Newly-built Facilities:

How to Manage Cost Without Compromising On Standards

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PDA Parenteral Drug Association

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CONNECTING PEOPLE SCIENCE AND REGULATION®

How to Manage Cost Without Compromising On Standards

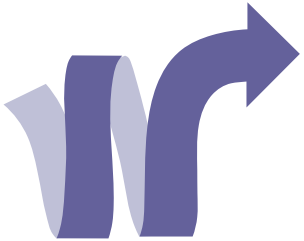
AGENDA:

- Background
- Challenges
- Approach
- Outcome
- Reflection

About Hilleman Labs:

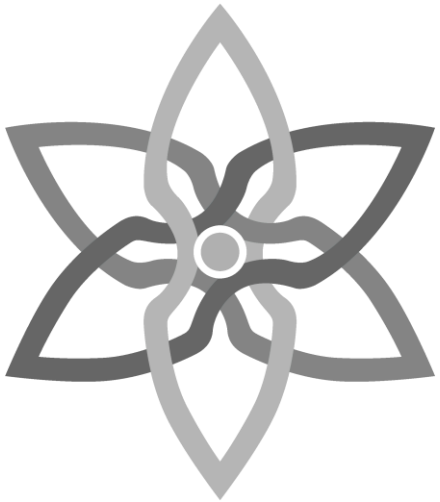
Merck Sharp & Dohme (MSD),
a global research-driven pharmaceutical company

Wellcome Trust,
a global charitable foundation dedicated to solving urgent health challenges



Established in 2009 as an equal **joint-venture partnership** between Merck Sharp & Dohme (MSD) and Wellcome Trust, **Hilleman Labs is focused on translating early discoveries to make vaccines** for infectious diseases and improve global health outcomes

Our Mission:



We are committed to developing

high impact, → Deliver impact to 100M+ people globally

affordable → Affordable by UNICEF and governments in low- and middle-income countries

vaccines for **LMICs** → With strong focus on Africa, Asia and Latin America

in a **safe, effective, novel** → Develop vaccines using existing and novel platform technologies

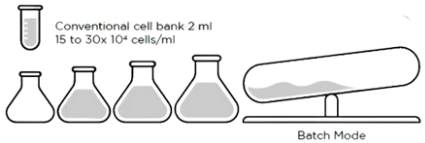
manner.

Hilleman Laboratories
MSD · Wellcome Trust Joint Venture

Our capabilities in CMC and preclinical R&D along with GMP manufacturing position us as a key partner for early development:

R&D Laboratory for CMC and Preclinical

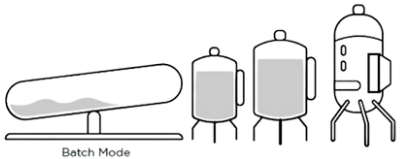
Upstream and downstream process development, drug product development, formulation and analytical development for vaccines and biologics



GMP Facility for Pilot-scale Manufacturing

Drug Substance suites which can be adapted for all platforms, including nucleic acid

Pilot-scale Drug Product Formulation and Fill & Finish bench-scale lyophilization suite



Scale Up

- 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
- Critical analytical assay validation

- Fill & Finish
- Established manufacturing process

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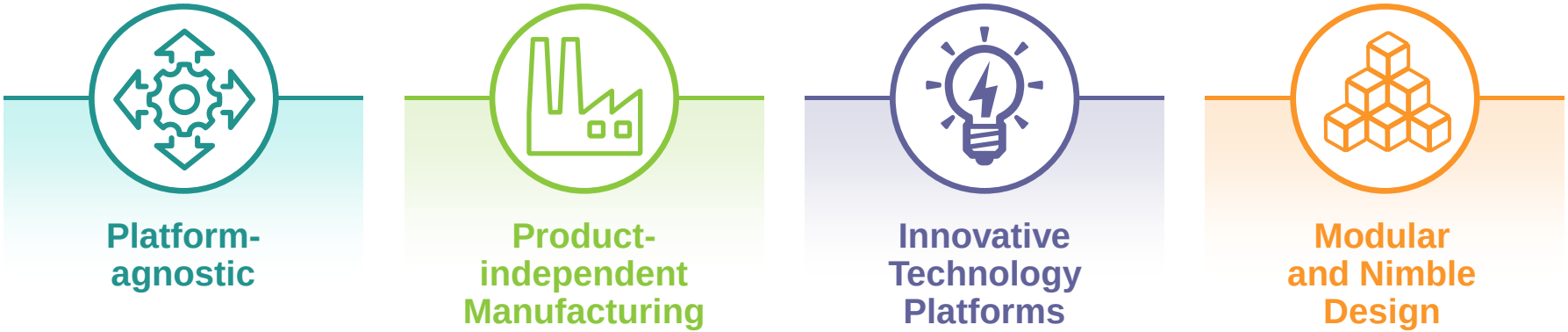
Highlights of ACES Facility:

