ESCO HEALTHCARE

*"Discovery to Delivery"*

# MiniTide®

## The Tiny Titan of Adherent Bioprocessing


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MiniTide® bioreactor leverages the proprietary Tide Motion® technology in a compact and user-friendly design. This facilitates linear scalability for research-oriented experiments. The streamlined bioprocess design expedites licensing due to the consistent application of the core Tide Motion® technology across all scales. This consistency ensures a seamless transition from initial discovery stages to in-vivo studies, GLP compliance testing, clinical trials, and ultimately, commercialization. This approach optimizes the patent lifespan by employing the same core technology throughout the entire development pipeline.

Esco MiniTide® simplifies the high-throughput screening of exosomes derived from diverse biological sources, covering primary tissues, cancer cells, and immortalized cell lines. This capacity is especially advantageous for the development of diagnostic and screening assays. It acknowledges the substantial variability in therapeutic potential between exosome populations, potentially influenced by culture conditions. The capability of MiniTide® to generate exosomes through cell culture enables researchers to investigate these contributing factors and pinpoint functionally potent exosome subsets.

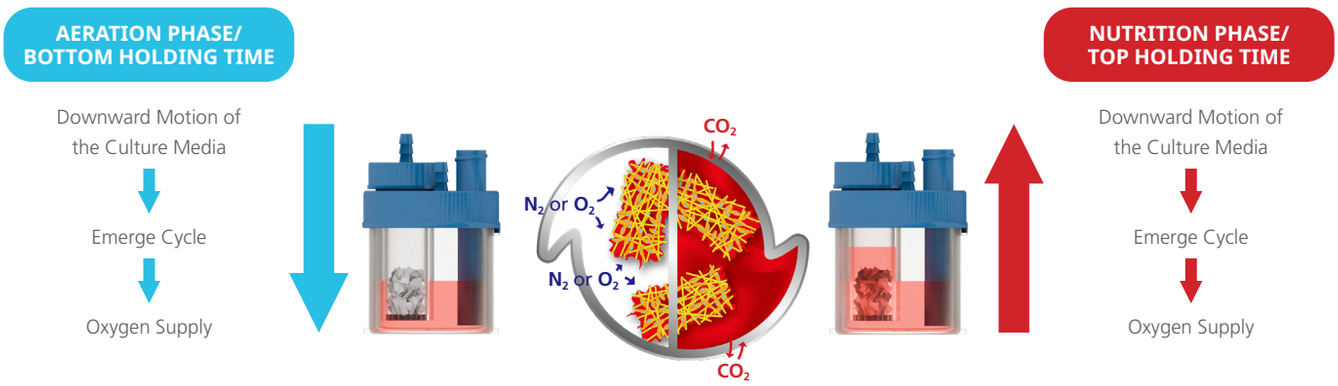

## Features

- Utilizes proprietary Tide Motion® technology in a compact, user-friendly design
- Disposable, single use vessel
- Siemens HMI PLC-based monitoring system
- Enables efficient research with limited samples, costly media, and expensive analyses
- Facilitates rapid exosome generation from primary tissues, cancer cells, and immortalized cell lines

## Applications

- Supports exosome-based research for therapeutic and diagnostic development
- Culture of anchorage-dependent cells with BioNOC II® and BioMESH® macrocarriers
- Proof-of-concept for 3D carrier culture
- MSC/EVs study or process optimization
- Vaccine/virus study or process optimization
- Tissue engineering

# The Motion Principle of MiniTide®




MiniTide® functions based on the Tide Motion principle, where cells adhere to macroporous carriers and are alternately exposed to aeration and nutrients from the culture medium. The gentle vertical movement of the medium creates a dynamic interface between air and liquid at the cell surface, ensuring an environment with minimal shear stress, high aeration and nutrient availability, no foaming, and unrestricted oxygen supply. This efficient transfer of nutrients and oxygen effectively replicates the alternating exposure to nutrients and oxygen that cells experience in their native environment.

# Macroporous Carriers

Anchorage-dependent cells require a surface for growth, traditionally provided by T-flasks or roller bottles. However, scaling up these methods is challenging, leading to the development of macroporous carriers. These matrices support the attachment, growth, and proliferation of adherent cell lines, including animal, mammalian, and insect cells. Commonly used in packed-bed and Tide Motion® bioreactors, they offer scalable solutions for large-scale cell culture. With diverse physical and chemical properties, the choice of carrier depends on the specific anchorage requirements of the cultured cells.

