ELECTROLAB

Your Quality, Our Assurance

Flow-Through Cell Dissolution Tester

Ophthalmic Suspensions

Medical Devices

Nanoparticles

Microspheres

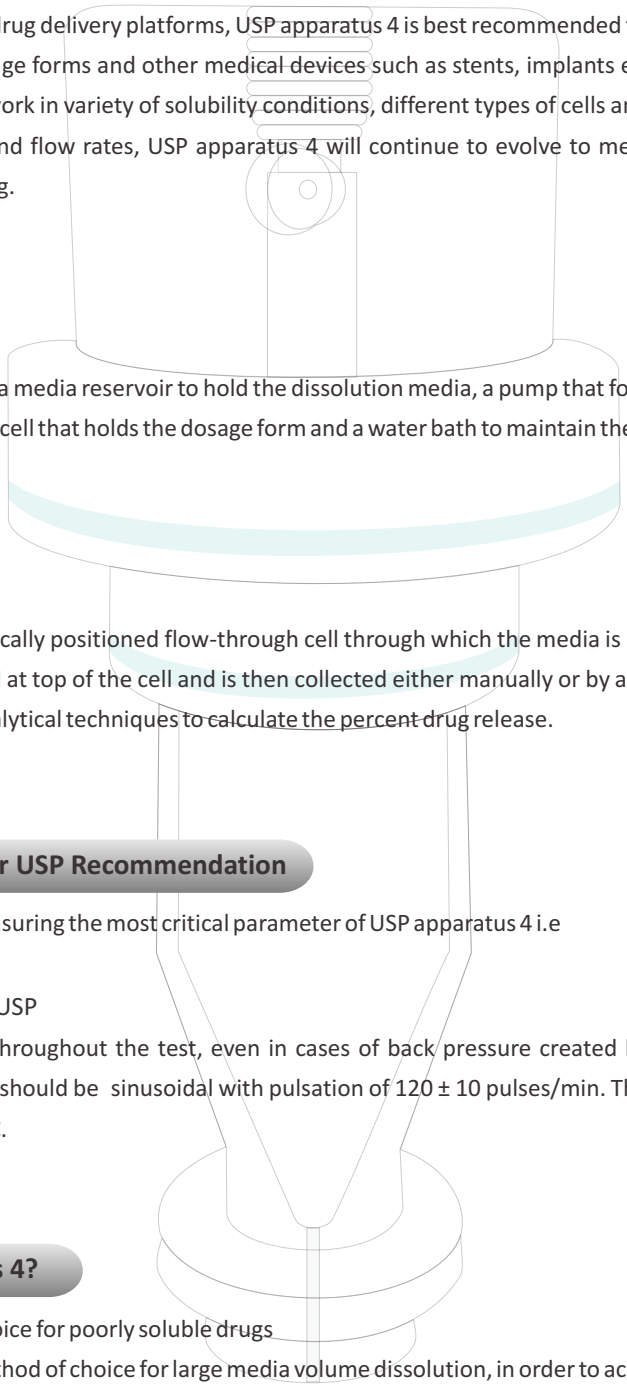
IVIVC Studies

Injectables

Granules

Flow-Through Cell Dissolution Tester (USP Apparatus 4)

Flow-Through cell dissolution tester is widely recommended for poorly soluble, modified release and extended release dosage forms. With the evolution of new drug delivery platforms, USP apparatus 4 is best recommended for studying the dissolution profile of solid, liquid, oral, non-oral dosage forms and other medical devices such as stents, implants etc. As this apparatus offers highly flexible configurations, ability to work in variety of solubility conditions, different types of cells and positioning of the dosage form, hydrodynamics, sink conditions and flow rates, USP apparatus 4 will continue to evolve to meet the changing needs of today's dissolution and drug release testing.



System Components

The USP apparatus 4 comprises of a media reservoir to hold the dissolution media, a pump that forces the media upwards through a vertically positioned flow-through cell that holds the dosage form and a water bath to maintain the cell temperature.

