Agilent Vacuum-Formed (VF) Molded Dissolution Vessels

Technical Overview

Figure 1. An Agilent VF Molded Vessel.

Introducing a Premium Dissolution Vessel for Optimal Reproducibility

"Dissolution is a technique used in the pharmaceutical industry to determine the rate at which pure active pharmaceutical ingredients enter into a solvent to yield a solution. The newly introduced VF molded vessels are vacuum formed around a set of Agilent mandrels, rather than through traditional hand-blown manufacturing, to maintain consistency and ensure exact specifications. This process guarantees proper geometry and eliminates warps and flaws, all with the intent to avoid possible interference from the vessels being used. The results should be indicative of the dosage form itself, not the equipment."

–Allan Little, Director of Marketing, Dissolution

As the transition to enhanced Mechanical Qualification (MQ) continues to gain traction throughout the industry, these vessels fill a void created by not performing the USP Performance Verification Test (PVT) using Prednisone tablets. The vessels are available in standard and verified versions of TruAlign for the 708-DS Dissolution apparatus, as well as the legacy EaseAlign for the 7000/7010 apparatus and TruCenter for the legacy 7025 apparatus. The verified versions include individual Certificates of Conformance (COCs) – a requirement for enhanced MQs. These vessels provide users of Agilent dissolution instrumentation a way to acquire premium accessories and continue to not just meet but exceed current regulatory requirements.

What makes this process unique?

Dissolution vessels are traditionally manufactured by hand-blowing and shaping standard stock glass tubing. This can cause variability in height, diameter, and specific geometry of the inner vessel among vendors and even from the same vendor. While hand-blown vessels produced today generally meet the specifications in USP <711> Dissolution[1], the quality of the vessels varies tremendously around the world. This variability can lead to significant differences in the hydrodynamics of the dissolution environment, which, in turn, is reflected in the dissolution rates.

Vacuum-formed (VF) molded vessels are made using a different process than conventional hand-blown glass vessels, offering tighter control over vessel dimensions that are critical to ensure a reproducible dissolution test. The vessels are manufactured by forming the glass around a mandrel, which maintains consistency and eliminates warps and other flaws which can occur with traditionally made vessels. Though the manufacturing process is time consuming, Agilent invested in a proprietary set of mandrels to ensure the tightest specification possible to provide far better control over the key parameters.

Why replace standard vessels with VF vessels?

A key objective when performing dissolution testing is controlling external sources of energy and variability. The dissolution test should be indicative of the dosage form, not the apparatus or accessories. At Agilent, we go to great lengths to eliminate or minimize every source of variability.

Vessel dimensions are one of the highest areas of risk and can create potential sources of variability in the suitability of a dissolution apparatus[2]. Because of this risk, guidance for documentation of individually measured components through a Certificate of Conformance (COC) or Certificate of Analysis (COA) was mandated in the FDA[3] and ASTM[4] mechanical qualification procedures.

Vessel inconsistency can also be a key source of variability, especially in the USP PVT. In fact, vessel irregularities were identified as the second highest potential cause of variability in Prednisone testing, with the first being dissolved gasses[5]. A key finding of this USP study was "...that switching from one set of vessels to another, similar set of vessels leads to significant differences in both mean percent dissolved and standard deviation, suggesting that the current geometric acceptance ranges may not be appropriate[5]."

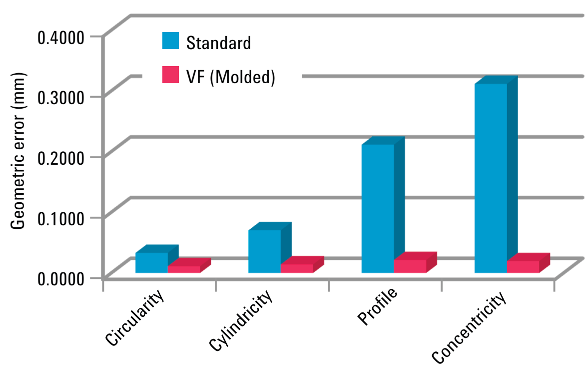
Vessel dimensions are critical in dissolution testing because they are directly correlated with differences in hydrodynamic mixing patterns and the volume present below the shaft. Analysis of multiple vessel vendors found high levels of variability between vessel suppliers resulting in "...as much as an 18% change in the volume of the dissolution media surrounding the paddle[6]." This study found that not only do vessels vary between vendors, but "...differences among dissolution vessels from the same source were also observed[6]." In addition to differences in volume below the paddle, differences were found in the distance between the paddle tip and vessel wall leading to:

