

AGILENT TECHNOLOGIES PRACTICAL SOLUTIONS NEWSLETTER

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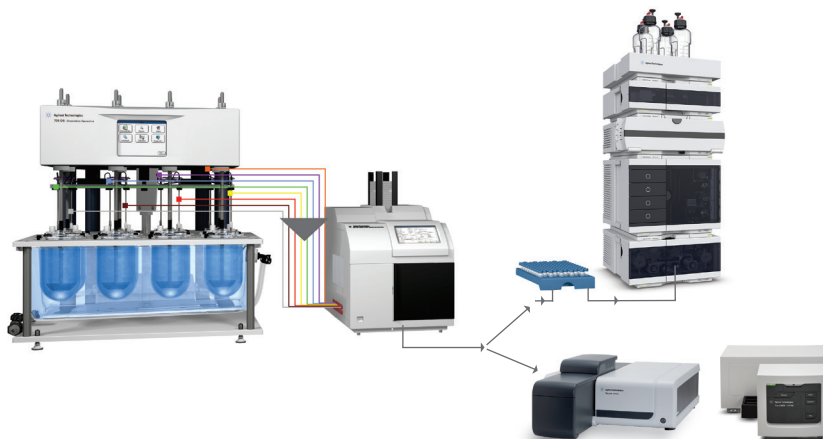
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DAN SPISAK, PRODUCT MANAGER, DISSOLUTION SYSTEMS

AUTOMATION OPTIMIZATION FOR UV-VIS AND LC DISSOLUTION SAMPLE ANALYSIS

There's no doubt that automating your dissolution testing makes life easier. In fact, once the system validation is performed for your product(s), the right solution allows you to complete other tasks without having to worry about taking that next sample. The benefits of automation, however, aren't just about productivity; having the correct instrumentation in place also brings reproducibility advantages. By having automated components perform the sample removal, filtration, and collection, analyst variability is eliminated, creating a consistent, repeatable workflow for each test.



Agilent Technologies

For many years, online UV-dissolution systems have led the way when it comes to simplifying both the dissolution test as well as the UV-Vis analysis and data processing. The Agilent Cary 60 and Cary 8454 UV-Vis spectrophotometers both provide complete solutions that automate this entire process.

But what about products that require a different type of analysis? Does your online system now sit idle and become useless for these methods? Not anymore.

Recent releases of software that power Agilent's UV-dissolution systems now fully accommodate the 850-DS Sampling Station. This is important because the integrated design of the 850-DS – comprising a pump, optional filter module, and sample tray – allows for movement of samples to the spectrophotometer for UV-Vis analysis or collection of samples into vials for subsequent LC injection.

Online UV-Dissolution system details with 850-DS sampling station and filter module

	Cary 8454	Cary 60
Closed Loop Sampling	Yes	Yes
Path Lengths (mm)	1, 2, 5, 10	1, 2, 5, 10
Automated Dosage Delivery	Yes	Yes
Automated Sampling	Yes	Yes
Temperature Monitoring	Yes	Yes
In-situ Fiber Optic Measurement	No	Yes
Sample Filtration	0.2 µm or 0.45 µm	0.2 µm or 0.45 µm
Sample Archival	Yes	Yes
Number of Apparatus	1	1 or 2

This means that the same instrumentation may be used for all your products, irrespective of the analytical technique required. The addition of the 850-DS filter module provides the 0.2 or 0.45 µm filtration often necessary for sample cleanup prior to injection. Not only that, but now all your dissolution methods and test data can be stored in a single, centralized database. Each system – comprising a 708-DS Dissolution Apparatus, 850-DS Sampling Station, Cary 60 or Cary 8454 UV-Vis spectrophotometer, and the respective software package – has its own distinct advantage depending on your specific method requirements, preferences, or familiarity.

The Cary 60 system utilizes Cary WinUV Dissolution software to control the dissolution system, data capture, and report processing. Compliance is governed by the Spectroscopy Database Administrator (SDA) and Spectroscopy Configuration Manager (SCM) to ensure that the necessary 21 CFR Part 11 requirements are met.

A new version of UV-ChemStation software powers the Cary 8454 system and provides the instrument control, method management, and reporting. Depending on your specific environment, compliance is managed by either the latest version of Security Pack software or can be integrated with Agilent's OpenLab Enterprise Content Manager software. Both versions of software have now been validated for use in a Microsoft Windows 10 environment as well.

Ultimately, your own internal requirements should determine what level or type of automation is right for your dissolution laboratory. These UV-Dissolution systems deliver all the advantages of online UV-Vis and offline LC sample collection with an organized, compliant software package at their core.

Either way, Agilent has you covered. For more information on the dissolution, spectroscopy, HPLC, or software solutions available, please contact your Agilent representative or visit www.agilent.com.

