PERMEGEAR

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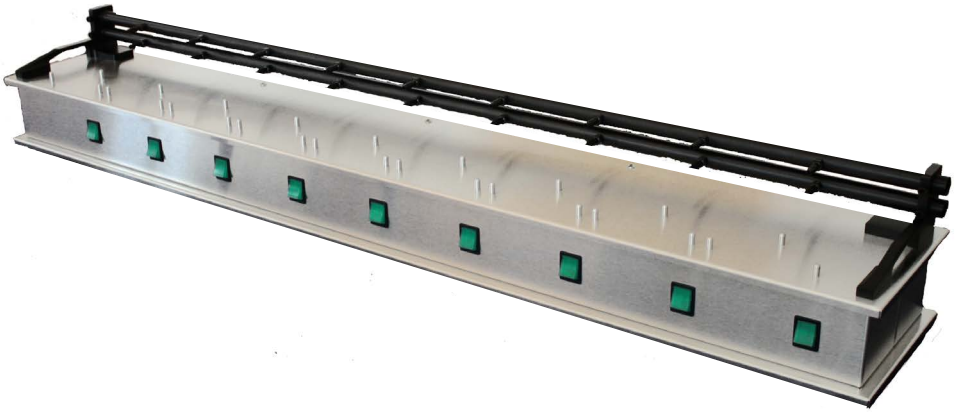
H9 Side-Bi-Side Manual Diffusion System



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Introduction

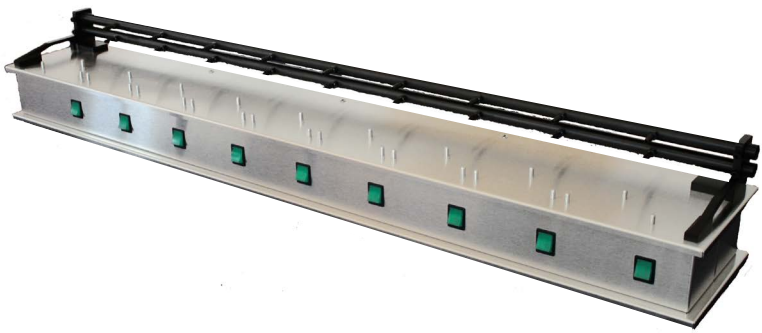
Description

PermeGear's H9 Side-Bi-Side Manual Diffusion System is an apparatus employing nine Side-Bi-Side Cells for carrying out testing that enables a researcher to measure the release or permeation of a compound into or through membranes. Side-Bi-Side Cells are currently in laboratories around the world and used for everything from measuring the migration of molecules through biological membranes to an instrument of measurement in the development of fuel cells. To best mimic *in vivo* conditions, permeation experiments are typically done at near normal body temperature. Therefore, the fluid inside each chamber of a Side-Bi-Side Cell is heated and stirred.

Components

PermeGear's Side-Bi-Side Cell Manual Diffusion Systems include one or more Side-Bi-Side Cells, an H-Series Stirrer and a heater/circulator. Each half cell is surrounded by a "jacket" through which heated water is circulated. Cell Clamps securely locate the Side-Bi-Side Cells directly above individual magnets. H-Series Stirrers provide easy access for connecting the jackets to a heater/circulator (not shown in the photo below). PermeGear provides heater/circulators, but often these are already available in users' labs.

Figure 1 - An H9 station magnetic stirrer



Setting up a PermeGear H9 Side-Bi-Side Manual Diffusion System

1 Connect the stirrer to the heater circulator

Install the stirrer on a level surface. The long tubes at the rear of the stirrer are manifolds that supply warming water to the Side-Bi-Side Cells. Fittings are supplied with each stirrer enabling the user to connect the manifolds in two ways. In both cases the output from the heater/circulator is connected to one end of either manifold tube and the same end of the second tube is connected to the return fitting of the heater/circulator. The other ends of the manifold tubes should be plugged with the fittings supplied, but a loop of tubing may also be used to connect the two ends. PermeGear supplied heater/circulators can pump enough water for two stirrers which may be connected with Y-connectors joining the pump outputs to both stirrers and joining both returns to the heater/circulator.

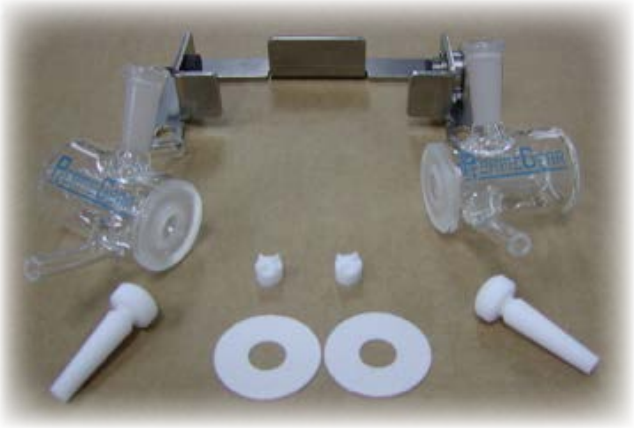


Figure 2 - Components of a Side-Bi-Side Cell and a Cell Clamp. The two white ring Teflon® foam gaskets can be used to prevent leakage between the cell halves and the membrane, if necessary.

