

Semisolids

Background: Semisolids Testing

Most pharmaceutical dosage forms applied directly to the skin for topical action are classified as semisolid, a group of products which include ointments, creams and gels. They are typically applied for immediate, localised relief.

These products are typically hydrocarbon-based or oil-in-water emulsions incorporating additional ingredients such as emulsifiers, stabilisers, pH buffers, preservatives, absorption promoters and perfumes.

USP Chapter <1724> details the performance testing required for semisolid drug products.

Semisolids

Test Apparatus & Method

There are three different apparatuses for the *in vitro* determination of drug release from semisolid drug dosage forms:

- Vertical Diffusion Cell (VDC)
- Immersion Cell
- Flow Through Cell (Apparatus 4)

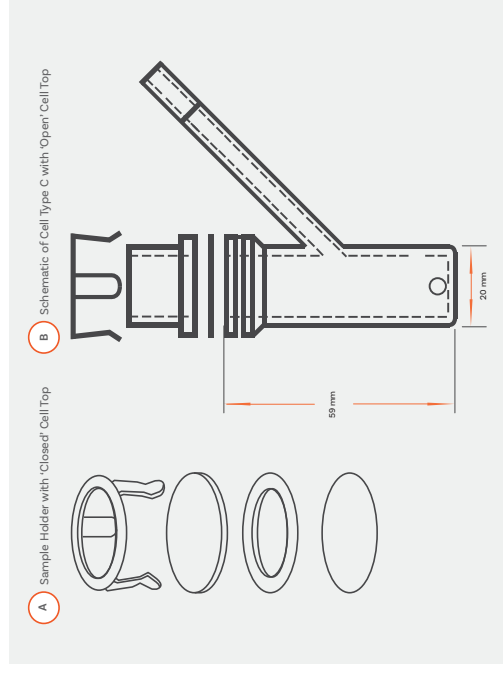
Due to its simplicity and reproducibility, the VDC, or Franz Cell, is typically the apparatus of choice.

The VDC comprises two parts: (a) the donor chamber containing the sample to be tested and (b) the receptor chamber containing the receptor medium.

The two parts are separated by an inert, highly permeable support membrane that acts as a conduit through which diffusion occurs.

The receptor chamber temperature is usually set to 32°C, to simulate normal skin conditions. At least 6 samples should be taken over a 6-hour period and analysed using HPLC or a similar analytical technique.

Results are calculated and expressed as the amount of drug released per unit membrane area (mcg/cm^2) vs square root of time. This should yield a straight line. The slope of the line (regression) represents the release rate of the product.



Annex 1 of the EMA 'Guideline on quality of transdermal patches' suggests the use of the VDC for permeation studies on transdermal patches

Vertical Diffusion Cell System: HDT 1000

Simple, reproducible semisolid drug release measurement

With precision heating and integrated powerful magnetic stirrers, Copley's compact HDT 1000 test system offers full control over all test parameters and has become the benchmark vertical diffusion cell test system for many labs.

Using an innovative heating block approach, the HDT 1000 eradicates the difficulties and the "spaghetti" of tubing associated with water-jacketed cell systems and accommodates either endpoint, discrete manual or fully automatic sampling techniques. A dedicated stirrer mounted beneath each station ensures thorough mixing throughout testing for accurate sampling.



USP compliant



Innovative dry heating system simplifies test set-up



Precision control over all test parameters



Powerful magnetic stirrers ensure consistent mixing during testing



Novel cell clamps simplify cell preparation and sample collection



Small footprint saves precious benchtop space



HDT 1000: Key Features



Control is provided via a user-friendly membrane keypad with test parameters displayed clearly on a backlit LCD screen



Up to 10 cells accommodated per test run



Easy to access sampling ports



Insulation to help maintain temperature stability



Heating block eradicates use of water-jacketed cells



Small unit footprint saves previous benchtop space

Choose your HDT System



HDT 1000

For higher throughput semisolids testing

Cat. Number
7290

Pharmacopoeial Compliance
USP <1724>

User Interface
Touchpad and LED display

Cell Capacity
Up to 10 diffusion cells

Heating System
Dry heating block

Temperature Range
Ambient - 150 °C

Stirrer Speed Range
400 - 2,000 rpm

Sampling Technique Compatibility
End-point
Discrete manual
Fully automatic

Unit Dimensions (w x d x h)
80 x 325 x 145 mm



HDT 1

Basic, low cost test system for entry-level semisolids testing

Cat. Number
7276

Pharmacopoeial Compliance
USP <1724>

User Interface
Touchpad and LED display

Cell Capacity
1 single diffusion cell

Heating System
Water bath

Temperature Range
Ambient to 300 °C

Stirrer Speed Range
200 - 1,300 rpm

Sampling Technique Compatibility
End-point
Discrete manual
Fully automatic

Unit Dimensions (w x d x h)
190 x 300 x 100 mm

Choose your HDT Accessories

Cells

All cells supplied with Copley's Vertical Diffusion Cell systems are designed to simplify cell preparation and sample collection procedures.

