



# THE HEALTH QUARTERS

QUARTERLY NEWSLETTER

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## ONWARD VACCINE MANUFACTURING TECHNOLOGY AND SOLUTIONS

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Esco Pharma - <https://www.escopharma.com/>

Esco TaPestle Rx - <https://escotapestlerx.com/>

Esco VacciXcell - <https://escovaccixcell.com/>

Esco Aster - <https://escoaster.com/>

With the first half of 2021 over, we realize the importance of vaccines in reducing the effect and continued prevalence of pandemics. We saw the unprecedented speed of COVID-19 vaccines granted with emergency use authorizations, the rise of new types of vaccines such as mRNA (from non-replicating to self-amplifying), to outpouring vaccine donations from one country to another.

We are in the era where solutions in vaccine manufacturing make a difference in the clinical setting in a short period of time.

In this issue, the HQ tackles Esco Healthcare technologies from upstream aseptic processing, cell attachment, to downstream processing tools that help improve vaccine production.

### Inside this Issue



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Adherent culture in 2D systems such as flasks have been used for some time now but growing these cells for manufacturing renders obstacles in scale-up.



Take A Minute!

#### Sharpen Your Vision with These Mind-boggling Optical Illusions!

In search of a way to jumpstart your visual senses? Try cracking these deceiving visual illusions in a minute.

## HQ Breakthrough

# Esco Downflow Booths and Air Shower Unit Installed at a Leading Pharmaceutical Company in UAE

One of the leading pharmaceutical manufacturing companies in the United Arab Emirates (UAE) has partnered with Esco to be their chosen manufacturer for one unit of air shower and three units of downflow booths. These are designed according to the user's requirements, and serve as an essential addition to their manufacturing facility to cope with the increasing market demands and to consistently comply with cGMP guidelines.

The units had been delivered in September 2020 and the installation for the Esco Air Shower (EAS) and the first Downflow Booth (DFB) were commenced. Installation Qualification (IQ) and Operational Qualification (OQ) tests for both units were conducted afterward to ensure that both units are functional. After the first set of equipment passed the IQOQ testing, the second and third DFBs were simultaneously installed in March 2021. There were some minor customizations and adjustments made for the filler plates upon installation followed by the IQOQ tests on both units. Finally, in May 2021 upon completion of the necessary documentation, the units were handed over to the client.

**Esco Air Shower (EAS)** is a specially designed, self-contained, air recirculating chambers installed at the entrance/exit of cleanrooms and other controlled environments. The unit is equipped with disposable

prefilters with 85% arrestance and ULPA filters with an efficiency of > 99.9995% at 0.3 µm particle sizes.

During operation, the chamber uses high-velocity jets supplying filtered air through stainless steel nozzles with an initial air velocity of 18-30 m/s. This helps reduce risk of cross-contamination by producing a "scrubbing effect" to potential surface contaminants from personnel, equipment, or supplies entering or exiting the area. The EAS is suitable for cleanrooms used for industries including micro-electronics, semiconductors, pharmaceuticals, spray painting, and food markets. This is also applicable for pharmaceutical and lab animal research applications to reduce potential for egress of hazardous substances and allergens from the controlled environment.

The installed EAS has a programmable micro-processor control system which supervises all functions and operation modes. There are also emergency buttons and indicator lights mounted on both sides of the unit to regulate traffic flow to the cleanroom. The unit is constructed with powder-coated electrogalvanized steel, impervious to wear and tear, flaking and corrosion through the time of use. The unit is also installed with uniform lights and heavy-duty, durable doors constructed with glass windows to permit visibility.

The **Pharmacon™ Downflow Booths (DFBs)**, commonly called dispensing/sampling/weighing booths, are designed in compliance with cGMP and are capable of providing an ISO Class 5 environment at rest conditions. All installed DFB units operate with a recirculating airflow and are equipped with a series of filtration systems which all work together in providing operator, process, and/or product protection during dispensing or charging and sampling of bulk, pilot, and small-scale raw materials. These make the DFB's design suitable and effective for contained processing such as in vaccine/biological manufacturing, particularly when weighing raw materials during formulation of buffers and growth media, and when making these into solutions.

The terminal H14 filters of the booth are knife-edge gel sealed which allows for rapid tool-less replacement from within the unit. Another feature installed are closed loop ECM fans, which are energy-efficient blowers that can automatically adjust their speed in response to the filter load.

DFB units installed are constructed of 304-grade stainless steel material, and provided with add-on front PVC curtain for extra barrier to the external environment while still facilitating easy access in and out from the booth. Each DFB is equipped with a control cabinet and HMI control system, which supervises all functions and operation modes. To add to the functionality of the equipment and in order to ensure that all the required operational parameters are maintained, audible alarm, indicator lights, and emergency stop button are also provided.