ACES: Agile Manufacturing, Highly Compact & Configurable, End-to-End Production Facilities & Flexible Single-Use Technology



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

What ACES has to offer:

Advanced Design and Operation Innovations; Unparalleled Flexibility; Speed to Clinic

Transformative Flexible Manufacturing

- Plug-and-play, modular, reconfigurable manufacturing
- Integrated continuous processing increases processing speed and efficiency

Concurrent Multiproduct Production

- Each DS suite can support bioreactor production at a scale of up to 250 L

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 for forward processing

End-to-End Production Capability

- Integration of platform-agnostic DS production suites and a pilot scale fill-and-finish drug product (DP) suite

GMP Manufacturing Facility Overview: ACES
Agile, highly Compact & configurable, End-to-End Production & Single-Use Technology

- GMP Facility at 138 Depot Road #04-01, *in close proximity to the Hilleman HQ in Biopolis*
- ~30,000 sq feet BSL2+ clinical GMP facility supplying clinical trial materials (CTM) from drug substance to drug product for clinical development and manufacturing
- GMP facility is integrated with Zone C/D manufacturing suites, QC laboratory, warehouse and supporting utilities
- Design provision for manufacturing of vaccines to supply Singapore's needs during pandemics (EUL)
- Quality Management System (QMS) has been established based on PIC/S and ICH guidelines I

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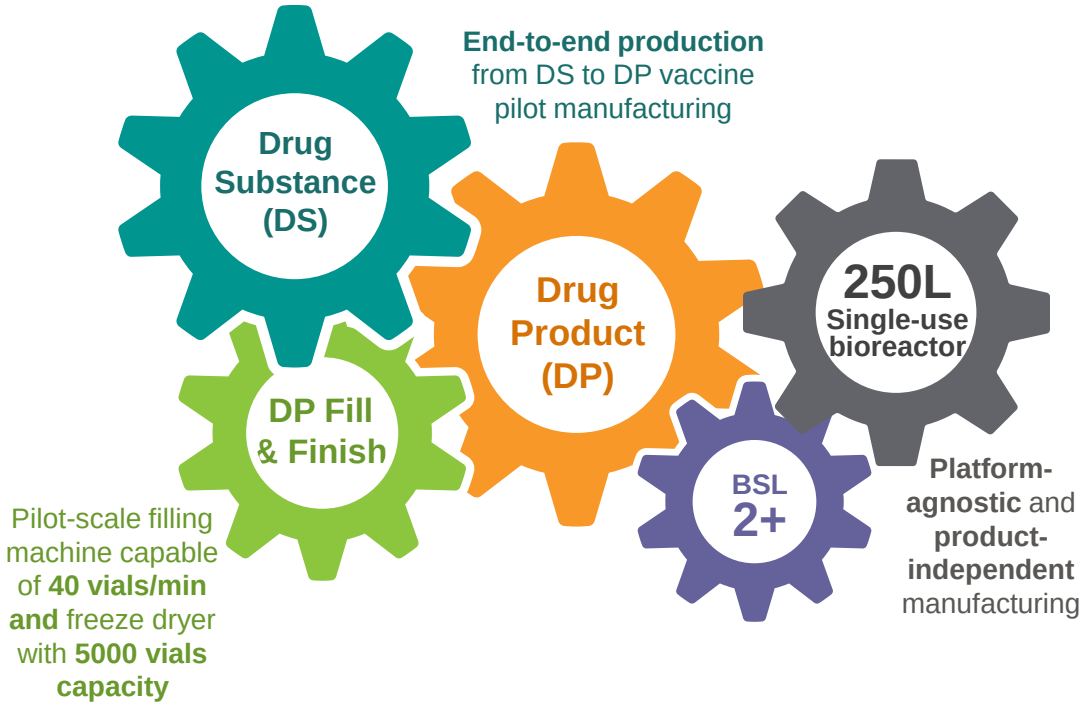
Key Features of the GMP Manufacturing Facility: ACES
Agile, highly Compact & configurable, End-to-End Production & Singe-Use Technology



