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Trace Elements Injection

» Trace Elements Injection is a sterile solution in Water for Injection of two or more of the following: Zinc Chloride or Zinc Sulfate, Cupric Chloride or Cupric Sulfate, Chromic Chloride, Manganese Chloride or Manganese Sulfate, Selenious Acid, Sodium Iodide, and Ammonium Molybdate. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amounts of zinc (Zn), copper (Cu), chromium (Cr), manganese (Mn), selenium (Se), iodine (I), and molybdenum (Mo).

Packaging and storage—Preserve in single-dose or in multiple-dose containers, preferably of Type I or Type II glass.

Labeling—Label the Injection to specify that it is to be diluted to the appropriate strength with Sterile Water for Injection or other suitable fluid prior to administration. The label shows by an appropriate number juxtaposed to the official name, the number of trace elements contained in the Injection according to the following: zinc and copper (2), and then cumulatively, chromium (3), manganese (4), selenium (5), iodine (6), and molybdenum (7). Other combinations are indicated separately by citing the number of trace elements contained in each followed by an asterisk that is repeated with the list of labeled ingredients. Label the Injection for its contents of zinc chloride ($ZnCl_2$), zinc sulfate ($ZnSO_4 \cdot 7H_2O$), cupric chloride ($CuCl_2$), cupric sulfate ($CuSO_4$), chromic chloride ($CrCl_3$), manganese chloride ($MnCl_2$), manganese sulfate ($MnSO_4$), selenious acid (H_2SeO_3), sodium iodide (NaI), and ammonium molybdate [$(NH_4)Mo_7 \cdot 4H_2O$], and for elemental zinc (Zn), copper (Cu), chromium (Cr), manganese (Mn), selenium (Se), iodine (I), and molybdenum (Mo), as appropriate in relation to the ingredients claimed to be present.

Identification—

A: The Assay preparation prepared as directed in the Assay for zinc, the Assay for copper, the Assay for chromium, the Assay for manganese, the Assay for selenium, and the Assay for molybdenum, as appropriate, based on the elements claimed in the labeling to be present, exhibit maximum absorption at the relevant wavelengths specified when tested as directed for the Procedures in the respective Assays.

B: If iodine is claimed in the labeling to be present, the retention time of the iodine peak in the chromatogram of the Assay preparation corresponds to that in the chromatogram of the Standard preparation as obtained in the Assay for iodine.

Pyrogen—When diluted with Sodium Chloride Injection so that each mL contains not more than 20 μ g of zinc, 20 μ g of copper, 0.1 μ g of chromium, 4 μ g of manganese, 4 μ g of selenium, 5 μ g of iodine, or 5 μ g of molybdenum, it meets the requirements of the [Pyrogen Test \(151\)](#).

pH (791): between 1.5 and 3.5.

PARTICULATE MATTER IN INJECTIONS (788): meets the requirements.

Other requirements—It meets the requirements under [Injections and Implanted Drug Products \(1\)](#).

Assay for zinc—

Standard preparations—Prepare as directed in the Assay under [Zinc Chloride Injection](#).

Assay preparation—Using the Injection, proceed as directed for Assay preparation in the Assay under [Zinc Chloride Injection](#).

Procedure—Proceed as directed for Procedure in the Assay under [Zinc Chloride Injection](#). Calculate the quantity, in μ g, of zinc (Zn) in each mL of the Injection taken by the formula:

$$5C/V$$

in which C is the concentration, in μ g per mL, of zinc in the Assay preparation, and V is the volume, in mL, of Injection taken.

Assay for copper—

Sodium chloride solution, Copper stock solution, and Standard preparations—Prepare as directed in the Assay preparation under [Cupric Chloride Injection](#).

Assay preparation—Using the Injection, proceed as directed for the Assay preparation in the Assay preparation under [Cupric Chloride Injection](#).

Procedure—Proceed as directed for Procedure in the Assay preparation under [Cupric Chloride Injection](#). Calculate the quantity, in mg, of copper (Cu) in each mL of the Injection taken by the formula:

$$2C/3V$$

in which C is the concentration, in μ g per mL, of copper in the Assay preparation, and V is the volume, in mL, of Injection taken.

Assay for chromium (if present)—

INJECTIONS CONTAINING 3 μ g OR MORE OF CR PER mL—

Sodium chloride solution, Chromium stock solution, Standard preparations, Assay preparation, and Procedure— Proceed as directed in the Assay under [Chromic Chloride Injection](#). Calculate the quantity, in μg , of chromium (Cr) in each mL of the Injection taken by the formula:

$$25C/V$$

in which C is the concentration, in μg per mL, of chromium in the Assay preparation, and V is the volume, in mL, of Injection taken.

INJECTIONS CONTAINING LESS THAN 3 μg OF CR PER mL—

Sodium chloride solution and Chromium stock solution—Proceed as directed in the Assay under [Chromium Chloride Injection](#).

Standard preparations—Prepare as directed in the Assay under [Chromic Chloride Injection](#). If the Injection is not labeled as containing sodium chloride, omit the addition of the Sodium chloride solution.

