Dissolution News

Issue #012 – End of Summer 2020

Dear all

These eight first months of the year 2020 have shown that things can get worse without notice. So, we wish you and your families all the best for the end of this complicated year.

Enjoy the read and stay healthy.

René Fässler
Product Manager Dissolution
USP 1,2,5,6

Michel Magnier
Product Manager Dissolution
USP 4

Responsibilities

Product Management Dissolution
USP 1,2,5,6: René Fässler
USP 4: Michel Magnier

Business Development Management
Due to recent organizational changes, the BDM MUE (Market Unit Europe) team is now reporting to Rui Fraga. This will combine the project management of Development Projects with the organization of the BDM efforts throughout the MUE team. No procedural changes between the BDM MUE team and Sales is expected to occur.

Rui Fraga
Project Management Officer

Why is Dissolution so beautiful?

Dissolution testing remains a supra-indicator of solid and semi-solid dosage forms manufacturing quality. It also helps generic companies obtaining biowaivers to offer patients lower cost treatments while increasing the understanding of APIs and formulations. Ultimately, thousands of batches are released each year using dissolution results as a Key Performance Indicator (KPI).

In-Silico models and Data Management systems require data from an analytical measurement. There is no analytical finish without a sample preparation! At SOTAX, our historical start was preparing samples via the Dissolution test and dissolution testing remains our baseline today. As the Pharma industry has rapidly changed and consolidated over the years, our SOTAX disso systems have been continuously sold, installed and qualified without interruption.

In the following pages you will find new success stories, improvements, components, features, accessories, software versions and documents to help you further in your dissolution testing projects.

https://youtu.be/su2NlMFD4wk

Success stories

ATF Xtend™

Fully automated
self-cleaning dissolution

Our new generation of USP 2 Fully Automated Systems, the ATF Xtend™ is now operational and several systems on-line and off-line have now been installed, qualified and put in operation in the UK, Sweden and Switzerland. The ATF is already the next industry standard for Fully automated Dissolution testing. Our UK installed base is already impressive and has grown naturally on our successful MultiDose™ legacy and our recent strengthening of Services in the area.

Thanks to our new data management platform q-doc™ combined with EasyTouch™ control, the ATF Xtend™ is now working 24/7 in parallel with the ATS Xtend™ and AT Xtend™: semi-automated and manual systems.

No other generation of Dissolution testing systems has ever reached this level of synchronization which allows SOTAX customers to organize their whole workflow orthogonally: using the right automation level for the right method.

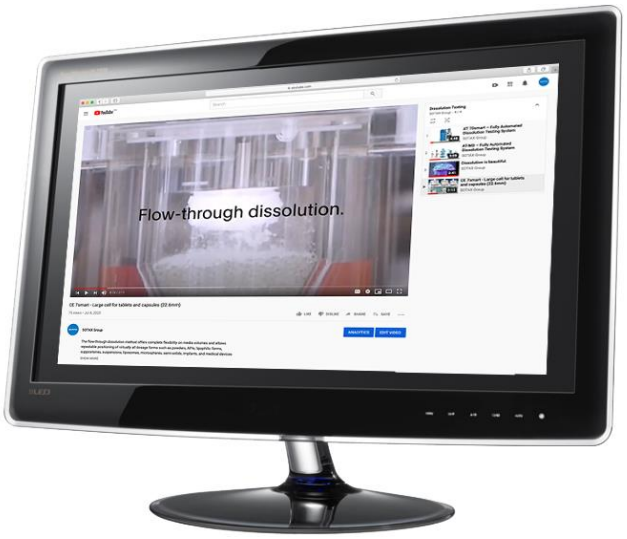
CE 7smart

The Flow-Through Cell CE 7smart systems are steadily spreading worldwide is support of various applications: tablets, capsules, powders, gels and creams, injectable suspensions and nano suspensions, suppositories, patches, medical devices. Several On-line seminars and continuous CE 7smart ordering made the lockdown pass more quickly.