## BioNOC II®

BioNOC II® is a macroporous carrier that supports the growth of anchorage-dependent cells including **animal, mammalian,** and **insect cells** in either serum-containing or serum-free culture media.

### Features

- Made of 100% PET
- Complies to <85>, <87>, <881>, ISO 10993-5: 2009
- High porosity (50 - 200 µm between fiber), and biocompatible to coating reagents for better
- attachment
- High surface area* up to 15,000 cm2 per 0.1 L packed bed volume for Vero cells
- Enhanced hydrophilicity, coating factors can be added

## BioMESH®

BioMESH® is a low-lint macrocarrier designed specifically for cell harvesting applications. It is suitable for use with **skin fibroblasts, cardiac fibroblasts, multipotent/pluripotent stem cells, epithelial cells,** and **chondrocytes.**

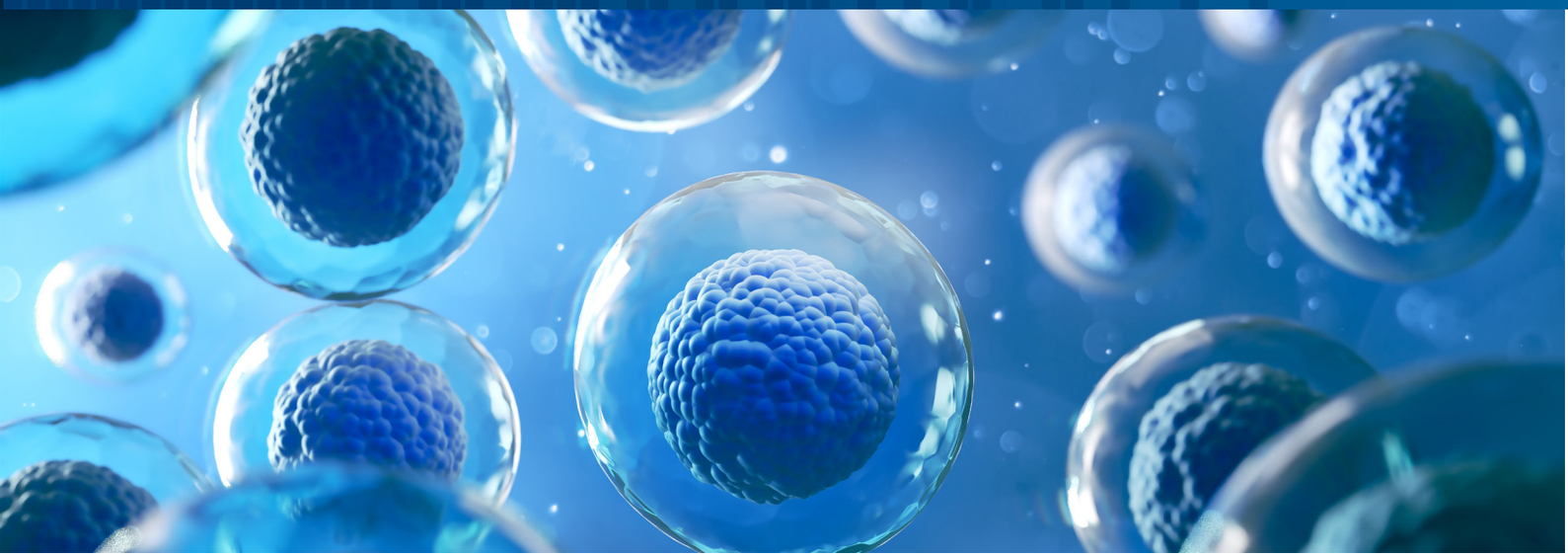
### Features

- Made of a combination of polypropylene (PP) netting and PET mesh
- Complies to USP <83> <87> <788>, USP Class VI, ISO 10993-5: 2009
- High porosity (200 µm space between PET fiber; 670 µm space between PP fiber)
- High surface area* for cell growth: up to 10,000 cm2 per 0.1 L packed bed volume for MSCs
- Enhanced hydrophilicity, coating factors can be added

**Note: Surface area varies on the cell line used*

## Your Own Scaffold or Bioedible Scaffold

Choose your preferred carrier system or opt for a bioedible scaffold designed for seamless integration.