Assay preparation—Use the undiluted Injection.

Procedure—Proceed as directed for *Procedure* in the Assay under [Chromic Chloride Injection](#). Calculate the quantity, in μg , of chromium (Cr) in each mL of the Injection taken by the formula:

$$25C/V$$

in which C is the concentration, in μg per mL, of chromium in the Assay preparation, and V is the volume, in mL, of Injection taken.

Assay for manganese (if present)—

Sodium chloride solution, Manganese stock solution, and Standard preparations—Prepare as directed in the Assay under [Manganese Chloride Injection](#).

Assay preparation—Using the Injection, proceed as directed for the *Assay preparation* in the Assay under [Manganese Chloride Injection](#).

Procedure—Proceed as directed for *Procedure* in the Assay under [Manganese Chloride Injection](#). Calculate the quantity, in μg , of manganese (Mn) in each mL of the Injection taken by the formula:

$$0.5C/V$$

in which C is the concentration, in μg per mL, of manganese in the Assay preparation, and V is the volume, in mL, of Injection taken.

Assay for selenium (if present)—

Selenium stock solution and Standard preparations—Prepare as directed in the Assay under [Selenious Acid Injection](#).

Assay preparation—Using the Injection, proceed as directed for *Assay preparation* in the Assay under [Selenious Acid Injection](#).

Procedure—Proceed as directed for *Procedure* in the Assay under [Selenious Acid Injection](#). Calculate the quantity, in mg, of selenium (Se) in each mL of the Injection taken by the formula:

$$LC/D$$

in which L is the labeled quantity, in mg per mL, of selenium in the Injection taken, C is the concentration, in μg per mL, in the Assay preparation, and D is the concentration, in μg of selenium per mL, of the Assay preparation on the basis of the labeled quantity in the Injection and the extent of dilution.

Assay for iodine (if present)—

Mobile phase—Prepare a suitable mixture of 0.05 M dibasic sodium phosphate, 0.0025 M cetyltrimethylammonium chloride (prepared by diluting 3.20 g of a 25% solution of cetyltrimethylammonium chloride with water to 1000 mL), and acetonitrile (45:25:25). Filter this mixture through a suitable filter of 0.5 μm or finer porosity, adjust with phosphoric acid to a pH of 6.8 ± 0.1 , and mix. Make adjustments if necessary (see *System Suitability* under [Chromatography \(621\)](#)).

Standard preparations—Transfer about 52 mg of potassium iodide, accurately weighed, to a 250-mL volumetric flask, dissolve in and dilute with water to volume, and mix. Transfer 5.0 mL of this solution to a 200-mL volumetric flask, dilute with water to volume, and mix. This solution contains about 5.2 μg of potassium iodide per mL (equivalent to about 4 μg of iodine per mL).

Assay preparation—Dilute an accurately measured volume of Injection quantitatively with water to obtain a solution containing about 4 μg of iodine per mL.

Chromatographic system (see [CHROMATOGRAPHY \(621\)](#))—The liquid chromatograph is equipped with a 226-nm detector, a precolumn containing packing L3, and a $4.6 \times 25\text{-cm}$ column that contains packing L1. The flow rate is about 2.5 mL per minute. [Note—Equilibrate the column with *Mobile phase* recirculating at a rate of about 1 mL per minute for at least 12 hours before use.] Chromatograph the *Standard preparation*, and record the peak responses as directed under *Procedure*: the tailing factor for the iodine peak is not more than 2, and the relative standard deviation for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 20 μL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the areas for the iodine peaks. Calculate the quantity, in μg , of iodine in each mL of the Injection taken by the formula:

$$(126.9/166.0)(CL/D)$$

in which 126.9 is the atomic weight of iodine, 166.0 is the molecular weight of potassium iodide, C is the concentration, in μg per mL, of potassium iodide, calculated on the dried basis, in the *Standard preparation*, L is the labeled concentration, in μg per mL, of iodine in the

Injection, and D is the concentration, in μg per mL, of iodine in the *Assay preparation* based on the labeled concentration and the extent of dilution.

Assay for molybdenum (if present)–

Ammonium hydroxide diluent, Sodium sulfate solution, Molybdenum stock solution, and Standard preparations—Prepare as directed in the *Assay* under [Ammonium Molybdate Injection](#).

Assay preparation—Using the *Injection*, proceed as directed for the *Assay preparation* in the *Assay* under [Ammonium Molybdate Injection](#).

Procedure—Proceed as directed for *Procedure* in the *Assay* under [Ammonium Molybdate Injection](#). Calculate the quantity, in μg , of molybdenum (Mo) in each mL of the *Injection* taken by the formula:

$$25C/V$$

in which C is the concentration, in μg per mL, of molybdenum in the *Assay preparation*, and V is the volume, in mL, of *Injection* taken.

Auxiliary Information - Please [check for your question in the FAQs](#) before contacting USP.

Topic/Question	Contact	Expert Committee
TRACE ELEMENTS INJECTION	Documentary Standards Support	SM52020 Small Molecules 5

Chromatographic Database Information: [Chromatographic Database](#)

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