2 Connect the Side-Bi-Side Cells

Place the Side-Bi-Side Cells into the Cell Clamps supplied with the stirrer. The barbed fittings of the manifolds can be connected with short sections of the latex tubing supplied with the stirrer to the ports of the Side-Bi-Side Cells' heating jackets. If you wish you can use Quik-Disconnect® fittings

which must be purchased from your supplier separately. In either case the cells need to be removed from the stirrer from time to time for cleaning.

Preparing the PermeGear H9 Side-Bi-Side Manual Diffusion System for use

3 Cleaning Side-Bi-Side Cells

Prior to using the cells, clean the stirbars and stoppers by rinsing them with methanol (MeOH) first and then deionized water several times. Let them dry. Fill both chambers with methanol. Then use a disposable plastic pipette to suck and release methanol from the chamber several times to clean both chambers as well as the contact surfaces of the chambers and the sampling ports. Replace methanol with deionized water. Repeat the previous cleaning step. Finally dry the chambers of each cell in the air before use. Repeat the cleaning procedures after use.

Figure 3, a Side-Bi-Side Cell

4 IVPT Diffusion Testing

Before testing, the following should be determined based on the project: The composition and concentration of the donor solution, composition of receptor fluid, type of membrane (polymeric or biological), temperature of the receptor fluid, sampling volume, and sampling time points.

Prior to starting, set the temperature of the heater/circulator to a predetermined value and place a stir bar into each side of each cell. Place a membrane between the two chambers and clamp the chambers together. If necessary, place Teflon® foam gaskets between the chambers and membrane. Designate one side as the receptor chamber and begin filling with receptor fluid while tilting the clamped cell up to force any bubbles out. Likewise, fill the donor chamber with donor solution. Insert the chamber stoppers and turn on the stirrers. Place the cell assembly onto the stirrer. The pins on the stirrer locate the Cell Clamp correctly so the rotating magnets inside the stirrer are directly below the magnet wells of the Side-Bi-Side Cells' chambers.

At each predetermined sampling time, remove the stopper from the sampling port. Withdraw a volume of sample specified in the test protocol by inserting a suitable pipette or syringe needle into the sampling port so that the sample will be removed from the middle of the chamber. The same amount of fresh fluid is refilled into the cell through the sampling port and the stopper is reinserted into the sampling port. Be sure to fill each chamber so the membrane is not in contact with air.

In some applications, the donor chamber may be sampled as well. Follow the same procedure as for sampling the receptor chamber.

5 Q&A

a - Can Side-Bi-Side cells be autoclaved? YES. They can be sterilized in an autoclave.

b - Can I use the mobile phase for the HPLC analysis as the receptor chamber's fluid? YES. In general, you can use any solvent for the receptor chamber's medium as long as the solvent provides "sink" conditions for the test compound. Generally, sink conditions are such that the concentration of the compound remains below 10% of the compound's solubility in the receptor chamber's medium. This ensures the permeation or release profile is not rate-limited by the compound's solubility in the receptor chamber fluid. The effect organic solvents have on the membrane should also be considered.

c - How do I select a membrane for In Vitro release testing? According to the "FDA Guidance for Industry: Nonsterile Semisolid Dosage Forms: Scale-Up and Postapproval Changes: Chemistry, Manufacturing, and Controls; In Vitro Release Testing and In Vivo Bioequivalence Documentation, May 1997, SUPAC-SS CMC 7", any "appropriate inert and commercially available synthetic membranes such as polysulfone, cellulose acetate/nitrate mixed ester, or polytetrafluoroethylene membrane can be used." Hydrophilic polymeric membranes with a pore size of .45µm are widely used. After determining a suitable membrane during the IVRT method development phase, the same membrane should be used for the duration of the project.

d - How do I decide how much sample volume to remove, i.e. the entire receptor volume or a couple of hundred microliters? If the study has only one time point, the entire receptor chamber's volume can be sampled out. If sampling more than one time point, any size aliquot is acceptable as long as no air bubbles are introduced at the junction of the cell halves. All of a chamber's fluid may be removed from the chamber, if necessary, but full replacement necessitates having to lift each clamped cell from the H-Series Stirrer to refill the chamber. Sample volume considerations include the maximum volume that can be removed without introducing bubbles and the minimum volume required for sample analysis.

Your System Includes:

1. The stirrer itself with a Cell Clamp for each station.

2. Side-Bi-Side Cells

3. The appropriate power cord

4. A bag of fittings to connect the multi-station stirrer to a system that provides warm water. (PermeGear supplies two sizes of fittings which both have 3/8NPT pipe threads on one end to screw into the tubes. Four of the fittings of the smaller size have a hose barb on the other ends from the NPT threads for 5/16” (8mm) tubing and the other four have 1/2” hose barbs (12.8mm) for larger tubing both of which seem to be common sizes for heater/circulators. You can choose which size you will need and discard the other.)

If PermeGear supplies the heater/circulator with the stirrers, we then supply only the correct fittings for our heater/circulator.

4. A roll of 3/16” ID soft silicone tubing, 3 feet for each cell, that the user will use to connect the cells to the manifolds.

5. A Manual with assembly instructions, operation, proper care and cleaning and frequently asked questions/answers.

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