



## Abstract

Disintegration tests measure the time it takes for a tablet or capsule to break apart under specific controlled conditions. It is one of several important tests used for quality control of these dosage forms. For the Dietary Supplement Ingredient Database (DSID) studies, supplements representative of the US market are identified and analyzed for their ingredient content. In addition to ingredient assays, tablets and capsules from adult multivitamin/minerals (MVMs) and over-the-counter prenatal MVMs were tested for disintegration. They were immersed and agitated in the appropriate media where a visual inspection of the material for all six tablets/capsules determined the result. Results were designated as pass or fail, according to US Pharmacopeial standards, which specify that disks are used in the testing of all MVM capsules and tablets except delayed-release enteric-coated tablets. The pass rate for adult MVMs was 92.2% (95 of 103 products). For these prenatal MVMs, the disintegration testing was run without (unintentionally) and with the addition of the disk to the apparatus. The pass rate improved from 51.8% (42 of 81 products) to 86.4% (70 of 81 products), respectively. DSID studies will continue to use disintegration to assess the quality and content uniformity of supplement tablets and capsules.

## Introduction

The Nutrient Data Laboratory (NDL), Beltsville Human Nutrition Research Center (BHNRC), Agricultural Research Service (ARS), USDA, has been working with the Office of Dietary Supplements (ODS), National Institutes of Health (NIH) and other federal agencies to plan and develop a DSID to evaluate dietary supplement products. For the DSID, priority product types and ingredients were identified based on prevalence reports from national surveys where the highest priority product types were MVM products. The third release of the DSID will be released by 2015.

The main objective of the disintegration studies was to evaluate tablet and capsule disintegration results for MVM products. Table 1 lists the procedures for disintegration testing based on the type of tablet or capsules. A disk was used where necessary in the disintegration apparatus. The disks are cylindrical in shape and  $9.5 \pm 0.15$  mm thick and  $20.7 \pm 0.15$  mm in diameter. Throughout this document, the word 'tablet' includes both product forms 'tablet' and 'capsule' unless otherwise noted.

**TABLE 1 – USP 36 Disintegration Method and Immersion Media Information for MVMs**

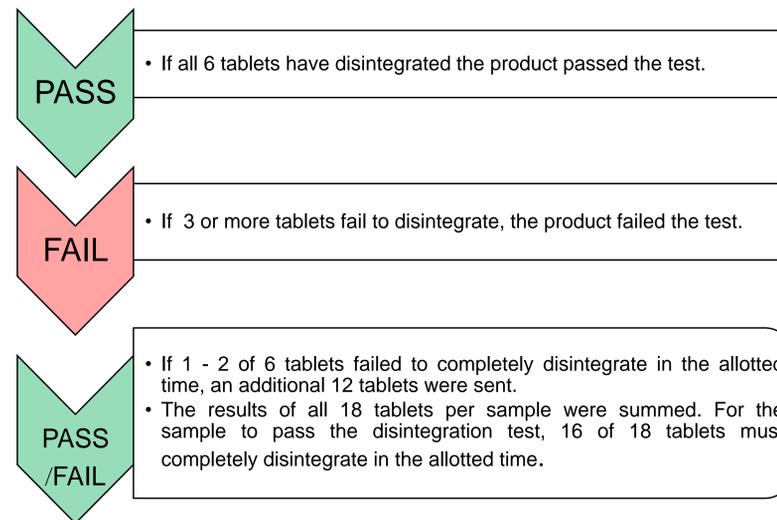
Dosage Form	Form Preparation	Procedure	Immersion Fluid	Media Temp.	Immersion Time	Pre Immersion required?	Disc needed?
Tablet	uncoated, sublingual	standard disintegration	water	37° C ± 2° C (body temperature {BT})	30 minutes	No	Yes
	coated (plain and film)	standard disintegration	water	37° C ± 2° C	30 minutes at BT	Yes (5 minutes at RT)	Yes
Capsule	hard gelatin, hard shelled	standard disintegration	acetate buffer (pH 4.5 ± 0.05)	37° C ± 2° C	30 minutes	No	Yes
	soft shelled, soft gelatin (soft gels)	rupture	water	N/A	15 minutes	-	-
Tablet Capsule	delayed-release (enteric-coated)	standard disintegration	simulated gastric fluid (SGF), simulated intestinal fluid (SIF)	37° C ± 2° C	SIF for the allotted time according to form preparation	Yes (1 hr in SGF)	No

## Materials and Methods

USP chapters <701> (disintegration equipment standards and setup) and <2040> (disintegration test methods for dietary supplements) were followed.

- Each test sample included six (6) tablets from a randomly selected lot of an MVM product. Samples were shipped to a certified laboratory with 10% of the products sent as blinded duplicates to verify method reproducibility.
- The appropriate immersion fluid and allotted disintegration time (see Table 1) were based on the coating of the tablet (coated or uncoated) or tablet matrix (soft gel). Each tablet was placed in a separate transparent receptacle, immersed, and agitated in the appropriate fluid for the allotted time. The temperature of the fluid was monitored and recorded for each tablet in accordance with USP standards (see Table 1).

