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Reference Standards in the Pharmaceutical Laboratory: Procurement and Characterisation

by Stephanie Blum, PhD

Reference standards

Pharmacopoeial standards are obtained by the chemicals officer from the issuing body and do not require further characterisation before use. They are used exclusively for the following purposes:

- Analytical testing in accordance with the specifications of the relvant monograph or the general pharmacopoeia chapter
- Reference for establishing an in-house secondary standard

For *all other reference standards,* the following specifications apply:

Procurement

The responsible head of laboratory instructs the chemicals officer to procure from one of the sources listed below:

- In-house production, research or development
- Active ingredient and excipient manufacturers
- Chemicals trade
- Synthesis service provider

If the standards are not manufactured by Peither Pharma GmbH itself, the supplier must be qualified in accordance with the "Supplier Management" SOP. When procuring standards, ensure that they are of sufficient purity for the intended use; for content standards, a purity ≥ 98% should be aimed for. If the reference standards are manufactured at Peither Pharma GmbH, the manufacture must be adequately documented. If the reference standards are from external sources, sufficient information on the production (synthesis route, purification) must be requested and retained when ordering.

The information on synthesis and purification of reference substances is necessary as it provides information on the impurities that may be present. This information is necessary to define appropriate characterisation tests.

Characterisation – general specifications

The head of laboratory defines and describes in advance the tests intended for the characterisation of the reference standard, including the respective acceptance criteria, in a test plan. He or she also specifies which of the tests will be performed in-house at Peither Pharma GmbH and which will be performed by a qualified contract laboratory. The head of quality control approves the test plan. The extent of the characterisation depends on the intended use of the reference standard, which must be specified accordingly in the test plan. The following applies

- for primary standards, the specifications of table 1,
- for secondary standards, the specifications of table 2.

The characterisation work must be carried out in accordance with the approved test plan in a GMP-compliant manner and shall be documented in accordance with the requirements of the SOP for record keeping, logbooks and laboratory journals.

Table 1

Characterisation of Primary Standards			
Characterisation by means of	**Primary standard for the analysis of**		
	Identity	**Content**	**Impurities**
Structure elucidation*	x	x	x
Assay	x	x	x
Content analysis with second independent method (plausibility check)	-	x	-
Stability test**	x	x	x

* on the first batch, usually using a selection of the following methods: NMR, IR, MS, elemental analysis; other or additional methods may be used on scientific grounds

** if corresponding information is not already available

Table 2

Characterisation of Secondary Standards			
Characterisation by means of	**Secondary standard for the analysis of**		
	Identity	**Content**	**Impurities**
Identification test (against primary standard)	x	x	x
Assay (against primary standard)	-	x	x

The head of laboratory summarises the results obtained during the characterisation of a reference standard in a test report. He or she evaluates the results against the acceptance criteria defined in the test plan to determine whether the reference standard can be released for use. The head of laboratory shall also indicate in the report the specific storage conditions and the period of usability. In the case of secondary standards, the primary standard used as reference shall also be indicated. The head of quality control approves the test report and thereby releases the reference standard for use.

The article is a translated excerpt from the German sample SOP-205-02 'Umgang mit Proben, Reagenzien und Referenzstandards im Labor' (Handling of samples, reagents and reference standards in the laboratory).

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