



Enhancer Cell

Provided to Help You Get the Most from Your Agilent Dissolution Products!

The performance testing of ointments, creams and gels has presented challenges. It is difficult to properly evaluate the in vitro release of the active ingredient from the formulation and quantitate the rate of diffusion across a barrier such as an artificial membrane.

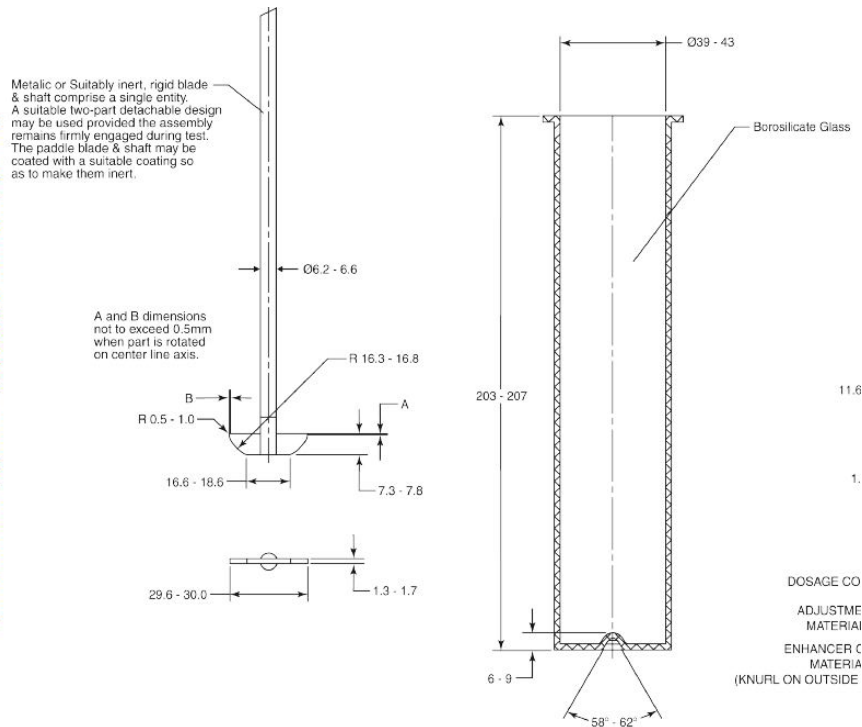
The skin is extensive and one of the most readily accessible organs of the human body. It has a surface area of approximately 1.7 to 2 square meters. It is comprised of three main tissue layers: Epidermis (stratum corneum), Dermis and Hypodermis (subcutaneous tissue). Topical products for systemic use include not only transdermal drug delivery systems but also, ointments creams and gels. The stratum corneum is the principle barrier to systemic drug administration and the in vitro system should simulate the release of the drug at this route of administration.

The enhancer cell provides a reproducible and accurate means of quantitating in vitro semisolid drug release. In all diffusion cells a layer of semisolid product under evaluation is placed in contact with a highly permeable membrane, with characteristics similar to human skin. This membrane acts as the barrier between the semisolid and the receptor medium representing the fluid characteristics of the dermis and hypodermis and generally consists of an isotonic saline buffer of fairly neutral pH. The membrane should not be rate controlling and should offer the least possible diffusional resistance. Samples are obtained over a 4 to 6-hour period as samples are withdrawn from the receptor medium typically at 1-hour intervals.

What diffusion testing has in common with traditional dissolution testing of solid dosages is rate determination especially for extended and sustained release products. However, diffusion testing is different from traditional testing of solid dosage forms due to the fact there is no dose. Topical semisolids are applied to tissue of various surface areas and thus testing for extent of release is not performed since there is no dose. Labeling for topical semisolid products typically contain the percentage of active ingredient such as 1% Hydrocortisone Ointment. Amounts of semisolid to be tested vary depending on rate limitations of the formulation but not less than 200 mg are commonly used. The most important thing to