"... heterogeneous shear rates... in the hemispheric region of the dissolution vessel. Given the differences in both the paddle-vessel wall clearance and in the volume of dissolution media surrounding the paddle, hydrodynamics in the hemispheric region of the vessel could be influenced by variability of the dimensions of this critical region of the dissolution vessel[6]."

Changes in the diameter between the vessels are also important as "inconsistent diameters will result in differing angular momentum[7]."

Of additional concern are aberrations in the vessel which can occur as spurs, fans, draws, depressions, and plains.

Standard versus VF Molded Vessels Comparison



Definitions:

Circularity (Roundness)
The measure of the sharpness of a particle's edges and corners.

Cylindricity
A three-dimensional geometric tolerance that controls how much a feature can deviate from a perfect cylinder.

Profile
A three-dimensional profile tolerance that describes the allowable variability in the contour of a surface.

Concentricity
A three-dimensional locational tolerance that describes the location of opposing points in cylidrical features with respect to a datum reference.

Figure 1. Shape comparisons between standard vessels and Agilent VF molded vessels.

These various deformations will also lead to increased variability versus a molded vessel. Further discussion of these deformations are found in Peter Scott's article "*Geometric Irregularities Common to the Dissolution Vessel*[7]."

Vacuum-formed or molded vessels offer tighter tolerance for one of the most critical components of the dissolution process. Agilent produces VF vessels to the tightest specifications possible to eliminate the variability often seen with hand-blown vessels. These vessels have tolerances that, for certain parameters, are more than 10 times tighter than what is specified on standard dissolution vessels. Although some manufacturers state that vessels should be fully interchangeable from position to position – or if one should need replacing – your company SOP's should ultimately dictate your actions.

Conclusion

Molded vessels provide a high level of confidence in vessel geometry and better consistency in hydrodynamics within the dissolution vessel. This consistency will help to achieve more ideal dissolution environments and better discrimination of dissolution samples.

Specification Comparisons

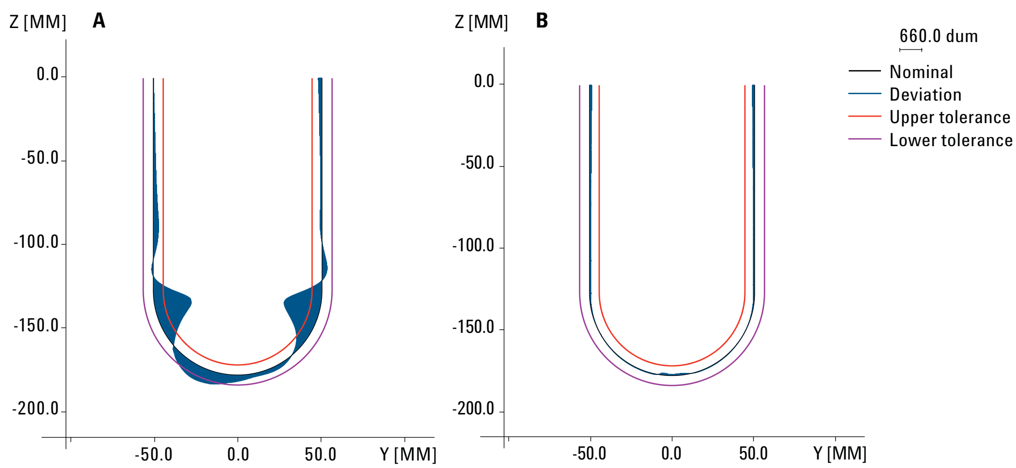


Figure 2. Variation in vessel shape between standard vessels tested by Agilent (A) and Agilent VF molded vessels (B), which exceed USP vessel tolerances. The center of the three lines indicates the ideal shape of the cylinder and hemisphere. The two lines drawn on both sides represent ± 0.3 mm from the center line. Visual images are not to scale, but have been enhanced to illustrate deviations in traditionally manufactured vessels.

