# **OPERATION MANUAL**

# For



# **Rotary Cell Culture Vessel**

# **Continuous Flow Perfusion System**

8977 Interchange Drive Houston, TX 77054 (T) 713-741-2582 (F) 713-741-2588 <u>rccs@synthecon.com</u> <u>www.synthecon.com</u>

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### **1.0** General Introduction to the Rotary Culture Max<sup>TM</sup>

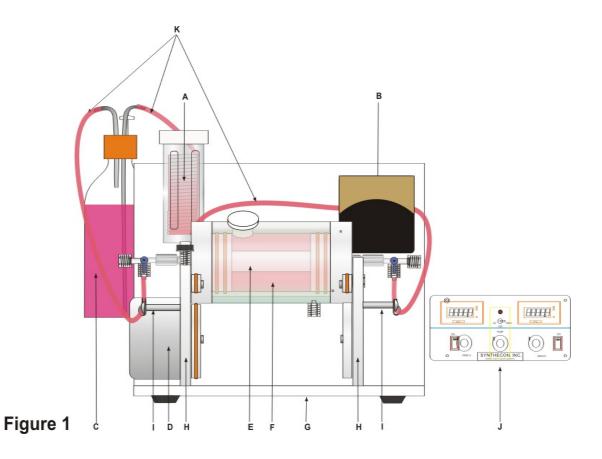
Synthecon, Incorporated is the industry leader in the design and utilization of unique Rotary Cell Culture Systems<sup>TM</sup> widely applicable in industrial, academic, and aerospace environments. A great variety of cell types from different species have been successfully grown in these systems to date including: osteoblasts, chrondrocytes, skeletal muscle, human and murine tumors, primary human hepatocytes, and a variety of human explant tissues (see bibliography at the end of the manual and <u>www.synthecon.com</u> for a continuously updated list). Cells have been successfully grown both in the absence of solid supports or using any of a variety of support structures; i.e., microcarrier beads, collagen macro beads, alginate beads, and various scaffolding materials. Cells subcultured in the unique bioreactor environment have been shown to exhibit unique properties; i.e., enhanced gene expression, enhanced production of bio-products, spontaneous formation of three-dimensional tissue assemblies, etc.

The advanced design ROTARY CULTURE  $Max^{TM}$  (*RCMW*<sup>TM</sup>) represents the next generation of Continuous Perfusion Bioreactors exclusively manufactured by Synthecon, Inc. The RCMW<sup>TM</sup> rotates the cell culture chamber horizontally to maintain the seeded cells suspended in the culture medium and provides an exceptional cell culture environment that enhances cell growth through the

> absence of air bubbles in the zero head space cell culture vessel, minimal shear forces, high mass transfer of nutrients, effective waste removal, and efficient oxygenation.

The RCMW<sup>™</sup> incorporates a number of design changes providing increased applicability, durability, and ease of use compared to earlier prototypes. These innovations include:

- 1. An *advanced design cell culture vessel* incorporating a microporus perfusion core which provides nutrient and gas exchange with cultured cells.
- 2. The new *in-line oxygenator* system provides external gassing of the media insuring a low stress culture environment
- 3. A new *direct drive rotation system* provides ease of operation and eliminates the older belt driven pulley and gear assembly found in earlier systems.
- 4. For increased ease of use, access and serviceability, the culture vessel is now rotated in a *cradle roller assembly*. The culture vessel is perfused through rotating fluid couplings located at the vessel endcaps. For removal, simply lift the culture vessel from the cradle for service, thus eliminating the need for manipulation of metal shafts and complex gear assemblies.
- 5. The media circulation loop now has two 3-way stopcock valves to simplify media management in the circulation loop. The RCMW<sup>TM</sup> is now equipped with *one media reservoir bottle* located on the rear face of the vertical support.



