Practical Solutions Newsletter

Agilent
Trusted Answers

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Dissolution Mysteries Solved: Interview with a Dissolution Expert, Part 3

Eleanor Lovelock, Technical Writing, Dissolution Systems

In the previous editions of Practical Solutions, we've been interviewing a true dissolution expert: Mr. Bryan Crist. Bryan is a deeply respected dissolution expert who has sat on committees for the USP and overseen some critical changes within dissolution. This is the final part of the series with Bryan.

Figure 1. Getting formulations to market faster.

Interview, part three

We sat down with Bryan to ask him some questions about both the fundamentals and more complex aspects of dissolution.

Practical Solutions (PS): In terms of companies' manufacturing processes, could you give some insight into how you think QC/QA automation increases the productivity of getting new drug formulations to market faster?

Bryan Crist (BC): Dissolution is one of those areas that has to be developed as a drug product is being developed. We need to know how well a drug performs, down to its particle size and its release rates and how soluble it is in order to design, test, and apply the best apparatus to test that product. Selecting automation wisely can really help the whole process. In the beginning, you're testing so many different formulations that you're really trying to optimize the process.

"Working with Bryan is very satisfying and educational, as he has the best hands-on experience ever. We have been able to compare notes of problems and mishaps in the field to improve the guidance for analysts as we share the quest for the best, most accurate test possible."

– Vivian Gray,
Editor of Dissolution Technologies

Automated or semi-automated approaches actually get very good utilization out of your analytical equipment, as it also allows a lot of work to be done unattended outside the normal workspan. If there are long runs that need to run for a day or two, these can be automated.

Figure 2. Drug formulations are always improving.

Or you may be able to start another run in the middle of the night when you're not there, then you come in, and in the morning the samples are there to process. It's a lot like buying time. You can achieve a lot of advantages via this throughput to assist the formulators and their drug form optimization process.

Automation is like buying time

PS: You were one of the cofounders of the Dissolution Discussion group (DDG). It's been very important connecting chemists with chemists, getting a conversation going, and really engaging in topics that are hot to that particular group. From your experience moderating the DDG, what would you say are the key interferences that a dissolution tester should aim to eliminate during their test?

BC: It's interesting. I teach a lot of method development seminars for dissolution. When I begin, it seems that all the questions are of a fundamental nature. Like any building that requires a good foundation, I think sometimes we jump right into the meat of developing something without paying very close attention to the status and condition of the instrument and how we're interacting with it.

The reason I bring that up is because one of the biggest interferences in dissolution is simply vibration. It produces an action that can help in physically breaking down a product. If instruments such as fume hoods, ultrasonic baths, shakers, different mixers and so forth are present, these impart vibrations through the bench.

"[Bryan's] awareness of technique and vast experience has made him well-suited to be a teacher, advisor, and researcher.

He has been a regular contributor to the literature through articles in Dissolution Technologies, along with several book chapters, [and] he has been a valuable advisor to the mission of Dissolution Technologies."

– Vivian Gray,
Editor of Dissolution Technologies

This can affect the apparatus to a point where, for example, an immediate release product that is defective and isn't performing correctly can release faster and pass thanks to the vibration.

It's a little scary when you think about it. We don't think of many immediate release drugs as being lifesaving but there are quite a few that are. They need to perform well. The analyst's job is to find and detect those that don't perform correctly under validated conditions. There are many other things that could affect the dissolution test, but what takes a lot of attention and good training in the fundamentals is ensuring the test is carried out correctly.

One of the biggest interferences in dissolution is simply vibration

PS: What do you envisage as the greatest challenges coming up for formulation chemists and manufacturing teams delivering twenty-first century drug-compliant dosage forms?

BC: It seems like in a dissolution world we're in a constant game of catch-up. The innovators of the drug product are creating dosage forms that are very good. For instance, the development of our Agilent 400-DS Apparatus 7 was done in coordination with laboratories that were developing coronary and arterial stents. Again, these release nanogram or picogram levels over a period of time; a very small volume, and no traditional dissolution apparatus at that time could go to those levels. Looking ahead we have to realize that there are even more numerous challenges and we have to be able to work with the industry to accomplish those. We've been very, very fortunate to have good collaboration efforts, not just in the pharmaceutical companies manufacturing, but also with academia.

Some of these early challenges can be resolved, and then, of course, also collaborating with major pharmaceutical manufacturers is key.

PS: Bryan, thank you so much for your time today. It's been a real pleasure to interview you.

BC: You're very welcome. Dissolution is a two-way street; I've only learned from somebody that's learned from someone else. Thank you very much for the interview—I very much appreciate it.

Questions and answers have been adjusted for clarity.