All other relevant features of the manufactured EAS and DFB units are factored in according to the user-required specifications of the client and validated accordingly on-site before turnover.

Esco Pharma is committed to producing high-quality, safe, consistent, and reliable equipment to meet the developing market demands and dynamic regulatory requirements. Contact Esco Pharma to learn more about the wide variety of products served. Esco Pharma's well-experienced staff and specialists will be happy to assess your needs and develop solutions to your specific requirements.

Click [here](#) for more information or contact us at [csis.pharma@escolifesciences.com](mailto:csis.pharma@escolifesciences.com)



DFB-G2



EAS-1B1

## Insight Scoop

# Isolators in Aseptic Processing of Vaccines

Ensuring the sterility of vaccines in manufacturing is of utmost priority. Consequences of failing to meet such sterility standards include shortage of supply due to the penalizing of manufacturing companies failing to ensure the sterility of vaccines, increased vaccine hesitancy among the general public due to such incidents, and serious injury or even death in the case of victims inoculated with contaminated vaccines. Thus, vaccine manufacturing companies and regulatory bodies have the immense responsibility of ensuring that their processes are thoroughly validated. The challenge lies in how most vaccines are manufactured: aseptic processing.

In the United States, vaccines are regulated as biologic products under the US Food and Drug Administration (USFDA) Center for Biologics Evaluation and Research (CBER), and unlike small molecules which can be steam-sterilized, most vaccines are prepared aseptically. As explained by the USFDA in its Guidance for Industry: Sterile Drug Products Produced by Aseptic Processing released in 2004, aseptic processing involves steps wherein the drug product, container, and closure are first subjected to sterilization methods separately, as appropriate, and then brought together. This differs from terminal sterilization, wherein only the final drug product is subjected to a sterilization process, such as heat or irradiation.

Many regulatory agencies recommend that terminal sterilization should be used for any product that can withstand it. Aseptic processing is only reserved for any operation wherein the drug cannot withstand the heat cycle of terminal sterilization. Many biologic products, including most vaccines, cannot withstand heat sterilization and are therefore aseptically processed. Furthermore, aseptic processing requires highly trained personnel and entails substantial costs, both for infrastructure and for everyday operation. For instance, based on the CBER's Guidance for Biological Drug Products, aseptic processing areas (e.g., filling and lyophilization) should

be designed using 21 CFR 211.42(c)(10), the Guideline on Sterile Drug Products Produced by Aseptic Processing, and the Draft Guidance for Industry – Sterile Drug Product Produced by Aseptic Processing – Current Good Manufacturing Practices as guides. This is because overall, aseptic processing involves more variables than terminal sterilization, and each step requires validation and control. With such complexity, each process could introduce an error that ultimately could lead to the distribution of a contaminated product. Any manual or mechanical manipulation of the sterilized drug, components, containers, or closures before or during aseptic assembly poses the risk of contamination, and thus necessitates careful control.

Over the years, an increasing number of pharmaceutical companies are choosing to use closed systems, such as isolators and restricted access barrier systems (RABS), in their aseptic vaccine manufacturing process. The move to closed systems is attributable to one crucial fact: operators are the predominant source of microbial contamination in aseptic processing. Direct contact between the operator and the process must be minimized. This is to ensure that the process remains sterile/aseptic, and avoid the catastrophic results of contaminated vaccines, especially since the injection of contaminated drug products has been historically proven to lead to serious adverse events, including death.

Esco Pharma's line of products includes isolators that meet the demand of closed system vaccine manufacture. The General Processing Platform Isolator (GPPI), which has an advanced control system that allows the operator to select either positive or negative chamber pressure as well as single pass or recirculating airflow patterns, can be used for pilot scale manufacturing, as well as in the harvesting, purification, and concentration steps. During the formulation and filling steps in downstream processing, filling line isolators can house a whole filling line system for vaccine manufacture. They can

be configured for either traditional filling line systems or flexible multi-format ready-to-use (RTU) filling line systems. Other isolators for virus production and/or vaccine research, which are crucial steps in vaccine production, include the Cell Processing Isolator (CPI), which is highly modular and can be integrated with general bioprocessing equipment, and the Turbulent Flow Aseptic Isolator™ (TFAI™) and Aseptic Containment Isolator (ACTI), both of which are capable of temperature and CO<sub>2</sub> control.

Aseptic processing will always continue to challenge vaccine manufacturing companies. Advances in cleanroom technology and further improvements in closed systems such as isolators and RABS will continue to address these challenges. The emergence of increased levels of automation is also promising. Aside from increasing production capacity, the increased use of robotics would consequently reduce the number of operators, who are the main sources of microbial contamination, and this would mean a lower overall risk of contamination. As more challenges arise and as we try to address them, the goal has always been the same: to provide safe, pure, effective, and affordable vaccines accessible to everyone.

