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U.S. Pharmacopeial Convention

## Guideline for Donors of USP Reference Standard Candidate Materials

USP's Reference Standard program relies on the generosity of donors, who, as experts in the field, provide high-quality candidate materials intended for use as official public standards. This guidance document describes the general USP requirements for such materials. (In addition to this, USP specifications for a particular material are provided to potential donors at appropriate times.)

1. **Purity-** The minimum purity is dependent upon intended or official uses. Default purity values are listed below, but in special cases, lower-purity materials may be acceptable.
   If used in USP Assay tests (e.g., USP Acetaminophen RS): ≥ 99.5%
   If used in USP Limit tests (e.g., USP Captopril Disulfide RS): ≥ 98.0%
   If used in non-quantitative applications: case-by-case

2. **Amount-** USP accepts candidate materials in various presentations, most frequently in bulk containers or pre-packaged units (e.g., sealed ampuls). For a first-time reference standard, a minimum quantity is established in consideration of the uses of the reference material, its properties (e.g., hygroscopicity and stability), and the anticipated market demand for it. In the absence of complete information, default quantities are requested. Examples of such default values are 400 g for an active pharmaceutical ingredient, excipient, or food ingredient, and 25 g for an impurity.

   USP can work with smaller quantities. Donors are encouraged to discuss individual cases with USP to reach a mutually-acceptable quantity for first time materials.

3. **Supporting information-** USP recognizes that the donated material is precious to the donor and to USP. To maintain the integrity of the material, and to ensure its efficient development into an official USP standard, USP requests that the shipment is accompanied by a Certificate of Analysis (C of A), a Safety Data Sheet (SDS), origin information (country and material) and a completed copy of the attached reference material information form.

   Ideally, the C of A includes all pertinent test results and the methods used to generate the results. Inclusion of IR and/or NMR spectra, other physiochemical data (eg. Raman, XRD), as well as stability data, when applicable, in the donated package, assists USP. Information about the likely impurities present in the candidate material, including late-stage process impurities, degradation products, and processing solvents, also aids development of the standard.

   The reference material information form provides USP scientific staff with additional information needed to maintain the high quality of the donated material during evaluation, packaging, and storage, including special precautions necessary for proper handling. USP experience is that timely receipt of this information saves subsequent USP and donor resources and facilitates the development of the public standards.

   Origin information (requested on the reference material information form) is required. USP requires a BSE-TSE statement.

4. **Post-donation activities-** Upon receipt of a donated bulk, USP sends an acknowledgement letter to the donor and commences the development process, which includes a multi-laboratory evaluation of the material. At the conclusion of the evaluation, USP compiles a summary data package, subdivides and labels the material, and ultimately releases the batch as a new lot of USP Reference Standard. A copy of the summary data package is sent with an acknowledgement letter to the donor. Donors also become eligible for USP's Donor Recognition Program, details of which are described on USP's website.

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USP–Switzerland
Basel

USP–India
Hyderabad

USP–China
Shanghai

USP–Brazil
São Paulo

USP–Ghana
Accra

USP–Ethiopia
Addis Ababa

USP–Indonesia
Jakarta

**Candidate Material for USP Reference Standard Shipping Requirements**

Please include the following in your USP Reference Standard candidate bulk material shipment:

1. Completed USP Reference Material Information Form
2. Certificate of Analysis for specific reference material candidate lot
3. Safety Data Sheet (SDS)
4. Supporting data, spectra (eg. NMR, MS, XRD, IR, Raman, DSC), chromatograms etc.
5. BSE-TSE Statement

# REFERENCE MATERIAL INFORMATION FORM

## 1. Reference Material Information

Reference Standard Candidate Name: _____

_____

CAS Registry Number (if available): _____ Supplier lot/Batch number: _____

## 2. Supplier Information

Supplier: _____

Contact Name: _____

Phone number: _____ E-mail address: _____

Signature: _____ Date: _____

## 3. Origin of Material – REQUIRED

Country of Origin: _____

** For USA Country of Origin, are the goods "wholly produced or obtained" in the United States or are the goods produced from materials not of USA origin but meet the Free Trade Agreement rules of origin?