Bryan Crist
Dissolution Expert

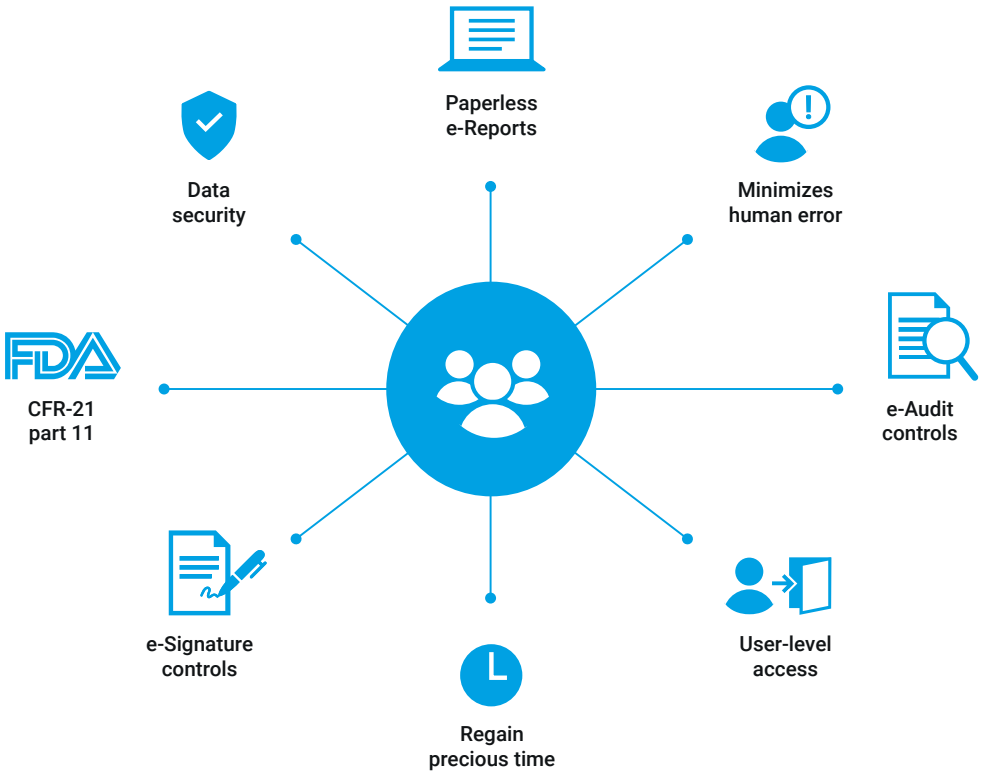
Bryan is internationally recognized as an expert in the field of dissolution, with more than 35 years of pharmaceutical testing experience.

The DWS Advantage: A Triple Release for Dissolution Success

Lorraine Kay, Global Product Manager

We're focused on making your lab successful, and that's exactly what our new triple release of Agilent Dissolution Workstation Software (DWS) version 1.7 offers. The key focus is to empower you to deliver in your role by facilitating a compliant environment, delivering paperless reporting, offering easy auditing and secure operations, and maintaining data integrity.

The Agilent Dissolution Workstation Software (DWS), including core software, 280 DS, and 400 DS versions offer you and your team a dissolution ecosystem of knowledge while ensuring that you're working in a compliant environment. The DWS advantage enables complete operational control and automation, structured user-level permissions and access, multilevel e-Signature reporting and so much more.



Set and forget with automated backups

Your SQL database is safely backed up as regularly as you need, and at a time that is convenient for you.

The choice is yours to overwrite previous files or append the current backup. What's more, you can select the local workstation or client server destination of your choice, giving you the option to set up your backup hassle-free.

Enhanced e-Signatures

Offering up to five authority levels with optional forced priorities, customizable to suit your needs gives the ultimate flexibility with control. Also, all electronic signatures are permanently linked to the test results and any attempt to sign a set of results using an invalid user identification or password is automatically recorded in the system audit trail. This security feature enables users to successfully work in a compliant environment and ensures data integrity.

Audits made easy

DWS 1.7 provides a System Audit Trail at your fingertips. Every action is date and time stamped, with user ID, reason codes, and event descriptions documented. You can even create a Difference Report that shows and documents exactly what was changed, by whom, when and why.

Together, these features offer laboratory managers and their analysts paperless, secure reporting functionality with user-defined labels, optional displays, and detailed e-Audit trails.

Controlled flexibility that delivers security and structure for your analysts' accounts

Structured permissions and defined user-level access is implemented with ease. Adding or restricting users to specific groups allows for easy access management and establishes operational access in the laboratory.

Each analyst can have predefined, tailored user access. This is extremely valuable for laboratories that wish to control access to hardware configurations and method files.

