Sections included in this document

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Document History

Version 2 The procedure was modified to allow its use with all of the manufacturer's dissolution equipment at DPA.

Document history					
Version #	**Status (I, R, C)**	**Date Approved**	**Location of Change History**	**Name & Title**	
				Contact	**Approving Official**
1.0	I	November 21, 2005	In Document	James Allgire	Lucinda F. Buhse
2.0	R	May 31, 2006	In Document	James Allgire Chemist, DPA	Lucinda F. Buhse Acting Dir. OTR

Chronologically track the original document and/or approved revisions or cancellations.

(a) Version # of the Document
(b) Status: I = Initial; R = Revision; C = Cancel
(c) Date Approved by the Approving Official
(d) Location of the Change History
(e) Name, Title of Contact/Approving Official: Include the organization abbreviation in the title. The contact may or may not be the author.

1. Purpose

The purpose of this document is to establish the setup, mechanical calibration, and operation checks for dissolution Apparatus 1 (Basket) and 2 (Paddle).

2. Scope/Policy

This procedure applies to all Apparatus 1 and 2 dissolution equipment at the Division of Pharmaceutical Analysis (DPA).

3. Responsibilities

3.1 Analyst

- Check the vessel, basket, and paddle dimensions on receipt.
- Perform the maintenance procedures as per the manufacturer's recommendation.
- Perform the mechanical calibration on receipt, after the instrument is moved, after the instrument is repaired, and six months after the previous calibration. If the instrument is not being used routinely the six month mechanical calibration can be performed before performing the first dissolution test after the six month time interval.
- Perform the operation checks at each time of use.

4. Background

The setup, mechanical, and operational checks are used to minimize variability during dissolution testing.

5. References

- USP General Chapter <711>
- <1092> The Dissolution Procedure: Development and Validation, Pharmacopeial Forum, 31(5), 2005, p.1463

6. Procedure

Wherever possible, tools should be traceable to NIST.

6.1 Apparatus setup

During apparatus setup or after replacement of parts, verify the following dimensions. Certificates of Analysis (COA) or Certificates of Conformity (COC) may be used to document the measurements. Discard any parts that do not meet specifications.

Vessel Dimensions

Use an appropriate measuring device to verify that the vessel dimensions conform to the specifications listed in the USP General Chapter <711> Dissolution. The vessel must have cylindrical sides and a hemispherical bottom which must be smooth and without defects.

Basket Dimensions

Each basket must conform to the dimensions shown in the USP General Chapter <711> Dissolution in Figure 1, Basket Stirring Element. An appropriate measuring device is used to make the measurements.

Paddle Dimensions
Each paddle must conform to the dimensions shown in the USP General Chapter <711> Dissolution in Figure 2. An appropriate measuring device is used to make the measurements.

6.2 Maintenance
Follow the manufacturer's maintenance recommendations and maintenance schedule**.**

6.3 Mechanical Calibration
Perform the following in the order given for mechanical calibration of each apparatus. Some iteration may be necessary if extensive adjustments are needed. Perform these tests every 6 months or after any repair, move, etc. If the instrument is not in routine use, the mechanical calibration may be performed prior to performing the first dissolution test after the six month interval. Some dissolution instruments require the use of manufacturer's supplied special tools or incorporate automatic mechanical devices to perform the following tests. These may be used provided they follow the general principle of the procedure.

Shaft Wobble
A runout gauge is placed on top of the vessel plate, and the drive module is positioned so that the gauge probe touches the shaft about 2 cm above the top of the paddle blade or basket. The gauge is placed so that the probe slightly presses in on the turning shaft. If a mechanical gauge is used, the gauge's pointer should read slightly more than zero. The pointer will vary from a minimum to a maximum reading, and the difference is called the wobble. The specification is ≤1.0 mm total runout.

Paddle and Basket Shaft Verticality
Lower the drive unit to where it would be during an actual dissolution test. If necessary the shaft verticality may be checked with the shafts raised above the drive unit. Place an accurate bubble level on the front edge of each of the shafts. The bubble should be within the lines of the level. Rotate the level 90º so it is on the side of the shaft. The bubble should again be within the lines of the level for each shaft. If the shafts are not vertical adjust the feet of the apparatus until they are vertical.

A digital leveling device may also be used to determine the shaft verticality. The shaft must be ≤0.5° from vertical.

Basket Wobble
A runout gauge is placed on top of the vessel plate and the drive unit is positioned so that the gauge probe touches the bottom rim of the basket. The gauge is placed so that the probe slightly presses in on the turning shaft. If a mechanical gauge is used, the gauge's pointer should read slightly more than zero. The pointer will vary from a minimum to a maximum reading and the difference is called the wobble. The specification is ≤ 1.0 mm total runout.

