

# AGILENT TECHNOLOGIES PRACTICAL SOLUTIONS NEWSLETTER



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DAN SPISAK, AGILENT PRODUCT MANAGER, DISSOLUTION

## THE 280-DS MECHANICAL QUALIFICATION SYSTEM— NOT JUST AN AGILENT THING

Qualification of your dissolution apparatus doesn't have to be a dreaded event... or time-consuming... or risky

In fact, the Agilent 280-DS Mechanical Qualification System (MQS) can make qualification of your dissolution apparatus quite the opposite of time-consuming or risky. By taking full advantage of the capabilities of the 280-DS, qualification actually becomes your best friend.

### **The current accepted practice: Waiting six months between qualifications**

For years, dissolution laboratories have heeded the tried-and-true recommendations from various regulatory agencies to qualify instrumentation every six months. This interval is extensively ingrained into maintenance calendars. If a qualification failure occurs—whether using the USP Performance Verification Test (PVT) or the ASTM/FDA recommended enhanced Mechanical Qualification (MQ)—an investigation ensues. First, to determine a reason for the failure; and second, to examine all the dissolution tests performed on the particular instrument. Much can happen in six months—and many experiments can be performed, especially in a busy laboratory.



**Agilent Technologies**

When Prednisone testing was the norm, and the procedure took a day or two to complete, the six-month interval may have made sense. Over the past few years, however, the situation has evolved. More and more laboratories are adopting the MQ procedure and measuring devices are greatly improved.

### **Rethink the six-month interval— and reduce potentially expensive, time-consuming investigations**

Using the 280-DS to complete the MQ takes about 15 minutes for paddles or baskets. If your entire qualification now only takes 30 minutes, there's no need to wait six months between procedures. By shortening the interval—let's use once per month as an example—you can:

- Reduce the amount of data generated that could potentially be called into question.
- Provide visibility to the actual data. No guessing as to the status of each individual parameter. The 280-DS software will even trend this data.
- Monitor specific conditions and resolve an issue before it becomes an "out-of-tolerance" value.

### **Redefine dissolution qualification and impart a "culture change" to your dissolution laboratory**

Use the innovative 280-DS with Agilent dissolution instruments as well as most other manufacturers that have an open-head design. Recent modifications have been made that expand this offering to Hanson Vision G2 models. Existing units can be updated to include this capability at the time of recalibration. Check out the 280-DS MQS or request a demonstration from your Agilent representative today!



Agilent 280-DS MQS Vessel Module

KAREN KRAUEL-GÖLLNER, AGILENT PRODUCT SUPPORT, DISSOLUTION  
 DAN SPISAK, AGILENT PRODUCT MANAGER, DISSOLUTION

## YOU ASKED, WE LISTENED: NEW INLINE FILTRATION FOR USP APPARATUS 3 AND 7

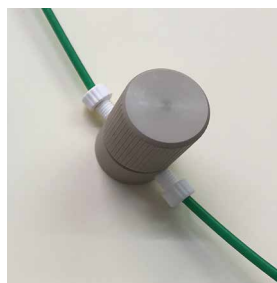
Filtration is an essential step in the dissolution process. Because dissolution continues until the sample is filtered, it is critical to filter immediately. A Full Flow Filter, when attached to a manual or automated sampling cannula, provides immediate filtration, which preserves the integrity of the dissolution sample.

Until now, the use of Agilent Full Flow Filters was limited to “rotating” apparatus (USP types 1, 2, 5 and 6). For “reciprocating” apparatus (USP types 3 and 7), inline syringe filters or a separate filtration module have been required when taking samples with an autosampler, due to limited space within the vessel itself.

### Introducing PEEK filter housings that can accommodate standard Full Flow Filters

The filter housing is placed inline—connected as part of the sample flow path—and supports any of the Full Flow Filter options available from Agilent. With these innovative filter housings, you can:

- Automate sample filtration prior to collection, an important step in stopping the dissolution process.
- Prevent undissolved particles from reaching the internal components of the sampling station—extending valve and tubing life.
- Simplify the cleaning process.



BIO-DIS Inline Filter



This option can be ordered with new systems as well as added to existing ones. Contact your Agilent representative for more information or ordering details. For questions related to the use of the filter housing or filtration in general, contact the Dissolution Hotline at [dissolution.hotline@agilent.com](mailto:dissolution.hotline@agilent.com).