Methodology

The test sample is placed in a vertically positioned flow-through cell through which the media is pumped at a desired flow rate and temperature. The eluate is filtered at top of the cell and is then collected either manually or by a sample collector. The samples are further analyzed using suitable analytical techniques to calculate the percent drug release.

System Specifications as per USP Recommendation

The pump unit is responsible for ensuring the most critical parameter of USP apparatus 4 i.e

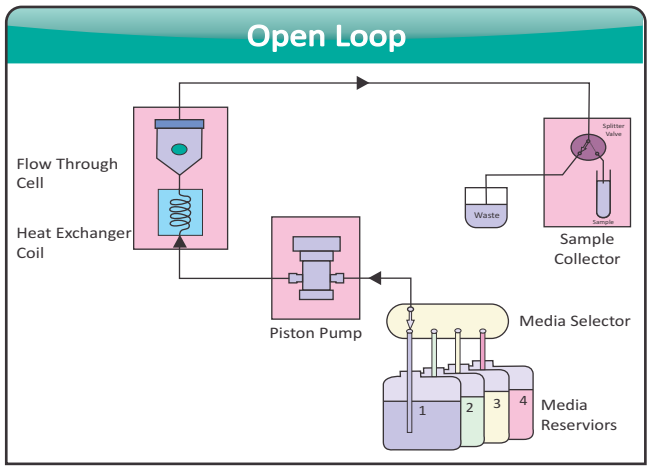
1. Flow rate of the media
2. Temperature ±0.5 as per USP

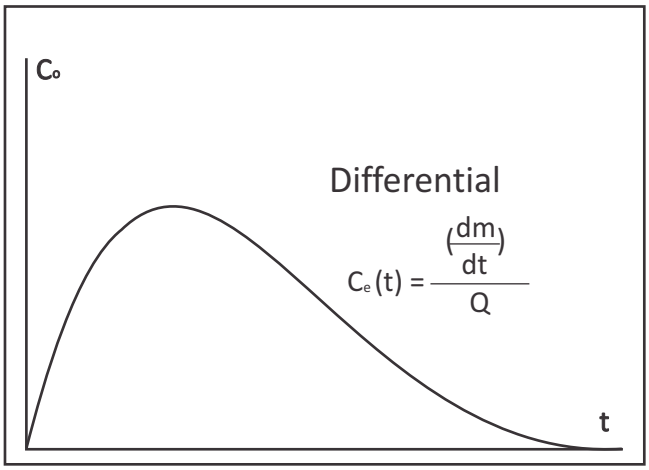
The flow rate must be constant throughout the test, even in cases of back pressure created by the filters. The USP regulation recommends that the flow profile should be sinusoidal with pulsation of 120 ± 10 pulses/min. The USP recommends the optimum media temperature should be 37^{0}C.

Why choose USP Apparatus 4?

- USP apparatus 4 is the ideal choice for poorly soluble drugs
- USP apparatus 4 is the best method of choice for large media volume dissolution, in order to achieve infinite sink condition
- For IVIVC studies, automated media changeovers can be easily achieved for solid as well liquid dosage forms
- Flow rates can be easily changed to allow 'accelerated' test studies
- Many challenges such as tablet floating, sticking etc. are eliminated

Open Loop Configuration





Although USP apparatus 1, 2 and 3 can be used for studying the dissolution profile of poorly soluble drugs, but they fail to offer the optimal sink conditions required. Whereas, USP apparatus 4 has always been linked to "optimal sink conditions" as it offers the flexibility in terms of media volume required. In an "open loop" configuration, there is a continuous flow of fresh media across the dosage form and hence, the total media volume used can be infinite. This means, that the influence of poor sink conditions on the test can be avoided by using larger volumes of media without the need for solubilizing agents. Samples can be collected as a fraction over a timed interval and analyzed using suitable analytical technique. The total amount of media passing through the dosage form is determined by the flow rate. In an open loop configuration, results are calculated as a differential curve or rate of drug release over the time.

