Status: Currently Official on 15-Feb-2025
Official Date: Official as of 01-Jul-2018
Document Type: USP Monographs
DocId: GUID-3B1D0C2E-6968-4CA8-A9A1-2FB27478D57D_2_en-US
DOI: https://doi.org/10.31003/USPNF_M35820_02_01
DOI Ref: ia1w7

Chorionic Gonadotropin for Injection

DEFINITION

Chorionic Gonadotropin for Injection is a sterile, dry mixture of Chorionic Gonadotropin with suitable diluents and buffers. Its potency is NLT 80.0% and NMT 125.0% of the potency stated on the label in USP Chorionic Gonadotropin Units. It may contain an antimicrobial agent.

ASSAY

• **Procedure**

Diluent: Saline TS, freshly prepared to contain 1 mg/mL of bovine serum albumin and adjusted with sodium hydroxide TS to a pH of 6.9–8.0

Standard stock solution: 10 Units/mL of USP Human Chorionic Gonadotropin RS in *Diluent*

Standard solutions: From the *Standard stock solution*, prepare three *Standard solutions* in *Diluent* such that the respective concentrations of chorionic gonadotropin constitute a geometric series such as 1: 1.2: 1.44 or 1:2:4 and such that the activity in each mL lies within the range of 0.1–1.0 Unit.

Sample solutions: Dilute a portion of the solution prepared for the test for *Estrogenic Activity* quantitatively and stepwise with *Diluent* to obtain three *Sample solutions* corresponding to those of the *Standard solutions*.

Animals: Select 20- to 23-day-old female rats, but restrict the selection so that no rat is more than 30% heavier than the lightest. House the animals under uniform conditions of temperature, lighting, feeding, and watering. Mark the animals for identification, and divide them at random into groups of the same number but NLT 10 animals. Assign one group to each of the three *Standard solutions* and three *Sample solutions*, respectively.

Analysis: Inject each rat subcutaneously in the dorsal area with 0.20 mL of the solution to which it was assigned, at approximately the same time on each of 3 consecutive days. On the afternoon of the fifth day, sacrifice the animals, and excise the uterus from each animal by cutting through the cervix, stripping off the surrounding tissue, and severing at the utero-tubal junction. Gently press out the uterine fluid on moistened absorbent paper, and weigh the uterus to the nearest 0.2 mg, using a suitable balance.

Calculation: Tabulate the observed uterine weight for each rat, designated by the symbol *y*, for each dosage group of *f* rats. If the data from one or more rats are missing, adjust to groups of equal size by suitable means. Total the values of *y* in each group, and designate each total as *T*, subscripts 1 to 3 for the three successive dosage levels, and subscripts *S* and *U* for the *Standard solutions* and *Sample solutions*, respectively. Test for parallelism and linearity between the results for the *Standard solutions* compared to the *Sample solutions* by suitable statistical methods.

Determine the logarithm of potency of the Injection:

$$\text{Result} = (4iT_a/3T_b) + \log R$$

i = interval between successive log doses of the *Standard solution* and *Sample solution*

$$T_a = \Sigma(T_U - T_S)$$

$$T_b = \Sigma(T_3 - T_1)$$

$$R = v_S/v_U$$

v_S = high dose of the Standard (USP Units)

v_U = high dose of the sample (mL)

Compute the log confidence interval, *L* (see *Design and Analysis of Biological Assays* ⟨111⟩). If the confidence interval is more than 0.1938, which corresponds at $P = 0.95$ to confidence limits of 80% and 125% of the computed potency, repeat the *Assay* until the combined data of two or more assays, redetermined as described under *Design and Analysis of Biological Assays* ⟨111⟩, *Combination of Independent Assays*, meet this limit.

Acceptance criteria: 80.0%–125.0% of the potency stated on the label

PERFORMANCE TESTS

• **Uniformity of Dosage Units**

Analysis: Open 10 containers, and accurately weigh each individual container and its contents, taking care to preserve the identity of each container and removing any labeling that might be altered in weight during the removal of the container contents. Remove the contents of each container by rinsing thoroughly with water, dry at 105° to constant weight, and reweigh. Calculate for each container the net weight of its contents by subtracting the weight of the dry, empty container from its initial gross weight. Determine the average weight of the contents and the relative standard deviation.

Acceptance criteria: The requirements are met if the weight of the contents of each container does not deviate from the average weight by more than 5.0%, and the relative standard deviation of the 10 containers is NMT 3.0%.

If the requirements of the test are not met, test 20 additional containers. The requirements are met if the net weight of NMT 1 container of the 30 deviates by more than 7.5% from the average weight of the contents of the 30 containers and the relative standard deviation of the 30 containers is NMT 3.3%.

SPECIFIC TESTS

• **pH ⟨791⟩:** The pH of the solution prepared for the test for *Estrogenic Activity* is between 6.0 and 8.0.

• **Estrogenic Activity**

Sample solution: Reconstitute as directed in the labeling.

Analysis: Into each of five rats that have been ovariectomized NLT 2 weeks previously, inject subcutaneously 0.25 mL of the *Sample solution* in the morning and in the afternoon of 2 successive days. On each of the 3 following days, take a vaginal smear from each animal.

Acceptance criteria: The requirements of the test are met if the cellular elements in the smears consist mainly of leucocytes and a few nucleated epithelial cells, but no cornified epithelial cells.

• **Other Requirements:** It meets the requirements in *Labeling ⟨7⟩, Labels and Labeling for Injectable Products*.

• **Bacterial Endotoxins Test ⟨85⟩:** It contains NMT 0.03 USP Endotoxin Unit/USP Chorionic Gonadotropin Unit.

• **Sterility Tests ⟨71⟩:** Meets the requirements

• **Constituted Solution:** At the time of use, it meets the requirements in *Injections and Implanted Drug Products ⟨1⟩, Specific Tests, Completeness and clarity of solutions*.

ADDITIONAL REQUIREMENTS

• **Packaging and Storage:** *Packaging and Storage Requirements ⟨659⟩, Injection Packaging, Packaging for constitution* .

• **Labeling:** Label it to indicate the expiration date.

Change to read:

• **USP Reference Standards ⟨11⟩**

▲▲ (ERR 1-Jul-2018)
USP Human Chorionic Gonadotropin RS

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
CHORIONIC GONADOTROPIN FOR INJECTION	Rebecca C. Potts Associate Scientific Liaison	BIO2 Biologics Monographs 2 - Proteins

Chromatographic Database Information: Chromatographic Database

Most Recently Appeared In:
Pharmacopeial Forum: Volume No. PF 39(5)

Current DocID: GUID-3B1D0C2E-6968-4CA8-A9A1-2FB27478D57D_2_en-US

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