Vessel Centering
The vessel plate of an apparatus may warp or bend or the thickness of a vessel lip or centering collar lip may not be perfectly uniform. If either of these occurs, even though the shafts are vertical and the vessel plate is level, the vessel walls may not be vertical.

Use centering tools which measure centering inside the vessel. Two centering tools are used to center the vessels around the paddle or basket shafts and to align the vessels so that their sides are vertical. For the paddle method, the bottom of one centering tool is placed 2 mm above the top of the paddle blade and the bottom of the second centering tool is clamped on the shaft 80 mm above the blade with the probes positioned in the same direction towards the glass vessel wall. For the basket method, the bottom of one centering tool is placed 2 mm above the top of the basket and the bottom of one centering tool is placed 60 mm above the top of the basket with the probes positioned in the same direction towards the glass vessel wall. Carefully lower the shaft and centering tools into the vessels so that the paddle blade or basket bottom is about 2.5 cm above the bottom of the vessel. Manually rotate the shaft slowly and check the centering at both levels. If the vessel is not centered at either level, adjust the vessel to center it. Adjustments can be made by rotating the vessel or the vessel with the centering collar inside the vessel plate, moving the vessel sideways within the vessel plate or placing shims (such as tape) under one side of the lip of the vessel or vessel centering collar. Repeat this process until both bottom and top positions are centered within 1.0 mm from the center line.

An alternative procedure is to use a mechanical or digital centering device that centers the inside of the vessel around the shaft or a surrogate shaft. The centering is measured at two positions inside the vessel in the cylindrical portion, one near the top but below the rim and one just above the bottom portion of the vessel. The shaft or surrogate shaft must be centered within 1.0 mm from the center line.

Vessel Verticality
The vessel verticality can be calculated using the centering measurements and the difference in height between the two measurements or it can be determined using a digital leveling device placed on the inside wall of the vessel. The verticality should be determined at two positions 90° apart. Adjustments can be made by placing shims (such as tape) under one side of the lip of the vessel or vessel centering collar. The vessel must be $\leq 1.0°$ from vertical.

After each vessel has been centered and made vertical, each vessel and vessel plate opening must be numbered and a mark must be placed on the lip of each vessel and on the vessel plate directly next to the mark on the vessel lip. Each vessel must be returned to the same vessel plate opening and positioned in the exact same position inside the vessel plate opening for all future dissolution tests.

Basket and Paddle Depth
The actual distance between the bottom of the vessel and bottom of the basket or paddle is determined. If the depth of the basket/paddle is adjustable, first a depth gauge is used to set the distance between the bottom of the paddle blade or basket and the bottom of the vessel. The depth gauge is set at 25 mm and placed on the bottom of the vessel. Each shaft is raised into the apparatus drive module. The drive unit is then lowered to its operating position. The paddle or basket is then lowered into the vessel until it touches the top of the depth gauge. The shafts are locked into this height. This is repeated for each shaft. The specification is 25 mm ± 2 mm.

Rotational Speed
A tachometer should be used to measure the rotational speed of the paddle or basket. The shafts should be rotating smoothly at ± 2 rpm of the target value.

6.4 Operation
Before each test perform the following:

Basket Examination
Each basket must be visually examined for defects such as rusting, corrosion, wires sticking out beyond the basket, clogged mesh holes or deformed mesh sides.

Paddle Examination
Each paddle must be visually examined for defects such as rusting, corrosion or loose pieces of coating on the paddles (for paddles coated with Teflon or another coating).

Vessel Examination
Each vessel must be free of scratches, cracks, pits and residue.

Vessel Temperature
The temperature of the medium inside each vessel is measured at time of use. The limit is ± 0.5°C of the target temperature. The target temperature is usually 37°C for Apparatus 1 and 2.

Vibration
The USP criteria of: "No part of the assembly, including the environment in which the assembly is placed, contributes significant motion, agitation, or vibration beyond that due to the smoothly rotating stirring element" is followed.

6.5 Additional Variables

Basket Shafts (Clips versus O rings)
The diagram of the basket stirring element in the USP General Chapter <711> shows that the basket shaft has clips to hold the basket. Some basket shafts have O rings to hold the basket in place instead of clips. The clips change the hydrodynamics of the medium causing slightly increased dissolution results with certain formulations. In order to conform to the USP diagram, DPA chemists must use basket shafts with clips or use detachable basket clips unless the dissolution method states otherwise.

Sinkers
Sinkers are required for capsules that float when the Apparatus 2 (Paddle) method is used. Some commercial sinkers have too many coils that trap the capsule material inside the sinker. DPA

uses sinkers that are recommended by the USP. A detailed procedure on how to make them is in the proposed USP General Chapter <1092> The Dissolution Procedure: Development and Validation, USP Pharmacopeial Forum, 31(5), 2005, p. 1463. If a method states to use a particular commercially available sinker, the DPA chemist must use the specified sinker.