The RCMW<sup>™</sup> allows the growth and maintenance of a variety of cell and tissue types in monocultures, co-cultured three-dimensional tissue-like cell aggregates and explants. The RCMW<sup>™</sup> accomplishes this by continuously perfusing fresh nutrients and gas, and effectively removing of waste products while maintaining a low shear suspension environment. The large 500 ml media reservoir along with the culture chamber volume, insure an extended culture. The media reservoir being outside the culture chamber, essentially, eliminates the need to remove the growth chamber from the incubator to replenish the medium. The key advantages of a perfused cell culture system include:

- 1. Ability for long-term un-interrupted cell culture
- 2. Clear unobstructed viewing of culture chamber environment.
- 3. Closed loop circulation of fluid, which reduces risk of contamination.

### The RCMW<sup>™</sup> is composed of the following components shown in Figure 1.

- A. Oxygenator assembly- externally facilitates oxygenation/CO2 exchange for cell and tissue cultures in the vessel. The assembly is mounted on the face of the vertical plate. The unit contains 46 square inches of surface area within thin wall silicone tubing. The fluid volume is about 10 cc. The oxygenator is easily removed for cleaning/sterilization. DO NOT REMOVE THE TUBING FROM THE HOUSING. It is mounted on the upper left side of the vertical plate of the support assembly.
- **B. Peristaltic pump-** clockwise rotation provides the force to pump culture medium through the culture vessel. It is mounted on the far upper right side of the vertical plate of the support assembly. Lift the tan colored faceplate upward to gain access for insertion of the media circulation tubing. Power is provided to the peristaltic pump via a multi-colored ribbon cable, which is connected at the power supply and then at the pump. To insure proper pumping, the tubing must be aligned in the center of the rotating rollers, and locked into the v-notches on the inlet and outlet sides of the pump. The pump flow rate is adjusted using the panel control knobs on the right front of the power supply. One rpm on the peristaltic pump is approximately equivalent to a flow rate through the circulation tubing of 0.5 ml/minute. Adjust flow rate as necessary
- C. Culture media reservoir- a 500 ml Pyrex glass bottle with orange cap containing a *long* stainless steel media supply tube that extends to the bottom of the bottle, a short steel media return tube, and a Whatman micro filter to vent the bottle. It is located in the middle of the rear face of the vertical plate of the support assembly.
- **D. Direct motor drive-** used to rotate the culture vessel horizontally at speeds from 2-42 rpm. It is equipped with one extended service life stepper motor (no brushes or gear head). The rotational speed switch, located on the left face of the power supply, has three settings: "Low"- adjustable range of 6-27 rpm; "Off" or "High" -adjustable range of 10-52 rpm.
- E. Perfusion Core- the plastic cylindrical core fits in the center of the culture vessel. Media is pumped through the center of the core until it reached the plastic plug where the flow is directed through the pores into the culture vessel. Media re-enters the core on the other side of the plug and exits the culture vessel. The core is to be used once and discarded. The plastic plug is reuseable and should be recovered after each culture.
- F. Culture vessel- culture vessels can range in volume from 25 ml to 1L. The standard size vessel is 125 ml. The vessel is composed of two white polyacetyl endcaps. Affixed to the endcaps are white delrin luer fittings for attaching rotating fluid couplings. Assembled, the vessel is comprised of two white endcaps, a perfusion core, and a clear vessel wall. The vessel wall contains two sampling/injection Luer lock ports with rubber septums and drain/fill port with a Delrin plastic plug insert.
  - **G. Rotator Base/Assembly Support-** serves to support and rotate the culture vessel. It is constructed of two rectangular white Delrin/Acetyl plastic plates (one horizontal and one

vertical) creating an envelope 12" wide X 10" long X 10.5" high. Components are mounted on each of the plates. Located on the vertical plate are the oxygenator assembly, peristaltic pump, and media bottle. The roller cradle assembly is attached to the horizontal base plate. It consists of two white Delrin uprights creating a roller cradle in which the vessel is aligned, supported and rotated.

