

Status: Currently Official on 16-Feb-2025
Official Date: Official as of 01-May-2023
Document Type: USP Monographs
DocId: GUID-44F6450B-5265-4982-9904-8CFC99F35DF0_5_en-US
DOI: https://doi.org/10.31003/USPNF_M77490_05_01
DOI Ref: fs952

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Somatropin

FPTIPLSRLF DNAMLRAHRL HQLAFDTYQE FEEAYIPKEQ KYSFLQNPQT
SLCFSESIPT PSNREETQQK SNLELLRISL LLIQSWLEPV QFLRSVFANS
LVYGASDSNV YDLLKDLEEG IQTLMGRLED GSPRTGQIFK QTYSKFDTNS
HNDDALLKNY GLLYCFRKDM DKVETFLRIV QCRSVEGSCG F

C₉₉₀H₁₅₂₈N₂₆₂O₃₀₀S₇ 22,124.77 CAS RN®: 12629-01-5; UNII: NQX9KB6PCL.

DEFINITION

Somatropin is a protein hormone consisting of 191 amino acid residues, and its structure corresponds to the major component of the growth hormone extracted from human pituitary glands. It is produced as a lyophilized powder or bulk solution by methods based on recombinant DNA technology. The presence of host-cell DNA and host-cell protein impurities in Somatropin is process specific—the limits of these impurities are determined by validated methods. Manufacturers must demonstrate a correlation between the Assay and a validated and approved growth-promotion-based bioassay. It may contain excipients.
[NOTE—One mg of anhydrous Somatropin is equivalent to 3.0 USP Somatropin Units.]

IDENTIFICATION

- **A.** The retention time of the somatropin peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the test for *Chromatographic Purity*, except that a *Standard solution* is also chromatographed and prepared by reconstituting a vial of [USP Somatropin RS](#) with *Diluent* to obtain a known concentration of about 2 mg/mL.
- **B. PEPTIDE MAPPING**
 - Solution A:** Trifluoroacetic acid and water (1:999). Filter, and degas.
 - Solution B:** Water, trifluoroacetic acid, and acetonitrile (100:1:899)
 - Solution C:** 0.05 M solution of tris(hydroxymethyl)aminomethane (Tris). Adjust with hydrochloric acid to a pH of 7.5.
 - Mobile phase:** See [Table 1](#).

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	100	0
20	80	20
40	75	25
65	50	50
70	20	80
71	100	0
86	100	0

Trypsin solution: 1 mg/mL of trypsin in *Solution C*. Store in a freezer, if necessary.
Standard stock solution: 2.0 mg/mL of [USP Somatropin RS](#) in *Solution C*

Standard solution: To 1 mL of the *Standard stock solution* add 30 µL of *Trypsin solution*. Cap the tube, and place it in a water bath at 37° for 4 h. [NOTE—If this solution is not injected immediately, store it in a freezer.]

Sample stock solution: 2.0 mg/mL of Somatropin in *Solution C*

Sample solution: To 1 mL of the *Sample stock solution* add 30 µL of *Trypsin solution*. Cap the tube, and place it in a water bath at 37° for 4 h. [NOTE—If this solution is not injected immediately, store it in a freezer.]

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 214 nm

Column: 4.6-mm × 25-cm; packing L7

Column temperature: 30°

Flow rate: 1 mL/min

Injection volume: 100 µL

Analysis

Samples: *Standard solution* and *Sample solution*, separately injected

[NOTE—Condition the chromatographic system by running a blank gradient program before injecting the digests.]

Acceptance criteria: The chromatographic profile of the *Sample solution* is similar to that of the *Standard solution*.

Change to read:

- **C.** ▲ [SOMATROPIN BIOIDENTITY TEST \(126\)](#) ▲ (CN 1-MAY-2023) : Meets the requirements

[NOTE—The bioidentity test may be performed either on the Somatropin bulk drug substance or on the finished pharmaceutical product.]

ASSAY

• SOMATROPIN CONTENT

Buffer solution: Dissolve 5.18 g of dibasic sodium phosphate and 3.65 g of monobasic sodium phosphate in 950 mL of water. Adjust with phosphoric acid or sodium hydroxide solution to a pH of 7.0. Dilute with water to 1000 mL.

Mobile phase: Isopropyl alcohol and *Buffer solution* (3:97). Filter, and degas.

Diluent: *Buffer solution* and water (1:1.5)

System suitability solution: Place 1 vial of [USP Somatropin RS](#) in an oven at 50° for 12–24 h. Remove from the oven, and dissolve the contents of the vial in *Diluent* to obtain a solution with a known concentration of about 1 mg/mL and a dimer content of 1%–2%.

Standard solution: Known concentration of about 1 mg/mL of [USP Somatropin RS](#) in *Diluent*

Sample solution: About 1 mg/mL of accurately weighed Somatropin in *Diluent*, or by diluting a bulk solution of Somatropin with *Diluent*. [NOTE—If necessary, the amount of protein in the solution can be determined with the test for *Total Protein Content*.]

Chromatographic system

(See [Chromatography \(621\)](#), [System Suitability](#).)

Mode: LC

Detector: UV 214 nm

Column: 7.8-mm × 30-cm; packing L33

Column temperature: Ambient

Flow rate: 0.6 mL/min

Injection volume: 20 µL

System suitability

Sample: *System suitability solution*

Suitability requirements

Resolution: NMT 0.4 for the ratio of the valley height, between the dimer and the monomer, and the dimer peak height

Tailing factor: NMT 1.7 for the monomer (major) peak

Analysis

Samples: *Standard solution* and *Sample solution*, separately injected

Record the chromatograms for NLT twice the retention time of the somatropin monomer (major) peak, and measure the peak responses for the monomer.

Calculate the concentration, in mg/mL, of somatropin in the *Sample solution* taken:

$$\text{Result} = (r_U/r_S) \times C_S$$

r_U = peak response of the monomer from the *Sample solution*

r_S = peak response of the monomer from the *Standard solution*