In an open loop configuration, EFD-07 can be integrated with a sample collector with splitter that enables sample collection for 14 sampling intervals (21 optional) with 75 mL of sample collection volume. Sample collector with splitter, automatically splits the sample volume into collection and waste depending upon the sample volume required.

Sample Collector with Splitter

Completely covered to prevent contamination and air drafts which cause excess evaporation of the collected samples

D'light™ technology
for audio and visual indication of instrument status from anywhere in the laboratory

- Power on
- Needle diving up / down
- Communication with dissolution tester

Movement of arm to :

- Sample position
- Waste tray / home position

Error due to :

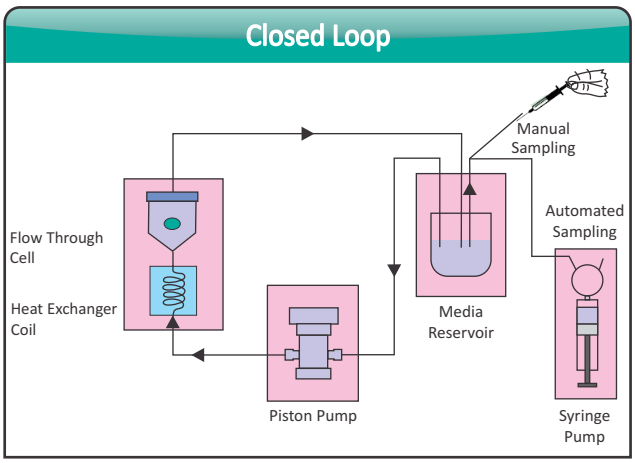
- Absence of sample collector tray
- Absence of waste tray
- Sample collector hood ajar

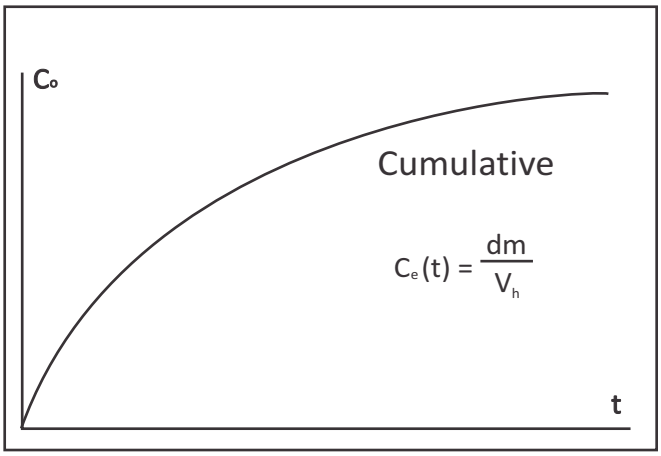
Media Selector

Automated media changeover :

Unlike the USP apparatus 1 and 2 involving media changeovers, where physical removal of the dosage and change to a new media is cumbersome and tedious, USP apparatus 4-open loop configuration facilitates easy media changeover at predefined time intervals. The flow-through method is the only method that allows for a media changeovers of suspensions and powders. This feature is useful while performing IVIVC studies, where the dosage form naturally passes through different pH of the digestive tract within sink conditions. It is also useful for enteric coated products, modified and extended release drug products. Using EFD-07 media selector, 4 different media can be automatically drawn from different sources at predetermined intervals.

Closed Loop Configuration





The closed loop configuration of USP apparatus 4 is similar to USP apparatus 1 and 2 where a fixed volume of media is recirculated through the dosage form. Samples can be withdrawn from the media reservoir at predetermined time intervals either manually or by a syringe system. The samples can be analyzed using suitable analytical technique. In case of closed loop, result of percent drug release dissolved is expressed as a cumulative curve. Closed loop configuration is ideal for dosage forms where solubility and sink conditions are optimal in a limited media volume range from 40 mL to 4 L. For low dose formulations such as drug eluting stents, implants, coated medical devices, injectable and microspheres; closed loop configuration has been utilized to fulfill lower media volume testing. The problems such as tablet sticking, floating, coning or dead zones seen in USP 1 and 2 as well as sampling issues and sample introduction effects are eliminated using the USP apparatus 4.