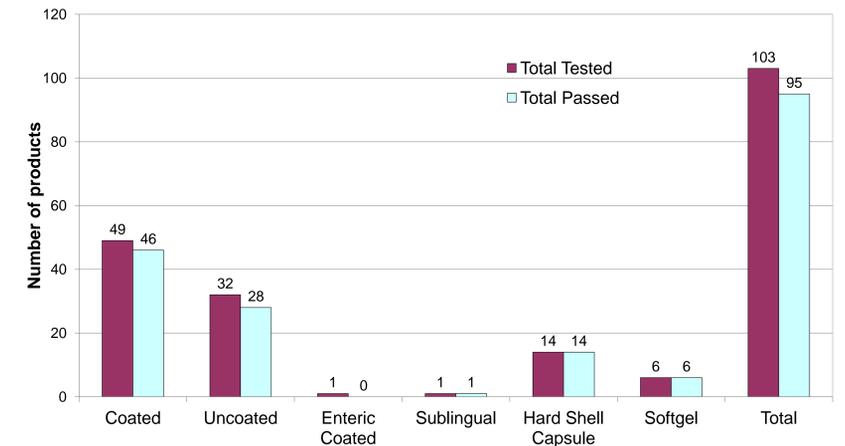
According to chapter <701> of the USP, complete disintegration is defined as *...that state in which any residue of the unit, except fragments of insoluble coating or capsule shell, remaining on the screen of the test apparatus or adhering to the lower surface of the disk, if used, is a soft mass having no palpably firm core.*" (2)



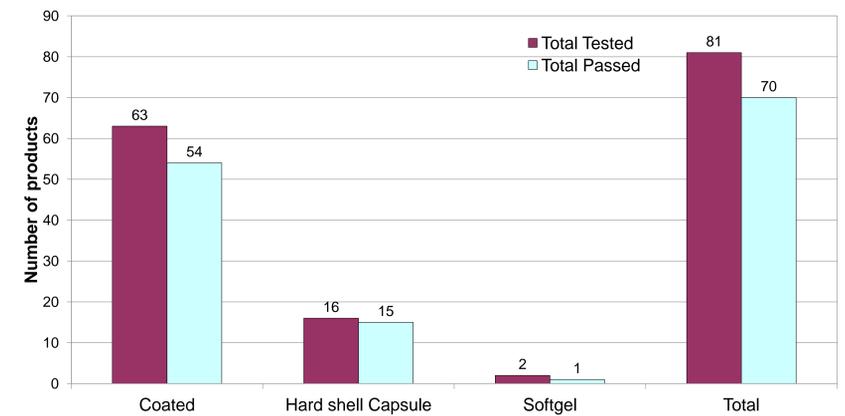
## Results

For the Adult MVM study 103 products were tested for disintegration. The pass rate was 92.2% or 95 of 103 products. Tablet types soft gel, sublingual, and capsules all passed. The tablet type/coating of failed samples included enteric-coated, coated, and uncoated. Each failed sample had all six tablets fail. To double-check these results, a second sample set of the same products was sent for testing. In all cases, all six tablets in the second sample set failed as well. This method consistency was also observed among the duplicate samples. The one duplicate sample that failed was sent again as a duplicate sample and all 12 tablets of the retested duplicate sample failed.

For the 81 over-the-counter prenatal MVM supplements tested, initial results showed a pass rate of only 52%. Additional investigation revealed that for these samples, the disk was not added to the test receptacles, as required. None of the products were enteric coated. The 42 products that had initially failed were retested with a disk and 10 of these failed disintegration again. Of the 10 retest samples that failed, 5 samples were from a second lot and 5 were a retest of the original lot. The three duplicates that initially failed, passed the retesting with disks. The final pass rate was calculated at 86.4%. Table 1 gives an overview of the different types of dosage forms and the usage of disks.



**FIGURE 1 – Adult MVM products with the total number of samples tested for disintegration and the total number of samples that passed.**



**FIGURE 2 – Over-the-counter Prenatal MVM products with the number of samples tested for disintegration and the number of samples that passed.**

## Conclusions

- Approximately 92% of samples tested (95/103) passed disintegration testing in the adult MVM study and 86.4% of the samples tested (70/81) passed disintegration testing study for over the counter prenatal MVMs. This shows that a large percentage of the MVM tablets have good content uniformity and quality.
- It can be clearly seen that the usage of disks increased the probability of disintegration for Over-the-Counter prenatal MVM products.
- DSID studies will continue to use disintegration to assess the quality and content uniformity of supplement tablets and capsules for the next pilot studies, including botanicals (green tea study and flavonoids study) and a prescription prenatal MVM study

## References

- <http://www.usp.org>; United States Pharmacopeia and National Formulary (USP 36-NF 31)
- Loebenberg, R; Steinke, W. Investigation of vitamin and mineral tablets and capsules on the Canadian market. J Ph Pharm Sci: 40-49, 2006.
- May Almukainzi, Mahnor Salehi, Nadia Araci Bou-Chacra, and Raimar Löbenberg, Investigation of the Performance of the Disintegration Test for Dietary Supplements. The AAPS Journal, Vol. 12, No. 4, December 2010

\*\*Information in this table was obtained from USP 36. The equipment used was the Hanson Research QC-21, 2 basket test system (6 tablet capacity per basket).