## Key Benefits

**Highest Yield**
MiniTide® employs advanced macroporous carriers, BioNOC II® and BioMESH®, to optimize cell culture applications. BioNOC II® offers a 100% PET, fibrous culture matrix, while BioMESH® utilizes a combination of polypropylene (PP) netting and PET mesh. These macrocarriers offer several advantages:

**High surface area:**
The macroporous design provides cells with a significantly increased surface area for optimal attachment and growth.

**Biomimetic environment:**
The 3D structure closely mimics a cell's natural in vivo environment, promoting healthy cell behavior.

**Efficient mass transfer:**
The matrix vessel facilitates efficient exchange of oxygen and nutrients, ensuring optimal cell proliferation and high bioproduct yields.

## Affordable Cost

MiniTide® scaled down bioreactor also offers significant advantages for research applications utilizing precious starting materials, high-cost culture media, or expensive analytical techniques. This translates to a substantial reduction in the overall cost per experiment.

## Linearly Scalable Quality

Esco Adherent Cell Tide Motion® platform offers a groundbreaking solution for adherent cell cultures. This innovative, world-first packed bed bioreactor system boasts full linear scalability. Starting with research-scale units

designed for standard $CO_2$ incubators, the platform seamlessly expands to production volumes while maintaining the core Tide Motion® principle. This ensures consistent and reliable cell growth throughout the development and manufacturing process.

| Cells | Estimated Cell Number per MiniTide Vessel | Carriers |
|---|---|---|
| MSC | $1.2 \times 10^6$ | BioNOC II®** |
| | $1.3 - 2.8 \times 10^7$ | BioMESH®*** |
| IPSC | $1.2 - 3.1 \times 10^6$ | BioNOC II® |
| Fibroblast | $1.2 \times 10^7$ | BioNOC II® |
| Vero | $6.2 \times 10^6$ | BioNOC II® |
| HEK293 | $8.8 \times 10^7$ | BioNOC II® |
| MDCK | $3.5 \times 10^7$ | BioNOC II® |
| BHK-21 | $1.5 \times 10^8$ | BioNOC II® |
| Sf-9 | $1.7 \times 10^8$ | BioNOC II® |
| Sf-21 | $1.2 \times 10^7$ | BioNOC II® |
| HuH-7 | $7.1 \times 10^7$ | BioNOC II® |

*The density of MSCs varies depending on the tissue of origin, the donor's age and characteristics, and the composition of the culture medium.

**BioNoc II® is optimally suited for the culture of MSCs when the goal is to obtain secretomes or small exosomes as the final products.

***BioMESH® is optimally suited for the cultivation of MSCs when the primary goal is cell harvesting as the final product. However, in cases where it is essential to maintain the cells' morphology, particularly if they have been extensively characterized in a 2D environment, BioMESH® may be more appropriate for harvesting small exosomes.

*The choice of carrier type will ultimately depend on the specific requirements of the client's final experiment.*

# Environmental Control

For both normoxic and hypoxic cell cultures, temperature is carefully regulated using Esco $CO_2$ incubators or compatible third-party models. To maintain aseptic conditions, these incubators should ideally have HEPA or ULPA filters. Additionally, a cooling function is recommended to counteract the heat generated by MiniTide®

## Top Holding Time

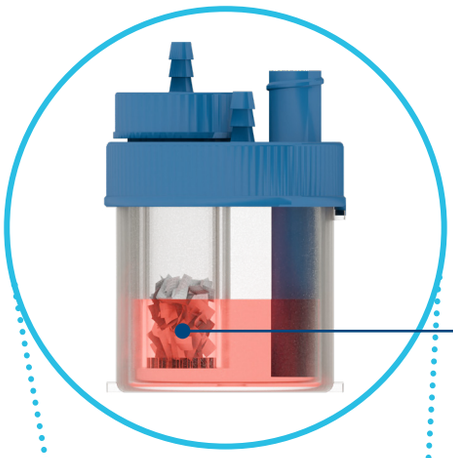
**Top holding time** refers to the phase in the Tide Motion® cycle where macroporous carriers are fully submerged in the culture medium, allowing for efficient nutrient exchange. During this stage, essential nutrients and growth factors diffuse into the carriers, while waste products produced by the cells are removed. This process ensures a continuous supply of nutrients to support cell growth and metabolism, optimizing the culture conditions for anchorage-dependent cells.

