Practical Solutions Newsletter

Year 2022 Volume 2

Agilent
Trusted Answers

10 Tips to Increase Productivity

Breaking Bad Dissolution Habits

Ten tips to help you identify and break bad habits in the lab that can save you time and cut costs.

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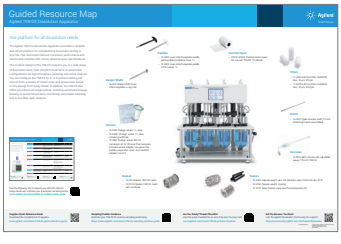

New Dissolution Poster Guides

Optimize the productivity of your Agilent dissolution instruments with our new quick-start guides.

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Questions You Asked

Read our expert's advice on how to best maintain the water bath for your dissolution instrument.

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Breaking 10 Bad Dissolution Habits

Bryan Crist, DissoAssist Consulting

Anecdotal evidence suggests it takes seven to 21 days to form a habit, although bad ones seem to become entrenched much quicker. What is clear is that once established, it can take much longer to replace bad habits with good ones. This might not be a problem unless those bad habits relate to lab tests, which could result in costly, time-consuming investigations into nonconforming data, or worse.

1 After all, it's just a dissolution test, isn't it?

Dissolution is one of the predominant tests for confirming the product performance of batches of dosage forms. It remains a technique-dependent test, in a practical sense, and should never be underestimated. Although laboratories maintain standard operating procedures (SOPs) and analytical procedures for their staff to follow during routine testing, problems can arise as a result of poor training, unapproved shortcuts, or unvalidated techniques, which could jeopardize the quality of the test results.

2 We don't have much time and I need to quickly get replacement media back into the vessel.

If your method calls for media replacement after each sample, this should be performed carefully. The recommended technique is to gently replace it against the shaft, just above the surface of the media.If it is pushed back into the vessel with force, it will upset the undissolved drug on the bottom of the vessel. This may alter dissolution results with a positive bias. The media replacement procedure must also comply with USP temperature and volumetric requirements.

Some important questions:

- **Did you learn about dissolution “on the job”?**
- **Have you adopted your mentor’s good practices?**
- **Have you found quicker ways to do your work?**
- **Are your SOPs properly reflecting the requirements specified in USP chapters <711> and <1092>?**

3 Deaeration of media? What a lot of hot air!

Although time consuming, deaeration is a critical issue for nearly all disintegrating solid oral dosage forms due increased turbulence from bubble formation. Dissolved gasses in the media form bubbles on all contact surfaces when heated, causing extensive turbulence for particles moving centrifugally along the vessel wall, which causes them to dissolve faster. Additionally, a paddle surface covered with bubbles has increased surface area and generates more agitation. Conversely, baskets covered with bubbles may slow dissolution as they can block the flow through mesh openings. It’s important to use only validated deaeration techniques.

4 Physical parameters? We don’t verify that stuff; metrology comes and checks the apparatus every six months.

An analyst is responsible for the verification of physical parameters prior to each test to ensure the apparatus remains in a qualified state and is clean and free from sources of residue and vibration. ASTM E2503 recommends operational checks to ensure proper mechanical alignment and condition of the apparatus’ components: paddle, basket, and vessel. If defective components are found, they should be replaced with components that possess certificates of conformance.

5 We just dump the media in and start the test when vessel 1 reaches 37 °C.

Dissolution media should be introduced carefully to minimize splashing and to protect the integrity of deaerated media. The media can be preheated to 37 ± 0.5 °C in the apparatus, but each vessel’s temperature must be checked and recorded minimally at the beginning and end of a run to document that the temperature tolerance was maintained. For accuracy of measurement at the end of the test, the stirring components should continue at their set speed until measurements are recorded. Evaporation covers should always be in place even for short (e.g., 30 minute) tests.

