occurs within 2 min and maintain boiling for exactly 10 min. Cool and add 3 g of potassium iodide R dissolved in 3 ml of water R. Carefully add, in small amounts, 25 ml of a 25 per cent m/m solution of sulphuric acid R. Titrate with 0.1 M sodium thiosulphate using starch solution R, added towards the end of the titration, as indicator. Carry out a blank titration using 25.0 ml of water R.

Calculate the content of reducing sugars, expressed as anhydrous glucose (C₆H₁₂O₆), using Table 0128-4:

<table>
<thead>
<tr>
<th>Volume of 0.1 M sodium thiosulphate (ml)</th>
<th>Anhydrous glucose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>19.8</td>
</tr>
<tr>
<td>9</td>
<td>22.4</td>
</tr>
<tr>
<td>10</td>
<td>25.0</td>
</tr>
<tr>
<td>11</td>
<td>27.6</td>
</tr>
<tr>
<td>12</td>
<td>30.3</td>
</tr>
<tr>
<td>13</td>
<td>33.0</td>
</tr>
<tr>
<td>14</td>
<td>35.7</td>
</tr>
<tr>
<td>15</td>
<td>38.5</td>
</tr>
<tr>
<td>16</td>
<td>41.3</td>
</tr>
</tbody>
</table>

See the information section on general monographs (cover pages)
In haemofiltration and in haemodiafiltration, the following formulations may also be used:

<table>
<thead>
<tr>
<th>Component</th>
<th>Expression in mmol</th>
<th>Expression in mEq</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>130 - 167</td>
<td>130 - 167</td>
</tr>
<tr>
<td>Potassium</td>
<td>0 - 4.0</td>
<td>0 - 4.0</td>
</tr>
<tr>
<td>Hydrogen carbonate</td>
<td>20 - 167</td>
<td>20 - 167</td>
</tr>
<tr>
<td>Chloride</td>
<td>0 - 147</td>
<td>0 - 147</td>
</tr>
</tbody>
</table>

Antioxidants such as metabisulphite salts are not added to the solutions.

IDENTIFICATION
According to the stated composition, the solution to be examined gives the following identification reactions (2.3.I):

- sodium: reaction (b);
- calcium: reaction (a);
- potassium: reaction (b);
- carbonates and hydrogen carbonates;
- acetates:
  - if the solution is free from glucose, use reaction (b),
  - if the solution contains glucose, use the following method: to 5 ml of the solution to be examined add 1 ml of hydrochloric acid R in a test-tube fitted with a stopper and a bent tube, heat and collect a few millilitres of distillate; carry out reaction (b) of acetates on the distillate;
- lactates;
- carbonates and hydrogen carbonates;
- magnesium: to 0.1 ml of titan yellow solution R add 10 ml of water R; 2 ml of the solution to be examined and 1 ml of 1 N sodium hydroxide; a pink colour is produced;
- glucose: to 5 ml of the solution to be examined, add 2 ml of dilute sodium hydroxide solution R and 0.05 ml of copper sulphate solution R; the solution is blue and clear; heat to boiling; an abundant red precipitate is formed.

TESTS

Appearance of solution. The solution is clear (2.2.I). If it does not contain glucose, it is colourless (2.2.2, Method I). If it contains glucose, it is not more intensely coloured than reference solution Y (2.2.2, Method I).

pH (2.2.3). The pH of the solution is 5.0 to 7.5. If the solution contains glucose, the pH is 4.5 to 6.5. If the solution contains hydrogen carbonate, the pH is 7.0 to 8.5.

Hydroxymethylfurfural. To a volume of the solution containing the equivalent of 25 mg of glucose, add 5.0 ml of a 100 g/l solution of p-toluidine R in 2-propanol R containing 10 per cent V/V of glacial acetic acid R and 1.0 ml of a 5 g/l solution of barbituric acid R. The absorbance (2.2.25), determined at 550 nm after allowing the mixture to stand for 2 min to 3 min, is not greater than that of a standard prepared at the same time in the same manner using a solution containing 10 µg of hydroxymethylfurfural R in the same volume as the solution to be examined. If the solution contains hydrogen carbonate, use as the standard a solution containing 20 µg of hydroxymethylfurfural R.

Aluminium (2.4.17). Take 200 ml, adjust to pH 6.0 and add 10 ml of acetate buffer solution pH 6.0 R. The solution complies with the limit test for aluminium (10 µg/l). Use as the reference solution a mixture of 1 ml of aluminium standard solution (2 ppm Al) R, 10 ml of acetate buffer solution pH 6.0 R, and 10 ml of water R. The absorbance (2.2.25), determined at 550 nm, is not more than 0.025.

Table 0861.2.

<table>
<thead>
<tr>
<th>Component</th>
<th>Expression in mmol</th>
<th>Expression in mEq</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium</td>
<td>130 - 167</td>
<td>130 - 167</td>
</tr>
<tr>
<td>Potassium</td>
<td>0 - 4.0</td>
<td>0 - 4.0</td>
</tr>
<tr>
<td>Hydrogen carbonate</td>
<td>20 - 167</td>
<td>20 - 167</td>
</tr>
<tr>
<td>Chloride</td>
<td>0 - 147</td>
<td>0 - 147</td>
</tr>
</tbody>
</table>

When hydrogen carbonate is present, the solution of sodium hydrogen carbonate is supplied in a container or a separate compartment and is added to the electrolyte solution immediately before use.