dx.doi.org/10.14227/DT310224P66

Impact of Vessel Inner Diameter in USP Dissolution Apparatus 2

David Curran[1,*], Geoffrey Neil Grove[2], Manasa Tsundupalli[3], and Xiaoling Zhang[4]
[1]*Medicine Development and Supply, GSK, Collegeville, PA, USA.*
[2]*Molecular Diagnostics Division, Bio-Techne, Waltham, MA, USA.*
[3]*TechOps, Incyte Corporation, Wilmington, DE, USA.*
[4]*CMC Regulatory Affairs, GSK, Collegeville, PA, USA.*

email: david.w.curran@gsk.com

ABSTRACT

Commercially available dissolution vessels used with United States Pharmacopeia (USP) apparatus 1 and 2 typically have nominal inner diameters of 100 or 104 mm. Little data are available in the literature to evaluate whether equivalent dissolution results are obtained when the same product is tested in both types of vessels. This study provides some additional data. Three immediate-release tablet products and a suspension product were tested in the two vessel types, across a range of paddle speeds. Superimposable dissolution profiles were obtained for all experiments. These data, although not exhaustive, suggest that these two vessel diameters may be considered equivalent from a hydrodynamic perspective, and thus, represent a low risk for method transfers between instruments that use vessels with 100-mm and 104-mm inner diameters.

KEYWORDS: Dissolution, vessel, inner diameter, *USP* <711>, rate, extent, paddle

INTRODUCTION

Dissolution is an analytical technique for assessing the likely pharmacokinetic performance of pharmaceutical formulations and is widely used for both quality control and research purposes. Transfers of dissolution test methods between laboratories, for example from a research and development site where the method is validated to a commercial manufacturing site, are critical to ensure consistent analytical results and proper control of product quality. However, method transfers are occasionally unsuccessful. Root cause analyses sometimes identify the use of different brands of equipment at different sites as a potential factor, but it may be less clear exactly which attributes of the instruments (if any) are causing different dissolution results. Minor differences in vessel geometry within United States Pharmacopeia (USP)-defined tolerances can exist and are sometimes postulated as a source of variability (*1*). The inner diameter of the vessel is one element of vessel geometry, but little data are available in the literature regarding the effect of this variable. Perivilli et al. conducted a computational study of the potential impact of this and other variables on fluid dynamics in the vessel, finding no significant impact from vessel inner diameter across the *USP* <711> specification range of 98–106 mm (vessel radius 49–53 mm) (*2*, *3*).

The present study aimed to investigate, across multiple products using different paddle speeds, whether changing the vessel inner diameter from 100 to 104 mm could give rise to variations in dissolution results. Vessels with inner diameters at the extremes of 98 and 106 mm were not available for this study. Although the same vessel is used for USP apparatus 1 (baskets), apparatus 2 (paddles) is more commonly used. Therefore, this study examined apparatus 2 only.

METHODS

USP Performance Verification Tests (PVT)

The USP performance verification tests (PVTs) were conducted with Prednisone Tablets RS (USP-proposed lot #: R072M0, Bulk Lot #: B160351, Item #: B559505) at Sotax (Westborough, MA) to establish a baseline with the specific vessels used in this study. Current USP guidelines for apparatus 2 testing were followed with manual sampling

*Corresponding author

(*4*). All runs were performed by the same operator on the same equipment. A Sotax AT Xtend dissolution bath and SOTAX Specord 200 plus UV spectrophotometer were used. Vessels with 100-mm and 104-mm inner diameters were tested. The exact dissolution vessels were shipped to GSK for use in this study.

GSK Pharmaceutical Products

Tests of four GSK products (three immediate-release tablets and a suspension) were performed using the same Sotax MultiDose G3 fully automated dissolution system with a Sotax AT bath. Vessels with inner diameters of 100 mm and 104 mm were tested over a range of paddle rotation speeds (20–65 rpm). Additional method details are proprietary.

Sample solutions were analyzed using online UV spectroscopy (Agilent 8453), with the exception of one tablet product (Product #3), for which samples were analyzed by reverse phase high-performance liquid chromatography (HPLC) (Agilent 1100 series). Dissolution profiles were generated according to each product's test method at GSK (Upper Merion Township, PA).

RESULTS AND DISCUSSION

The comparison of vessels with 100-mm and 104-mm inner diameters did not result in a significant change in either the mean result or repeatability (coefficient of variance) with USP apparatus 2 dissolution testing. This was true for both the USP PVT tablets (Table 1) and all GSK products tested in this study (Fig. 1–3), representing a range of rotation speeds from 40–65 rpm. Even with a suspension dosage form at very low rotation speed (20 rpm), where maximum sensitivity to hydrodynamics might be expected, no significant difference was observed (Fig. 4).

Table 1. PVT Results for Vessels with 100-mm and 104-mm Inner Diameter

Run Number	Geometric Mean (% Dissolved)	%CV	Vessel inner diameter (mm)
1	36	3.1	104
2	34	4.9	104
3	35	2.8	104
4	35	2.7	104
5	36	3.6	100
6	35	3.7	100
7	35	7.5	100
8	34	3.3	100

CV: coefficient of variation.

These results suggest that there is no significant difference in hydrodynamics when the vessel inner diameter is 100 or 104 mm, which is consistent with the predictions of CFD modelling (*2*).

