

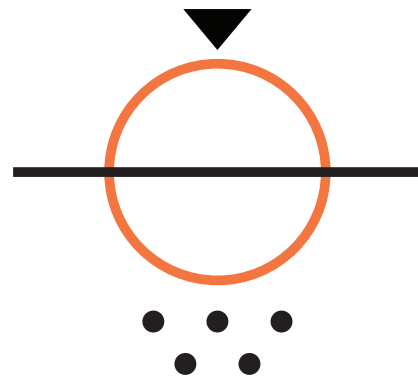
The Performance Verification Test (PVT)

Assessing dissolution assembly performance and providing evidence of instrument suitability





The performance verification test (PVT) in the context of dissolution testing



Dissolution is the transfer of a drug substance from a solid into a solution. The dissolution test is used throughout the product life cycle for most solid oral dosage forms, typically as an in vitro performance test in early product development and in later stages as a quality control test for monitoring stability and performance of the finished dosage form.

Dissolution testing is commonly performed using USP Apparatus 1 (basket) or USP Apparatus 2 (paddle). The dissolution test assembly generally consists of six or more individual vessel/stirring-element combinations with individual components that may be independently adjusted. The purpose of the dissolution test assembly is to simulate drug release from the dosage form in a reproducible manner.

The PVT serves multiple roles in dissolution test assembly qualification — initially, as a Performance Qualification test to demonstrate the “fitness for purpose” of USP Dissolution Apparatus 1 and USP Dissolution Apparatus 2, and, subsequently, as a periodic performance check to demonstrate the ongoing reliability of the apparatus.

PVT Benefits

A Holistic Test

The PVT can serve as a final performance check of the Installation Qualification/ Operation Qualification/ Performance Qualification process, a necessary requirement for Analytical Instrument Qualification.

Instrument Suitability Test

Performing regular PVTs throughout the usable life of the dissolution assembly improves overall dissolution data quality by providing periodic performance checks to demonstrate that the instrument is performing as intended.

Proficiency Test

The PVT can also be used as a proficiency test (e.g., for analyst qualification, internal and/or external dissolution laboratory qualification).

Benefits of using the USP Dissolution Performance Verification Standard – Prednisone Reference Standard (USP DPVS – Prednisone RS) for PVT

Sensitivity to Instrument Setup

In addition to being sensitive to test assembly setup parameters that are easily measured (e.g., rotation speed, paddle height, vessel alignment), the dissolution of USP DPVS – Prednisone RS is also sensitive to parameters that are not easily measured or characterized by the end user (e.g., vessel quality, vibration).

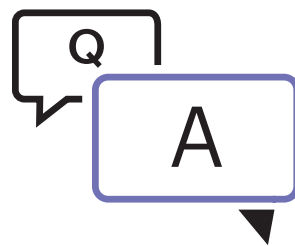
Independent Reference Standard

USP provides an independently established Reference Standard approved by a committee of independent experts from industry and academic organizations.

Global Comparability

The acceptance ranges provided with each lot of USP DPVS – Prednisone RS are established through collaborative studies with multiple international laboratories.





PVT Explained

Q: What is the purpose of the PVT?