New developments, new publications: our Flow-through Cell story remains robust thanks to our combined efforts. We thank you for that.

The first video of a new series of FTC videos has been posted in SharePoint and on our YouTube™ channel. It describes the large tablet for cells and capsules and provides nice insight to the flow-through cell technique in general.

Youtube LINK:
https://youtu.be/XNuVuuLx30c?list=PLHaNfBeN5qBNxjn1BOIZn5LRFkVsPc38H



Application Services in US

The US Analytical Group in Westborough has seen an increase in activity this year as our customers have had to change their way of working in order to continue to provide quality medications to patients in a timely manner. Based in Westborough's AR&D Laboratory, the US Analytical Group also acts as a BDM resource to Market Unit America (MUA).

Projects completed in the Westborough laboratory are at an all-time high this year and the scope of the work has been incredibly diverse. The group has completed or is currently working on the following types of applications:

- **Method Feasibility & Validation:** CE 7smart, AT Xtend, ATF, TPW, and AT50
- **Data Management:** q-doc, EmpowerLink for ASP

Carol Moynihan

Vivek Shah

Two Case Studies

Product and USP Apparatus Comparison

A dissolution customer was interested in comparing various forms of their product in a standard USP type 4 open loop apparatus. Because they did not have equipment in house and were interested in gaining both product and general dissolution knowledge, they decided to contract this work out to us.

Vivek Shah (Application Scientist) helped the customer to understand the compendial apparatus and was instrumental in guiding them through the typical application use as it related to their specific dosage form. They decided that they were interested in answering two fundamental questions:

- Can dissolution differentiate product types and are release rates relevant to in-vivo performance?
- What type of influence does USP apparatus have of the release rate and is there an ideal setup to be applied going forward?

Our lab found that the CE 7smart did a nice job differentiating the product types and that the release rates were relevant to the performance of the product in-vivo!

TPW Method Development and pre-validation

An existing TPW customer was having difficulties with a filed low dose product where the manual method was not very consistent. They had hoped that the TPW could help to improve throughput and repeatability of an inconsistent manual process.

While they had the instruments in house, they did not have the resources to investigate the automated method feasibility. The customer therefore placed an order to work with Carol Moynihan (SOTAX Application Scientist) to develop a plan to evaluate automation feasibility and upon success, run a series of pre-validation steps so that the customer could "on-board" the method in various commercial facilities.

This particular product was incredibly complex, but Carol was able to successfully navigate a series of challenges to guide the customer through the entire process.

In the end, this work will help the customer immensely by improving a cumbersome manual process with a more repeatable automated procedure. It was also a success story for SOTAX as the TPW as a tool became more valuable for them and they plan to invest in more units throughout their global sites to support to improved workflow… a true Win/Win!

DKSH Japan (previously known as Nihon Siber-Hegner) is one of the first foreign trading companies that was established in Yokohama in 1865. With strong Swiss heritage and an uninterrupted presence in Japan for more than 150 years, the company has contributed greatly to Japan and its culture, becoming today the leading Market Expansion Services provider in Japan. DKSH Japan offers products and services in the three specialized areas of Consumer Goods, Performance Materials and Technology.

We wish Nuoh Shin Lew and Nagashima Hideki all the best!

Changes in UV-Vis qualification

The USP, JP and EP have different requirements for the Qualification of UV-Vis spectrophotometers. As a global company we are supporting our customers but wish to harmonize our procedures. In partnership with Mettler and Analytik Jena we have now updated our Qualification procedures to the latest guidelines.