Part Number	Description	Qty	Comment
K1200-00855	Apparatus 3/7 filter housing	7	Use when upgrading an existing installation
K1005-01956	Tubing assembly – sample cannulas to filter housing	1	Use when upgrading an existing installation
1005-1729	Tubing assembly – filter housing to sampling station	1	Use when upgrading an existing installation
5022-2155	Pack of tubing unions	1	Tubing connections for when filter housing is not required
G7977A or G7978A Option #150	Apparatus 3/7 filter housing kit	1	Use the option when ordering a new Apparatus 3/7 with 850-DS

BRYAN CRIST, AGILENT SCIENTIFIC AFFAIRS MANAGER

## DISSOLUTION SPECIFICATION SETTING FOR IR PRODUCTS: EMA DRAFT

Earlier this year, the European Medicines Agency released a draft entitled *Reflection Paper on the Dissolution Specification for Generic Oral Immediate Release Products*. Its contents were discussed during our last Dissolution Discussion Group (DDG) Online Meeting in August, and its primary focus pertains to immediate release dosage forms with at least 75 % of their active ingredient dissolving in 45 minutes or less.

The paper outlines general requirements for dissolution method development, including:

- **Suitable dissolution medium:** pH should be consistent with the physiological pH, and with sufficient volume to allow sink conditions.
- **Surfactants use:** Discouraged, and must be well justified for poorly soluble active drugs.
- **Method speed:** Suggested to begin with 50 rpm paddle, with higher speeds only allowed through justification. The focus on speed is primarily to reduce variability in the initial time points; higher speeds must not be employed if there is a loss of discriminatory power.
- **Demonstrating the discriminatory power of the method:** Use batches intentionally manufactured with different quality attributes that will adversely affect the disintegration or dissolution of the finished product.
- **Waiver of in vivo bioavailability:** Supported for highly soluble products if the equivalences of the test batches are equivalent to the reference drug product when run in physiological media at three different pH levels.

In addition, a concise decision tree is presented that outlines the principles for specification setting based on the biobatch dissolution results. Specifications are set after the previously mentioned discriminating dissolution method has been developed.

The decision tree describes the conditions for the Q value at a given time, as well as compliance at the stage 2 level consisting of 12 dosage units. It also outlines acceptance criteria based on Q values of 75, 80, or 85 % within time limits of 15, 30, and 45 minutes, relative to the results of the biobatch, within 10 %.

The document in its entirety may be obtained at [www.ema.europa.eu/docs/en\\_GB/document\\_library/Scientific\\_guideline/2016/05/WC500206407.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2016/05/WC500206407.pdf)

A recording of the applicable DDG meeting in August can be downloaded from the DDG Web site.

[www.dissolution.com](http://www.dissolution.com)



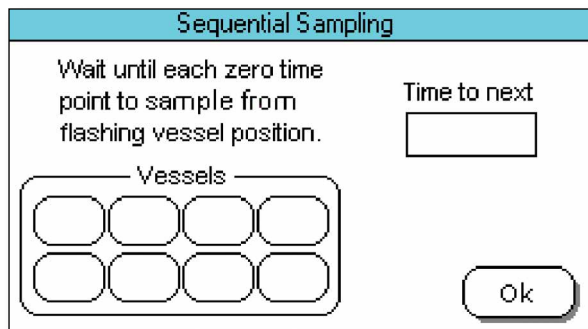
DAN SPISAK, AGILENT PRODUCT MANAGER, DISSOLUTION

## 708-DS DISSOLUTION APPARATUS – IMPROVED ACCESS CONTROL AND NOTIFICATIONS

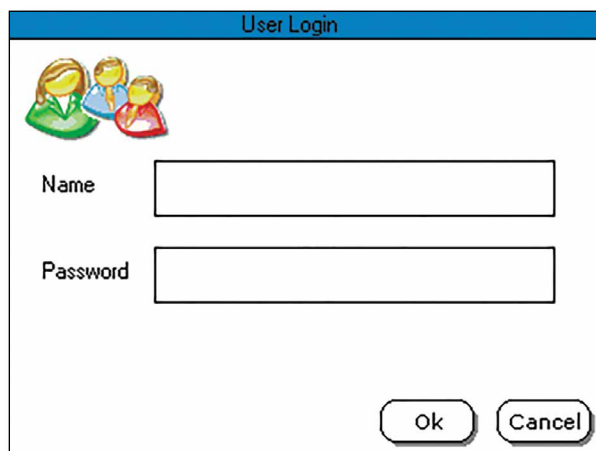
The capabilities of the Agilent 708-DS Dissolution Apparatus continue to expand. Our latest development, in the form of a firmware update, introduces several new features that bring clear benefits to any dissolution laboratory.