DAN SPISAK, PRODUCT MANAGER, DISSOLUTION SYSTEMS

PROGRESS REPORT: STAY CURRENT WITH 708-DS AND 850-DS FIRMWARE UPDATES

In keeping with our commitment to continuous improvement, Agilent is announcing updates to the firmware versions of both the 708-DS Dissolution Apparatus and 850-DS Sampling Station. The development and internal evaluation of these updates are now complete. All new units will be delivered with this firmware; existing units in the field may be upgraded at the user's discretion. We recommend coordinating an upgrade with Agilent's service team at the time of a periodic qualification or system maintenance.

The firmware updates add the following functionality:



708-DS – version 2.07

- Individual usernames/passwords added for access control
- Improved alarms for sample point notifications
- Additional graphics for user when performing sequential manual sampling
- Vessel temp probes enabled to measure temperatures down to $5\text{ }^{\circ}\text{C} \pm 0.5\text{ }^{\circ}\text{C}$



850-DS – version 3.0

- Individual usernames/passwords added for access control
- User levels customization now available by system administrator
- Volume calibration guide and storage of calibration history added
- Automated rinsing of internal reservoirs included as system clean option

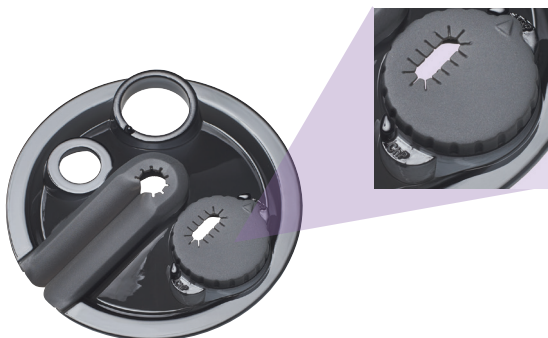
Your feedback is appreciated

Agilent is always looking for ways to make your dissolution testing easier. In fact, many of the improvements listed above came from our customers. If you have a suggestion or idea, let us know! We'd love to hear from you. Feel free to contact us at any time at dissolution.hotline@agilent.com. Please put "Feedback" in the subject of your message so we can filter these responses appropriately. You can also use the Dissolution Hotline for any dissolution-related questions.

ALLAN LITTLE, DIRECTOR OF MARKETING, DISSOLUTION SYSTEMS

DISSOLUTION SAMPLING LOCATION: MEET THE LATEST CP REQUIREMENTS

The internationally accepted current and historical position for withdrawing dissolution samples is “from a zone midway between the surface of the Dissolution Medium and the top of the rotating basket or blade, not less than 1 cm from the vessel wall.” (USP <711>) A recent change in the Chinese Pharmacopeia (CP) 2015 specifies this distance at 10 mm from the wall of the vessel. While this change may appear minor, it could have an impact on dissolution test results for products tested per previous CP or other international pharmacopeias. It will be critical for multinational companies to ensure their dissolution methods specify the sampling location.



Fortunately, the Agilent 708-DS Dissolution Apparatus is designed to accommodate this change. Simply repositioning the sampling cannula on the sampling manifold ensures that the samples are taken at the properly specified location. A new evaporation cover is available for the 708-DS that has a rubber gasket through which the sample and return cannula pass. Simply rotate this removable gasket 180 degrees to switch between the USP-prescribed location or the new CP requirement.

All new 708-DS instruments include the adjustable manifold and the newly designed evaporation covers. If you have an earlier 708-DS and would like to order a new manifold with the CP sampling location or new evaporation covers with USP/CP sampling capabilities, use the following catalog numbers. Please note that both the updated manifold and covers are required to achieve sampling from the CP location.

Description	Part Number	Quantity
708-DS evaporation cover, standard, for CP/USP sampling	K1005-05225	6 or 8
AND one (1) of the following:		
708-DS manifold, sampling only, 8-position, 1L	K1001-01172	1
708-DS manifold, sampling only, 8-position, 2L	K1001-01176	1
708-DS manifold, sampling/temperature, 8-position, 1L	K1001-01184	1
708-DS manifold, sampling/temperature, 8-position, 2L	K1001-01188	1

BRYAN CRIST, SCIENTIFIC AFFAIRS MANAGER

USP PHARMACOPEIAL FORUM UPDATE: <1236> SOLUBILITY MEASUREMENTS

The proposed new chapter "Solubility"—published in the USP Pharmacopeial Forum 43 edition, Volume 2 in March of 2017—provides greater understanding of thermodynamic equilibrium. It covers methods for estimating aqueous solubility, factors that affect solubility and solubility measurements, experimental methods for determining equilibrium solubility, methods for determining apparent solubility, and suggested bio-relevant media for conducting the studies.

