

	Standard Operating Procedure		SOP Number D-106	Revision 8
	Analytical Standards		Effective Date 05/09/23	Page Page 1 of 6
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1.0 Purpose

The purpose of this procedure is to define logging, labeling, use, and certification of reference materials used for analytical testing in the QC laboratory.

2.0 Scope

This procedure applies to all analytical reference materials to be used in drug product, dietary supplement, companion animal supplement, and cosmetic raw materials and finished products where strength testing is required. These guidelines specifically apply to USP, USP secondary, fine chemical, and certified standards. Qualitative standards for FTIR, TLC, HPLC spectral analysis, and other qualitative methods will be addressed in SOP D-109 Qualitative Standards.

3.0 Responsibility

- 3.1 It is the responsibility of QC and Analytical Chemists to follow this procedure.
- 3.2 It is the responsibility of QC Laboratory Management to implement this procedure and to ensure that the procedure is being followed.
- 3.3 It is the responsibility of QC Laboratory Management and/or Analytical Development personnel to keep this procedure aligned with current practices.

4.0 Definitions

- 4.1 **USP** – United States Pharmacopeia
- 4.2 **CofA** – Certificate of Analysis

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- 4.3 **USP Secondary Standard** – A reference standard purchased from a vendor other than USP that is traceable to the USP primary standard. A fine grade chemical characterized against a USP standard.
- 4.4 **Analytical Standard** – A traceable reference standard or fine chemical purchased from a vendor that has not been evaluated against a USP standard
- 4.5 **ACS** – American Chemical Society
- 4.6 **NIST** – National Institute of Standards and Technology
- 4.7 **SDS** – Safety Data Sheet
- 4.8 **QC** – Quality Control
- 4.9 **PQV** – Process Quality Verification

5.0 References

- 5.1 D-109, SOP, Qualitative Standards
- 5.2 D-106-F1, Form, Analytical Standard Log
- 5.3 A-106, SOP, Documentation Guidelines for cGMP Records
- 5.4 C-502, SOP, Record Storage, Retention, and Destruction

6.0 Procedure

- 6.1 Purchasing
 - 6.1.1 Traceable reference standards and fine chemicals can be purchased through any approved vendor (Sigma, Spectrum, Fisher, etc.) or through any foreign or domestic pharmacopeia when accompanied by a CofA.
- 6.2 Receiving
 - 6.2.1 Analysts will log all Analytical Standards on Form D-106-F1 Analytical Standard Log, and will include the following information:
 - 6.2.1.1 Unique identifier

- 6.2.1.2 Chemical name
- 6.2.1.3 Designator
- 6.2.1.4 Purity
- 6.2.1.5 Time of Use Adjustments
- 6.2.1.6 Source / Catalog number
- 6.2.1.7 Lot number
- 6.2.1.8 Expiration date
- 6.2.1.9 Notebook Reference for Recertified
- 6.2.1.10 Logged by/Date
- 6.2.2 A unique identifier for each bottle reference material will be generated with the following format: XXASYYY.
 - 6.2.2.1 XX is the last two digits of the year received.
 - 6.2.2.2 AS is the abbreviation for Analytical Standard.
 - 6.2.2.3 YYY is the sequential order of logging the standard, 001, 002, 003, etc.
- 6.2.3 The Designators apply as follows:
 - 6.2.3.1 USP Primary Reference Standard- "USP Primary"
 - 6.2.3.2 USP Traceable Standard- "USP 2nd Std"
 - 6.2.3.3 Traceable Standard (non-USP)- "Traceable"
 - 6.2.3.4 Fine Chemical Standard- "Fine Chemical"
 - 6.2.3.5 Japanese Pharmacopeia- "JP"
 - 6.2.3.6 British Pharmacopeia- "BP"
 - 6.2.3.7 European Pharmacopeia- "EP"

6.2.4 A copy of each Analytical standard CofA will be added Form D-106-F1 Analytical Standard Log in alphabetical order based on analyte name with the unique identification number (ex. 13AS002) added to the top of the CofA.

6.2.4.1 When a standard is expired then recertified one line is drawn through the log entry with “recertified” noted on the line along with the new line number for the recertified standard and the analyst’s initials and date. The standard will be re-entered into the log with the original unique identifier along with updated expiration information.

6.3 Hierarchy of use for analytical standards:

6.3.1 Drug products and raw materials for use in drug products should be tested using only First or Second tier reference standards.

