1.0 Purpose

This procedure provides detailed instructions on the calibration and use of the Hanson Phase One and the PTZ AUTO 4 Disintegration Testers for disintegration evaluation of various products.

2.0 Scope

2.1 This procedure applies to the following items:

2.1.1 Uncoated, film coated, plain coated, delayed release and enteric coated tablets.

2.1.2 Hard and soft gelatin and vegetable capsules used in final products or as raw materials.

2.2 This procedure does not apply to the following items:

2.2.1 Chewable tablets, powders, liquids, and gummies

2.3 Specialty formulations not covered in this procedure can follow official USP and NSF monographs.

3.0 Responsibility

3.1 It is the responsibility of QC and Analytical Chemists to follow this procedure.

3.2 It is the responsibility of R&D to assign disintegration specifications when customer does not provide a specification.

3.3 It is the responsibility of QC Laboratory Management to implement this procedure and

to ensure that the procedure is being followed.

3.4 It is the responsibility of QC Laboratory Management to keep this procedure aligned with current practices.

4.0 Definitions

4.1 **QC** – Quality Control

4.2 **NIST** – National Institute of Standards and Technology

4.3 **NSF** – National Science Foundation

4.4 **NMT** – Not More Than

4.5 **CPM** – Cycles per minute

4.6 **Disintegration** – As defined by USP <2040> *Disintegration and Dissolution of Dietary Supplements,* the state in which any residue of the unit, except fragments of insoluble coating or capsule shell, remaining on the screen of the test apparatus or adhering to the lower surface of the disk, if used, is a soft mass having no palpably firm core

5.0 References

5.1 USP <2040> Disintegration and Dissolution of Dietary Supplements

5.2 USP <701> Disintegration

5.3 NSF/ANSI 173-2012, Section 5.4.1

5.4 D-703-F1, Form, Disintegration Test Ticket

5.5 C-501, SOP, Document Control Procedure

5.6 C-502, SOP, Record Storage, Retention, and Destruction

6.0 Equipment

6.1 Apparatus

6.1.1 For tablets or capsules that are NMT 18mm long, use the apparatus that meets the requirements and specifications of USP <701> *Disintegration,* Apparatus A (6 positions).

6.1.2 For tablets or capsules greater than 18mm long, use the apparatus that meets the requirements and specifications of USP <2040>, Apparatus B (3 positions).

7.0 Calibration

7.1 Calibration - the apparatus is calibrated for stroke length, stroke rate, and bath temperature.

7.1.1 The stroke length is calibrated by holding a marker to the base of the shaft during operation and then measuring the line left on the shaft. The length of the mark is measured by a calibrated, NIST traceable micrometer. The acceptable stroke length tolerance is 5.5 cm +/- 0.2 cm.

7.1.2 The stroke rate is measured by a calibrated, NIST traceable timer. A cycle is defined by the up and down stroke of the basket assembly. Time the apparatus for 30 cycles and divide 30 by the time taken in minutes. The acceptable stroke rate tolerance is 29 to 32 strokes per minute.

7.1.3 The bath temperature is calibrated by placing a calibrated, NIST traceable thermometer next to the thermocouple in the water bath. The set point for the thermocouple is 37°C. The acceptable temperature tolerance is 35 °C to 39 °C.

8.0 Procedure

9.1 The specification for disintegration is the maximum disintegration time allowable.

9.2 Testing will be performed using deionized water as the immersion fluid unless a USP/NSF monograph or product specific test detail states otherwise.

9.3 1L beakers are used as vessels. Place vessel into water bath and add 800 mL of Millipore water. Check to make sure the basket does not completely submerge. Adjust water level as necessary.

9.4 Check water bath level against the fill line. Adjust water level to the fill line as necessary.

9.5 Equilibrate the vessel to 37°C +/- 2°C. Equilibration can be determined at any point by testing the temperature of the contained fluid using a calibrated thermometer.

9.6 Place 1 dosage unit in each of six tubes before allowing basket to submerge.

9.7 If using the PTZ Auto 4, select the appropriate method given the required time. Select basket position for desired apparatus. Press Start button.

9.7.1 It is important to note that while standard functionality for the PTZ Auto 4 is the independent operation of each basket assembly; all simultaneous runs must be the same method.

9.8 Operate the apparatus for the duration using the described parameters for stroke, CPM, and temperature.

9.8.1 Use of disks is permitted.

9.8.2 If the tablet has a soluble external coating a five minute presoak of the tablet in room temperature water is permitted to remove coating.

9.8.3 If the product is predominately hydrophobic or has poor wettability the use of bile salts, 0.2% SDS, or 0.2% Triton X-100 maybe used.