Nanoparticle success has arrived

We are pleased to present the newly-introduced Agilent NanoDis System. New functionality delivers end-to-end operational control, complete system automation, and nanoparticle dissolution testing success.

NanoDis functionality ensures that only compatible parameters are permitted and available. The new NanoDis comes preloaded with default settings to enable your success.

Looking for more info?

To find out more about the DWS advantage and how you can benefit from paperless reporting, having auditable, secure operations and data integrity, contact your Agilent representative or email the dissolution hotline at dissolution.hotline@agilent.com

850-DS Sampling Station Gains Major Firmware Update

Lee Dowden, Product Manager, Dissolution Systems

The Agilent 850-DS Dissolution Sampling Station continues to be a valuable choice for improving efficiency in the laboratory and automating dissolution sampling. At Agilent, we understand that updates and changes are necessary as the field of Dissolution changes and progresses. Valuable user feedback helps us develop a continuous improvement plan to meet your needs.

Dissolution portfolio for small volume

This latest update to the 850-DS Dissolution Sampling Station includes the following key features:

- Tray replacement with new vials/tubes at any time during the test
- Replacement media function added for Agilent USP Apparatus 3 (Reciprocating Cylinder) and Agilent USP Apparatus 7 (Reciprocating Disk)
- Replacement media workflow improved
- Sampling manifold remains in the lowered position until media replacement is complete
- Simplified method table writing – RPM defaults to previous timepoint RPM
- Increased temperature monitoring range – now monitor below 30 °C
- Autocalculate accounts for waste-drop volume and sampled amount, the only volumes removed from the system during sampling
- Improved calibration sequence with filter plate module

Same filter plates, different name

You may have noticed a slight change to the filter plates. This is only in name, and not in quality. GE Whatman are now called Cytiva.

Figure 4. Agilent 850-DS Sampling Station

Contact us

You are still supported by the same team as before so for any questions related to these filter plates, please contact the Agilent dissolution hotline at dissolution.hotline@agilent.com or your local Cytiva representative.

Questions You Asked

Q We have been using the Agilent Cary 60 Fiber Optic UV Dissolution System with great success. We have, however, found a problem with a product where its placebo can influence the medium in the vessel, making a cloudy solution. The percentage of dissolved product in the medium was bigger than when we were using an autosampler with a filter and a manual spectrophotometer. We suspect it might be the placebo, but we're not sure. What would you suggest?

A We're glad to hear you have successfully implemented methods with the Agilent Cary 60 Fiber Optic UV Dissolution System.

For the issue of placebo effects, this is a problem with fiber optics. As you have stated, the results will be different with or without filtration. One thing to try is to use the correction wavelength in the software. This can be used to correct for any placebo or scatter affects you may have, which could account for the increase in percentage dissolved. The correction can be found in the spectrometer section of the method. You can then select to do the correction and enter the wavelength required. To determine the wavelength you should scan a standard solution and a placebo solution. You would then choose the best wavelength that has little/no absorbance from the API but shows an absorbance (or scatter) from the placebo. This scatter effect should be consistent across wavelengths.

Once the correction wavelength is applied, the method will perform all measurements at the analysis wavelength and the correction wavelength and then correct for the result. This should bring the percentage of dissolved results down as expected.

If you have any further questions, please let us know. Hopefully this helps resolve your problem.

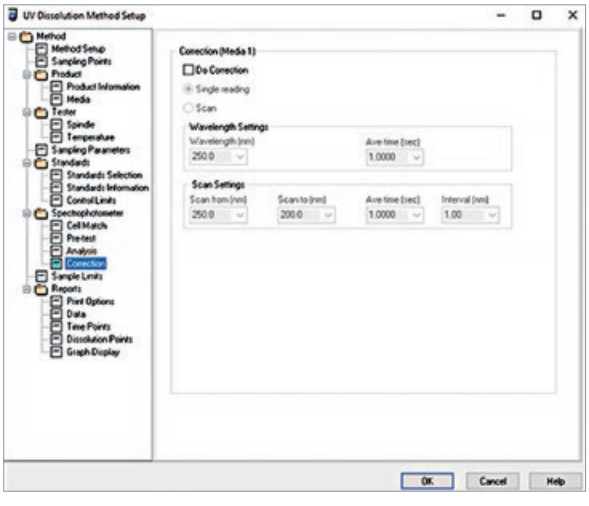


Figure 5. Correction for spectrometer section.

Got a question of your own?

Submit it to our dissolution hotline at dissolution.hotline@agilent.com for an answer.

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1-800-227-9770
agilent_inquiries@agilent.com

Europe
info_agilent@agilent.com

India
india-lsca_marketing@agilent.com

Asia
Pacificinquiry_lsca@agilent.com

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