dx.doi.org/10.14227/DT130106P36

USP Bulletin

Editor's Note: This announcement can be found on the USP Website at www.usp.org.

The USP Performance Test: Mechanical Calibration vs. a Periodic Performance Verification Test with Chemical Tablets (Calibrators)

Date: January 17, 2006

Topic: The USP Performance Test and the USP Periodic Performance Verification Test.

Background: For a non-solution orally administered dosage form, an important test in the public or private specification is the USP Performance test. USP provides instructions for the procedure in General Chapters *Dissolution* <711> and *Disintegration* (<701>), which may then be adapted by a manufacturer to a specific dosage form. USP is working to expand the USP Performance test to dosage forms given by other routes of administration.

FDA Advisory Committee Meetings: In May and October 2005, the FDA Advisory Committee for Pharmaceutical Science (ACPS) discussed dissolution testing and the use of USP's 'calibrator' tablets. Conclusions of the Advisory Committee were to recommend use of mechanical calibration as an alternative to the use of 'calibrator' tablets, and this recommendation may be incorporated in an FDA Compliance Policy Guide. USP has requested that FDA allow USP further opportunity to discuss some of the science and technical issues considered at the ACPS meetings (view on USP website)and has received a response (view on USP website) .

USP does not agree that mechanical calibration is an acceptable alternative for a periodic performance verification test and has provided FDA information in support of this position. USP hopes that this information will be taken into account in the development of any FDA Compliance Policy Guide on this subject and that USP will have the opportunity for further input before any such Guide is finalized. USP welcomes FDA's statement that multiple opportunities for public comment and discussion will occur before alternative test methods are substituted for dissolution.

Nomenclature: Part of the challenge in discussing the science and technical issues associated with the USP Performance test, the dissolution procedure, and a 'calibrator' tablet relates to terminology. Using nomenclature from the ISO 5725 series, the USP 'calibrator' tablet does not function in calibration of dissolution equipment. Instead it is a physical standard (etalon) that is associated with a periodic performance test, usually conducted at six month intervals by a pharmaceutical manufacturer. In the future, USP will avoid the use of the term 'calibrator' in describing its chemical tablets. A periodic performance verification test assesses a dissolution tester, the analyst, and the analytical procedure, and allows for inter-and intra-laboratory comparisons, which mechanical calibration does not. Mechanical calibration is usually performed prior to each dissolution study and is also part of new instrument qualification. Thus the two approaches are different and serve different purposes.

Science and Technical Information: USP is completing an extensive collaborative study on a new Lot P tablet containing 10 mg of prednisone, which has been manufactured under stringent conditions. In addition, USP is conducting extensive variance studies on this new physical standard. Both sets of data will be made available publicly, and USP looks forward to public discussion of the data. In particular, USP believes these data will clarify some of the misconceptions about chemical tablet variance presented at the ACPS meetings. USP plans additional laboratory studies and welcomes input from all stakeholders as additional data become available.

Procedural Matters: USP has formed an Advisory Panel (Chair: Ms. Vivian Gray) to consider the USP dissolution procedure and periodic performance verification test and associated chemical tablet physical standards. This Advisory Panel reports to the Biopharmaceutics Expert Committee (Chair: Dr. Thomas Foster) in USP's Council of Experts. USP will continue to work with the experts in these two bodies to assess both mechanical calibration and the USP periodic performance test, as well as the value of dissolution vis-à-vis alternate tests such as might arise in the application of PAT concepts. Additional science and technical approaches will be considered. USP believes that specific improvements are possible to USP's periodic performance test that will enhance its value to pharmaceutical manufacturers. As always, USP welcome public comment on its standards setting activities.