

INJECTION AND FOR INJECTION

The following is a template to be used when drafting an Injection or For Injection monograph. This is intended to serve as a guideline for drafting monographs in *USP* style. It is incumbent upon the monograph writer to be familiar with *USP General Notices* and the General Chapter tests. Note that not all tests would appear in any one monograph and that not every variation of individual tests is shown. Only those sections used most often are included. Tests are listed in the order in which they should appear in a monograph.

NOTES—See templates for Drug Substance, and Tablets and Capsules in the addendum of the *USP Guideline for Submitting Requests for Revisions for USP–NF* for sections that are required but not included here, whether stated explicitly in the template or not.

Add the following:

[_____] Injection

[_____] Injection is a sterile solution of [drug substance name] in [solvent, e.g., Water for Injection]. It contains not less than 95.0 percent and not more than 105.0 percent of the labeled amount of [drug substance or active ingredient] [C_xH_x ____ O_x].

Packaging and storage— Preserve in a [single-][multiple-] dose [specify container and type] and store at [specify temperature].

Appropriate Packaging and Storage statements are defined in the *General Notices and Requirements* of *USP–NF*. The packaging and storage information should agree with FDA- approved information. Specify the package type (e.g., well-closed, tight, single-dose, etc) and the temperature (e.g., controlled room temperature). Include special handling needed such as protect from light, store under and inert atmosphere, etc.

Labeling— Label it to indicate that it meets requirements for *Labeling* under *Injections* <1>. Label it also to state that the Injection is not to be used if its [color][other physical characteristics is darker than [indicate color or other physical characteristic]]. Injections containing antioxidant or antimicrobial agents indicate so prominently on its label. Injections containing no antioxidant or antimicrobial agents should indicate prominently on its label “antioxidant-free” or “preservative-free”. The label of an Injection should also indicate its routes of administration and the statement that it is not suitable for oral, intrathecal or epidural use and if it is single-dose or multiple-dose.

Monograph labeling (see *USP General Notices*) statements that are intended to affect the packaging are generally added only when there is a substantial risk to the public health. These statements indicate a requirement for specific packaging elements

(such as a red or black cap) or cautionary statements (such as Dilute before use). The labeling section of a package insert may also contain required labeling to indicate which tests and/or procedures in the drug product monograph are applicable.

USP Reference Standards— formatting examples: *USP Bupivacaine Hydrochloride RS. USP Lidocaine Hydrochloride RS. USP Endotoxin RS.*

Identification—

{Need at least one ID test for each active ingredient. If more than one ID test is incorporated, tests are alphabetized, e.g., **A:**, **B:**, etc., and ordered as follows: IR, UV, TLC, retention times comparison, and other tests. Also, retention time coincidence can be included. Also consult above templates for details.}

A: {ID tests for analyte(s). Varies by monograph. Examples: It responds to the (e.g., *Thin-layer chromatographic Identification Test <201>*).}

B: The retention time of the [analyte/major] peak in the chromatogram of the *Assay preparation* corresponds to that of the [major] peak in the chromatogram of the *Standard preparation* obtained as directed in the *Assay*.

Bacterial endotoxins <85>— It contains no more than [] USP Endotoxin Unit per mg of [].

Sterility <71> —It meets the requirements when tested as directed for [] under *Test for Sterility of the Product to be Examined*.

{The Sterility Test is applicable only to products labeled sterile. The Proposal should indicate whether a membrane filtration (procedure of choice) or direct inoculation procedure is employed. The direct inoculation procedure is used if the membrane filtration procedure is not applicable.}

Antimicrobial Preservative <341>—Proceed as directed for [name of the antimicrobial agent] under *Antimicrobial Agent Content--<341>*: not more than [_._] % is found.

{Because Injections and For Injections are usually sterile products, this test may not be necessary unless it is a multiple-dose injection.}

pH <791>— between [_._] and [_._].

Particulate matter <788>—meets the requirements for small-volume injections.

Deliverable volume <698>—For [Injection][For Injection] packaged in [package type] containers: meets the requirements.

Other requirements—It meets the requirements under *Injections <1>*.

Water, Method [] { 921 } : not more than [_._]0%. {for For Injection products only}

Residual solvents <467>: meets the requirements.

Impurity—

{Use templates for HPLC procedures for Impurities included in templates for Drug Substance, and Tablets and Capsules in the addendum of the *USP Guideline for Submitting Requests for Revision for USP-NF*.}

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Assay—

{NOTE: FOR COMBINATION DRUG PRODUCTS, AN ASSAY TEST FOR EACH DRUG IS NEEDED.}

Mobile phase—Prepare a filtered and degassed mixture of [] and [] (___:___). [Adjust with [] to a pH of [].] Make adjustments if necessary (see *System Suitability* under *Chromatography* <621>).

System suitability preparation—Dissolve suitable quantities of USP [Drug] RS and USP [] RS in [] to obtain a solution containing about [] [mg][μg] per mL and [] [mg][μg] per mL, respectively.

Standard preparation—Dissolve USP [] RS in [] to obtain a solution having a known concentration of about [__.] mg per mL.

Assay preparation—

{Use the following template for an Injection product.} Quantitatively dilute an accurately measured volume of [] Injection with [] to obtain a solution containing accurately known concentration of about [] mg per mL [active] [equivalent of active]. [Pass a portion of this solution through a filter having a ___-μm or finer porosity, and use the filtrate.]

{Use the following template for a For Injection product.} Dissolve [] in [], to obtain a solution having a known concentration of about [__.] mg [or μg] per mL.

Chromatographic system (see *Chromatography* <621>)—The liquid chromatograph is equipped with a []-nm detector and []-mm × []-cm column that contains packing L[]. The flow rate is about [] mL per minute. [The column temperature is maintained at __°.] Chromatograph the *System suitability preparation*, and record the peak responses as directed for *Procedure*: [the relative retention times are about __ for __ and 1.0 for ___ {name analyte};] [the resolution, *R*, between __ and __ is not less than __.][;] [the capacity factor, *k'*, is not less than __.][;] [the column efficiency is not less than __ theoretical plates][;] [the tailing factor is not more than __][; and] [the relative standard deviation for replicate injections is not more than __.%].

Procedure—Separately inject equal volumes (about [] μL) of the *System suitability preparation*, the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the [major] [analyte] peaks. Calculate the quantity, in mg, of [active ingredient] (chemical formula) in the portion of [Tablets][Capsules] taken by the formula:

$$[]C(r_U/r_S),$$

in which *C* is the concentration, in mg per mL, of USP [Drug] RS in the *Standard preparation*; and *r_U* and *r_S* are the peak responses obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Microbiological Assay—

{FOR ANTIBIOTICS }

{AN HPLC ASSAY PROCEDURE IS PREFERRED OVER A MICROBIAL ASSAY PROCEDURE FOR A USP–NF MONOGRAPH. THE MANUFACTURERS ARE URGED TO EXPLORE THE POSSIBILITY OF SUBMITTING AN HPLC PROCEDURE FOR ASSAY FOR ANTIBIOTICS. }

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Assay preparation—{Describe as required. Use template for the HPLC Assay above, but specify the appropriate buffer as directed in *Antibiotics—Microbial Assays* <81> .}

Procedure—Proceed as directed for [] under *Antibiotics—Microbial Assays* <81>, using accurately measured volume of Assay preparation diluted quantitatively to yield a Test Dilution having a concentration assumed to be equal to the median dose level of the standard. {OR, the sponsor should fill in the rest of this section with specific details, as appropriate.}