

Hilleman Laboratories' ACES Facility Factsheet

(ACES: Agile manufacturing, highly Compact & configurable, End-to-end production facilities & flexible Single-use technology)

Background

- Part of Hilleman Laboratories' dual-feature setup, ACES is a 30,000 sqft current Good Manufacturing Practices (cGMP) facility that works in tandem with the research and development (R&D) laboratory in Biopolis to provide comprehensive end-to-end biopharmaceutical product development solutions, from concept to the manufacturing of clinical trial materials (CTM) for phase I and II clinical studies.
- The platform-agnostic and product-independent manufacturing facility supports the development of affordable, high-value vaccines and biologics for Singapore as well as low- and middle-income countries (LMICs) using innovative technology platforms.
- Its modular and nimble design allows quick manufacturing pivots during times of crisis, such as switching from regular pilot-scale manufacturing of CTM to the production of vaccines for emergency use in Singapore should such a need arise. Such setup enables the ACES facility to respond rapidly to emerging public health threats, especially at the onset of a pandemic.
- ACES is expected to be completed in November 2023, with various commissioning and qualification processes to be completed by June 2024.

R&D Laboratory for CMC and Preclinical



GMP Pilot-scale Manufacturing



 Conventional cell bank 2 mL 15 to 30 × 10⁴ cells/mL



Scale Up

- Upstream and downstream process development, drug product development, formulation and analytical development for vaccines and biologics

- Technology transfer from R&D to manufacturing
- Adaptation of new manufacturing condition
- Antigen production

- Delivery system establishment
- Vaccines formulation development
- Manufacturing for safety studies

- Upscale manufacturing GMP
- GMP-grade product
- Equipment qualification
- Critical analytical assay validation

- Fill & Finish
- Full equipment qualification
- Full analytical assay validation
- Established manufacturing process

Value Proposition

- The ACES facility will be leveraged across the following domains:
 - Development of biopharmaceutical assets: Producing biological starting materials (BSM) and clinical trial materials (CTM) for internal usage, collaborators and external clients (contract manufacturing organization [CMO] model)
 - Capability building: Building and strengthening capabilities, skill sets and knowledge to support process optimization and new product development work
 - Manpower development: Create training opportunities for R&D entities in LMICs

Plant Operation & Capabilities

- The ACES facility is Hilleman Laboratories' state of the art vaccine and biologics manufacturing facility, equipped with advanced design and operation innovations that confer unparalleled flexibility, increase productivity, enhance compliance and enable speed to clinic.

- Specifically, the ACES platform includes the following highlights:

(i) Transformative Flexible Manufacturing

- Portable, skid-mounted, single-use systems empowered by Utility Poles enable plug-and-play, modular, reconfigurable manufacturing in all drug substance (DS) suites.
- Integrated upstream and downstream processes within the same suite optimize facility use and enable continuous processing. This helps to increase processing speed and efficiency.

(ii) Concurrent Multiproduct Production

- Concurrent Multiproduct Production in different suites is enabled by functionally closed operations that are performed in individual cleanroom served by dedicated air handling units. Supported by well-designed, unidirectional transport flows accessed via a dual system of supply-and-return hygienic corridor concept, the prevention of cross-contamination across different production areas is assured.

(iii) On-the-Floor Real Time Analytical Testing and Process Analytical Testing (PAT)

- Modern advancement in analytical technology allows for in-process testing to occur on-line with the process or near the production floor to rapidly generate test result to facilitate GMP decision-making. Very few samples need to be transported to the quality control lab. Other compendial compatible test samples will be tested at externalized controlled test labs.

(iv) End-to-End Production Capability

- First of its kind end-to-end manufacturing capabilities are augmented with the integration of platform-agnostic DS production suites and a pilot scale fill-and-finish drug product (DP) suite.
- Each DS suite can support bioreactor production at a scale of up to 250 L and the fill-and-finish line can process both liquid-filled and lyophilized vial format to enable the rapid release and deployment of ready-to-use CTM to support missions in LMICs.

(v) Manufacturing Support Infrastructure

- The DS and DP manufacturing capability is augmented by a slew of manufacturing support infrastructure such as combined media and buffer solution preparation, equipment preparation, waste staging, warehousing operation, quality control labs and utilities holding areas, among others.

The ACES cGMP facility and the R&D laboratory at Biopolis form a vaccines and biologics development and manufacturing hub capable of producing BSM and CTM - from early discovery through pilot manufacturing - to deliver global health impact (especially in LMICs) and for Singapore's strategic healthcare needs and pandemic preparedness.

Through expanded global strategic partnerships with LMICs, the ACES facility can hasten the development and scalability of new, cost-effective vaccines and biologics for early phase clinical development, and create more opportunities for technology transfers to larger manufacturers.

Gaining quick access to important CTM, particularly vaccines and biologics that are administered to clinical trial populations, will elevate Singapore's role in addressing global health needs and enhance the country's responsiveness to emerging epidemic and public health emergencies.

Consequently, high-value, life-saving vaccines and biologics can be made more affordable and widely accessible, especially to people living in LMICs.

GLOSSARY

Biosafety Level: Biosafety levels are used to identify the protective measures needed in a laboratory setting to protect workers, the environment, and the public. At any given biosafety level, there will be strict requirements for laboratory design, personal protective equipment, and biosafety equipment to be used.
[Source: <https://www.phe.gov/s3/BioriskManagement/biosafety/Pages/Biosafety-Levels.aspx>]

Current Good Manufacturing Practice (cGMP): CGMP provides for systems that assure proper design, monitoring, and control of manufacturing processes and facilities. Adherence to the CGMP regulations assures the identity, strength, quality, and purity of drug products by requiring that manufacturers of medications adequately control manufacturing operations.
[Source: <https://www.fda.gov/drugs/pharmaceutical-quality-resources/facts-about-current-good-manufacturing-practices-cgmp>]

Drug product (DP): Medicinal products that are manufactured beforehand and placed on the market in packaging intended for distribution to the consumer, or other medicinal products intended for distribution to the consumer in the preparation of which any form of industrial process is used, or medicinal products that are produced commercially, except in pharmacies. Finished medicinal products are not intermediate products intended for further processing by a manufacturer.
[Source: <https://mpl.loesungsfabrik.de/en/english-blog/think-out-of-the-box/ds-dp-excipients>]

Drug substance (DS): Active substances that are intended for use as medically active constituents in the manufacture of medicinal products or which, through their use in the manufacture of medicinal products, are intended to become medically active constituents.
[Source: <https://mpl.loesungsfabrik.de/en/english-blog/think-out-of-the-box/ds-dp-excipients>]