- **H.** Upright roller cradle supports- vertical white Delrin plastic plates equipped with white Delrin direct-drive disk and roller support disk to maintain the culture vessel in proper alignment in the roller cradle assembly.
- I. Silicone tubing standoff clips- be sure tygon tubing is inserted through the clip and does not put strain on the rotating coupler. The rotating coupler must remain parallel with the central axis throughout system rotation or it will cause excessive wear resulting in leakage.
- J. **Power supply** the blue control box that houses the electronic motor speed controls. The front panel knobs are used to adjust vessel rotation speed, as well as, to control the peristaltic pump. A digital tachometer displays rotation speed and rate of pump flow. A flat, multicolored, ribbon cable connects the rotator base to the power supply control box. The rotational speed of the vessel may be set on "Hi", "Low", or "Off". **THE CONTROL BOX SHOULD NEVER BE PLACED INSIDE AN INCUBATOR.**
- **K. Connecting tubing-** reusable, autoclavable Dow-Corning silicone rubber tubing used to complete the perfusion loop (3/32" inner diameter)
- L. External perfusion loop- consists of media supply/waste bottle, oxygenator assembly, peristaltic pump, media and rotating fluid couplings with three-way valves, connected with reusable, autoclavable, silicon rubber tubing.

### 2.0 Read before using-Limited Warranty

- ☑ Please read, complete and return the Limited Warranty Sheet found on the last page *immediately upon receipt* of your new RCMW<sup>™</sup>. The Warranty will **NOT BE VALID** unless it is signed and returned to Synthecon, Inc.
- ☑ The RCMW<sup>™</sup> is currently intended for **<u>RESEARCH USE ONLY</u>** (see warranty).

### ☑ Caution: performing any of the following can invalidate the warranty.

- Soaking any part of the vessel in bleach, acidic, or basic cleaning solutions can result in absorption of toxic chemicals into the rubber fittings and inhibit cell growth.
- Abrasive cleaners or strong organic cleaning compounds such as acetone *will destroy* the plastic.
- Corrosive chemicals such as chromates will damage the metal parts.
- **Do not** autoclave the rotator base/upright assembly (see Figure 1). Table 1 lists those components that can be autoclaved.
- Sterilizing the autoclavable components (Table 1) for more than the recommended temperature and time (120°C for 20 minutes).
- Storage of the rotator base/upright assembly in an incubator <u>while NOT in</u> <u>use</u> will corrode the motors eventually resulting in loss of function. *Synthecon reserves the right to make discretionary determination of the cause of damage to returned rotators and deem whether the repair is covered under the limited warranty.*
- Placing the power supply/control box inside an incubator will result in loss of function.

#### Table 1 Methods for sterilizing RCMW<sup>™</sup> components

# Autoclavable components

### 120°C, 20 min

Culture vessel

(Porous core and plug, Delrin drain/fill port, O-rings, two end caps, clear vessel wall) Silicone rubber tubing 0.2 micron vent filters medium bottle & cap oxygenator male and female type tubing connectors

### Do not autoclave

### Wipe/rinse with ETOH only

White Delrin cradle support assembly	
peristaltic pump	
power supply outer cover	
Ribbon cable	

# **Disposable Components**

(discard after each use)

Plastic three way stopcock with luer fittings
Rotating fluid couplings
Syringes
Rubber Septums, one way valves

### 3.0 Getting Started- Unpacking and Inspection

The RCMW<sup>TM</sup> is carefully packaged for shipment to ensure the arrival of an intact, functional unit. Unfortunately, on rare occasions, some damage may incur during handling by the freight carrier.

- Upon receipt, visually inspect each system component closely after unpacking for visible or concealed damage.
- IF DAMAGE IS EVIDENT OR SUSPECTED, DO NOT ASSEMBLE OR OPERATE THE UNIT. Please call Synthecon, Inc. at (800) 853-0740 if you are in the USA. For assistance outside the USA, please call your closest distributor listed at the end of the manual.

### 4.0 **RCMW<sup>TM</sup>** preparation required before culture initiation

Before initiating the growth of cultures, the RCMW<sup>™</sup> must be properly prepared.