Technical Details

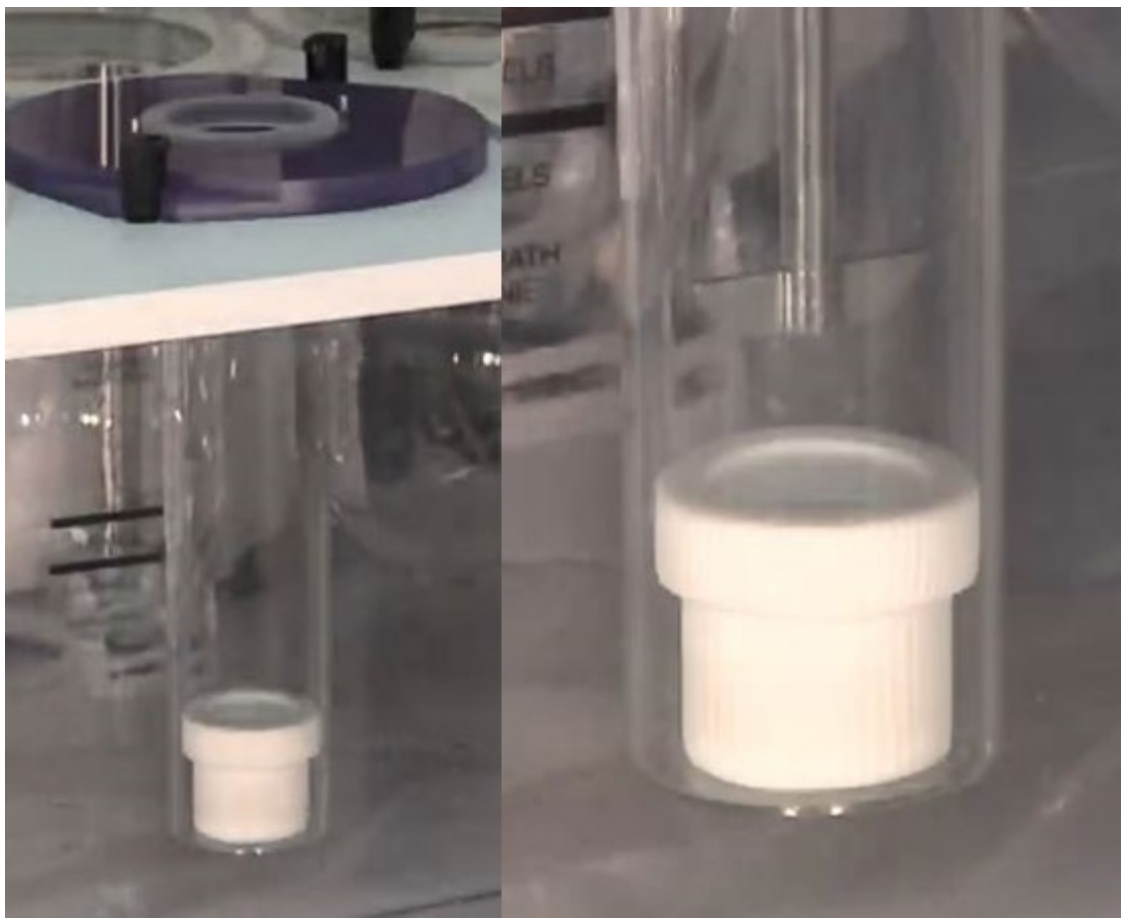
The Enhancer Cell is a Compendial device which is described in the USP Chapter <1724> Semisolid Drug Products - Performance Tests as the Immersion Cell, Model A. It is used in USP Apparatus 2 that is modified with 200 mL, flat-bottom vessels and mini-paddles for six positions. As the illustration shows, a dimple is built into the bottom of the vessel to keep the Enhancer Cell centered within the vessel during testing.



The temperature of the test is maintained at 32 °C during the test. One of the main advantages that the Enhancer Cell has over vertical diffusion cell (also called the Franz Cell) is the capacity for the donor and receptor compartments to be precisely temperature controlled.

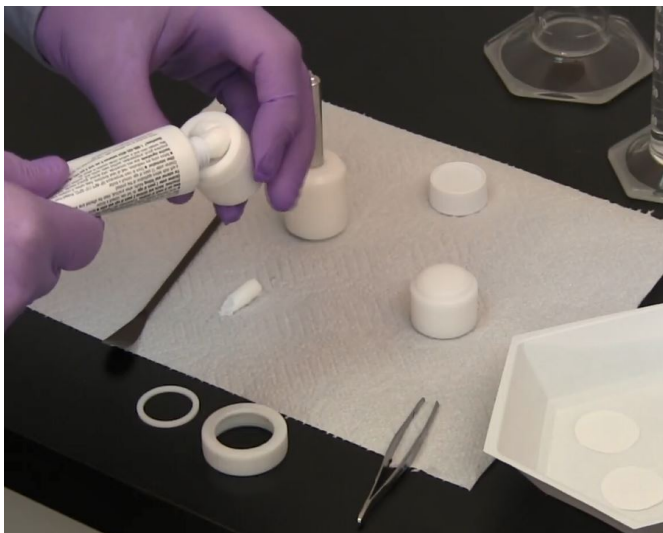
Conducting the test should occur as follows:

Setup: Before loading the cells, the Agilent 708-DS dissolution apparatus should have the 1 Liter vessels removed and replaced with the 200 mL Enhancer Cell vessels. The Apparatus 1 or 2 shaft should be removed and replaced with the mini paddle. Verify the height with the adjustment tool/height spacer to one of two typical heights; 1.0 or 2.5 cm. The physical parameters of the traditional USP 2 should be used to control level, verticality of the shaft and vessel, vibration, wobble and temperature which in this case is 32 °C.