For USP Models 'A', 'B' and 'C', vertical diffusion cells are supplied complete with individual cell tops for both 'closed' or occluded' operation (as per Model 'A') and 'open' operation (as per Models 'B' and 'C' respectively), maximising the versatility of the HDT series.

To accommodate 'full thickness' membranes or skin, and in contrast to the Type 'B' and 'C' cells, which use a 3-pronged spring clip, a screw-type cell closure mechanism has been developed for the skin specific

cell that ensures proper contact between the sample and the receptor medium. All components of the cell are made from FDA-approved inert materials and a side sampling arm facilitates easy filling, sample withdrawal and media replacement.

Samples are separated from the receptor media by a synthetic inert and highly permeable support membrane.



HDT

Cat. No.	Description
7290	10 Cell Vertical Diffusion Cell Test System HDT1000 (excl. cells)
7276	Single Cell Vertical Diffusion Cell Test System HDT 1 (excl. cells)
7298	Vertical Diffusion Cell 1128 mm x 7 mL Type 'B' (in Glass)
7299	Vertical Diffusion Cell 15 mm x 11 mL Type 'C' (in Glass)
7302	Vertical Diffusion Cell 15 mm x 12 mL for Skin (in Glass/Tecapro)
7295	Syringe 2 mL complete with Luer and sampling tube (Pk 10)
7296	Syringe 20 mL complete with Luer and media filling tube
7297	Parafilm Laboratory Film (250' x 2")
7289	Storage Rack for 10 Vertical Diffusion Cells (Types 'B', 'C' and Skin)
7277	IQ/OQ/PO Documentation Pack for HDT1/1000
7272	Qualification Tools for HDT1/1000
7282	Re-calibration of Qualification Tools for HDT1/1000

Cell Specification



Type 'B' Cell



Type 'C' Cell



Skin Cell

Cat. Number
7298

Sample Holder Type
Clip

Sample Holder Material
Glass

Receptor Material
Glass

Operation
Open, Closed/Occluded

Receptor Volume
7 mL

Max Membrane/Skin Thickness
Open 0.5 mm
Closed/Occluded 0.5 mm

Cat. Number
7299

Sample Holder Type
Clip

Sample Holder Material
Glass

Receptor Material
Glass

Operation
Open, Closed/Occluded

Receptor Volume
11 mL

Max Membrane/Skin Thickness
Open 0.5 mm
Closed/Occluded 0.5 mm

Cat. Number
7302

Sample Holder Type
Screw

Sample Holder Material
Tecaprot

Receptor Material
Glass

Operation
Open, Closed/Occluded

Receptor Volume
12 mL

Max Membrane/Skin Thickness
Open 4.0 mm
Closed/Occluded 2.5 mm

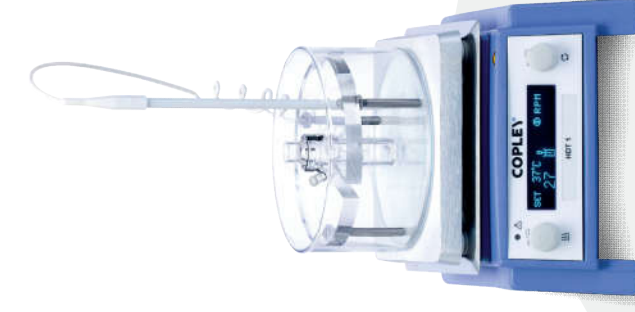
Membranes

Copley offers a range of three synthetic membranes:

- PVDF**
 A hydrophilic polymeric membrane
 Pore size: 0.45 microns.
- Supor Polyethersulfone**
 A hydrophilic polyethersulfone membrane with a 0.45 m pore size. These membranes have reduced protein binding and fewer leachables than Tuffryn membranes.
- Strat-M Membranes**
 Newer, multi-layered membrane offering higher correlation to human skin than simpler synthetic alternatives, without the high test variability associated with biological models and does not require wetting.

HDT Cell Membranes

Cat. No.	Description
7270	Pack of 100 PVDF Membranes 25 mm o.d.
7274A	Pack of 100 Supor Polyethersulfone Membranes 25mm o.d.
7275	Pack of 60 Strat-M Membranes 25 mm o.d.
7304	25 mm Punch For VDC Skin/Membrane



VDC HDT 1

A simple test system for a single diffusion cell.
This is a smaller alternative to the main HDT 1000, ideal for entry-level semisolids testing.