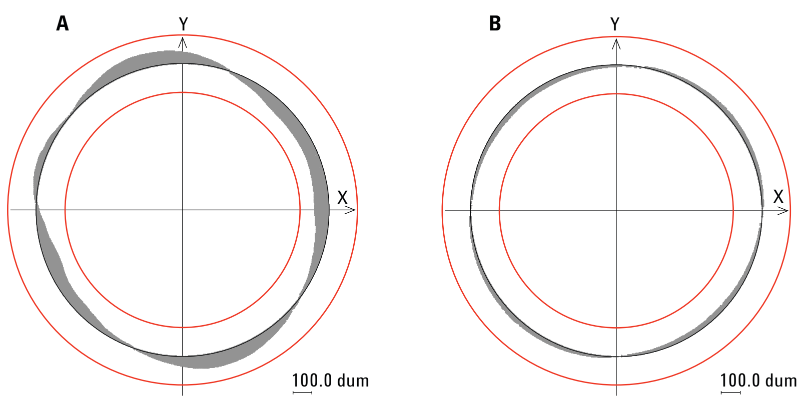


Figure 3. Variation in roundness between a standard vessel (A) and an Agilent VF molded vessel (B). The center of the three lines indicates the ideal shape of the cylinder and hemisphere. The two lines drawn on both sides represent ± 0.3 mm from the center line. Visual images are not to scale, but have been enhanced to illustrate deviations in traditionally manufactured vessels.

Ordering Information

Description	Part number
TruAlign VF molded vessel, 1L, for 708-DS	12-1501
EaseAlign VF molded vessel, 1L, for 7000/7010	12-1502
TruCenter VF molded vessel, 1L, for 7025	12-1503
TruAlign VF molded vessel, 1L, for 708-DS, verified	13-0010
EaseAlign VF molded vessel, 1L, for 7000/7010, verified	13-0020
TruCenter VF molded vessel, 1L, for 7025, verified	13-0030

Description	Part number
708-DS, 6-position - VF molded vessel option	G7910A #130
708-DS, 8-position - VF molded vessel option	G7911A #130
708-DS and 850-DS Dissolution Sampling System - VF molded vessel option	G7913A #130
708-DS and Cary 60 Multicell UV Dissolution System - VF molded vessel option	G7926A #130
708-DS and Cary 60 Fiber Optic UV Dissolution System - VF molded vessel option	G7927A #130

In addition to the standalone part numbers, the TruAlign version of the VF molded vessels is also an available option (#130) – replacing the standard TruAlign vessels – in all applicable Product Numbers as shown.

References

1. USP 35 - NF 30, Physical Test <711> Dissolution, p. 299. USP **2012**, Rockville, MD, USA.

2. Salt, Alger, “Enhanced Mechanical Calibration of Dissolution Test Equipment”, *Dissolution Technologies*, May **2011**.

3. “The Use of Mechanical Calibration of Dissolution Apparatus 1 and 2 – Current Good Manufacturing Practice (cGMP); Guidance for Industry”, U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), U.S. Government Printing Office: Washington D.C, January **2010**.

4. E 2503-07 Standard Practice for Qualification of Basket and Paddle Dissolution Apparatus; ASTM International; April **2007**.

5. J. Eaton, “Perturbation Study of Dissolution Apparatus Variables – A Design of Experiment Approach”, Dissolution Technologies, February **2007**.

6. G. Deng, “Evaluation of Glass Dissolution Vessel Dimensions and Irregularities”, *Dissolution Technologies*, February **2007**.

7. P. Scott, “Geometric Irregularities Common to the Dissolution Vessel”, *Dissolution Technologies*, February **2005**.

For more information, visit:

http://www.chem.agilent.com/en-US/products-services/instruments-systems/dissolution/dissolution-vessels/Pages/default.aspx

www.agilent.com/lifesciences/vfvessels

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