☐ Yes ☐ No

Synthetically Derived? ☐ Yes ☐ No

Animal Derived? ☐ Yes ☐ No

Animal type/organ/fluid:

_____

Were any animal materials used in the processing of intermediates or final product?

☐ Yes ☐ No

Biologically Derived? ☐ Yes ☐ No

Source (e.g., fermentation, recombinant (provide expression system, e.g., plasmid, *E. coli*, CHO cells)):

_____

Human Derived? ☐ Yes ☐ No

Fluid type: _____

Plant Derived? ☐ Yes ☐ No

Type/Part: _____

## 4. Basis of Purity or Value Assignment

| | |
|---|---|
| ☐ | *Official USP/NF Method* (USP/NF _____, page _____) |
| ☐ | *In-House Assay Method* |
| | ☐ Reference Standard used: _____ |
| | ☐ Number of assay replicates: _____ |
| | Comments: _____ |
| ☐ | *Mass Balance Method* (% purity = 100 - % impurities as specified below) |
| | ☐ Loss On Drying or Water: _____ |

| | |
|---|---|
| 4. | **Basis of Purity or Value Assignment (Cont'd.)** |
| | ☐ HPLC Impurities: _____ |
| | ☐ Residue On Ignition: _____ |
| | ☐ Additional Impurities: _____ |
| 5. | **Storage Conditions** |
| ☐ | Room temperature |
| ☐ | Cool Room (between 8° and 15° C) |
| ☐ | Refrigerator (between 2° and 8° C) |
| ☐ | Freezer (between -25° and -10° C) |
| ☐ | Other: _____ |
| ☐ | Not known : _____ |
| 6. | **Directions for Use** |
| ☐ | Dry before use<br>Temperature: _____°C time: _____ hrs vacuum: _____ mm Hg: _____ desiccant: _____ |
| ☐ | Do not dry, correct for volatiles ( _____ LOD) or correct for moisture ( _____ KF) |
| ☐ | Do not dry, use as-is |
| ☐ | Not known |
| 7. | **Sample Preparation Recommendations** |
| ☐ | Use immediately (solutions are unstable)_____ |
| ☐ | Protect from light _____ |
| ☐ | Refrigerate _____ |
| ☐ | Other _____ |
| ☐ | Not known _____ |
| 8. | **Material Information** |
| ☐ | Material is stable under stated storage conditions for _____years _____ |
| ☐ | Material is hygroscopic _____ |
| ☐ | Material is air sensitive _____ |
| ☐ | Material is light sensitive _____ |
| ☐ | Solvents used during the last stage (e.g., reaction, workup, purification):<br>_____ |
| ☐ | Information regarding salt, solvent, hydrate ratios _____ |
| ☐ | Information regarding known polymorphs _____ |
| ☐ | Not known _____ |

| 9. **Packaging Recommendations** | |
|---|---|
| ☐ | Ambient temperature and humidity conditions |
| ☐ | Rooms with a reduced relative humidity |
| ☐ | Inert gas-filled glove box |
| ☐ | Package under low actinic light |
| ☐ | Not known _____ |
| 10. **Shipping Documentation** | |
| ☐ | Certificate of Analysis (CoA) |
| ☐ | Material Safety Data Sheet (MSDS) |
| ☐ | Supporting analytical data |
| ☐ | BSE-TSE Letter |
| ☐ | Harmonized Tariff Schedule (HTS Code) (optional) _____ |
| ☐ | NAFTA/FTA Certificates (optional) |
| ☐ | FDA Product Code (optional) _____ |
| 11. **Regulatory Status** | |
| Is the Company/facility registered with any regulatory government agency(ies) (e.g. FDA, EU, TGA) or against any industry standard (e.g. ISO, USP, NSF)? ☐ Yes ☐ No Agency/ Standard: _____ | |