Off-line sample collection for the closed loop configuration is available with EFD-07 connected to a sample collector. Syringes pull the desired volume from the media reservoir and dispense them either into glass tubes (20 mL or 10 mL) or capped HPLC vials. The system can be programmed to collect the sample volumes at predefined time points. The syringe system also offers the facility for auto-replacement and dilution with fresh media. The sample collector enables sample collection for 24 sampling intervals. Automatic sample collector adapts to 5 different types of trays.

Sample Collector and Syringe Pump

Sample Collector Tray (ESC-08Dx)*	
HPLC vials	Glass tubes
• 1.5 mL (24 x 7)	• 20 mL (16 x 7)
Combination tray (with dilution option)	
HPLC and Glass tubes (2 Types) • HPLC vials 1.5 mL (8 x 7) + Glass tubes 20 mL (8 x 7)	

*Customized trays available

EFD-07 can also be integrated with a media manager to maintain the desired media temperature and provide continuous stirring of media in the media reservoir throughout the test.

Features of EFD-07

QbD Quality by Design

- Compliance with USP, Ph. Eur. JP and BP
- 7 cell dissolution tester
- Valveless ceramic pump heads
- Automatic flow rate adjustment for individual cells
- Individual cell temperature monitoring
- Media selector for easy media change (optional) for open loop
- Program support for gravimetric flow validation and calibration of individual pumps
- Isolated water circulating pump for precise temperature control of the water bath and to reduce vibrations
- User friendly intuitive 7" touch screen interface
- Flow rates can be adjusted from 2 mL/min to 32 mL/min
- 999 programmable protocols
- Saves upto 100 calibration and validation reports
- D'light™ technology for system and sample collector status. For eg.
  - Connected
  - Run
  - Error
- Test protocol can also be printed using in-bult thermal printer for better longetivity of data (optional)

EFD-07

Compliance


Touch Screen

Programmable Protocols

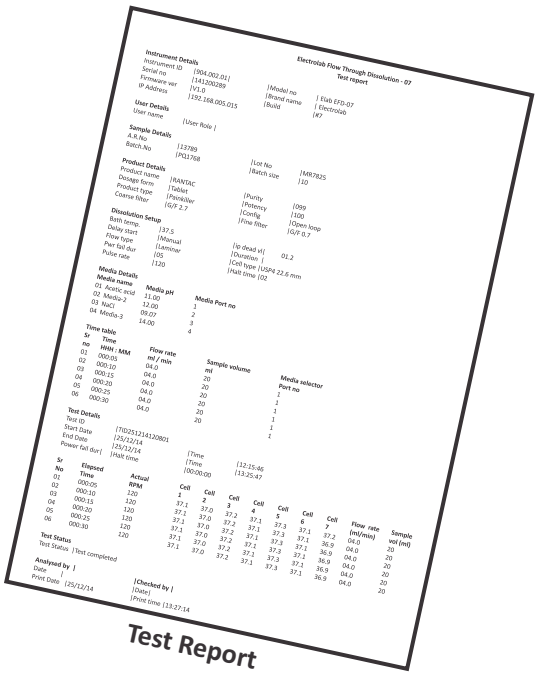
Individual Cell Temp. Monitor


Automated Offline Sampling


LAN


Print Report


Audio Output


Test Report

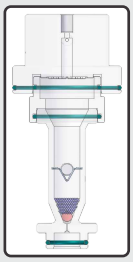
Applications

USP apparatus 4 facilitates dissolution testing of:

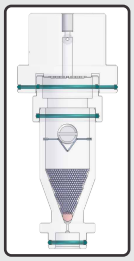
- Tablets
- Capsules
- Powder / granules / API's / bead formulation
- Injectable suspensions
- Suppositories / soft gelatin capsules
- Microspheres / liposomes / nanoparticles
- Inhaler drugs
- Drug eluting stents / implants
- Ointments / creams / gels
- Ophthalmic lenses

