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# Mechanical Qualification (MQ) for Apparatus 1 and 2

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- Installation Qualification (IQ)
- Operational Qualification (OQ)
- Performance Qualification (PQ)



- IQ Definition – the documented collection of activities necessary for installing an instrument in the user's environment
- Ensures the equipment and accessories have arrived undamaged and the order is complete
- Verifies that the user environment meets all vendor-specified requirements
- Instrument setup and verifying unit comes on usually completes the procedure



- OQ Definition – collection of basic functionality tests that ensure the instrument operates as intended by the manufacturer and the end user
- Tests performed are specific to the instrument being qualified
- Performed after the IQ or if the instrument undergoes service / modification or is moved to another location
- May be repeated at regular intervals if the instrument does not have a PQ or “calibration”



- PQ Definition – test(s) performed based on the typical on-site application of the instrument
- Performed after the IQ/OQ or at a pre-determined interval (usually every 6 months)
- Dissolution PQ includes the verification of basic physical parameters as well as execution of the PVT
- The USP Performance Verification Test (PVT) requires use of Prednisone and Salicylic Acid
- Used since 1978

- It has long been understood that the physical parameters of dissolution apparatus and their tolerances can have significant impact on the quality of dissolution test results
- Recently, several standard-setting groups such as the FDA, USP and ASTM officially released protocols and recommendations to perform mechanical calibration of dissolution apparatus
- The FDA's draft guidance recommends the use of mechanical calibration for dissolution apparatus "as an alternative to the use of calibrator tablets" (PVT and PQ)



- MQ Definition - measurement and verification of a dissolution apparatus' physical parameters, which impacts the results of a dissolution test
- Newly implemented procedure based on release of guidance from FDA, ASTM
- Executed in place of PQ for dissolution apparatus 1 and 2
- Does not require use of Prednisone or Salicylic Acid tablets



Physical parameter measurements performed on dissolution apparatus:

- Basket/paddle depth
- Shaft wobble
- Shaft verticality
- Basket wobble
- Vessel centering
- Vessel verticality
- Rotational speed (RPM)
- vessel temperature

- Measurement of vessels, baskets, and paddles dimensions (listed in USP General Chapter <711>)
- Regular maintenance schedule for any dissolution apparatus that includes MQ as a part of overall AIQ based on frequency of use or internal quality system requirements
- Daily or prior-to-use examination to:
  - Visually inspect vessels, baskets, paddles for scratches, cracks, residue and rusting
  - Check that vessel temperature is within 0.5° C of target temperature



The FDA draft guidance was issued in October 2007

- Online: <http://www.fda.gov/CDER/GUIDANCE/7232dft.pdf>
- FDA Draft Guidance for Industry: The Use of Mechanical Calibration of Dissolution Apparatus 1 and 2 – Current Good Manufacturing Practice (cGMP)
- It recommends the use of “appropriately rigorous methods” for mechanical calibration of dissolution apparatus and specifically references two such methods:
  - FDA - CDER Division of Pharmaceutical Analysis Document # DPA-LOP.002, “Mechanical Qualification of Dissolution Apparatus 1 and 2”
  - ASTM E 2503-07 Standard, “Standard Practice for Qualification of Basket and Paddle Dissolution Apparatus”



- The USP also issued a draft toolkit, which contains a section describing mechanical calibration preceding the section on the PVT
- Dissolution Procedure: Mechanical Calibration and Performance Verification Test; Version 1.0  
Draft 5.1 October 4, 2007  
<http://www.usp.org/pdf/EN/dissolutionProcedureToolkit2007-10-04.pdf>

# Comparison of MQ Tolerances

Parameter	FDA (DPA-LOP.002)	ASTM (E2503-07)	USP Toolkit, 2.0, includes PVT (Draft)	Current Physical Parameters
<b>Basket / Paddle Depth</b>	25 ± 2 mm	25 ± 2 mm (or within 8% of desired height)	23-27 mm above bottom of vessel	25 +/- 2mm
<b>Rotational Speed</b>	± 2 rpm of target	within 2% or ± 2 rpm of stated rate (use larger)	± 1 rpm of set value	+/- 4%
<b>Shaft Wobble</b>	≤ 1.0 mm total runout	≤ 1.0 mm total runout	≤ 1.0 mm total wobble	No significant wobble
<b>Shaft Verticality</b>	≤ 0.5° from vertical	Within bubble	<i>Not measured</i>	<i>Not measured</i>
<b>Basket Wobble</b>	≤ 1.0 mm total runout	≤ 1.0 mm total runout	≤ 1.0 mm total wobble	+/- 1.0 mm
<b>Vessel Centering</b>	≤ 1.0 mm from center line	≤ 1.0 mm from center line	NMT 2.0 mm diff. between smallest/largest measurement	NMT 2mm of center axis
<b>Vessel Verticality</b>	≤ 1.0° from vertical	≤ 1.0° from vertical at each point	NMT 0.5° from vertical	<i>Not measured</i>
<b>Vessel Plate Level</b>	<i>Not measured</i>	<i>Not measured</i>	NMT 0.5° deviation from horizontal	Within bubble
<b>Temperature</b>	<i>Not measured</i>	<i>Not measured</i>	NMT 0.2°C difference between set point / meas.	<i>Not Measured</i>

# Comparison of MQ Procedures – Frequency of Activities

<b>Parameter</b>	<b>FDA (DPA-LOP.002)</b>	<b>ASTM (E2503-07)</b>	<b>USP Toolkit, 2.0 - includes PVT (Draft)</b>	
<b>Operation (before every dissolution test)</b>	Basket Examination	Basket Examination	Basket Examination	
	Paddle Examination	Paddle Examination	Paddle Examination	
	Vessel Examination	Vessel Examination	Vessel Examination	
	Vessel Temperature	Vessel Temperature	Vessel Temperature	
	Vibration	Vibration	Vibration	
			Water Bath	
			Centering	
			RPM (single position)	
<b>Maintenance</b>	According to manufacturer	Established program; consult manufacturer	Routine maintenance / inspection	
<b>Frequency</b>	Upon move, repair or six-month interval	Upon move, repair, or quality system determination	Mechanical- every 3 months; PVT – every 6 months	

# PQ vs. MQ



- Takes less time to perform
- Does not require Calibrator tablets and standards
- Verification of accessory components (baskets, shafts, paddles, vessels) is a critical feature of all mechanical qualification protocols
- The quality of accessory components and their compliance of physical dimensions to USP, EP, and JP are critical factors that affect the performance
- Regular scheduled maintenance required
- No specifications for Vibration



- Time consuming
- Requires use of Calibrator tablets and standards
- Wide specification range and questions regarding stability of Prednisone Tablets
- PQ remains extremely valuable as a holistic test of the performance of a dissolution apparatus
- PQ is able to discern the effects of vessel imperfections and vibrations on the performance of the apparatus



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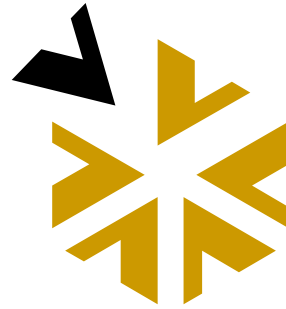
## Status of the Pharmaceutical Industry's Position on MQ

- The FDA draft guidance has invited comments and is currently in the process of consideration for issuance of final guidance

Comments?



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