Disassembly and discard of disposable components Cleaning/washing of autoclavable components Rinsing/soaking Autoclaving appropriate components Unit re-assembly

### CAUTION: ALL RCMW<sup>™</sup> COMPONENTS ARE NOT STERILE UPON ARRIVAL EXCEPT THOSE IN STERIL PACKAGES INCLUDING:

Three way stopcock/rotating fluid couplings Cannulas and Septums One way valves

The RCMW<sup>TM</sup> is shipped completely assembled with these non-sterile disposable components attached for instructional use ONLY and must be cleaned and sterilized, or discarded and replaced with pre-sterilized components before use.

## 4.1 System disassembly sequence for washing & sterilization

Please refer to Figure 1 for proper identification of parts to facilitate disassembly. Remove the following items to wash and autoclave or for replacement with pre-sterilized components *before initializing* a sterile cell culture in the RCMW

### Upon receipt of the RCMW<sup>TM</sup> unit and prior to actual operation-

- 1. Disconnect disposable rotating coupling from each end of the culture vessel and discard.
- 2. Carefully remove the culture vessel. Remove each of the white Delrin end caps while holding the vessel (a plastic screw is included to assist with removing the end caps. You will see screw holes in the Delrin end cap. Put the screw in one of the holes and screw in until the end separated from the vessel wall. Remove screw and reinsert into another hole to further separate the vessel from the end cap. A slight unscrewing twist of the end cap will make it easier to remove). Unscrew the white Delrin drain/fill port. Place all parts in a secure area where they cannot be knocked onto the floor and become damaged.
- 3. Remove tubing from the support clips located on the outer face of the upright support plates of the roller cradle.
- 4. Disconnect and remove the silicon rubber tubing forming the perfusion loop. Note how the tubing is connected to facilitate re-connection after washing and sterilization. Disconnect the tubing from the peristaltic pump. **NOTE**: *leave the tubing connected to the orange cap of the media bottle to facilitate re-assembly.*
- 5. Remove the oxygenator assembly by unscrewing the bolt on the bottom of the white bracket. Support the assembly by *using your fingers* while removing the oxygenator to prevent it from falling. DO NOT REMOVE TUBING FROM OXYGENATOR HOUSING!
- 6. Remove the media bottle from the holder in the rear of the vertical plate of the support assembly.

### 4.2 Washing the RCMW<sup>TM</sup> Components after disassembly

- 1. Use a mild liquid soap— a laboratory soap such as Liquinox or equivalent.
- 2. Soak all components (disassembled culture vessel,oxygenator, media bottle, connecting tubing) in the soap dissolved in warm water for about 10 minutes.
- 3. The RCMW<sup>a</sup> may be washed with a soft brush. Avoid sharp instruments as any damage to the vessel wall can cause progressive cracking after multiple autoclavings.

The oxygenator requires an injection of soapy water using a syringe and then allowing it to soak.

- 4. After cleaning, thoroughly rinse each component under gently running tap water until all traces of soap are completely removed.
- 5. The oxygenator will need to be rinsed by injecting water through the tubing or syringe port using a 20-60 cc size syringe several times. REMEMBER: DO NOT REMOVE THE TUBING FROM THE OXYGENATOR HOUSING.

### 6. Either of two rinsing protocols can be used.

Rinsing the components is a critical step since residual soap can be harmful to cell cultures. First, hand rinse all components in high purity, cell culture grade water (i.e., Millipore Milli Q water or the equivalent). Next, either

- 1. Completely immerse and soak all components in high purity water overnight or
- 2. Alternatively, rinse components in continuously running high purity (Milli Q or equivalent not deionized)water for 45-60 minutes.

(Do not forget to use a syringe to rinse the oxygenator)

7. Before the porous perfusion core is placed in the bioreactor vessel, a reusable delrin plug must be placed inside the core to direct the flow of media into and out of the vessel (see figure 2a). The plug is placed in the end of the core (see figure 2b) and pushed into the core with the metal rod provided. The mark on the metal rod is the distance that the plug should be pushed into the core.