6 We found this dissolution vessel cleaning brush that works great!

Laboratory suppliers offer a dissolution vessel cleaning brush fitted with stiff bristles held in place with a twisted wire core. This tool absolutely destroys dissolution vessels by causing deep gouges and scratches on the interior vessel wall. A verified cleaning method should typically use a hot water/detergent wash and a soft cloth or nonabrasive pad, followed by several rinses with purified water. This will keep vessels in good condition. An alcohol rinse step may be needed for residues left by tablet coatings or gelatin capsule fragments. Top tip: line the sink bottom with a rubber mesh mat and the faucet with a rubber bumper to avoid vessel breakage during cleaning.

7 We remove six dosage units from the container and introduce them all when we start the apparatus.

Individual dosage units should be evaluated for defects prior to testing, and gloves should be worn to protect the dose and coating from moisture and oils on skin. Dosage units can be dropped at the same time, but they should be allowed to settle to the bottom of the vessel prior to paddle rotation. When manually sampling, it may be necessary to stagger the introduction of individual dosage forms to ensure that samples can be obtained and filtered within the required time. This is especially helpful if additional sample handling, dilution, or media change for enteric-coated products is required.

8 The ± 2% rule? We just stop the spindle rotation after 30 minutes to end the test, then pull and filter samples or centrifuge them.

USP chapter <711> states that samples must be withdrawn within ± 2% of the time that they are introduced. For a 30 minute test, the ± 2% window translates as ± 36 seconds (a 72 second window) centered on exactly 30 minutes. If sampling manually, it is useful to stagger dosage introduction. The sample must also be filtered during this timing window to stop the dissolution process. A centrifuge is not a replacement for clarifying dissolution samples since the 2% rule is violated by keeping particles in contact with media, where they continue to dissolve.

Summary

Many of these ten bad habits were discovered during investigations of aberrant data or by live audits of a dissolution environment. Unfortunately, these practices can be inherited through analyst-to-analyst training, or seen as a way to get more things done in a shorter time. They may have innocently developed over time, or procedures may lack sufficient rigor to prevent these types of issues occurring in routine dissolution testing.

9 We switched to plastic graduated cylinders for measuring due to breakage of costly glass Class A cylinders.

The USP requires a volumetric accuracy of ± 1%, which should be maintained during dissolution tests. Obviously, this begins with accurate measurement and introduction of media into the vessel. Since a one liter Class A volumetric graduated cylinder has an accuracy of ± 1%, it should be apparent that a plastic Class B cylinder cannot meet this accuracy specification. Dissolution media can also be measured by weight using a vessel placed onto a top-loading balance. This is highly accurate and especially useful for surfactant-containing media, due to inaccuracies that foaming media present in a graduated cylinder or volumetric flask.

10 It's time for lunch… I'll clean the apparatus when I get back.

Leaving acidic media to dry will affect the integrity of baskets over time as the acid dries and becomes highly corrosive on the surface of the mesh. The corroded baskets will no longer meet wire and aperture specifications if they are not cleaned or at least placed in water immediately after each test. Additionally, vessels, spindles, and any automated equipment should be cleaned according to validated cleaning methods. This will ensure that the apparatus is free of residue from the product or media under test. Each product or method should have its own validated procedure as some are more difficult to clean.

However they came about, these bad habits need to be replaced with good ones, no matter how long it takes. Too much is at stake to let them linger on. Analysts can refresh their day-to-day dissolution best practices by visiting the Agilent repository of dissolution webinars. These cover a variety of topics ranging from basic tips and tricks, to advanced applications.

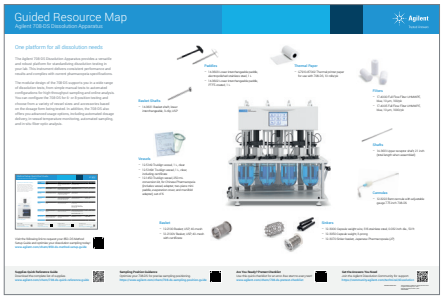
For more details, visit: www.agilent.com/chem/dissolution-webinars

New Dissolution Poster Guides Available for the 708-DS and 850-DS

Lee Dowden, Product Manager Dissolution Systems, Agilent

The Agilent 708-DS Dissolution Apparatus and Agilent 850-DS Dissolution Sampling Station are two of the most popular solutions available for your dissolution testing requirements.