Degassing

The Vacuum Deaeration Apparatus Model (VDA) from Copley is an easy-to-use and inexpensive unit designed to degas receptor medium prior to its use, ensuring that diffusion is unimpeded by the collection of gas beneath the membrane. Once deaerated, the system can be used to maintain the temperature of the degassed dissolution medium to the required temperature for testing.

Used in combination with a vacuum pump, pressure meter and dissolved oxygen meter, the VDA system guarantees oxygen levels below 4 ppm, exceeding the recommendations set out in the pharmacopoeias (USP suggests an oxygen concentration <6 ppm is an adequate level of dissolution media deaeration).



The VDA system comprises of:

- 500 mL pressure bottle containing receptor medium
- Water bath to heat the contents of the bottle to 45°C
- A magnetic stirrer/heater to stir the content of the bottle whilst heating it and the surrounding water bath
- A condensate filter to prevent condensate from damaging the vacuum pump

The following items are required in addition to provide a full system:

- A vacuum pump
- A differential pressure meter to display pressure and test for leaks
- A dissolved oxygen meter to measure and display dissolved oxygen levels in the media

Immersion Cell

An alternative to the Vertical Diffusion or Franz Cell for testing semisolids, the Immersion Cell (USP Model A) is described with the conventional USP Apparatus 2 for Dissolution testing on Page 75.

Accommodating a 25 mm diameter membrane, the Immersion Cell is comprised of 4 main parts:

1. A retaining ring to secure the membrane to the cell body
2. A washer to hold the membrane in contact with the sample
3. The membrane or skin
4. The cell body which contains the compartment in which the sample to be tested is placed

The immersion cell is used with a special flat-bottomed version of the 200 mL Small Volume Conversion Kit (see Page 38) to eradicate the issue of dead space under the cell that would occur with a round-bottomed vessel.



Immersion Cell with 200 mL Small Volume Conversion Kit

Immersion Cell & Accessories

Cat. No.	Description
7280	Immersion Cell
7281	200 mL Small Volume Conversion Kit for Immersion Cell
7270	Pack of 100 PVDF Membranes 25 mm o.d.
7274A	Pack of 100 Supor Polyethersulfone Membranes 25mm o.d.
7275	Pack of 60 Strat-M Membranes 25 mm o.d.



Immersion Cell

Suppositories

Background: Suppository Testing

Suppositories, which advantageously avoid the risk of digestion of the active drug in the gastrointestinal tract, are classified as either:

Hydrophilic: made from a water-soluble base such as polyethylene glycol, which dissolves in rectal or vaginal fluids.

Lipophilic: made from a greasy base such as cocoa butter, which melts at body temperature.

There is no single method of drug release testing suitable for all types of suppository formulations.

Suppository Testing

Test Apparatus & Method

The suppository is a more common and accepted dosage form in Europe than in the USA which may explain why references to specific test methods relating to suppositories and associated dosage forms are mainly confined to the European Pharmacopoeia.

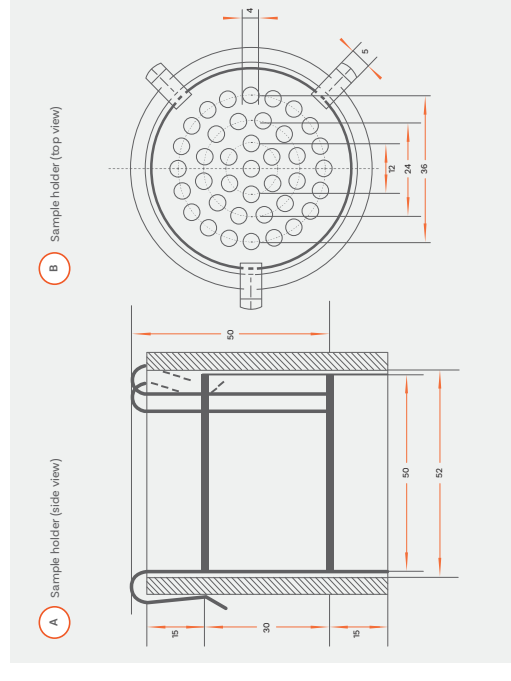
The rate of drug release (dissolution) for hydrophilic suppositories can be measured using the standard basket, paddle or flow through methods described in USP Chapter <711> and Ph. Eur. 2.9.3 (see Page 24-25). Methods for lipophilic suppositories include:

- a modified basket method (see Page 39)
- a paddle method (see Page 24)
- a modified flow method (see Ph. Eur. 2.9.42)

In addition to this, the European Pharmacopoeia references two other technical procedures relating to **disintegration** and **softening** time of suppositories:

2.9.2 Disintegration of suppositories and pessaries

2.9.22 Softening time determination of lipophilic suppositories



Suppository Tester: SDT 1000

Straightforward suppository testing

Designed in accordance with the specifications laid down in Ph. Eur. 2.9.2, the SDT 1000 is a single unit tester optimised for assessing the disintegration properties of suppositories and pessaries and with the appropriate attachment; for measuring the softening time of lipophilic suppositories (as per Ph. Eur. 2.9.22.-2).

