



Question and Answer Section

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The following questions have been submitted by readers of *Dissolution Technologies*. Margareth Marques, Ph.D. and Will Brown, United States Pharmacopeia, authored responses to each of the questions.

*Note: These are opinions and interpretations of the authors, and are not necessarily the official viewpoints of the USP. Email for correspondence: web@usp.org

Q What concentrations of hydrochloric acid are appropriate for use as dissolution media?

A The dissolution medium should be biorelevant, it should have a composition and a pH representative of what is found in vivo. Therefore, a range of hydrochloric acid from 0.1 N about 0.001 N is recommended to be used as dissolution medium.

Q Which agitation rates are the most appropriate for use with USP apparatus 1 and 2?

A When using Apparatus 1 and 2, the agitation rate should be kept within the range of 25 to 150 rpm. Rates outside this range are usually unacceptable because of possible irreproducibility of the stirring below 25 rpm and the introduction of turbulence above 150 rpm. The use of 50 to 100 rpm with Apparatus 1 and 50 or 75 rpm with Apparatus 2 is recommended in the FDA Guidance, Dissolution Testing of Immediate Release Solid Oral Dosage Forms. An agitation rate of 100 rpm with Apparatus 2 may be useful for testing some modified-release dosage forms.

Q Regarding dissolution testing of suspensions, which test parameter is the most critical?

A The dissolution process for suspensions is similar to that for tablets, with the difference that the disintegration/deaggregation step is bypassed. For suspensions one of the most critical aspects of the dissolution test is the introduction of the sample. The development of the dissolution test for suspensions should include a careful evaluation of the location within the test vessel used for sample introduction. If the sample is simply poured on the top of the medium, a homogeneous dispersion throughout the entire volume of dissolution medium may not result. In some cases, dispensing the sample in the bottom of the vessel using a syringe or a pipet can be used to advantage.

Q How should the tablets or capsules be introduced into the dissolution vessel?

A When using Apparatus 1, the tablet or capsule should be placed inside the basket with the basket dry, and then the whole system should be lowered down inside the vessel. Once at the proper height, the agitation is initiated. For Apparatus 2, the tablet or capsule should be introduced into the vessel with the medium still and the paddle motionless, the agitation is started up after the dosage form has come to rest on the bottom of the vessel.

Q What pore size filters should be used in dissolution testing?

A The filter pore size can range from 0.45 μm to 70 μm . However, if the filtrate has a cloudy appearance, or the filter becomes clogged, an alternative type of filter or pore size should be evaluated. Occasionally, depth filters grading from coarse to fine porosity may be necessary where the suspended materials might otherwise block the ultimate filter.

Q Should the tablet weight be included in the calculation of the quantities of active ingredient dissolved from a tablet?

A No, all the calculations in dissolution are done considering the label claim and not the actual content of drug (or tablet weight) in each individual tablet.

Q Can I use filter paper or cotton to filter the sample solution withdrawn from the dissolution vessel?

A Filter Paper and cotton are not the most appropriate filtration material to be used in dissolution. Gravity filtration is typically much slower than filtration from the syringe through a membrane filter assembly. Since the filtration should be carried out as soon as possible to stop the dissolution process from the active ingredient still present in the particulates, gravity filtration is not favored. Furthermore, the filter should be able to retain all the insoluble particles present in the dissolution aliquot. Any filter should be evaluated with respect to adsorptive interference of the analyte on to the filter. Interference to the analysis through the contribution of substances leached from the filter should also be examined.

Q Should I evaluate other dissolution medium if I know that the active ingredient has a good dissolution profile in a particular medium?

A The dissolution profile of an active ingredient is greatly influenced by the excipients present in the formulation, and for extended-release dosage forms this influence is much more important. If you are analyzing two different immediate-release formulations containing the same active ingredient, there is a good chance that the same dissolution medium could be used for both. But if you are working with modified-release dosage forms you need to find which is the most discriminating medium for each particular formulation.