7. Records

The date, analyst, dissolution vessels' manufacturer, and the dissolution apparatus's manufacturer, model number, and serial number will be recorded on the appropriate Mechanical Calibration Report Sheet (see Attachment A and B) along with the appropriate observations. The completed report sheet will be placed in the report sheet folder for that apparatus. Each dissolution apparatus will have its own report sheet folder.

8. Glossary

Not Applicable

9. Attachments

Attachment A - Mechanical Calibration Report Sheet--Apparatus 1 (Basket)
Attachment B - Mechanical Calibration Report Sheet--Apparatus 2 (Paddle)

Signatures
Approving Official's Signature:

BJ Westenberger_____ 6/1/06
Benjamin J Westenberger, Deputy Director Date

LF Buhse_____ 6/1/06
Lucinda F Buhse, Director Date

ATTACHMENT A

BASKET APPARATUS QUALIFICATION REPORT SHEET

Date _____ Analyst _____

Dissolution Apparatus: Manufacturer _____ Model #_____ Serial #_____

Dissolution Vessels: Manufacturer _____

MECHANICAL CALIBRATION REPORT SHEET -- APPARATUS 1 (BASKET)

Calibration Parameter	Point of Measurement	Results & Comments	Tools Used	Specifications
Shaft wobble	2 cm above top of basket	1. _____ 2. _____ 3. _____ 4. _____ 5. _____ 6. _____		≤ 1.0 mm total runout
Shaft verticality	Along shaft	Record results at 2 points that are 90° apart. Shaft is vertical.: (Y/N) Shaft1 Pt1:_____ Pt2:_____ Shaft2 Pt1:_____ Pt2:_____ Shaft3 Pt1:_____ Pt2:_____ Shaft4 Pt1:_____ Pt2:_____ Shaft5 Pt1:_____ Pt2:_____ Shaft6 Pt1:_____ Pt2:_____		Bubble must be with-in the lines of bubble level ≤ 0.5° from vertical
Basket wobble	Bottom of basket rim	1. _____ 2. _____ 3. _____ 4. _____ 5. _____ 6. _____		≤ 1.0 mm total runout
Vessel/Shaft centering	Step 1: Measured lower position Step 2: Measured upper position	Step 1: 1. _____ 2. _____ 3. _____ 4. _____ 5. _____ 6. _____ Step 2: 1. _____ 2. _____ 3. _____ 4. _____ 5. _____ 6. _____		≤1.0 mm from centerline
Vessel verticality	Straight portion of vessel at two places 90° apart	1. _____ 2. _____		≤1.0 ° from vertical
Height check/Basket depth	Basket bottom	1. _____ 2. _____ 3. _____ 4. _____ 5. _____ 6. _____		25 ± 2 mm
Rotational speed		50 rpm _____ 100 rpm _____		± 2 rpm

Attachment B

PADDLE APPARATUS QUALIFICATION REPORT SHEET

Date _____ Analyst _____

Dissolution Apparatus: Manufacturer _____ Model #_____ Serial #_____ Dissolution Vessels: Manufacturer _____

MECHANICAL CALIBRATION REPORT SHEET -- APPARATUS 2 (PADDLE)

Calibration Parameter	Point of Measurement	Results & Comments	Tools Used	Specifications
Shaft wobble	2 cm above top of paddle blade	1. _____ 2. _____ 3. _____ 4. _____ 5. _____ 6. _____		≤ 1.0 mm total runout
Shaft verticality	Along shaft	Record results at 2 points that are 90° apart. Shaft is vertical: (Y/N) Shaft1 Pt1:_____ Pt2:_____ Shaft2 Pt1:_____ Pt2:_____ Shaft3 Pt1:_____ Pt2:_____ Shaft4 Pt1:_____ Pt2:_____ Shaft5 Pt1:_____ Pt2:_____ Shaft6 Pt1:_____ Pt2:_____		Bubble must be with-in the lines of bubble level ≤ 0.5° from vertical
Vessel/Shaft centering	Step 1: Measured lower position Step 2: Measured upper position	Step 1: 1. _____ 2. _____ 3. _____ 4. _____ 5. _____ 6. _____ Step 2: 1. _____ 2. _____ 3. _____ 4. _____ 5. _____ 6. _____		≤1.0 mm from centerline
Vessel verticality	Straight portion of vessel at two places 90° apart	1. _____ 2. _____		≤1.0 ° from vertical
Height check/Paddle depth	Paddle bottom	1. _____ 2. _____ 3. _____ 4. _____ 5. _____ 6. _____		25 ± 2 mm
Rotational speed		50 rpm _____ 100 rpm _____		± 2 rpm