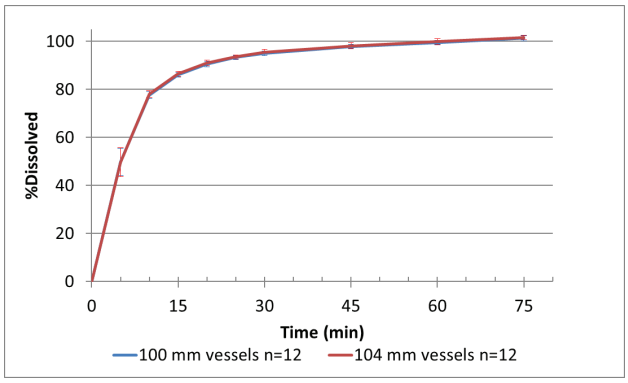

Figure 1. Dissolution profile of immediate-release tablets at 60 rpm in USP paddle apparatus (product #1). All error bars represent ± one standard deviation.

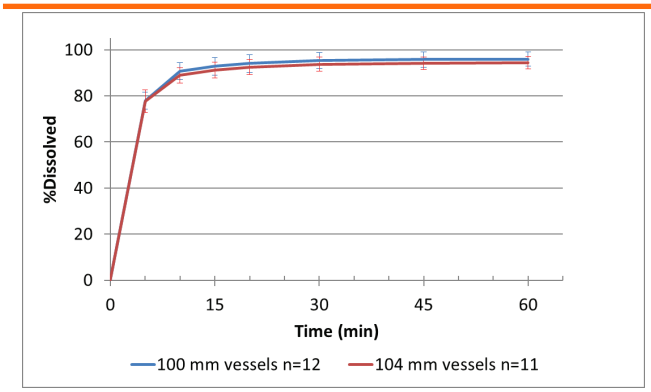

Figure 2. Dissolution profile of immediate-release tablets at 40 rpm in USP paddle apparatus (product #2). All error bars represent ± one standard deviation. Some experiments provided n = 11 replicates due to isolated instrument malfunction.

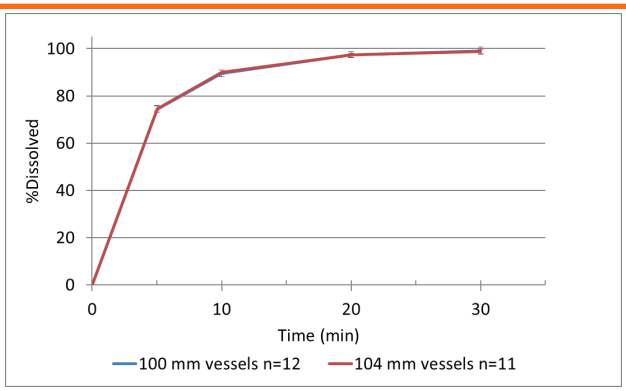

Figure 3. Dissolution profile of immediate-release tablets at 65 rpm in USP paddle apparatus (product #3). All error bars represent ± one standard deviation. Some experiments provided n = 11 replicates due to isolated instrument malfunction.

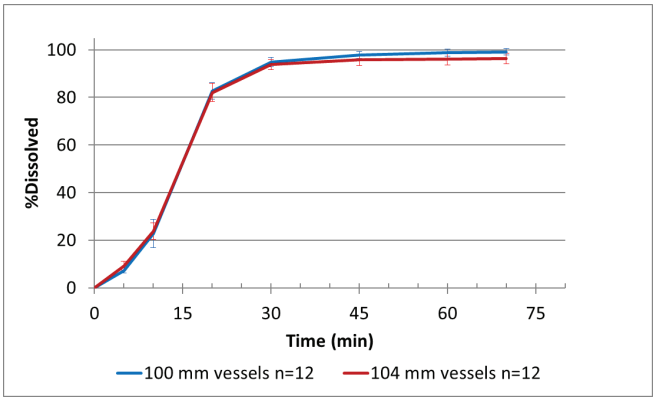

Figure 4. Dissolution profile of immediate-release suspension at 20 rpm in USP paddle apparatus (product #4). All error bars represent ± one standard deviation.

The authors cannot project whether extending the testing range to 98 and 106 mm, the minimum and maximum of the USP tolerance, would have an impact on results.

CONCLUSIONS

The data obtained in this study suggest that use of vessels with 100-mm and 104-mm inner diameters may be considered low risk for any cross-platform dissolution method transfer.

ACKNOWLEDGEMENTS

The authors would like to thank Sotax and the steering committee of the American Association of Pharmaceutical Scientists (AAPS) In Vitro Release and Dissolution Testing (IVRDT) community for their support of this study.

DISCLOSURES

David Curran and Xiaoling Zhang are paid employees of GSK. The other authors have no conflicts of interest.

REFERENCES

1. Liddell, M. R.; Deng, G.; Hauck, W. W.; Brown, W. E.; Wahab, S. Z.; Manning, R. G. Evaluation of glass dissolution vessel dimensions and irregularities. *Dissolut. Technol*. **2007**, *14* (1), 28–33. DOI: 10.14227/DT140107P28.
2. Perivilli, S., Walfish, S., Stippler, E., Liddell, M. R. Impact of select geometric and operational parameters on hydrodynamics in dissolution apparatus 2 (paddle apparatus): a design of experiments analysis based on computational fluid dynamics simulations. *Pharm. Res*. **2022**, *39*, 919–934. DOI: 10.1007/s11095-022-03272-4.
3. <711> Dissolution. In *USP–NF*. United States Pharmacopeia, 2010.
4. Dissolution Toolkit Procedures for Mechanical Calibration and Performance Verification Test; Apparatus 1 and Apparatus 2; version 2.0. Dosage Form Performance Laboratory, United States Pharmacopeia, 2010.