The SDT 1000 has a simple design, which uses manual inversion controlled via a water-resistant pulley system. Test parameters including water bath temperature and stirrer speed are easily set using the touch key interfaces.



Ph. Eur. compliant



Easy-remove components for straightforward cleaning



Single unit assesses both disintegration and softening time (with necessary attachments)



SDT 1000: Key Features



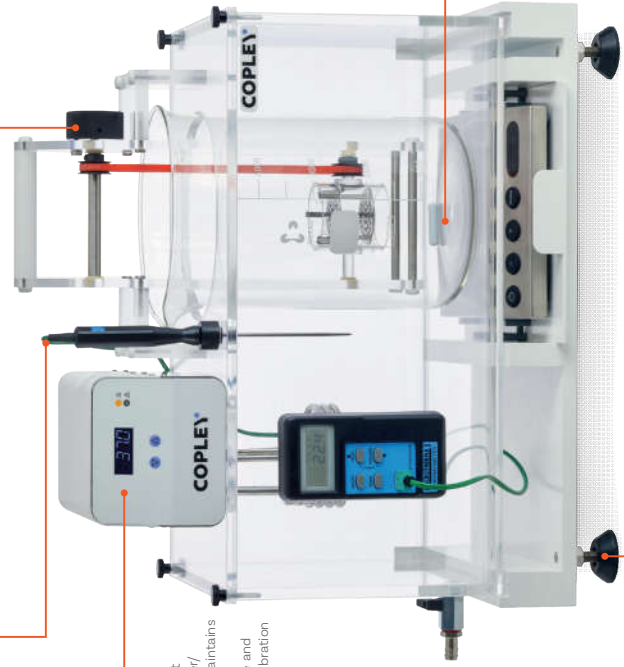
Integrated PT100 probe for precision temperature control and measurement



Manual sample inversion offers users ultimate control and flexibility



Independent digital heater/circulator maintains a constant temperature and minimises vibration



Powerful magnetic stirrer ensures consistent mixing during testing



Small unit footprint saves previous benchtop space

Softening Time Attachment

A special attachment is used in place of the disintegration test station, in combination with a 4-litre beaker containing three glass rods (C1) for measuring the softening time of lipophilic suppositories, in accordance with Ph. Eur. 2.9.22.-2.



Softening Time Attachment



SDT 1000

Cat. No.	Description
1704	Suppository Disintegration Tester SDT 1000
1705	Electro-Magnetic Stirrer for SDT-1000
1706	Softening Time Attachment (Ph. Eur. 2.9.22.-2)



SDT 1000 Accessories

Cat. No.	Description
1707	Qualification Tools
1712	Re-calibration of Qualification Tools
1708	IQ/OQ/PQ Documentation
1710	Digital Timer with Audible Alarm (including calibration)



SDT 1000: Technical Specifications

Pharmacopoeial Compliance
Ph. Eur. Test 2.9.2
Ph. Eur. 2.9.22.-2 (with suitable attachments)

User Interface
Touchpad buttons, LED display

Test Stations
Disintegration: 1
Softening Time: Up to 3

Temperature Range
Ambient - 50 °C

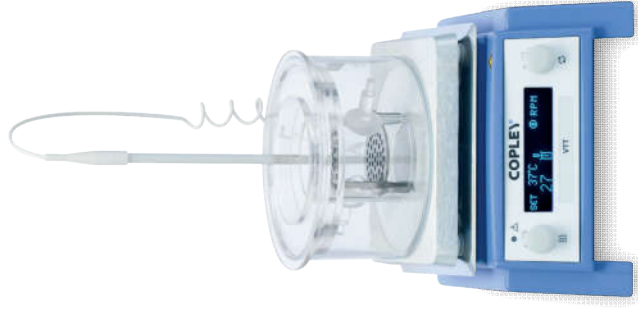
Sample Inversion
Manual

Stirrer Speed
80 - 2000 rpm (in 10 rpm intervals)

Unit Dimensions (w x d x h)
510 x 280 x 500 mm

Vaginal Tablet Tester (VTT)

Using the same sample holder as the SDT 1000 together with a low form beaker and heater/stirrer, Copley's VTT is a reliable, easy-to-use and compliant (Ph. Eur. 2.9.2) solution for assessing the disintegration properties of vaginal tablets.



Vaginal Tablet Tester

Cat. No.	Description
1800	Vaginal Tablet Tester (VTT)
1709	Glass Plate for use with Vaginal Tablets