9.9 At the end of the testing cycle, lift the basket assembly, observe the tablets and determine if each unit has disintegrated.

9.9.1 If all the dosage units have disintegrated then the product has passed.

9.9.2 If three or more dosage units fail to completely disintegrate then the product has failed.

9.9.3 If one or two tablets fail to disintegrate completely, repeat the test on 12 more dosage units. The product passes if not less than (NLT) 16 of 18 tablets tested are disintegrated.

9.10 Delayed Release/ Enteric Coated Tablets

9.10.1 Simulated Gastric Fluid TS Prep: Dissolve 2.0 g of sodium chloride and 3.2 g of purified pepsin, that is derived from porcine stomach mucosa, with an activity of 800 to 2500 units per mg of protein, in 7.0 mL of hydrochloric acid and sufficient water to make 1000 mL

9.10.2 Simulated Intestinal Fluid TS Prep: Dissolve 6.8 g of monobasic potassium phosphate in 250 mL of water, mix, and add 77 mL of 0.2 N sodium hydroxide and 500 mL of water. Add 10.0 g of pancreatin, mix, and adjust the resulting solution with either 0.2 N sodium hydroxide or 0.2 N hydrochloric acid to a pH of 6.8 ± 0.1. Dilute with water to 1000 mL

9.10.3 Omit the use of a disk. Place 1 tablet in each of the six tubes of the basket, and if the tablet has a soluble external sugar coating, immerse the basket in water at room temperature for 5 min. Then operate the apparatus using simulated gastric fluid TS, maintained at 37 ± 2°, as the immersion fluid. After 1 h of operation in simulated gastric fluid TS, lift the basket from the fluid and observe the tablets: the tablets show no evidence of disintegration, cracking, or softening. Operate the apparatus using simulated intestinal fluid TS, maintained at 37 ± 2°, as the immersion fluid for the time specified in the monograph. Lift the basket from the fluid and observe the tablets.

9.11 Delayed Release/ Enteric Coated Capsules

9.11.1 Place 1 softgel capsule in each of the six tubes of the basket. Omit the use of a disk. Operate the apparatus using simulated gastric fluid TS, maintained at 37 ± 2°, as the immersion fluid. After 1 h of operation in simulated gastric fluid TS, lift the basket from the fluid and observe the softgels: the softgels show no evidence of disintegration or rupture that would permit the escape of the contents. Operate the apparatus with disks using simulated intestinal fluid TS, maintained at 37 ± 2°, as the immersion fluid for NMT 60 min. Lift the basket from the fluid and observe the capsules.

9.12 Documentation D-703-F1 Disintegration Test Ticket

9.12.1 Results for finished product testing are recorded on Form D-703-F1 Disintegration Test Ticket.

9.12.2 All documentation will be distributed and maintained as outlined in SOP C-501 Document Control and SOP C-502 Record Storage, Retention, and Destruction.

10.0 Revision History

Revision	Date	Description of Changes	CCR #	By
0	05/06/10	Original	-	-
1	01/24/12	Update SOP format	-	-
2	02/25/13	Increased specificity of instructions and tolerances, reformatted	13-079	B. Johns
3	01/20/15	Updated format, added NIST traceable standards, added NSF requirements. Expanded procedure for testing non-monograph formulations. Biennial Review.	15-0015	B. Johns
4	04/15/15	Added test parameters for products that are predominately hydrophobic or have poorly wettability.	15-0330	B. Johns
5	08/01/17	Added new equipment. General clarifications.	17-0765	N. Zhang
6	02/23/21	Updated to reflect correct disintegration apparatus. Minor changes	CC-21-0098	J. Sassman
7	03/23/22	Minor changes for clarity.	CC-22-0115	S. Sassman
8	07/17/24	Updated for PTZ Auto 4 use. Updated Scope and Procedure for testing. Added documentation requirements and references.	CC-24-0323	J. Nicholson

ION Nutritional Labs	Disintegration Test Ticket		
	Form: D-703-F1	CCR No. CC-24-0323	Revision: 8

Logbook Number: _____ Logbook Page: _____ of _____

Disintegration Bath & Basket Assembly Ion # :				**Calibration Due Date**	
Apparatus Type				☐ **A** (6 tube)	☐ **B** (3 tube)
Temperature:		**Thermometer Ion # :**		**Calibration Due Date**	
Configuration (Check one)					
☐ **DISKS**		☐ **TOP SCREEN**		☐ **NONE**	

Sample Information	
Sample Name/ Time Point:	
Dosage Form:	
Sample Batch/Lot #:	
Test Date:	
Test Result (notate if multiple stages):	
Specification (notate if multiple stages):	

Determination (circle one): **Pass** **Fail**

Comments:

Performed By/Date: _____

Reviewed By/Date: _____

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