CE 7smart
Flow-Through Dissolution System

In-vitro drug release testing in compliance with USP apparatus 4, EP, and JP
Configurations for various methods and analytical requirements
Specific flow-through cells for novel dosage forms
Ideal for small volume dissolution and poorly soluble compound testing

Tablets (immediate and extended release)

Capsules, pellets

API's, powders, granules

Soft-gelatin capsules, suppositories

Medical devices, stents, implants, coated lenses

Microspheres, nano-suspensions

Injectable suspensions

Semi-solids, gels, creams

Transdermal patches

CE 7smart

The flow-through cell is widely recommended for poorly soluble, modified / extended release, and low dose products. With the evolution of new drug delivery platforms, USP apparatus 4 has also been used for IVIVC studies and a growing range of dosage types.

Because of the highly flexible configurations, the ability to work in a variety of solubility conditions, different flow-through cell types, and enhanced control over the hydrodynamic environment, USP apparatus 4 continues to evolve to meet the changing needs of today's in-vitro release testing.

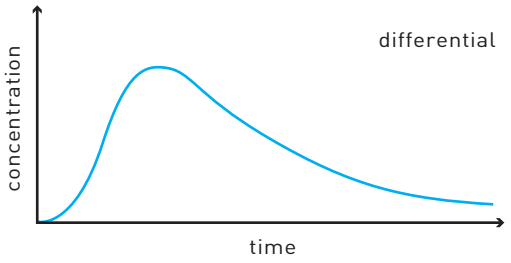
SOTAX is the pioneer in flow-through cell dissolution technology designing and having manufactured the very first instrument in 1973. Today, SOTAX is 1st in class with hundreds of companies using the CE 7smart for their important dissolution workflow.

→ CE 7smart
flow-through cell dissolution tester

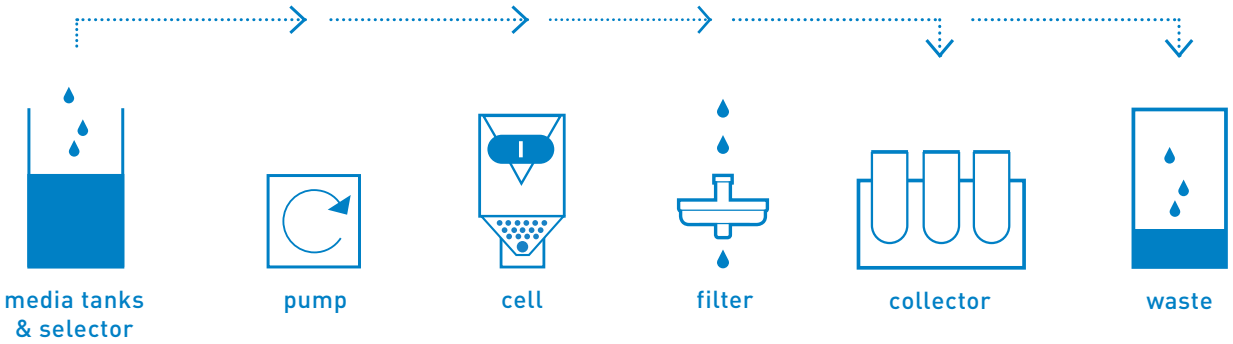
Open loop configuration

Originally designed for poorly soluble compounds where more than the compendial USP 1, 2 and 3 media volumes are required, the flow-through cell system has always been linked to "optimal sink conditions" allowing for flexibility in terms of media volume required.

In the "open loop" configuration, fresh media crosses the dosage form. Samples are collected as fractions within a defined time interval, analyzed on-line by a UV-Vis spectrophotometer, or collected off-line. The total amount of media is determined by the flow rate. This means that the influence of poor sink conditions on the test can be avoided altogether by using larger volumes of media without the need for solubilizing agents.



→ Open loop configuration



→ Open system off-line with media selector and splitting valve on fraction collector

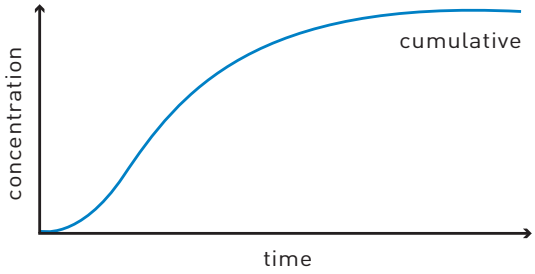
Automated media change

In the open loop configuration, it is possible to change the type of media that passes through the flow cell after predefined time intervals. Using the media selector, media is automatically switched to draw from a different source. Up to 3 different media can be programmed. Bio-relevant dissolution media can be used depending on filter performance. This feature is useful for performing IVIVC studies where the dosage form is exposed to the different pH's of the digestive tract. Studies have shown improved correlations due in part to maintaining sink conditions as well as differing hydrodynamics in the flow-through cell. It is also useful for enteric coated products, modified release and extended release products. Unlike the USP apparatus 1, 2 and 3 methods, where changing to a new media can be tedious, USP 4 simplifies this workflow allowing for a straightforward and documented media change.