After a lengthy thermodynamic discussion, the chapter reveals the importance of evaluating the solubility of an API with a good understanding of the three factors that affect the accuracy of solubility testing:

- Physicochemical properties: surface area, particle size, and crystallinity or amorphism
- Media properties: pH, polarity, surface tension, surfactants, co-solvents, and salts
- Measurement properties: temperature, time, and agitation method

With an understanding of these factors, the primary means of determining equilibrium solubility rests with the shake-flask method, which has been widely used for at least 40 years and is considered to be the most reliable method for determining solubility. This method has proven to be the most relevant way to determine aqueous solubility; although methods exist

for determining apparent solubility (potentiometric titration, turbidity measurements, and miniaturized screening), such methods are not considered suitable alternatives for true equilibrium solubility determined by the shake-flask method. The shake-flask method contained in the proposed chapter describes in detail the sample preparation, experimental conditions for equilibration of the solution, analysis of the solution, and reporting solubility results.

The final sections include bio-relevant media. The section on human media primarily covers human fed and fasted states for simulated gastric and intestinal fluids along with simulated colonic fluid. In veterinary medicine, however, solubility of API is the key to understanding the bioavailability of the drug over typical dissolution and drug-release testing. This is because it would be difficult to conduct drug-release testing for the diverse and complex GI conditions of the world's animal species. Several simulated fluids are contained for veterinary products, however, representing canine gastric and intestinal fasted state, as well as bovine gastric media representing a variety of pH levels and the presence or absence of short-chain fatty acids.

Although the comment period for this new chapter expired on May 31, 2017, it should appear soon as an official informational chapter in the USP based on the comments received.



QUESTIONS YOU ASKED

Enhancer Cell for Ointment Testing

Question: I am looking for in vitro study on an ointment and I would like to know more about the Agilent Enhancer Cell and if possible to use this instead of a Vertical Diffusion Cell (VDC).

Answer: The Enhancer Cell is an official compendial device for testing ointments, creams, and gels, and is contained in USP Chapter <1724> as the Immersion Cell. Both the VDC and the Immersion Cell are diffusion cells and should be interchangeable, but if an existing method for an ointment references the VDC exclusively, then a validation would need to be performed to allow the use of the Enhancer Cell as an alternative method. Otherwise, either cell may be used in analytical and product development.

The Enhancer Cell offers many advantages over the VDC; temperature control of the membrane and donor compartment, ease of sampling and media replacement, ruggedness over the fragile VDC components, and most importantly, the ability to use with existing dissolution apparatus and sampling equipment.

Several online sources are provided below where you may obtain additional information on the Enhancer Cell.

- **Agilent Dissolution Source Book**

http://www.nxtbook.com/nxtbooks/agilent/dissolution_sourcebook/#/16

- **Agilent Video Tutorial**

<https://www.youtube.com/watch?v=K9eiVPOLoNM>

- **Agilent Website**

[http://www.agilent.com/en/products/dissolution/accessories/enhancer-cell-\(immersion-cell\)](http://www.agilent.com/en/products/dissolution/accessories/enhancer-cell-(immersion-cell))

- **Access Agilent Newsletter Article**

<https://www.agilent.com/en-us/newsletters/accessagilent/2015/jul/topicals?cid=11649>

Routine Maintenance for 850-DS Sampling Station

Question: How often should I replace the tubing that connects the sampling cannulas of the dissolution bath to the sampling station?

Currently during annual preventive maintenance, we also replace all the internal tubing of our sampling station. But I am concerned that the external connection tubing will start to wear, and this tubing is easy to kink.

Answer: Actually, the tubing may last years without replacement depending on how well it is routinely cleaned; even the internal tubing that you are regularly replacing should last for years. Otherwise, it may be replaced in the event of damage from excessive crimping such as setting something on the tubing and crushing it. Buildup of residue or the appearance of discoloration may occur, but these may be kept to a minimum with regular cleaning cycles immediately after the run.

So, there is really no minimum period for replacement, and we would suggest that the instrument should not be disturbed, or should at least be moved around as little as possible to avoid potential damage to the tubing by keeping it away from other equipment which may be placed on top of the tubing. The connections may wear from repeatedly changing the sample tubing connections, but this should be minimized for a dedicated online collector.

Agilent Sites and Services for Your Dissolution Workflow



Agilent Dissolution Systems Digital Source Book

www.nxtbook.com/nxtbooks/agilent/dissolution_sourcebook/index.php

Dissolution Exchange

www.dissolution.chem.agilent.com

Dissolution 1-on-1 Training

www.dissolution.chem.agilent.com/learn/dissolution-1-on-1

Dissolution Hotline (Email Address)

dissolution.hotline@agilent.com

Dissolution Discussion Group (DDG)

www.dissolution.com

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