Flow-Through cells for different dosage forms

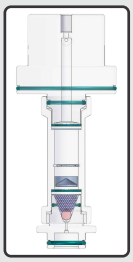
As USP apparatus 4 has wide range of applications, several flow-through cells have been developed and optimized according to the different dosage form like tablets, suspensions, stents, suppository etc. EFD-07 is capable of employing the method to accommodate most dosage forms.



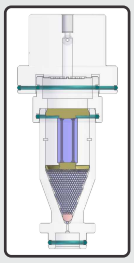
1 : 12 mm cell



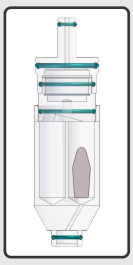
2 : 22.6 mm cell



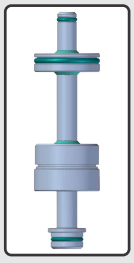
3 : Cell for powders and granules



4 : Dialysis adapter in 22.6 mm cell



5 : Cell for suppositories and soft gelatin capsules



6 : Aerosol/ Inhaler cell

1. **12 mm cell :** This cell is described as a small cell for tablets and capsules in the USP, Ph. Eur. and JP. As per the specifications, a detachable tablet holder is also available. This cell can also be used for suspensions, injectables, small medical devices and stents.
2. **22.6 mm cell :** This is the most widely used cell of all flow-through cells. It is described as a large cell for tablets and capsules in the USP, Ph. Eur. and JP. As per the specifications, a detachable tablet holder is also available. It can also be used for larger doses of suspensions and microspheres. There are a variety of holders developed for holding different dosage forms in this cell.
3. **Cell for powders and granules :** This cell is described in the Ph. Eur. and is based on the 12 mm cell. It is used to determine the dissolution rate of pure solid substances (API characterization), active substances in preparations used as powders, granules and bead formulations.
4. **Dialysis adapter in 22.6 mm cell :** This cell is based on the 22.6 mm cell and is used to study the dissolution profile of nanoparticles, microspheres, micro-suspensions and injectables etc. A dialysis adapter along with dialysis membrane inside the cell allows testing on these dosage forms. Adapter to accommodate 1 mL Float-A-Lyzer is also available.
5. **Cell for suppositories and soft gelatin capsules :** This cell is described in the Ph. Eur. and has a special two chambered design which blocks the lipidic excipients from the suppository/soft gelatin capsules and allows only the dissolution media to pass up to the filter.
6. **Aerosol/Inhaler cell :** This cell is manufactured in stainless steel and is specially designed to study the elution rate of inhaler drugs.

7. **Cell for drug eluting stents** : This cell is manufactured in PTF and is used for medical devices like drug eluting stents. The inner diameter can be customized to fit the medical device accordingly.
8. **Cell for large medical devices** : This cell has a maximum length of 80 mm and is designed to hold longer medical devices.
9. **Cell for implants** : This cell has a small chamber to house the dosage and is used for smaller implants.

10. Customized flow-through cells :

Using the above cells as the main models, specific holders have also been designed to hold other dosage forms. Customization can be based on the dosage form, media, inner diameters, cell length and holding devices etc.

- **Holder for creams and gels :** An inserted cup facilitates testing on ointments, gels and creams using a permeation membrane. This modification is based on 22.6 mm cell.
- **Holder for ophthalmic lens :** This modification is based on 22.6 mm cell and has an inverted holder that allows testing on ophthalmic lenses coated with drugs.