Figure 2a



Figure 2b

The side of the core with the longest distance from the plug is the influx side and shortest distance is the efflux side. When the core is placed in the vessel before autoclaving, one of the endcaps should be marked so that the vessel can be properly oriented.

The core should be placed in the bioreactor vessel and autoclaved in the assembled vessel. It is suggested that plastic caps be placed on the luer fitting **loosely** and secured with autoclave tape to protect them from contamination when the system is assembled prior to initiating a culture. See figure 3





8. Autoclave components at 120°C for 20 minutes. **CAUTION:** *Higher temperatures and longer autoclave times must be avoided as these can damage components and void the warranty*. The entire flow loop may be assembled and autoclaved as a unit. It is recommended that the free ends of the loop with plastic fittings be wrapped with aluminum foil to protect them from contamination while the system is being prepared for culturing. Figure 4

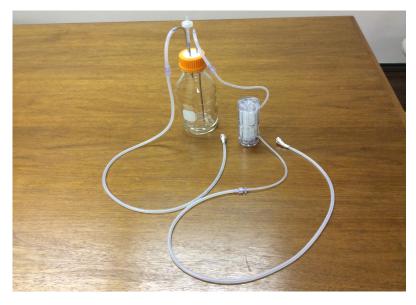


Figure 4

## **Re-assembly** after sterilization

Refer to Figure 1 for guidance in re-assembly.

1. Take all sterilized components to a sterile work area; i.e., a laminar flow biological safety cabinet (sterile tissue culture hood).

2. Remove the tape on each of the Luer fittings on the endcaps and attach a 3 way stopcock/rotating coupling. Try to avoid touching the Luer fittings or sampling ports. If these areas are accidentally touched, wipe them immediately with a sterile alcohol swab. Attach sterile disposable one-way valves or rubber septums to the Luer ports on the vessel wall for sampling media. The septums are meant to be used with the plastic cannulas provided.

3. Remove the protective foil cover from one end of the tubing and attach to the rotary coupling on one endcap. Repeat the process on the other endcap. (Figure 5)

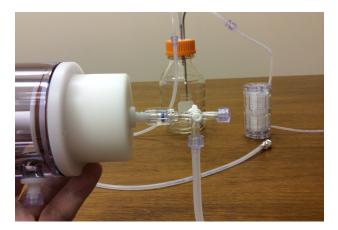


Figure 5

4. Filling the Culture vessel with media. Fill the media bottle with the desired volume of media. Remove the fill port plug on the vessel wall and place it on a alcohol swab. Fill the cell chamber of the vessel with media and cells until it reaches the fill port. Microcarriers or other scaffolding material can also be added at this time. Replace the fill port plug being careful not to contaminate the plug. Since it is difficult to maneuver the rotator base in the hood, it is more convenient to take the complete the flow loop and assemble it on the rotator base on a bench and then place the whole system in the incubator. (Figure 6 shows the completely assembled system) Note the clamp on the left upright should be tightened to assure that the vessel rotates properly.



Figure 6

Note in figure 6 that one syringe port has a septum and the other port has a one way valve. This is just for demonstration purposes. Either can be used on the syringe ports depending on the user's preference.

5. Open the cover of the peristaltic pump so that the tubing is not pinched. Place a sterile syringe on one of the luer ports on the rotating coupling and turn the valve to open that port to the syringe. Using the syringe, prime the tubing by drawing media from the bottle until it reaches the syringe. Rotate the valve so that the media flow is directed into the vessel through the perfusion core. Close the cover of the peristaltic pump. Place a 5 or 10 ml syringe with a plastic canula on the sampling port (wiping the septum with a sterile alcohol swab whenever it is to be punctured is recommended). Maneuver the bubble in the cell chamber beneath the sampling port and draw the bubble out. Media will be pulled through the core to replace the volume of the bubble. During the culture, if bubbles appear in the vessel, they can be removed by this procedure. The tubing directly attached to the rotating coupling should be inserted into the support clips to prevent the rotating coupling. The system

is now ready to be placed in an incubator and connected to the power supply. During the initial stage of the culture (approximately 24 hours), the bioreactor should be rotated without flow to allow cells to form spheroids or attach to scaffolds. Otherwise the cells will pass through the pores in the core and accumulate in the media reservoir.