## Bottom Holding Time

**Bottom holding time** refers to the phase in the Tide Motion® cycle where the macroporous carriers are exposed and transition into the oxygenation stage. During this phase, the oxygen or suppressed oxygen diffuse from the headspace within the vessel to the surface of the macroporous carriers.

*Approximately 20% of the culture medium remains in contact with the macroporous carriers throughout the phase. This facilitates the passive diffusion of oxygen, or limited oxygen in the case of hypoxic cultures, from the surrounding air into the cell layer adjacent to the carriers, ultimately reaching the 3D cell culture within the macroporous matrix.*

| **Application/ Macrocarriers** | **EV/Exosomes** | **Cell Therapy** *(when harvesting the cells as final product)* | **Intracellular Virus** *(when harvesting the cells containing the virus)* | **Secreted Bioproducts** *(Virus, Viral Vectors, Proteins)* |
|---|---|---|---|---|
| BioNOC II® | +++ | ++ | ++ | +++ |
| BioMESH® | +++ | +++ | +++ | ++ |

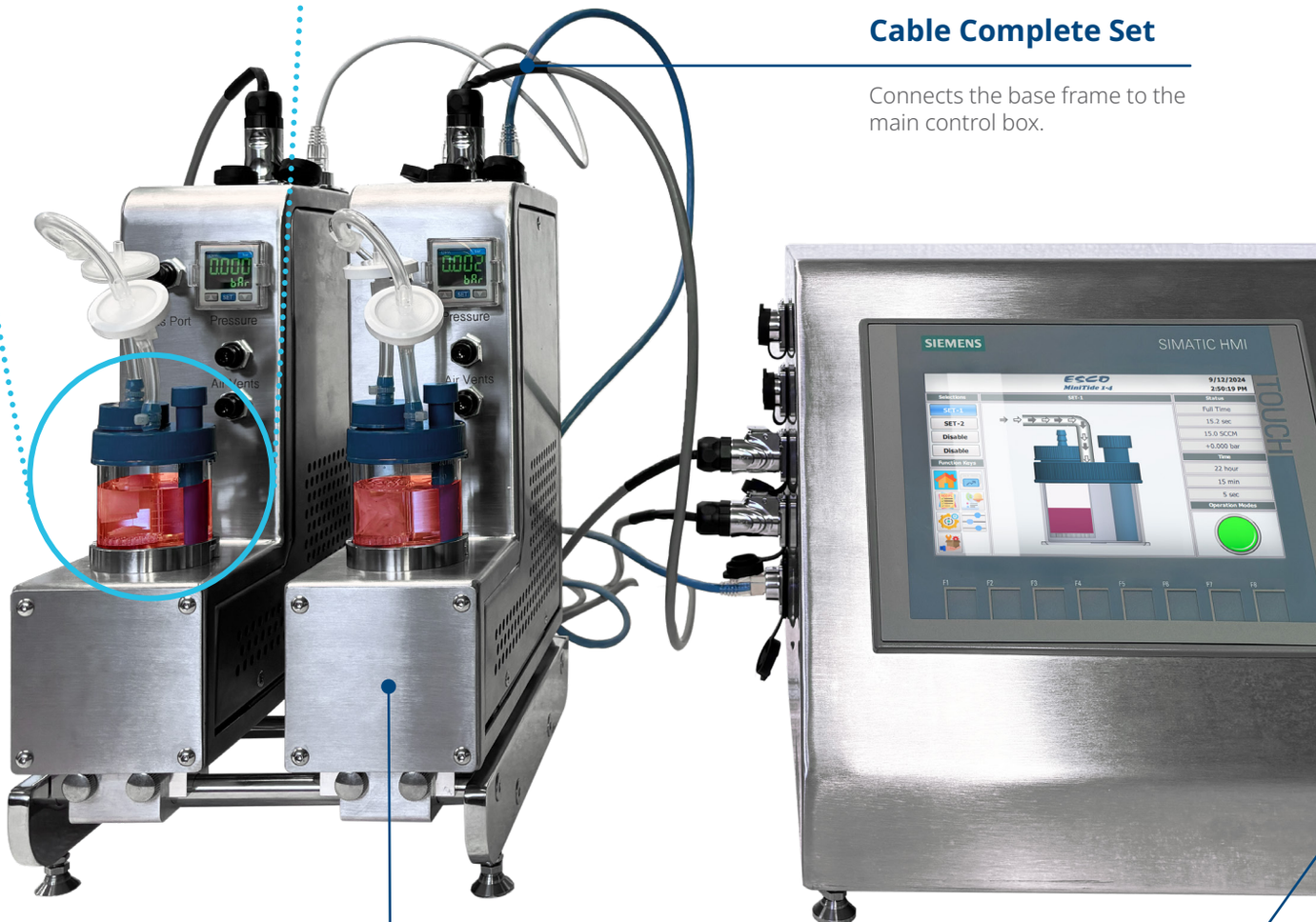


## BioNOC II® / BioMESH® (Packed Bed)

Cells remain entrapped in the carriers, simplifying media replacement and product harvesting.