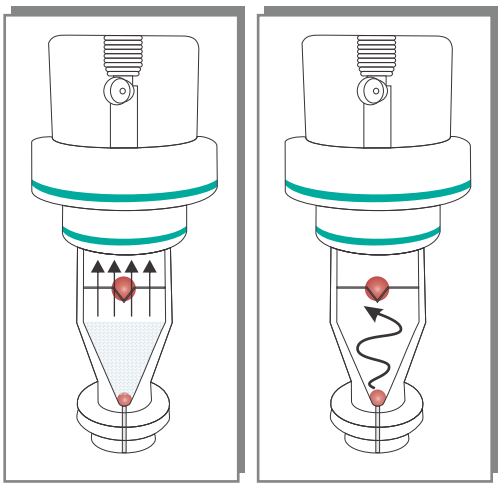
For intended use of hydroalcoholic media, specially designed PEEK cells are also available

Experimental Conditions

- **Types of flows :**

There are 2 types of hydrodynamic flow within a flow-through cell viz. a laminar flow and turbulent flow. Laminar flow is achieved by filling the flow-through cell with a 5 mm ruby bead bottom of the cell followed by a layer of 1 mm glass beads as described in the USP. The laminar flow is more controlled as it crosses the dosage form in unidirectional flow.

The turbulent type of flow is obtained by placing only the ruby bead in the flow-through cell. The turbulent flow is more beneficial for dosage forms that require a higher agitation rate to release its actives.



Laminar Flow | Turbulent Flow

- **Sample filtration :**

Filtration occurs at the top of the flow-through cell with a filter insert of standard filter size of 25 mm. Different types of filters with variety of pore sizes can be used depending on the dosage form. In some cases, multiple filters can be used from larger to smaller pore size. The use of glass wool in the filter section is recommended for dosage forms with highly insoluble or oily particulates .

- **Dosage positioning :**

Solid dosage form: Tablet can be simply placed in the cell on the layer of glass beads or positioned uniformly on a tablet clip holder or directly on the ruby bead (turbulent flow). This factor can eliminate problems such as tablet sticking, swelling and floating as seen in other conventional dissolution methods.

Suspension : Liquid samples can be placed directly on layer of glass beads or sandwiched uniformly between single or multiple layers of glass beads. This ensures repeatability, reproducibility and reliability of results.

Powder : Using the powder granule cell, the powder is simply filled into the cell without any compression or compaction. The filter insert is placed on either side of the cell.

Specifications

Utilize ELECTROLAB's dedicated Dissolution Application Lab for confidential Method Development and Transposition to optimize parameters for NDDS

Model	**EFD-07**	
Product code	230 Volts	110 Volts
	M.S. : 1420100	M.S. : 1410100
Number of cells	7	
Pulses /min.	120 PPM ± 10	
Flow rate	2 mL/min to 32 mL/min	
Flow rate accuracy	± 5 %	
Temperature range	20°C to 45°C (55°C optional)	
Temperature accuracy	± 0.1°C	
Display	7" color TFT with resistive touch panel	
No. of samples	14/21 (Open loop), 24 (Closed loop)	
Sample intervals	1 min to 999 hrs 59 mins	
Individual sample volume	Open loop capacity : upto 75 mL Closed loop capacity : 1.5/10/20 mL	
Interface port	RS 232, Ethernet	
Water bath	SS	
Bath capacity	6 L	
Temperature controller	Heater : 1KW SS-316 with thermal protection Sensor : RTD Circulator : High flow BLDC pump	
Electrical Power	230V AC	110V AC
	50 / 60 HZ, 1.3 KW, 6 Amp	50/60 Hz , 12 Amp
Dimensions	Basic (Pump unit + Cell unit + Media Selector) L 1040 mm x W 750 mm x H 700 mm	
	Open loop with splitter L 1540 mm x W 750 mm x H 700 mm	
	Closed loop with sample collector and syringe pump L 1540 mm x W 750 mm x H 700 mm	

Our Products

• Complete range of Dissolution Testers • Dissolution Media Preparator • Disintegration Testers • Tablet Hardness Testers
• Electromagnetic Sieve Shakers • Tap Density Tester • Bulk Density Tester • Powder Flow Tester • Leak Testers • Peristaltic Pumps

CE ISO 9001

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