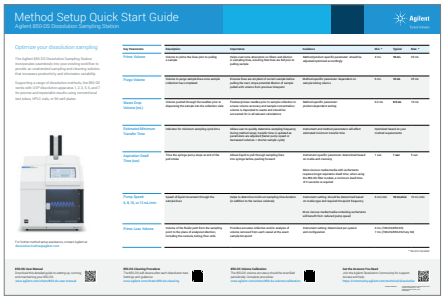
With so many of these instruments in use across the world we often get questions regarding parts, setup, and general use of these semi-automated systems. These new posters provide a quick resource tool for your laboratory, displaying critical information to help guide new and experienced users. If the information is not directly on the poster, QR codes will guide you to where to find exactly what you need.



708-DS Guided Resource Map

Whether you need to test oral dosage forms, topical products, implants, transdermal patches, or medical devices, the 708-DS offers ultimate flexibility. This poster keeps setup options at your fingertips. It also provides sample positioning instructions and a pretest checklist to eliminate testing errors.

PDF www.agilent.com/chem/708-DS-poster-guide



850-DS Quick Start Method Setup Guide

The 850-DS enables unattended sampling, filtering, and cleaning of your dissolution samples. This poster takes you step-by-step through the key parameters for method setup, and will quickly become a helpful reference for you in the lab. In addition, you'll get access to tips for volume calibration and cleaning.

PDF www.agilent.com/chem/850-DS-poster-guide

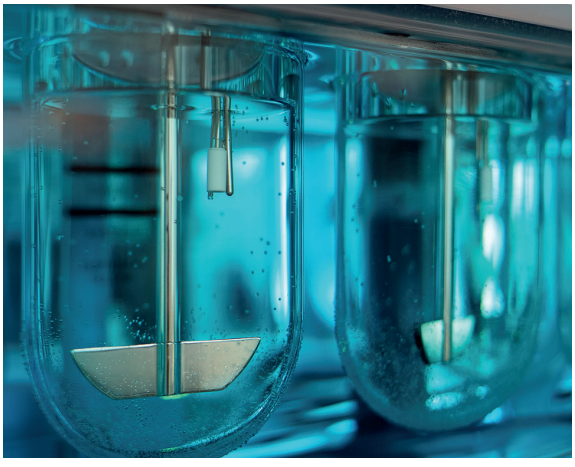
Request your printed copy

Customers in the U.S., Canada, Europe or India may request a free printed copy of each poster at the website listed below. The ordering terms and conditions listed on the website apply.

www.agilent.com/chem/dissolution-guides

Questions You Asked

Lee Dowden, Product Manager Dissolution Systems, Agilent



Advice for your water bath

Q What is the best way to maintain the water bath for my dissolution instrument?

A It is important to regularly check and maintain your water bath level and make sure it is free of contaminants. This will ensure the heater/circulator works efficiently and that there are no obstructions in the lines. Contaminants can include dissolution media, solutions from previous tests, cleaning agents, and algae growth. Also, over time the water will gradually evaporate – be sure to add water as needed to completely cover the media level in the vessels. This will improve heating efficiency and guarantee uniform vessel temperatures during your test.

It is also good practice to routinely clean out your dissolution water bath, ideally at least every three months and no longer than every six months. Additional cleaning may be required if the water bath is observed to be dirty and the vessels are not clearly visible. To clean the bath, first power off and unplug the heater/circulator. The water can then be drained with any residual liquid soaked up. The inside of the bath (including the underside of the vessel plate) can be wiped down with a soft cloth and a nonabrasive cleaner – be sure not to leave any towel debris in the bath, as this could potentially clog the tubing or pump.

Once clean, the bath is refilled with water to the appropriate level for the number of installed vessels. The heater/circulator may require an extra flush with clean water to remove any internal growth or accumulated debris. There are a few options available to inhibit any growth in the water bath – either using an algaecide or you may consider placing a UV light in-line, as found in aquariums.

Got a question of your own?

For specific advice, feel free to contact our Dissolution experts at the Dissolution Hotline (dissolution.hotline@agilent.com).

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DE72854594

Published in the USA, March 18, 2022
5994-4349EN

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