## Cable Complete Set

Connects the base frame to the main control box.




## MiniTide® Culture Stage

Stainless steel 304 that can hold up to 4 MiniTide® vessels.

## HDMI Box

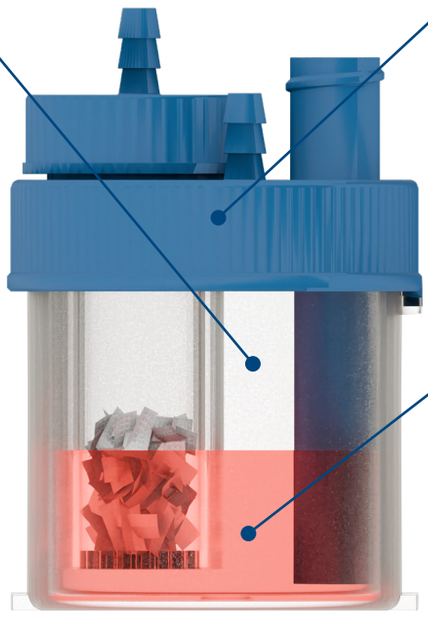
MiniTide® HMI utilizes Siemens HMI KTP700/PLC 1214C, which allows for independent control of the experiment conditions.

## Polystyrene

Polystyrene stands out as a preferred choice for cell culture flasks. This selection is driven by its key properties: superior optical clarity, ensuring unobstructed observation, exceptional durability for reliable performance, and minimal cytotoxicity.

## Polypropylene

Polypropylene exhibits exceptional resistance to moisture, a variety of acids, and alkalies. This material offers a robust combination of high impact strength and fatigue resistance, creating a favorable environment for cell growth and proliferation.



