November 01, 2020

Effective: November 01, 2020, until superseded

Subject: USP Reference Standard's Uses and Applications

Dear Valued USP Customer,

USP Reference Standards (RS) are not for use in humans or animals as drugs or medical devices. They are intended only for use in analytical or laboratory applications generally as specified in USP compendia. It may be possible to use a USP RS outside of its associated USP compendial applications; however, it is the responsibility of the user to determine the suitability of the RS for a non-USP use. All information required for the official use of a USP RS is provided in the associated USP compendial procedure, the label of the RS, and on its USP Certificate, if available. Test results and data that are not included in these sources cannot be shared as they are considered proprietary to the USP Reference Standard program.

USP RS's are generally considered primary compendial standards, with a few rare exceptions. Some of the biologic RS's are considered secondary compendial standards because they are calibrated and tested against World Health Organization (WHO) International Standards. Unlike a typical primary and secondary standard, primary and secondary compendial standards undergo rigorous testing in a collaborative study and are subject to statistical analysis. Compendial standards are considered to have the highest level of accuracy and traceability.

A USP RS, where explicitly mentioned in an official USP compendial procedure, is considered to be part of the official method. In the event of a dispute, it is the USP procedure with its associated USP RS(s) which determines compliance. This is also stated in Section 5.80. *USP Reference Standards* of the General Notices and Requirements in the USP-NF online publication: "Where USP or NF tests or assays call for the use of a USP Reference Standard, only those results obtained using the specified USP Reference Standard are conclusive." USP does not provide guidance on the qualification or use of non-USP reference materials in place of a USP RS. Users are advised to consult with the regulatory authority where their products are marketed for guidance on the qualification of in-house standards and the use of a non-USP reference material.

Regards,

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