6.3.2 First tier - A standard traceable to USP

6.3.3 Second tier - A standard traceable to a recognized organization (ACS, AOAC, NIST etc.)

6.3.4 Third tier - A highly refined chemical with a CofA from an approved vendor.

6.3.5 Raw materials may be used as reference standards under extreme exception when the purity is certified using a suitable reference standard or method.

6.4 Storage / Expiration

6.4.1 Standards will commonly be stored in a desiccator cabinet at room temperature in compliance with their labeling instructions or in an appropriate area if special storage conditions are stated on the CofA or in the SDS (Refrigerator, Freezer, Light Blocking, etc).

6.4.2 USP standards will be stored in a desiccator cabinet separately from non-Pharmacopeial standards in compliance with any special storage instructions listed on the CofA or in the SDS.

6.4.3 USP secondary standards, traceable and fine chemical standards are valid until the manufacturer’s expiration or re-test date listed on the CofA. If no expiration

or re-test date is given, the standard expires one year from the date of service entry.

6.4.4 Certified and traceable standards can be recertified against a valid USP Primary Standard.

6.5 Qualifying / Requalifying a Reference Standard

6.5.1 Qualification of a standard is specific to the type of test method.

6.5.2 Prepare the chemical in a manner appropriate for the type of determination technique (Example: HPLC, HPTLC, titration, etc.).

6.5.3 Prepare the test material sample in triplicate using no less than 50mg unless otherwise directed by a monograph or recognized procedure.

6.5.4 Prepare a single preparation of the traceable standard corrected for purity, water content, etc. at the same concentration as the test material.

6.5.5 Establish the system suitability of the measurement system according to the test method.

6.5.6 For HPLC make six standard injections and analyze results for system suitability. If system suitability passes make one injection of sample to analyze for purity. Adjustments to purity for water may be made after initial analysis.

6.5.7 Monograph requirements must be met for determining purity of a material by titration.

6.5.8 Certified / Recertified materials are valid for a period of 12 months.

6.5.9 Purities in excess of 100% are to be considered 100%. While ordinary analytical variation can result in a pure substance assaying in excess of 100%, no substance can be greater than 100% pure. Analyses exceeding 102.5% are invalid for certification / recertification purposes.

6.5.10 The qualification procedure will be fully recorded in the analyst's notebook and copies of the notebook pages and raw data will be stored in the analytical standard log for reference.

6.6 Documentation Requirements

6.6.1 A PQV check must be performed for each completed logbook page as outlined in SOP A-106 Documentation Guidelines for cGMP Records.

6.6.2 Documents will be maintained following SOP C-502 Record Storage, Retention, and Destruction.

7.0 Revision History

Revision	Date	Description of Changes	CCR #	By
0	05/06/10	New	-	-
1	02/04/13	Updated SOP to new format, expanded options to use USP secondary standards for direct use and for qualifying secondary working standards, changed the name of the SOP.	-	-
2	11/20/13	Clarified qualifying standards, defined tier system for selecting standards, added two new definitions, rewrote for better clarity and organization, changed SOP title	13-1067	B. Johns
3	12/02/14	Updated format. Added designators. Redefined logging methods. Updated responsibilities.	14-0965	B. Johns
4	03/26/15	Added additional information on the handling and selection of pharmaceutical standards.	15-0290	B. Johns
5	08/23/16	Added information on the use of non-USP standards for domestically released non-ANDA monograph pharmaceuticals.	16-0771	B. Johns
6	04-19-17	Reintroduce manual tracking of standards to meet 21 CFR 11 compliance. Separate SOP to support only Dietary supplement, companion animal and cosmetic standards. OTC standards to be addressed and logged under a separate SOP procedure. Make current certification process. Update paper log spreadsheets.	17-0437	B. Johns
7	07/20/20	Update formatting. Update scope to include drug products since a separate SOP for drug product standards was never created with rev 6. Remove unused definitions. Combine D-106-F1 with D-106-F2 for simplification and since F2 is not being used as intended. Add column for purity and notebook ref to D-106-F1. Remove references to electronic log as this is not being maintained any more. Require triplicate prep for standard recertification.	CC-20-0497	S. Sassman
8	04/12/23	Schedule review: update format and logo. Revise responsibilities section.	CC-23-0189	K. Burris