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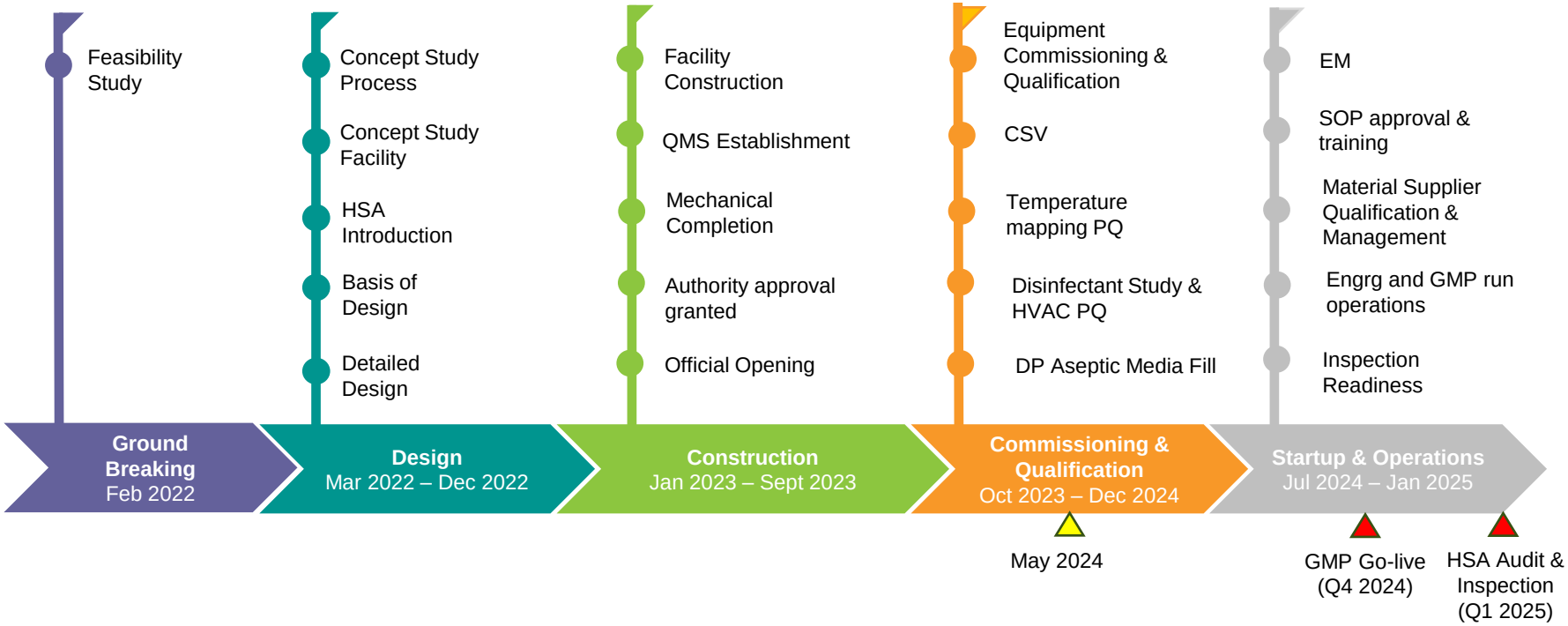
PRODUCT FLOW:

The following is the process/product flow overview of the future Early Phase Clinical GMP Facility:

- Unidirectional
- Dedicated Supply/ Return corridor
- Flows are made to reduce contamination risk
- Dedicated AHU to prevent cross contamination

Process/Product flow shifts from the east to the west of the facility.

ACES Journey & Plan:



CHALLENGES:

- Brown Field
- Clinical Manufacturing
- Platform Agnostic
- Fail Fast
- Building Drawings

- > 200 years of experience lean team
- Phase Appropriate
- Ballroom Concept
- Reconfigurable

CHALLENGES:

LIFTING

EXISTING PIPES, FIXED FLOOR

EXISTING PILLARS, CEILING CONSTRAINTS

APPROACH:

- Leverage Building Facilities, Utilities
- Logistics, Equipment Movement assessment
- Fit for Purpose
- Balance between short term and long term requirements
- Unidirectional
- Dedicated Air Handling Unit
- Height of the clean room
- Both DS and DP in one place

- Transparent collaboration with partners
- One Team
- Phase appropriate Quality Management System
- PM who manages schedule, cost
- Single Person approval for Drawings
- Active Sponsorship

OUTCOME:

- Outcome Met ✓
- Schedule ✓
- Cost ✓
- Resources ✓
- Authorities Approval ✓

REFLECTION:

- Periodic course correction from team input
- Commercial to Clinical Manufacturing
- Green Field to Brown Field
- Earlier regulatory engagement during construction, finishing

Thank You!