- **User notification for sequential manual sampling:** similar to initial dosage drop, the 708-DS screen will now display a graphic indicating when to pull the sample from each position.
- **Custom setting for vessel temperature probes:** the user can now determine how long to immerse the probes to obtain a stable, equilibrated temperature reading.
- **User access control added to manifold depth calibration screen:** an administrator can now govern who has access to the depth settings for the sampling manifold.
- **Enhanced sample point notifications:** additional alerts have been added—including increased frequency and volume settings—to signal when a sample time point is approaching.
- **Wider temperature range:** for special circumstances where a lower temperature is desired, the lower bath temperature limit is now  $5 \pm 0.5$  °C. Please note, temperatures below ambient require an external cooling source.
- **Individual user name and password control:** to better restrict actions and prevent unwanted changes, the 708-DS now supports specific user names and passwords.

Take advantage of these new features and upgrade today! Speak with your Agilent representative to coordinate a convenient time to install this update.



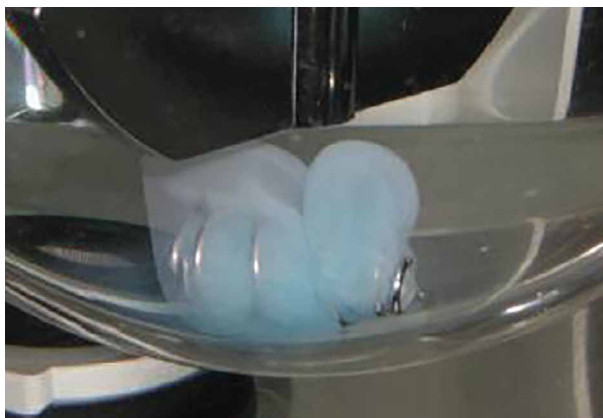
Sequential Manual Sampling



User Login

## QUESTIONS YOU ASKED

**Question:** My product requires an enzyme to break down cross-linked gelatin. The media already contains surfactants. Nevertheless, the product is still failing—even with the addition of the required enzyme.



Cross-linking and pellicle formation

**Answer:** The primary issue I think you are having is the incompatibility of the enzyme and surfactants in the media—namely, surfactants denature enzymes. Usually the enzyme helps to open the gelatin capsule (if the capsule has a cross-linking problem) and surfactants assist in solubilizing the drug product. In your case, the denatured enzyme is basically useless for breaking down cross-linked gelatin.

**USP Chapter <711> Dissolution was modified (official release August 1, 2016) to address this specific issue.**

It proposes a pretreatment step when surfactants or other ingredients are known to denature enzymes. During pretreatment, the test is repeated with the dissolution media without surfactant, yet containing the appropriate enzyme according to the media pH. The suggested pretreatment time is less than 15 minutes; at the end of this time, the missing surfactant contained in the remaining media is added.

The time for the pretreatment becomes part of the dissolution test, so if the total time for the test is 30 minutes and the pretreatment time is 10 minutes, the test continues for 20 minutes after the surfactant in the remaining media is added.

This approach must be scientifically justified, and we suggest that you follow the recommendations for *Dosage Forms Containing or Coated with Gelatin* section within the <711> Dissolution chapter.

## Agilent Sites and Services for Your Dissolution Workflow



Agilent Dissolution Systems Digital Source Book

[www.nxtbook.com/nxtbooks/agilent/dissolution\\_sourcebook/index.php](http://www.nxtbook.com/nxtbooks/agilent/dissolution_sourcebook/index.php)

Dissolution Exchange

[www.dissolution.chem.agilent.com](http://www.dissolution.chem.agilent.com)

Dissolution 1-on-1 Training

[www.dissolution.chem.agilent.com/learndissolution-1-on-1](http://www.dissolution.chem.agilent.com/learndissolution-1-on-1)

Dissolution Hotline (Email Address)

[dissolution.hotline@agilent.com](mailto:dissolution.hotline@agilent.com)

Dissolution Discussion Group (DDG)

[www.dissolution.com](http://www.dissolution.com)

Learn more

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