Next, each Enhancer Cell (EC) must be loaded with the formulation before placement into the dissolution apparatus.

Loading the sample product into the cell: Examine the test product for damage. Then one or two mL of the ointment, cream, or gel to be tested should be squeezed from the tube. The product is then squeezed into the EC body with the retaining and centering rings removed. The product should be pushed into the edges as the cell is rotated to fill the donor compartment evenly. excess of product should be in the cell.



Leveling the product: The leveling of the product is required to provide a consistent and even surface for the membrane to rest once it is applied. To accomplish this, a flat-edge spatula is used to push the product down and away as it is drawn across the top of the EC body. The excess is discarded.



Applying the membrane: The membrane must be presoaked in the receptor medium for at least 20 minutes. The membrane is then removed from the medium with tweezers taking care to only handle the edge and not damage the surface of the membrane. The membrane is then rolled onto the surface of the product to avoid the entrapment of air.



Attaching the surface area ring: The surface area ring controls the surface of the membrane to standardize the release area. These rings are available in three sizes; 4, 2 and 0.5 cm² with the 4 cm² size being the most common (shown following):



Attaching the retaining ring: The surface area ring is held in place by a retaining ring that is screwed onto the cell body until a small amount of resistance is felt:



Adjusting the centering ring: The centering ring is adjusted with an alignment tool that may also be used to set the height. The alignment tool is wiggled into place and the groove in the tool places the centering ring exactly in the middle of the cell. Once the centering ring is centered, the retaining ring is tightened slightly. Over-tightening may result in damage to the membrane. The alignment tool should remain in place during the adjustment step:



Adjusting product contact to the membrane: The product must be pushed up against the membrane while the alignment tool is in place. This is accomplished with an adjustment tool that looks similar to a screwdriver. Once the tool is inserted, about one-quarter turn clockwise is applied to press the product against the membrane.



Ready for testing: After tightening, remove the tool and the Enhancer Cell is prepared and ready to test. Prepare the additional 5 cells for the **drug release** testing:





The prepared cells are placed into the vessel and preheated media (32 °C) is added. Paddle rotation is started immediately and the test is underway with samples usually withdrawn each hour for up to 4 to 6 hours:



Agilent catalog numbers (or links to Digital Source Book)

Enhancer Cell may be found in the Agilent Digital Source Book along with ordering information:

http://read.nxtbook.com/agilent/source_book/dissolution_systems_2017_2018/enhancer_cell.html



Ordering Information:

Enhancer Cells and Accessories, compatible with Agilent, Varian and VanKel apparatus models

Description	Part Number
Enhancer Cell, 4 cm ² surface area membrane (one per position)	12-4000
Enhancer Cell, 2 cm ² surface area membrane (one per position)	12-4001
Enhancer Cell, 0.5 cm ² surface area membrane (one per position)	12-4002
Height spacer (1 cm) / alignment tool, for 4 cm ² Enhancer Cell (one required)	12-4020
Height spacer (1 cm) / alignment tool, for 2 cm ² Enhancer Cell (one required)	12-4021
Height spacer (1 cm) / alignment tool, for 0.5 cm ² Enhancer Cell (one required)	12-4022
Adjustment tool, for all Enhancer Cell sizes (one required)	12-4015
Cuprophane membrane, 126x345 mm, 10 sheets/pkg.	12-1370

Enhancer Cell Ordering Example

In addition to your apparatus, the following ordering example describes the items that should be ordered for Enhancer Cell use.

Enhancer Cell Ordering Example: 708-DS conversion, 6 positions, 4 cm² Enhancer Cell

Quantity	Description	Part Number
6	Enhancer Cell, 4 cm ² surface area membrane (one per position)	12-4000
1	Height spacer (1 cm) / alignment tool, for 4 cm ² Enhancer Cell (only one required)	12-4020
1	Adjustment tool, for all Enhancer Cell sizes (only one required)	12-4015
6	Mini paddle, lower interchangeable, electropolished stainless steel	13-3608
6	TruAlign vessel, flat bottom, 200 mL (one per position)	12-5170
6	TruAlign vessel 100/200 mL conversion kit (includes vessel adapter and evaporative cover)	12-6368

Agilent Enhancer Cell Operator's Manual:

http://www.agilent.com/cs/library/usermanuals/public/Enhancer_Cell_Op_Man.pdf

Link to video

<http://www.agilent.com/en-us/video/enhancercelltechnique>

Agilent Sites and Services for Your Dissolution Workflow



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www.nxtbook.com/nxtbooks/agilent/dissolution_sourcebook/index.php

Dissolution Exchange
www.dissolution.chem.agilent.com

Dissolution 1-on-1 Training
www.dissolution.chem.agilent.com/learn-dissolution-1-on-1

Dissolution Hotline (Email Address)
dissolution.hotline@agilent.com

Dissolution Discussion Group (DDG)
www.dissolution.com