

TECH OFFER

A Robust Cell Manufacturing Bioprocess For Clinical Usage



KEY INFORMATION

TECHNOLOGY CATEGORY:

Healthcare - Pharmaceuticals & Therapeutics
Life Sciences - Industrial Biotech Methods & Processes
Materials - Plastics & Elastomers

TECHNOLOGY READINESS LEVEL (TRL): **TRL8**

COUNTRY: **SINGAPORE**

ID NUMBER: **TO175092**

OVERVIEW

Bioprocessing technologies used in scaling manufacturing production typically uses scale-up and scale-out approaches through microcarrier-based stirred tank bioreactors, wave bags or cell stackers and multi-layered flasks. However, during the research and development process of cell and gene therapies, there is a significant technical gap between basic research methods and these manufacturing process development, which causes problems such as increase in time and cost of the development process. Cell and Gene Therapy manufacturing is an emerging area in the biopharmaceutical industry that must overcome high barriers of resource, capacity, and cost constraints. Therefore, it is extremely important to consistently consider and design a culture process from R&D to commercialization as a closed system with a certain size of scale-up and automation.

This technology introduces a robust and economically viable culture process in a closed culture system which comprises of an automated cell culture medium change device that can be installed in commercial CO₂ incubators, where the device is coupled with a patented microwell bag and V-shaped adhesion cell culture bag, capable of both spheroid culture (3D) and adhesion

culture (2D). This novel technology has established a culture method that meets the requirements of clinical use by improving sterility, reproducibility, and operability, and produces a large number of uniform-sized clusters.

The technology owner is seeking partnerships and collaborations with institutions, hospitals, biotechnology and biopharmaceutical firms.

TECHNOLOGY FEATURES & SPECIFICATIONS

This technology features three different components which can be applied separately or in combination with the automated cell culture system.

1. Spheroid culture bag designed in 2 measurements:

- A large scale 1,000cm² (290 mm x 410 mm) surface area with a diameter of 350um and 650,000 wells at a volume of 200-800ml.
- A small scale 50cm² (70 mm x 120 mm) surface area with a diameter of 500um and 18,000 wells at a volume of 10-20ml.
- Spheroid size can be controlled by changing the number of cells seeded.
- The microwells are treated with ultra-low adhesive substance to inhibit cell adhesion.
- Spheroid culture bag has a dedicated holder that is portable, stackable and observable to prevent the movement of spheroids between microwells and inhibit formation of large aggregates.

2. Adhesion culture bag for adherent cells designed in 2 types of surfaces:

- A flat surface bag usable for microscopic observation.
- A V-shaped micro-patterned surface area enabling more than 3x of cells per unit area to achieve high density cell culture. A 1,000 cm² bag would equate to an estimate of 3,000cm² in area.
- The inner surface are treated to allow for cell adhesion.
- This adhesion bag can be applicable not only for cell therapy but also for small volume production of antibody, cytokine and proteins.

3. An automated closed culture medium change device adaptable to both spheroid and adhesion bags:

- It allows for microscopic observation under a closed system.
- It is patented in enabling precise pumping control of medium change rate by controlling liquid thickness.
- For spheroid culture, it is possible to replace the entire medium while inhibiting the transfer of spheroids from one well to another.

POTENTIAL APPLICATIONS

- Organoids for high-throughput drug dosing tiration testing.
- High-throughput drug efficacy and toxicity screening.
- Restructuring of organoids.
- Cell therapies using adherent cells such as Mesenchymal Stem Cells (MSCs).
- Cell differentiation from ES or iPS cells
- Mass production of cells for *in vivo* mice studies injection.

MARKET TRENDS & OPPORTUNITIES

The development of new manufacturing technologies and processes that can scale up the production of cell therapies while maintaining quality and reducing costs is a critical factor driving market growth. The global allogeneic cell therapy market was valued at USD 255.6 million in 2022 and is projected to expand at a compound annual growth rate (CAGR) of 27.40% from 2023 to 2030 (Research and Markets). A major driver of this growth is the increasing incidence of chronic diseases that can be addressed with allogenic cell therapies. The stem cell therapies segment, particularly allogenic stem cell therapies, dominated the market with the largest share in 2022 due to their widespread application in treating blood cancers, leukemia, lymphoma, and autoimmune disorders. The non-stem cell therapies segment is expected to grow at the fastest CAGR of 31.32% by 2030 (Grand View Research).

The market size of this technology extends beyond the field of cell therapy manufacturing as it can be widely used for drug discovery screening and mass production of spheroids and organoids in other applicable areas including cultivated meat cultures.

UNIQUE VALUE PROPOSITION

UVP of the culture bag:

This technology's patent stems in the design of a culture vessel with a high gas permeable film engineered with different layers of film at a specific thickness ratio, enabling efficient gaseous exchange of O₂ and CO₂ which is superior to conventional plastic vessels and reduces plastic wastage. The material of the film allows passing of culture gas but does not allow passing of microorganism which contaminates the cell. The size of the bags can be designed according to the purpose of culture.

The culture bags has been proven safe and tested to use for clinical and manufacturing grade. Test conducted includes cytotoxicity, endotoxin, sterility, leachables and extractables. This novel microwell culture bag product has provided a superior alternative method for cell clustering.

UVP of the spheroid culture bag:

The spheroid culture bag has been optimized in its height to ensure consistent production of homogenous uniformed cell clusters while affirming that diameter does not affect cluster uniformity. The spheroid culture bag exhibits user-friendly operability. Firstly, it allows easy removal of air bubbles in microwells. By simply setting the bag in the holder and incubating overnight, air bubbles can be removed by specific pressure (200-400kgf/m²) applied by the pressing plate holder during incubation. Secondly, formed spheroids can be easily recovered from the bag without pipetting by simply turning the bag upside down. Thirdly, almost all clusters (>99% of total number of cells) after culturing could be collected. Lastly, the microwell bag consistently produces uniform sized clusters.

UVP of the adhesion culture bag:

Since the culture area is about three times larger than that of flat substrates, it is possible to perform adhesive culture at three times higher density. In addition, after treating cell detachment solution, cells can be detached without pipetting. The bag volume is smaller than that of rigid culture vessels, saving space during stocking, culturing and disposing.