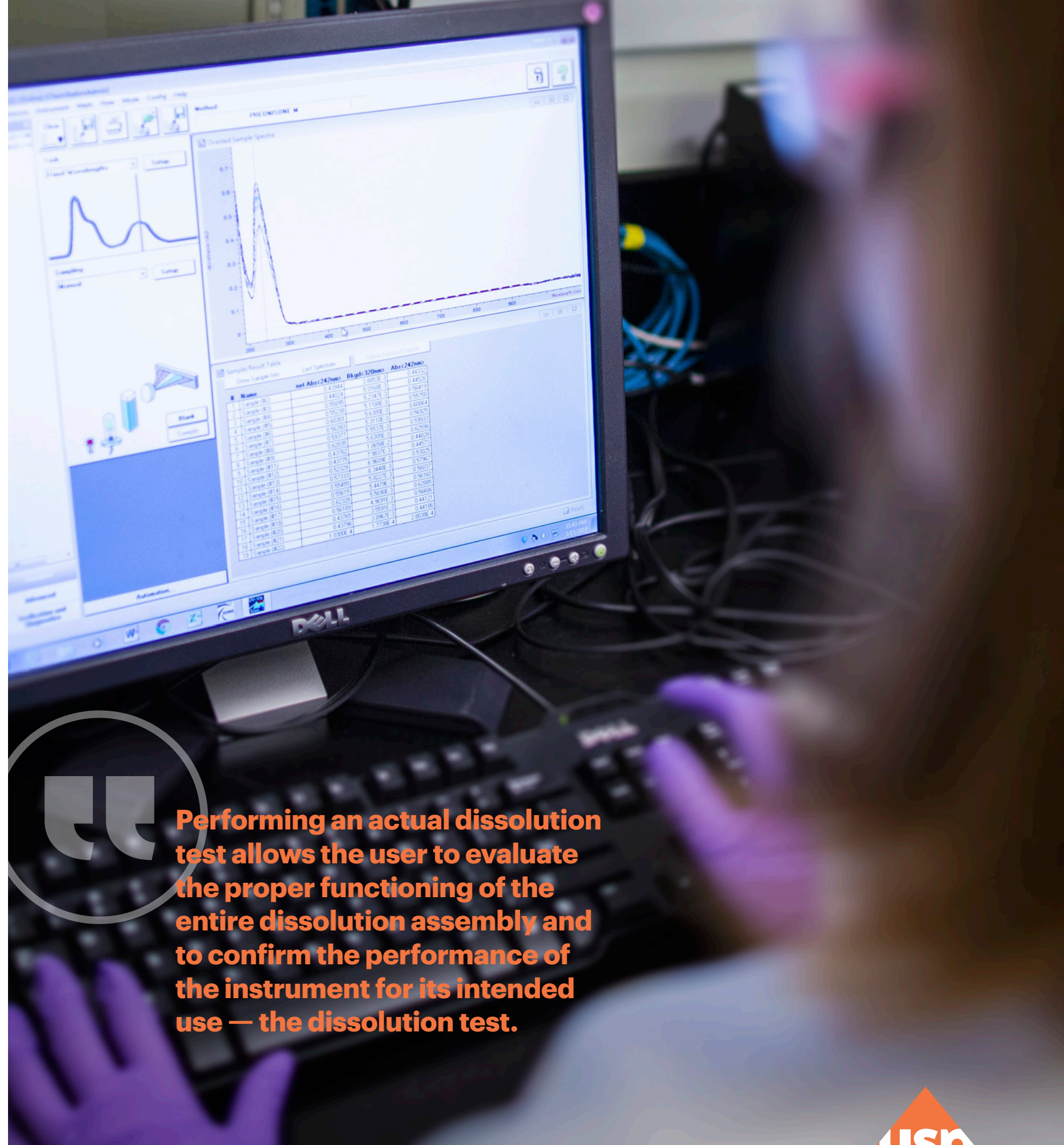
A: As part of the Analytical Instrument Qualification, the Performance Qualification assesses the instrument as a whole after each of the individual component dimensions has been verified and the operation of the instrument has been verified. Performing an actual dissolution test allows the user to evaluate the proper functioning of the entire dissolution assembly and to confirm the performance of the instrument for its intended use — the dissolution test.

Q: Why is the USP DPVS – Prednisone RS required for the PVT?

A: The USP DPVS – Prednisone RS has a long history as part of the PVT used with both USP Apparatus 1 and USP Apparatus 2, and it has been shown to be sensitive to the setup, vessel dimensions and operational parameters specified in *USP General Chapter <711> Dissolution*. To help achieve comparable performance, the acceptance criteria for each bulk lot of USP DPVS – Prednisone RS are established based on the analysis of data from collaborative studies involving multiple participants such as equipment manufacturers, regulatory agencies and pharmaceutical manufacturing and testing laboratories. By comparing the data from their own assembly with the acceptance criteria provided with the USP DPVS – Prednisone RS, end users can assess where their own dissolution test assembly performance stands in relation to the collaborative study results.

Q: What is the advantage of performing the PVT along with mechanical calibration?