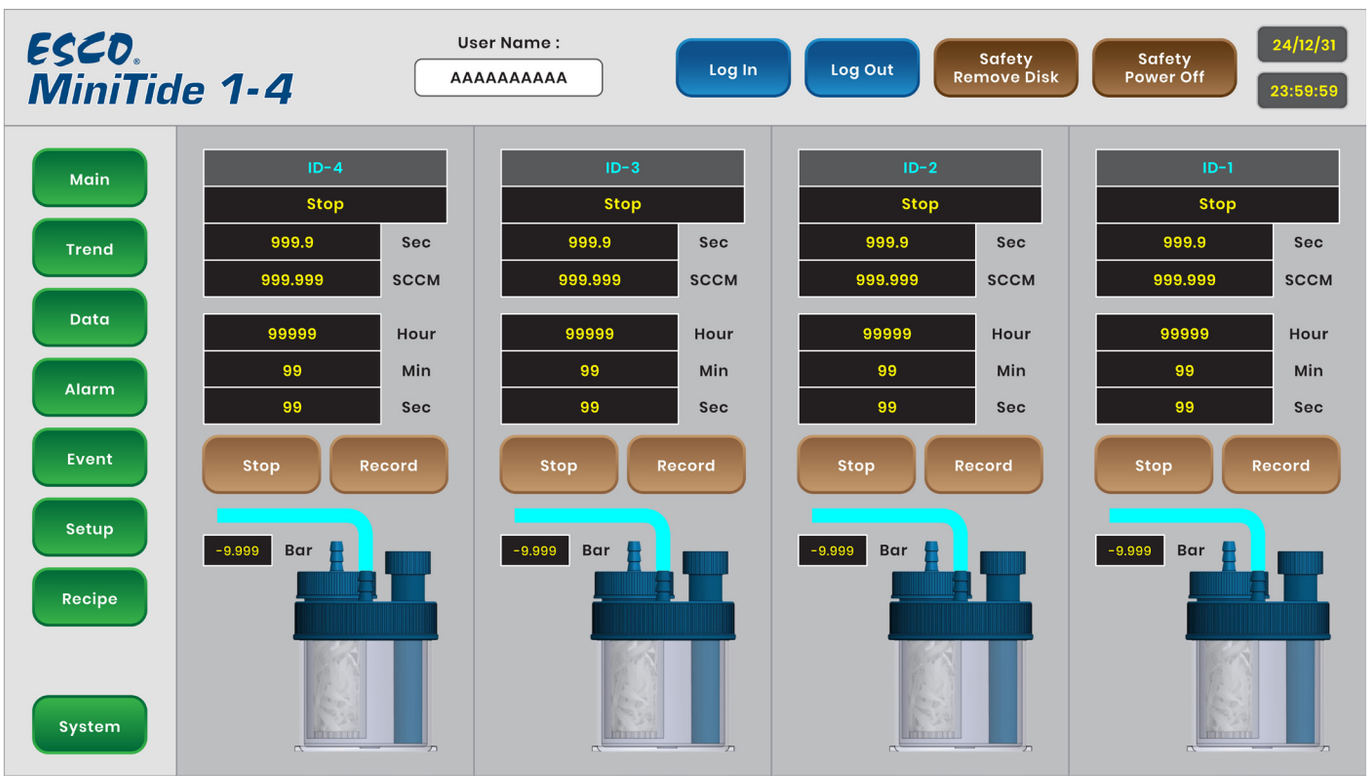
## Working Volume

The MiniTide® system employs a versatile cell culture vessel with a maximum capacity of 60 mL, but a working volume of 35 mL is recommended.


| | | |
|---|---|---|
| **Working Volume** | 35 mL | |
| **Pre-Packed Carrier** | BioNOC II® | 0.17 ± 0.005 g |
| | | 25 pcs |
| | BioMESH® | 0.5 ± 0.05 g |
| | | Initially supplied as 10 BioMESH® sheets (24 × 9 mm). These sheets are bisected to yield a total of 20 BioMESH® sheets (12 × 9 mm). |
| **Material** | Cap | Polypropylene |
| | Bottle | Polystyrene |

# MiniTide® HMI Main Screen

MiniTide-4 features independent control, enabling researchers to design diverse experiments. This allows for the exploration of various parameters, including independent manipulation of top holding (nutrient exchange) and bottom holding (aeration phase) durations, as well as the investigation of the impact of different media types.




| | |
|---|---|
| **HMI Main Screen** | Displays the main screen |
| **Trend** | Displays the trend graph |
| **Data** | Displays the data list |
| **Alarm** | Displays the alarm list |
| **Event** | Displays the operation history |
| **Setup** | Displays the programming settings page and the manual operation page |
| **Recipe** | Displays recipe operation page |
| **System** | Displays the system configuration settings page |
| **Log In** | Displays user login screen |
| **Log Out** | Logging out the current user |
| **Safety Remove Disk** | Ensuring the files are properly saved |
| **Safety Power Off** | Function key to confirm closing the background program |

# MiniTide® Product Specification

Esco Tide Motion® system bioreactors are a leading technology platform for global commercial production of human and animal vaccines. Additionally, Esco Tide Motion® system bioreactors play an essential role in clinical applications, supporting the development of adherent cell therapies and their derivatives. These derivatives include exosomes, extracellular vesicles, cell-derived nanovesicles, collagen for medical and cultivated meat applications, proteins for diagnostics and therapeutics, growth factors, and biomaterials like cultivated leather, all with applications in the biomedical field. MiniTide® is for research use or further manufacturing only and cGMP/GMP usage is subject to the site Quality Manufacturing Systems to be in place.

*Note: MiniTide® needs to be placed in a cooled $CO_2$ incubator to offset the heat it produces.*

| | | |
|---|---|---|
| **Weight** | HDMI Box** | 6.5 kg |
| | Main control box + 1 MiniTide® Module unit | 11 kg |
| | Main control box + 2 MiniTide® Module unit | 13.7 kg |
| | Main control box + 3 MiniTide® Module unit | 16.7 kg |
| | Main control box + 4 MiniTide® Module unit | 20 kg |
| **Required space (W × H × D)** | HDMI Box** | 290 × 360 × 290 mm |
| | Main control box + 1 MiniTide® Module unit | 210 × 270 × 460 mm |
| | Main control box + 2 MiniTide® Module unit | 295 × 270 × 460 mm |
| | Main control box + 3 MiniTide® Module unit | 380 × 270 × 460 mm |
| | Main control box + 4 MiniTide® Module unit | 465 × 270 × 460 mm |
| **Power supply** | 100-230 VAC, 50/60 Hz | |
| **Housing** | 304 stainless steel | |
| **Tide Motion® rate range** | 15 ~ 75 mL/min | |
| **Accuracy** | 1.5 mL/min[1] | |
| **Holding Time** | 0 ~ 9999 s | |
| **Other properties** | Data trend chart<br>Data sheet<br>Alarm list<br>Recipe management<br>User authority management<br>Export in PDF and CSV format | |