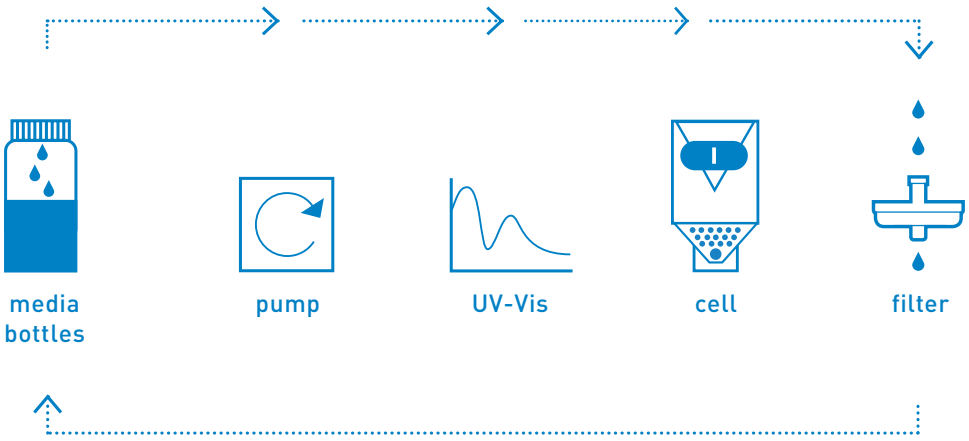
Closed loop configuration

In a closed system, the flow-through method is conducted much like a USP apparatus 1 and 2 experiment where a fixed volume of media circulates across the dosage form. Samples can be taken at predetermined times by an autosampler or read by an on-line UV-Vis spectrophotometer.

Results are expressed as a cumulative dissolution curve. Closed systems are ideal for dosage forms where solubility and sink conditions are optimal in a volume range from 25 mL to 5 L. USP 4 offers another possible way to compare results with traditional 250 mL, 500 mL, 900 mL, 1 L, 2 L paddle, baskets, and USP 3 methods. This method also provides advantages over other USP methods such as different hydrodynamic and mixing effects eliminating the coning or dead zones as well as sampling issues or sample introduction effects sometimes seen in USP apparatus 1 and 2.



→ Closed loop configuration



→ Closed system on-line with UV-Vis

Small volume dissolution and elution testing

As a direct result of low dose formulations such as drug eluting stents, implants, coated medical devices, injectables, and microspheres, the USP 4 method has evolved to fulfill even lower media volume testing. Within the medical device field, the term "dissolution" has been replaced by "elution" where the amount of drug released from a polymer coating or drug depot is measured.

These drug amounts are often so low that in order to meet LOQ issues for analysis, the total media volume had needs to be decreased. Note that (when compared with USP 1, 2) the dosage form remains in equivalent hydrodynamic conditions - whatever volume is used.

Cells for a variety of dosage forms

The CE 7smart is compatible with many different dosage forms.

① Tablets (12 mm cell)
This cell is described in the EP, USP, and JP as a small cell for tablets and capsules. An optional tablet holder is also described. It can also be used for suspensions, injectables as well as small medical devices and stents.
- EP 2.9.3 "Dissolution"
- USP <711> "Dissolution"
- JP 6.10 "Dissolution Test"

② Tablets (22.6 mm cell)
This cell is described in the EP, USP, and JP as a large cell for tablets and capsules. An optional tablet holder is also described. It can be used for parenterals, suspensions, and microspheres. There are a variety of holding devices developed for this cell. It is the most widely used of all flow-through cells.
- EP 2.9.3 "Dissolution"
- USP <711> "Dissolution"
- JP 6.10 "Dissolution Test"

③ Powders and granulates
This cell is used to determine the apparent dissolution rate of pure solid substances (API characterization) and of active substances in preparations presented as powders. It is also used for granule and bead formulations.
- EP 2.9.43 "Apparent Dissolution"

④ Drug-eluting stents
This cell is manufactured in PTFE and is used for medical devices like drug-eluting stents. It eliminates potential adsorption problems encountered with polycarbonate cells. The inner diameter can be custom manufacture to fit the medical device accordingly.