### References:

1. Agalloco, J., & Mestrandrea, L. (2017). Moving to Closed Systems for Aseptic Processing. In P. T. International, *Vaccine Development and Manufacturing 2017* (pp. 31-38). Iselin: UBM.
2. Center for Biologics Evaluation and Research. (2010). *Inspection of Biological Drug Products (CBER) 7345.848*. In C. f. Research, *Compliance Program Guidance Manual Chapter – 45 Biological Drug Products*.
3. CRB Group. (2021). *The Current State of Aseptic Processing & Fill-Finish Manufacturing*. 3BL Media.
4. Frantz, J. C. (n.d.). *Aseptic Processing Overview*. A3P.
5. Gomez, P. L., Robinson, J. M., & Rogalewicz, J. A. (2012). *Vaccine Manufacturing*. Elsevier Public Health Emergency Collection.
6. Parenteral Drug Association. (2011). *PDA Technical Report No. 22 (2011 Revision)*.
7. United States Food and Drug Administration. (2004, September). *Guidance for Industry: Sterile Drug Products Produced by Aseptic Processing - Current Good Manufacturing Practice*. The United States of America.

### Isolators for Closed System Vaccine Manufacturing



Aseptic Containment Isolator (ACTI)

Cell Processing Isolator (CPI)

Turbulent Flow Aseptic Isolator™ (TFAI™)

General Processing Platform Isolator (GPPI)

# Project Genesis

## No Culture Stress with BioMESH®

Adherent culture in 2D systems such as flasks have been used for some time now, but growing these cells for manufacturing renders obstacles in scale-up. Aside from being laborious and time-consuming culture, flat layers do not accurately represent the adherent cell's *in vivo* state. In comparison with 2D culture, three-dimensional (3D) cell culture allows adherent cells to grow in a larger surface area while being able to monitor and maintain important biological mechanisms like cell-to-cell communication.

The *in vivo* state of cells means that they are in a constant fresh supply of nutrients as well as their chemostatic environment is maintained. The spatial organization through which these adherent cells grow in 3D mimics its original state where intricate cell-cell and cell-matrix interactions dominate. Biological mechanisms like cell viability, morphology, proliferation, differentiation, and more are accurately depicted.

With recently developed BioMESH macroporous carriers, cells can grow undisturbed in 3D while maintaining a non-turbulent environment with minimal shear force through Tide Motion. BioMESH is the next generation of BioNOC™ II macroporous carriers, with a more defined surface area and configuration. Adherent cells such as mesenchymal stromal cells (MSCs), VERO, HEK293, C2C12, and more can be cultured using these 3D matrices.

### Features:

- Large surface area for growth
- Highly porous
- Mimics cell's *in vivo* environment
- Enhanced biocompatibility
- Rigid to support fixed-bed
- Gene and protein expression present
- Made from PP and PET material
- Culture cells in 3D geometry
- High cell and product yield

In the case of culturing stromal cells especially for cell therapy applications, the BioMESH scaffold shows advantageous features such as ECM secretion which is required for native cell function. It has also been shown that culturing using these carriers, stromal cells are able to maintain their fibroblastic morphology and re-attachment properties (Figure 1).

BioMESH macroporous carriers packed inside a Tide Motion bioreactor enables the precise control of important parameters such as pH, DO, and temperature required for cell culture. Tide Motion has been adapted and designed for 3D culture where the alternate exposure of cells to nutrition and aeration

via cyclical upward and downward motion produces high cell and product yield.

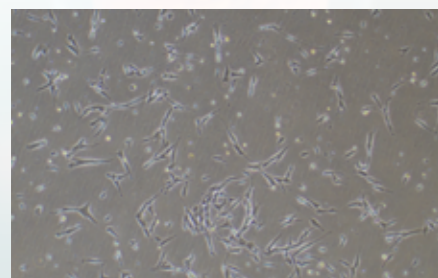
The geometrical material of the carriers allow cell culture monitoring through harvesting several carriers for staining and cell detachment through enzyme incubation and mechanical agitation. There is also ease of harvest for secreted products as the carriers remain packed and stable in the system, reducing additional downstream processing steps.

While most applications, especially viral vaccines, require high virus/cell produce for research and bioprocess manufacturing, culturing cells in 3D BioMESH® can enhance cell growth, expansion, and function. Partnered with Tide Motion bioreactors, different parameters can be manually or automatically controlled and run in different process modes to achieve high cell/product density. Let there be no culture stress with the BioMESH® culture model combined with the Tide Motion bioreactor design.