** The user needs to ensure that the third-party $CO_2$ incubator with a cooling function can withstand the weight*
*** The HMI box is placed outside of the $CO_2$ incubator*

| Item Code | Model Code | Description |
|---|---|---|
| **Main Unit** | | |
| 2231110 | MIT-1M10 | 1 VESSEL, MODULE, 110-230V, 50/60HZ, - M for Modular |
| 2231111 | MIT-2M10 | 2 VESSELS, MODULE, 110-230V, 50/60HZ |
| 2231112 | MIT-3M10 | 3 VESSELS, MODULE, 110-230V, 50/60HZ |
| 2231113 | MIT-4M10 | 4 VESSELS, MODULE, 110-230V, 50/60HZ |
| 2231097 | MINITIDE, MIT-16A-8 | 16 VESSELS, AUTO, 230V, 50/60HZ |

*Note: Existing MiniTide® from stages 1 through 4 are capable of being retrofitted as per user's requirement.*

# MiniTide® Product Specification

| Consumables | | |
|---|---|---|
| **MiniTide Vessel (MTMV)** | | |
| 1400309 | MINITIDE VESSEL-E, MTMV-E | 4 EMPTY VESSELS<br><br>*Matrix depends on client's requirement/s |
| 1400310 | MINITIDE-BIONOC II, MTMV-BII, 10 PCS | For virus and applications which are sensitive to pH<br><br>10 pieces of BioNOC II<br>Matrix:Media Ratio is 1:20<br>4 Vessel/Pack |
| 1400311 | MINITIDE-BIONOC II, MTMV-BII, 25 PCS | 25 pieces of BioNOC II<br>Matrix:Media Ratio is 1:7<br>4 Vessel/Pack |
| 1400312 | MINITIDE-BIOMESH 50 MICRON, MTMV-BM50 | MiniTide-BioMESH 50 micron<br>Matrix:Media Ratio is 1:7<br>4 Vessel/Pack |
| 1400313 | MINITIDE-BIOMESH 200 MICRON, MTMV-BM200 | MiniTide-BioMESH 200 micron<br>Matrix:Media Ratio is 1:7<br>4 Vessel/Pack |
| **MiniTide Base Frame** | | |
| 5012040 | BASE FRAME, MINITIDE-2 | SS CARCASS ONLY |
| 5012041 | BASE FRAME, MINITIDE-3 | SS CARCASS ONLY |
| 5012042 | BASE FRAME, MINITIDE-4 | SS CARCASS ONLY |

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Ceiling Laminar Airflow Units
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Containment Barrier Isolator (CBI)
Downflow Booth (DFB)
Dynamic Floor Laminar Hatch
Dynamic Pass Box
Evidence Drying Cabinet
Garment Storage Cabinet
General Processing Platform Isolator (GPPI)
Laminar Flow Horizontal Trolley
Laminar Flow Straddle Units, Single and Double
Laminar Flow Vertical Trolley
Pass Box
Soft Wall Cleanroom
Sputum Booth
Ventilated Balance Enclosure (VBE)
Weighing and Dispensing Containment Isolator (WDCI)

Since 1978, Esco has emerged as a leader in the development of controlled environment, laboratory and pharmaceutical equipment solutions. Products sold in more than 100 countries include biological safety cabinets, fume hoods, ductless fume hoods, laminar flow clean benches, animal containment workstations, cytotoxic cabinets, hospital pharmacy isolators, and PCR cabinets and instrumentation. With the most extensive product line in the industry, Esco has passed more tests, in more languages, for more certifications, throughout more countries than any biosafety cabinet manufacturer in the world. Esco remains dedicated to delivering innovative solutions for the clinical, life science, research and industrial laboratory community.

ESCO HEALTHCARE *"Discovery to Delivery"*

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