⑤ Suppositories and soft gelatin capsules
This cell has a special 2-chambers design which traps the lipidic excipients and allows the dissolution media to pass up to the filter.
- EP 2.9.42 "Dissolution Test for Lipophilic Dosage Forms"
- USP <1004> "Mucosal Drug Products - Performance Test"
- USP <2040> "Disintegration and Dissolution of Dietary Supplements"

⑥ Implants
This cell is used for small implants and has a small chamber to house the dosage form.

⑦ Large medical devices
This cell can be used for longer medical devices and has a maximum length of 83 mm.

Customized flow cells

Dosage form specific cells have also been created and designed based around these main models.
Customization includes inner diameters, cell length and dosage form holding devices.
A variety of holding devices can be designed for inside the flow-through cell:

⑧ Semi-solid adaptor
This cell is based on a 22.6 mm cell. An insert cup allows testing on gels, creams, and ointments with a permeation membrane.
- USP <1724 "Semi-solid Drug Products - Performance Tests"

⑨ Holding device for dialysis insert
This cell is based on a 22.6 mm cell. An insert holder allows testing on nano-particles contained in a dialysis bag such as the Float-A-Lyzer®.

⑩ Holding device for ophthalmic lenses
This cell is based on a 22.6 mm cell. An insert holder allows testing on drug coated ophthalmic lenses.

① ② ③

④ ⑤ ⑥ ⑦

⑧ ⑨ ⑩

Flow rate and importance of the pump

In the flow-through method, the pump is responsible for ensuring an important parameter: the flow rate of the media. The flow rate can be compared with the RPM speed of USP 1 and 2 or the DPM of USP 3.

The CP 7-35 digital piston pump has been specifically developed for the USP 4 method. This pump is equipped with 7 valveless ceramic pump heads ensuring a very high level of reproducibility and consistency. The flow rate can be adjusted between 4 and 35 mL/min, fulfilling the USP standard flow rate recommendations of 4, 8, and 16 mL/min. A useful method development tool is the pump's ability to have different flow rates per channel. This feature is advantageous during the development of a USP 4 dissolution method.

Another unique feature of the pump is the automatic calibration / validation option. For this purpose, the pump is linked to a balance (optional) and printer (optional). The pump automatically checks and adjusts its flow rate channel per channel based on user-defined volumes. The calibration protocol is then automatically printed out.

→ CP 7-35
piston pump

Analytical configurations

The CE 7smart can be fitted with either a UV-Vis spectrophotometer for on-line UV measurements or an autosampler for off-line collection into HPLC vials.

On-line analysis

For on-line analysis in an open loop configuration, a wide range of UV-Vis spectrophotometers can be directly linked to the CE 7smart. Using WinSOTAXplus Dissolution Software, on-line measurements can be taken at predetermined times.

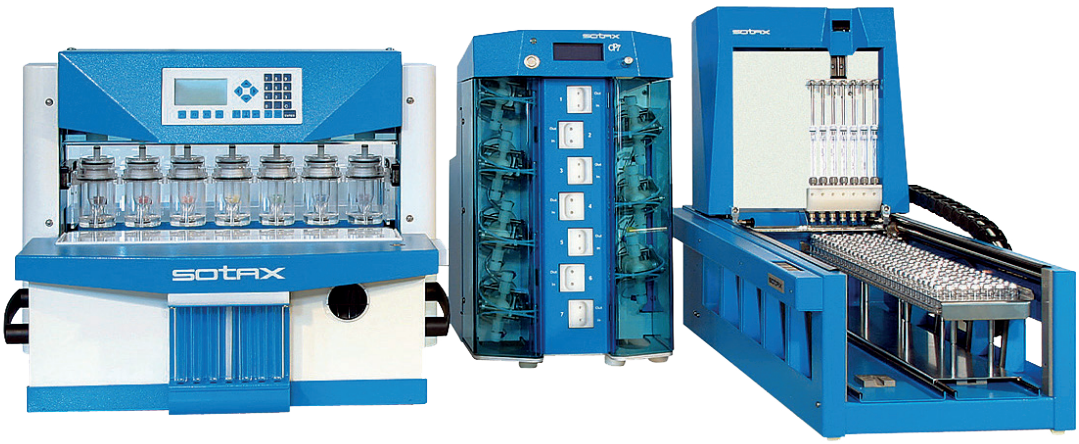
The system automatically reads the baseline for each cell, records raw absorbance data and corrected data, and calculates concentration and % drug release in a 21 CFR Part 11 software package.