6. Connect the ribbon cables from the power supply to the peristaltic pump and the rotator. The cables can be run between the door and the gasket. The rotational speed is usually set to 10-12 rpm initially. If visible aggregates are formed, the speed should be adjusted upward to maintain the aggregates in suspension without touching the wall of the vessel. The pump speed should be determined empirically according to the metabolic requirements of the cells being cultured. Media changes can be done by simply changing the media bottle in the flow loop to one with fresh media.

No special medium formulations are required for the growth of cells in the RCCS. Each cell type and application is unique. Cell culture medium formulations that you have previously used successfully with other cultivation methods (i.e., petri dishes, flasks, roller bottles, etc.) have generally been found to be appropriate for the RCCS. See the Bibliography and SYNTHECON website <u>www.synthecon.com</u> (bibliography periodically updated) for medium formulations successfully used in the past with the RCCS.

# 5.0 Troubleshooting

	Problem	Possible cause/solution
		check for loose connection tubing
В	bubbles present in cell culture vessel I	incubator could be dry causing excessive evaporation
		Ensure that the media bottle contains medium
C	culture medium leaking	Check valves, couplings, and tubing for tightness of fit
		Replace if defective
	Medium fails to recirculate	Check for proper positioning of steel tube below the fluid
	e	level in the media bottle
		Check position of three way valves and rotating coupling
		Make certain peristaltic pump is plugged in and speed
		control set on power supply
		insure that tubing is correctly installed in the roller asembly o
		f the peristaltic pump
V	Vessel rotation is inconsistent	Check that vessel is properly situated in the roller cradle and
	1	not bound up or jammed.
		The vessel can only achieve rotation if it is in contact with
	ľ	the rotating disk drive located on the inside of the left
		upright cradle support.
		Check to insure that the RPM are optimal for the selected
		high/low range of the power supply
Р	Perfusion tubing twisting C	Check that rotating coupling was installed and aligned
		appropriately with the tubing support clips and that it is
		turning without an orbital rotation. Replace and align
0		correctly if defective
C	Culture vessel will not fill	Check position of three-way stopcock valves
		look for crimp in tubing at inflow endcap
	oxygenator tubing removed from inside	Return to Synthecon for repair,
	oxygenator cylinder core	
		Empty waste bottle and replace filter unit.
b	bottle	

# 6.0 How to order disposable pre-sterilized parts

Contact Synthecon (713-741-2582 or rccs@synthecon.com) or telephone contract distributors for information on ordering disposable pre-sterilized parts.

### Equipment Usage Rights

SYNTHECON<sub>TM</sub> Inc. grants the purchaser a non-exclusive right to use the Rotary Cell Culture System equipment solely for the purpose of conducting research and specifically excluding use of this equipment for any purpose other than research. Synthecon technology is not intended for use on/in humans. Any desire by end user to manufacture commercial products in Synthecon, Inc. technology will require the end user to obtain a *User's License* from the National Aeronautics and Space Administration and/or Synthecon, Inc. Its use must comply with all laws, ordinances, and regulations relating to the possession, use, or maintenance of the equipment, including registration and/or licensing requirements, if any. **Patents in Force** 

The Rotary Cell Culture System<sup>TM</sup> is protected by patents exclusively licensed from the National Aeronautics and Space Administration (NASA) and patents owned by Synthecon Inc., with others pending. The patents Synthecon Incorporated operates under are listed below:

- Patent number 5,437,998 "GAS PERMEABLE BIOREACTOR AND METHOD OF USE" Patent issued August 1, 1995
- Patent number 5,665,594 "GAS PERMEABLE BIOREACTOR AND METHOD OF USE" Patent issued September 9, 1997
- Patent number 5,702,941 "GAS PERMEABLE BIOREACTOR AND METHOD OF USE" Patent issued December 30, 1997
- Patent number 5,763,279 "GAS PERMEABLE BIOREACTOR AND METHOD OF USE" Patent issued June 9, 1998
- Patent number 4,988,623 "ROTATING BIO-REACTOR CELL CULTURE APPARATUS" Patent issued January 29, 1991
- Patent number 5,026,650 "HORIZONTALLY ROTATED CELL CULTURE SYSTEM WITH A COAXIAL TUBULAR OXYGENATOR" Patent issued June 25, 1991
- Patent number 5,153,131 "HIGH ASPECT RATIO VESSEL AND METHOD OF USE" Patent issued October 6, 1992
- Patent number 5,155,035 "METHOD FOR CULTURING MAMMALIAN CELLS IN A PERFUSED BIOREACTOR" Patent issued October 13, 1992
- Patent number 5,153,133 "METHOD FOR CULTURING MAMMALIAN CELLS IN A HORIZONTALLY ROTATED BIOREACTOR" Patent issued October 6, 1992
- Patent number 5,998,202 "MULTIPLE CHAMBER DIFFUSION VESSEL" Patent issued December 7, 1999
- Patent number 5,989,913 "CULTURE VESSEL FOR GROWING OR CULTURING CELLS, CELLULAR AGGREGATES, TISSUES AND ORGANOIDS AND METHODS FOR USING THE SAME" Patent issued November 23, 1999

### **Alterations**

Alteration of the equipment voids the warranty on this equipment. In no case shall SYNTHECON<sup>TM</sup>, Inc. be responsible for any modifications or alterations to this equipment performed by anyone other than SYNTHECON<sup>TM</sup>, Inc.

# **IMPORTANT NOTICE**

# **Limited Warranty: Limited Liability**

SYNTHECON<sup>TM</sup> Inc. warrants that, for one year, under normal operating conditions and use, this equipment will be free from defects of materials and workmanship. SYNTHECON<sup>TM</sup> Inc. will repair or replace defective parts at our option. Contact SYNTHECON<sup>TM</sup> Inc. immediately upon discovery of a defect. SYNTHECON<sup>TM</sup> will provide you with a return authorization number and shipping instructions.

### **Components**

### **Oxygenator Membrane**

The oxygenator membrane is a very delicate component consisting of silicone rubber, .005 inches thick, covering a polyester cloth backing. Care and attention should be given to the membrane during cleaning, sterilization, and removal of cultured material. Synthecon reserves the right to make discretionary determination as to the cause of damage with returned oxygenators, and deem whether the repair is covered under the Synthecon Limited Warranty. See Operators Manual for appropriate procedures.

#### **Rotator Base**

Storage of the Rotator Base in an incubator while not in use will result in damage to the rotator components. Synthecon reserves the right to make a discretionary determination as to the cause of damage with returned rotators, and deem whether the repair is covered under the Synthecon Limited Warranty.

The equipment must be used and operated in a careful and proper manner. In no event shall SYNTHECON<sup>TM</sup> Inc. or its suppliers be liable for any indirect, special, or consequential damages, including but not limited to, loss of cells, medium, data, labor or equipment incurred by the purchaser or any third party arising from the use of, or inability to use this equipment.

### <u>Service</u>

For service during and after the expiration of the warranty, contact SYNTHECON<sup>TM</sup>, Inc. at (713) 741-2582 during 9 a.m. to 5 p.m., US Central Time Zone. Equipment being returned for service should be shipped to: Synthecon,- Customer Service Dept, 8977 Interchange Dr., Houston, TX 77054. Please include a short description of the problem, service required or reason for the return. Please pack equipment being returned in sturdy containers with adequate packing materials. Synthecon will not be liable for damage sustained during shipment.