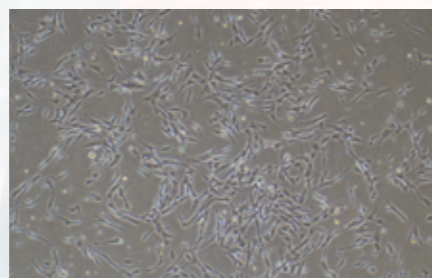
### Disclaimer:

*BioMESH® is still under development. The final product features and performance are subject to change. Know more about 3D matrices through here: <https://escovaccixcell.com/tide-technology/cell-attachment/BioNOC-II>*

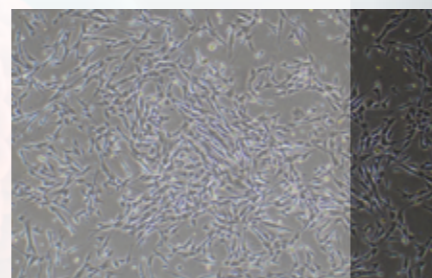
Figure 1. Post-harvest Monitoring (after centrifuge): Adipose-derived MSCs cultured in 5.5 grams of BioMESH in CelCradle™ Tide Motion bioreactor.



60,000 cells/well



100,000 cells/well



160,000 cells/well

# TAKE A MINUTE

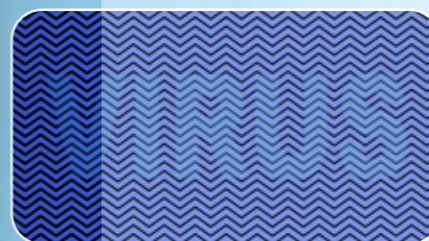
## OPTICAL ILLUSIONS: A memory game and a puzzle-in-one.

Have you ever wondered if your eyes have deceived you? It's not your eyes, but how the brain perceives and interprets an image. As the saying goes, the eyes look, but the brain sees. Unleash your mind's potential by outwitting these illusory images for a minute.

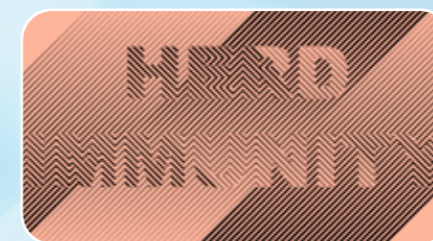
Part 1: In this image, how many Esco Healthcare equipment can you see?



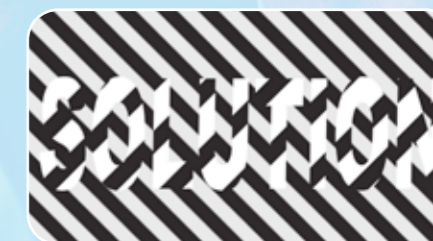
Part 2: Now let's play with some words, what do you see below?



1.



2.



3.



4.



5.



6.

Time's up! Curious if you got it right? See you in the next issue!

# TAKE A MINUTE

Answers from the Previous Issue

## FIND THE MISSING ITEMS:

Can you help these healthcare scientists look for some of their missing items before starting the experiment?

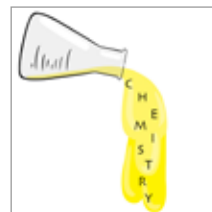
- |                                  |                              |
|----------------------------------|------------------------------|
| 1. Disposable pipettes           | 7. Crystal Violet Dye (CVD)  |
| 2. Esco Cell Processing Isolator | 8. Neubauer counting chamber |
| 3. Petri dishes                  | 9. Cryogenic tank            |
| 4. T-flasks                      | 10. CelCradle™ bioreactor    |
| 5. Gloveports                    | 11. BioNOC™ II macrocarriers |
| 6. Cryogenic vials               |                              |



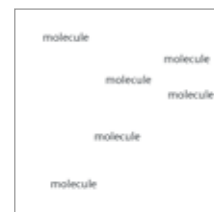
## WORD PICTURE PUZZLE:

Rebuses are pictures often made with letters, numbers or images, which vaguely represents a word, a phrase, or a saying. To help you solve them, make sure to look at word placements, sizes, colors, and quantities. So, can you decipher these rebus puzzles before your 1 minute runs out?

CLUE: SCIENCE & TECHNOLOGY, PHARMACY



1. FLOW CHEMISTRY



2. SMALL MOLECULES



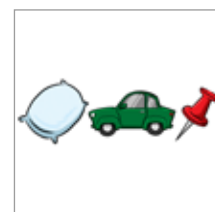
3. CALL IN SICK



4. DOWNSTREAM



5. VACCINE



6. PILOCARPINE



7. SOCIAL DISTANCING



8. FIRST AID



9. EYE SHADOW

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