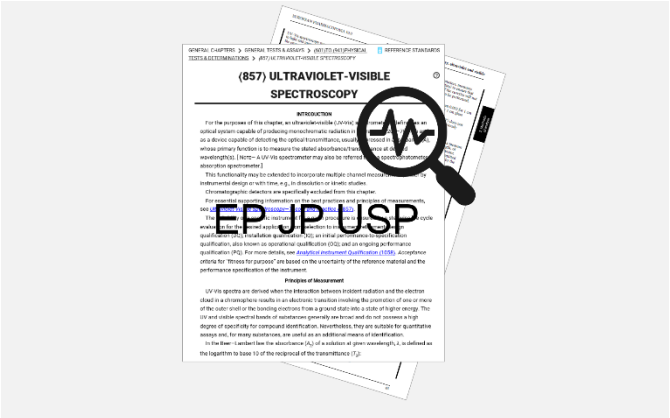
The following points should be taken into consideration

- the Qualification we are offering is based on the use of a UV-Vis spectrophotometer for Dissolution purpose
- our UV-Vis partners Mettler and Analytik Jena have different ways to handle these new requirements (additional modules or additional software modules). These parts will now be added by default to our system offers

Analytik Jena: the extra USP/EP Validation modules are only to be used in these two cases

- The customer does not want us (or dealer) to qualify the spectrophotometer with our own laptop
- The customer does not want to program qualification methods on ASpect UV main software.

Mettler-Toledo is using a combination of modules CertiRef™ and LinSet™



As a service for other UV-Vis brands the standard EP/USP UV-Vis Qualification will now be done including

- Baseline deviation
- Wavelength Accuracy will be done with Holmium, Didymium solution and filter
- Photometric Accuracy, precision and linearity will be done with Potassium dichromate (PDC) solutions (UV) and glass filters (Vis)
- Stray light will be done with Potassium Chloride, Sodium Iodide, Acetone and Sodium Nitrite
- Resolution will be done with Toluene in Hexane

Every additional requirement will be charged. (Special agreements in place being taken in consideration).

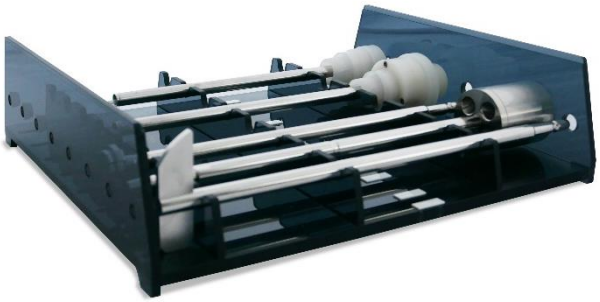
The Qualification according to JP will be done for the time being only in Japan. More details can be obtained through Video Conferences with our Dissolution PM Michel Magnier.

Dissolution accessories

New

We have redesigned our dissolution accessories to fit with our AT Xtend™ 6,7,**8** stirred positions design. The material used is Plexiglas GS. Note that the shaft holder can now accommodate manual, hollow shaft, USP 1,2,5,6 models.

P/N	DESCRIPTION
10692	Paddle Rack
10693	Basket Rack
10694	Shaft Rack
10696	Shaft cleaning station (bucket cover)



Low volume sampling with hollow shaft

New

An increasing number of customers are using biorelevant dissolution methods starting with a gastric phase of 250-300 mL before a media addition which moves the test to a higher pH. These methods were complicated to handle in the past due to sampling limitations.

P/N	DESCRIPTION
25230-01/-02 /-03	Hollow shaft PVDF for low Volume sampling elec. Polished / PTFE / gold coated (AT 70smart head*)
25213-01 /-02	Paddle / (PTFE)
25220-01	Inlet for Paddle

*Hollow shaft with standard AT head on demand.

Customized Insert for tablet drop (USP 2)

To insert oblong tablets in a repeatable way, we quickly engineered a guided insert (the insert fits in the existing tablet dropper). The modified guide helps the tablet to fall always in a reproducible way into the vessel. The ID of the guide hole was 8.5 mm. Other designs can be done on demand.