SYNTHECON<sup>TM</sup>, Inc. also provides biology and engineering contract support services. Special custom designed equipment can be built to meet the customer's needs. Customers can provide cell samples of their cell and tissue lines, and SYNTHECON<sup>TM</sup> Inc. will conduct growth and feasibility studies of the customer's cells on a contract fee basis. Sub-licenses are available which would include design, scale-up, and manufacture of production equipment.

### **Copying and Sale**

Duplication, modification or sale of copies of this equipment is prohibited. This equipment is patented by the U. S. Government. SYNTHECON<sup>TM</sup> Inc. holds the exclusive licenses to these patents.

### Acceptance of Equipment

The purchaser shall inspect the equipment delivered and immediately notify the seller of any discrepancies with the equipment. If the purchaser fails to provide notice in writing within 14 days after the delivery of the equipment, the purchaser will be presumed to have accepted the equipment. The acceptance and use of this equipment constitutes an agreement upon the purchaser's part to the usable condition of the equipment.

#### **Refurbished Products**

Refurbished products carry a separate warranty, this warranty does not apply. For details of refurbished

product warranty, please refer to the refurbished product warranty information packaged with each

refurbished product.

### WARRANTY WILL NOT BE VALID IF IT IS NOT SIGNED AND RETURNED.

Warranty valid to original purchasers only. Please sign and return by mail immediately to: For international locations see the very last page

Synthecon, Inc.	
Customer Service Department	
8044 El Rio	
Houston, TX 77054	

Purchaser: \_\_\_\_\_

Institution/Organization:	
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Purchase Date:
----------------

Invoice/PO#: \_\_\_\_\_/\_\_\_\_

Model #:	

Serial Number(s)

### (PLEASE NOTE THAT THIS PAGE IS FOR YOUR RECORDS. PLEASE USE THE YELLOW PAGE THAT ACCOMPANIES THIS MAUAL FOR WARRANTY REGISTRATION!)

# **IMPORTANT NOTICE**

PLEASE READ AND COMPLETE THE SYNTHECON LIMITED WARRANTY ON THE LAST PAGE

### **RETURN THE YELLOW COPY IMMEDIATELY**

WARRANTY WILL NOT BE VALID IF NOT COMPLETED AND RETURNED

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### **10 International Locations**

### <u>USA</u>

SYNTHECON, INC. 8977 Interchange Dr. Houston, TX 77054 Tel.: (713) 741-2582 Fax: (713) 741-2588 rccs@synthecon.com

### <u>Europe</u>

Cellon Zone d'Activites Economiques Robert Steichen 16, rue Heierchen L-4940 Bascharage Luxembourg Tel.: +352 26 33 73 - 1 Fax: +352 31 10 52 www.c e-mail: sales@cellon.lu

### <u>China</u>

East Lake Cell Co. 369 Guangshan Rd. East Lake Hi-tech Zone Wuhan, Hubei, China Tel: +86-1398239916 +86-27-87052473 www.eastlakecell.com

### <u>Taiwan</u>

Tseng Hsiang Life Science LTD. No 99-15 Sec. 2, Nan-Kang Rd Taipei, Taiwan R.O.C Tel: 02-785-1156 Fax: 02-788-5896 thlsl@ms9.hinet.net

### <u>Japan</u>

Tomy Digital Biology Co., Ltd. "EDGE" Building 2-9-1 Ikenohata Taito-ku Tokyo 110-0008 Tel: 81-3-5834-0810 Fax: 81-3-5834-1888"; E-mail: info@digital-biology.co.jp Website: www.digital-biology.co.jp

### Egypt

Noor Scientific & Trade 10 El-Salam St, Komish El-Nile Aghakhan, Shoubra, Cairo-11241 Egypt Tel: 202 4329148 Fax: 202 2034350 noor@access.com.eg

### <u>India</u>

Medi Analytika India Pvt. Ltd Adyar Bridge road Adyar, Madras - 600 020 India Tel: 0091-44-446 0988/490 8734/490 8572 Fax: 0091-44-446 3931/490 8572 mediana@vsnl.com