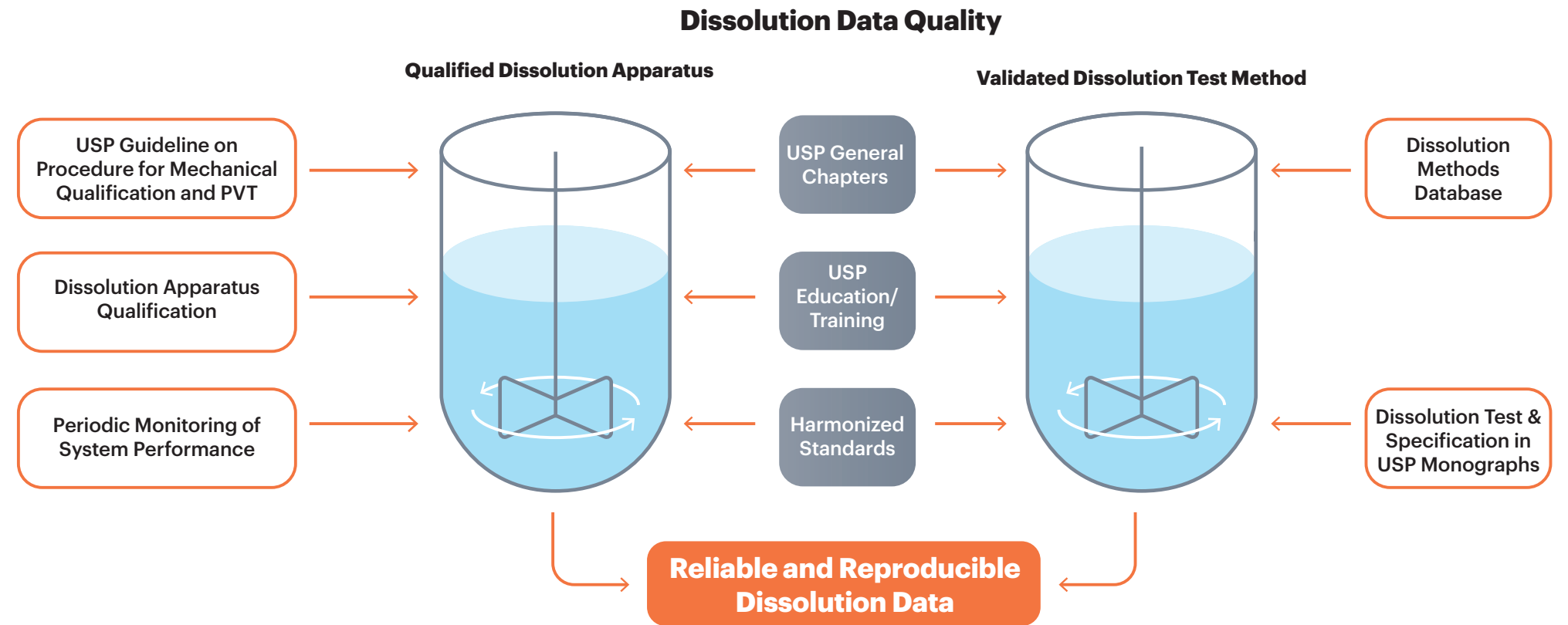
A: Approaches to instrument qualification that rely solely on the agreement of mechanical specifications with those described in *USP General Chapter <711>* and other sources assume there is no interaction of these easily quantifiable qualities with those that are more difficult to characterize. The PVT provides a test of the “fitness for purpose” of the entire dissolution system, including the environment in which the equipment is operating. The USP DPVS – Prednisone RS has been shown to be sensitive not only to the setup of the instrument but also to vibration from external sources, media degassing and other dissolution test conditions that are not easily quantified (e.g., vessel quality and consistency). The purpose of the PVT and using the USP DPVS – Prednisone RS is not to diagnose specific problems with the dissolution instrument but to provide confidence that the instrument is functioning properly.



Performing an actual dissolution test allows the user to evaluate the proper functioning of the entire dissolution assembly and to confirm the performance of the instrument for its intended use — the dissolution test.

How do USP resources support the reliability and reproducibility of dissolution data?

USP provides several resources to support the development of validated dissolution test methods and to support the proper and complete qualification of the dissolution instrument.



USP Resources

USP General Chapters

- ▶ <711> Dissolution
- ▶ <724> Drug Release
- ▶ <1058> Analytical Instrument Qualification
- ▶ <1090> Assessment of Solid Oral Drug Product Performance and Interchangeability, Bioavailability, Bioequivalence, and Dissolution
- ▶ <1092> The Dissolution Procedure: Development and Validations
- ▶ <1094> Capsules — Dissolution Testing and Related Quality Attributes

USP Education

- ▶ Fundamentals of Dissolution course — focuses on the theory and basics of dissolution and the qualification of USP Dissolution Apparatus 1 and USP Dissolution Apparatus 2
- ▶ Development and Validation of Dissolution Procedures course — used for batch release and stability testing

Harmonized Standards

- ▶ USP participates in international harmonization initiatives with standards-setting organizations to coordinate public standards.

Dissolution Apparatus Qualification

- ▶ Installation Qualification — evaluation of system requirements and confirmation of suitable environment
- ▶ Operational Qualification — verification that the instrument is operating within specifications in the selected environment (i.e., mechanical qualification)
- ▶ Performance Qualification — demonstration that the dissolution assembly is performing as intended (i.e., PVT)

USP DPVS – Prednisone RS

- ▶ The USP DPVS – Prednisone RS is a specifically formulated reference standard material to be used for the PVT of USP Apparatus 1 and USP Apparatus 2.

USP Guideline on Procedure for Mechanical Qualification and PVT

- ▶ Provides detailed descriptions of USP best practices for mechanical qualification and PVT of USP Apparatus 1 (basket) and USP Apparatus 2 (paddle) dissolution test assemblies

Periodic Monitoring of System Performance

- ▶ Regular preventative maintenance of dissolution system
- ▶ Periodic check of system performance using PVT to ensure fitness for purpose and system control

Dissolution Test and Specification in USP Monographs

- ▶ Provides instructions for the monograph dissolution test and related specifications

USP Dissolution Methods Database

- ▶ Provides USP monograph test conditions and a helpful search function in a downloadable database available at USP website

Your voice makes a difference!

USP works with independent experts from industry, academia and healthcare fields to develop USP standards that provide a foundation of quality in these critical areas, and now you can help advance public health by partnering, volunteering or providing input today.

Learn more about the PVT and PVT support — including guides, education/training and tip sheets — at www.usp.org/PVT.