In-line degassing unit for CE 7smart Open system

New

A new In-line degassing unit is now available to degas dissolution media in an open loop system. This unit is quieter than before and can handle a flow rate of up to 1L/min. This unit is space saving (L365 x H135 x W150 mm) and can be introduced between the media selector and the pump. The degassing is done on one channel.

MS 47

Degassing

CP 7-35

P/N	DESCRIPTION
25834-01	In-line degassing unit for CE 7smart Open (L365 x H135 x W150 mm)

Note: the same unit is now used in the AT 70smart “Vacuum Degassing option”

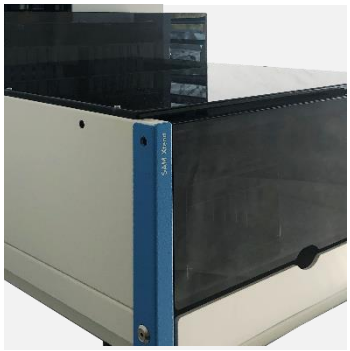
SAM M Cooling

Our cooling system is now available on the version M. The cooled racks are on the lower level of the SAM M. (No possible upgrade in the field). The cooling system principle is as described in Dissolution News 2 (cooling plates and Minichiller)

P/N	DESCRIPTION
24447-02	SAM M with cooling on Level 1 (at order)

SAM's new cover for light sensitive samples

Current protection shields mounted on the SAM are transmitting 92% of light. The new cover brings down the transmission to 21%, still allowing the vision of the process. These new covers can be selected as options or ordered as upgrade kits in the field.



Model	Part number (at ordering)	Part number (upgrade)
SAM SR	25777-01	25777-05
SAM S	25777-02	25777-06
SAM M	25777-03	25777-07
SAM M (cooling)	25777-04	25777-08

Various

Application Notes

- Gloss ←→ SOTAX Ref No.
  “BN10004EN_01_Reference Comparison”

- Remote Authentication q-doc
  “BN10016EN_01_Xtend RemoteAuthentication with q-doc”

Various documents

- Manual bath with q-doc
  https://www.sotax.com/sotax_worldwide/manual_dissolution_bath_audit_trail

- Excel spreadsheet for linearity calculation (OQ)

Current software versions

- EasyTouch™: 3.02.0
- WinSOTAXplus: 2.83
- q-doc: 4i

Note: drivers for Agilent 8453/4 are available in EasyTouch™ 3.02.0 / q-doc 4i

Recent publications

- Dissolution Technologies May 2020: description of Pr Diane Burgess (University of Connecticut), Dr Nikoletta Fotaki (University of Bath) and Mr Samir Hadouchi (SPS Pharma) presentations in AAPS (Association of American Pharmaceutical Scientist) / NIFDC (Chinese National Institutes for Food and Drug Control) joint workshop in Yantai (China) in May 2019.
  http://dissolutiontech.com/issues/202005/DT202005_A05.pdf
- Dissolution Technologies May 2020: A Look at Cleaning Effectiveness in Automated Dissolution Systems
  http://dissolutiontech.com/issues/202005/DT202005_A02.pdf
- In Situ Gelling Ophthalmic Drug Delivery System for the Optimization of Diagnostic and Preoperative Mydriasis: In Vitro Drug Release, Cytotoxicity and Mydriasis Pharmacodynamics
  P-L. Destruel, Ni Zeng, F. Brignole-Baudouin, S. Douat , J.Seguin , E. Olivier, M. Dutot, P. Rat , S.Dufaÿ , A.Dufaÿ-Wojcicki, M.Maury, N.Mignet, and V. Boudy
  https://www.mdpi.com/1999-4923/12/4/360
- Interpolymer Complexes of Eudragit® Coplolymers as novel carriers for Colom-specific drug delivery
  A.V. Bukhovets, N.Fotaki, V.V. Khutoryanskiy, R.I Moustafine
  https://www.mdpi.com/2073-4360/12/7/1459