→ CE 7smart on-line configuration

Off-line sample collection

For off-line analysis, the CE 7smart can be connected to an autosampler. Both off-line system configurations – open and closed loop – can be programmed via the firmware to collect sample volumes at predefined time points.

Methods can be protected as well as connected to a printer for temperature and method reporting. For 21 CFR Part 11 / Data Integrity compliance, it can also be controlled by WinSOTAXplus Dissolution Software.



→ CE 7smart off-line configuration

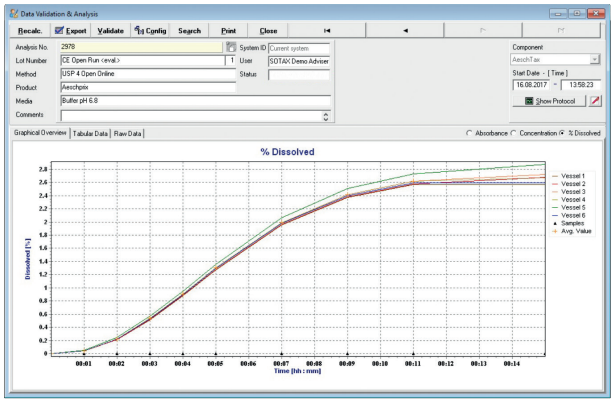
WinSOTAXplus Dissolution Software

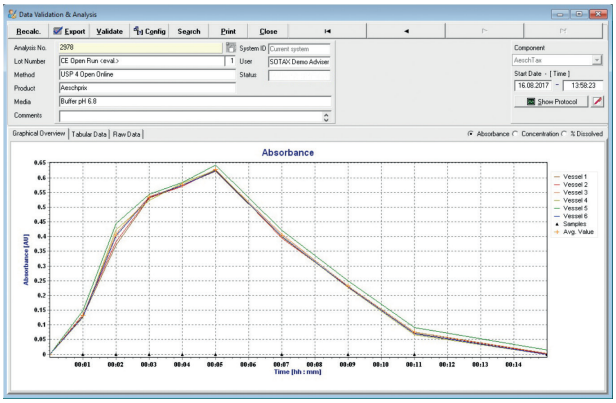
WinSOTAXplus has been developed under the latest regulations including GAMP, GALP, ISO 9001 software standards and completely complies with the rules and regulations of 21 CFR Part 11 and Data Integrity set out by the FDA.

WinSOTAXplus is an integrated dissolution software package that controls the CE 7smart and all connected components. WinSOTAXplus operates and has been validated on Windows 7. It is fully networkable and LIMS compatible. When installed, WinSOTAXplus is supplied with a complete validation IQ / OQ package and supported by SOTAX certified software engineers worldwide.

Other important features include:

- User-friendly method set-up, results reporting, hardware control
- Real-time data collection in % dissolved, abs or concentration
- Single or multi-component analysis
- Placebo or impurity subtraction
- Standard calibration and standard bracketing
- Flow rate and temperature reporting
- Control of UV-Vis (different drivers available), sampling time points, sample volume collection
- Scanning function during the run
- Cell grouping (allows the collection of data by grouping different cells with different testing conditions, e.g. different flow rates, different dose etc.).





Associated Services

Technical Service

Global. Reliable. Customer-focused. The SOTAX Global Service Network is available worldwide, whenever and wherever you need us.

- System installation and qualification
- User training
- Preventive maintenance
- Technical support (first line responder training)
- Repairs
- Updates, upgrades, and customization
- Compliance services (cGMP compliant qualification: IQ, OQ, PQ, MQ, PVT, and customer-specific qualification)
- Service contracts
- Relocations

Application Services

At SOTAX we engineer solutions for development and quality control.
We support you with expertise at each step of your process:

Feasibility study	Secure your instrument investment with data confirmation of capability with your products
Method development	Save time and resources by allowing SOTAX application scientists to develop your methods in accordance with your method development requirements
Method transfer	Use our trained hands to provide method training and facilitate the transfer of your dissolution methods across sites
Method validation	Speed rollout by allowing us to facilitate and document validation of your method
Application support at installation	Screen your applications and develop an efficient plan for integrating flow-through dissolution into your laboratory
Application training	Come to our labs or invite SOTAX into yours to work with our application experts to streamline the dissolution workflow

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