

Standard Operating Procedure

Title: Management of Reference Substances

Procedure

1. Primary and Impurity Reference Substance

1.1. Certified and reputable Primary and Impurity reference substances sources

1.1.1. Primary and Impurity Reference Substances as indicated under definitions, are substances manufactured and tested to compliance by a certified source. The certified sources from which these quality Reference Substances can be obtained from are, British Pharmacopoeia (BP), United States Pharmacopoeia.

1.1.2. Analytical reagents can be used as Primary Reference Substances under special circumstances, particularly if the substances are not obtainable through the above Certified sources. Where this is the case a Reputable Supplier should be used and a Certificate of Analysis for the substance should be obtained.

1.2. Ordering of Primary and Impurity Reference Substances

To arrange for an order of a Primary and Impurity Reference Substance to be ordered by the assigned Laboratory Staff doing Reference Substance maintenance, simply contact them with the complete details of:

- Reference Substance needed
- The Pharmacopoeia to buy from
- The Pharmacopoeia catalogue number
- The number of bottles needed (include weight per bottle, e.g. 2 x 25mg bottles)
- The urgency requirement

It is appropriate for the assigned Laboratory staff doing Reference Substances maintenance to advise Laboratory staff that an order has been placed and indicate an estimated time of receipt.

The following should than be sent to the Pharmacopoeia (**Note:** Send by registered mail.):

- Letter addressed to the department indicating enclosed items and indicating an order is being placed,
- Copy of Purchase Order Number,
- Copy of Licence to Import,
- Payment details where applicable,

If the pharmacopoeias requested a statement of use for the Reference Substance being ordered, so it is appropriate to include in letter a statement for appropriate use.

Note: Follow local regulatory guidelines for importing reference substances.

1.3. Registration of the Primary and Impurity Reference Substances

1.3.1. When the reference substance is received, sign it off as received on the Laboratory "Order book".

1.3.2. Assign a reference substance reference code and enter information as appropriate onto the "Reference Substances log" (see section 6).

1.3.3. Compile the data in the "Primary and Impurity Substance Summary Sheet" form **Form-330** with the relevant information to reflect Reference Substances log Book entries. File the manufacturer's "Certificate of Analysis" in the appropriate Laboratory office cabinet.

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- Collect the manufacturer's Certificate of Analysis of the sampled raw material from the Raw Material Specification and Test Report prepared, when the raw material was tested first in the laboratory. See SOP **LAB-060**. Check re-test/ expiry date of the raw material. This will enable a sample of longer shelf life.
- The standard used to test a batch, should not be the same batch number as the material used in the batch. Hence, when requesting a sample for SRMRS, ensure that the batch requested would not be used to manufacture future batches of finished Product.
- In some exceptional circumstances, there may be no other material in the warehouse other than the one being used by production to make batches. In such case, If the material is available as an Analytical Grade pure substance in chemical catalogues, purchase some and qualify it against a PRS to convert it into a SRMRS. When the material is not available as an analytical grade pure substance, then the standard SRMRS used to test a finished batch is allowed to be the same batch number as the material in the batch (as long as the SRMT2 has been qualified against a primary standard before use).
- The Secondary Raw Material Reference Substance arrives from the Warehouse to the Laboratory labeled as a "Secondary Sample", with Product Name, Product Code, and the Laboratory Batch number. See SOP **WAR-045**.

3.3. Registration of the Secondary Raw Material Reference (SRMRS)

- 3.3.1. Assign a reference substance reference code and enter information as appropriate onto the "Reference Substances log Book" (see section 6).
- 3.3.2. Compile a form **Form-325** with the relevant information to reflect the Reference Substance Log Book entries. Collect a copy of Manufacturer's Certificate of Analysis and a copy of the completed "Raw Material Specification and Test Report" for the material, attach all previous testing records for this bottle. File the documents in the designated folder of the laboratory office.
- 3.3.3. Place some "masking tape" around the lid of the bottle. This tape will serve as a reminder for the Technician to write down a "Date bottle opened" date for the bottle and advise authorised laboratory Staff to update information on the summary sheet (**Form-325**) and on Reference Substances Log.
- 3.3.4. Remove the Warehouse label off the bottle and replace it with an In-process SRMRS Label **Form-355**. This label serves to segregate the substance under quarantine and will remain in place until the substance has been tested to qualify for use as a Secondary Reference Substance in routine analysis.
- 3.3.5. Place the bottle for collection by the team members in either of the appropriate locations, for testing:
 - The Laboratory Fridge
 - The Laboratory Freezer
 - The Laboratory Desiccator.
 - The Laboratory Safe

Contact to the team to advise reference substance ready for collection.

3.4. Coding the Secondary Raw Material Reference Substance (SRMRS)

The Secondary Raw Material Reference Substance is coded to be included in the controlled standards referencing system. The reference code for Secondary Raw Material Reference Substance generated using the following format:

- SRMRS\ Iso\ XXXX\ YY\Z