A Platform Approach to Spray Dried, Thermostable, Mucosal Vaccines

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IPAC-RS
International Pharmaceutical Aerosol Consortium on Regulation & Science

IPAC-RS Workshop:
Inhaled Biologics: Preparing for a Future Beyond Small Molecules

September 4-5, 2024

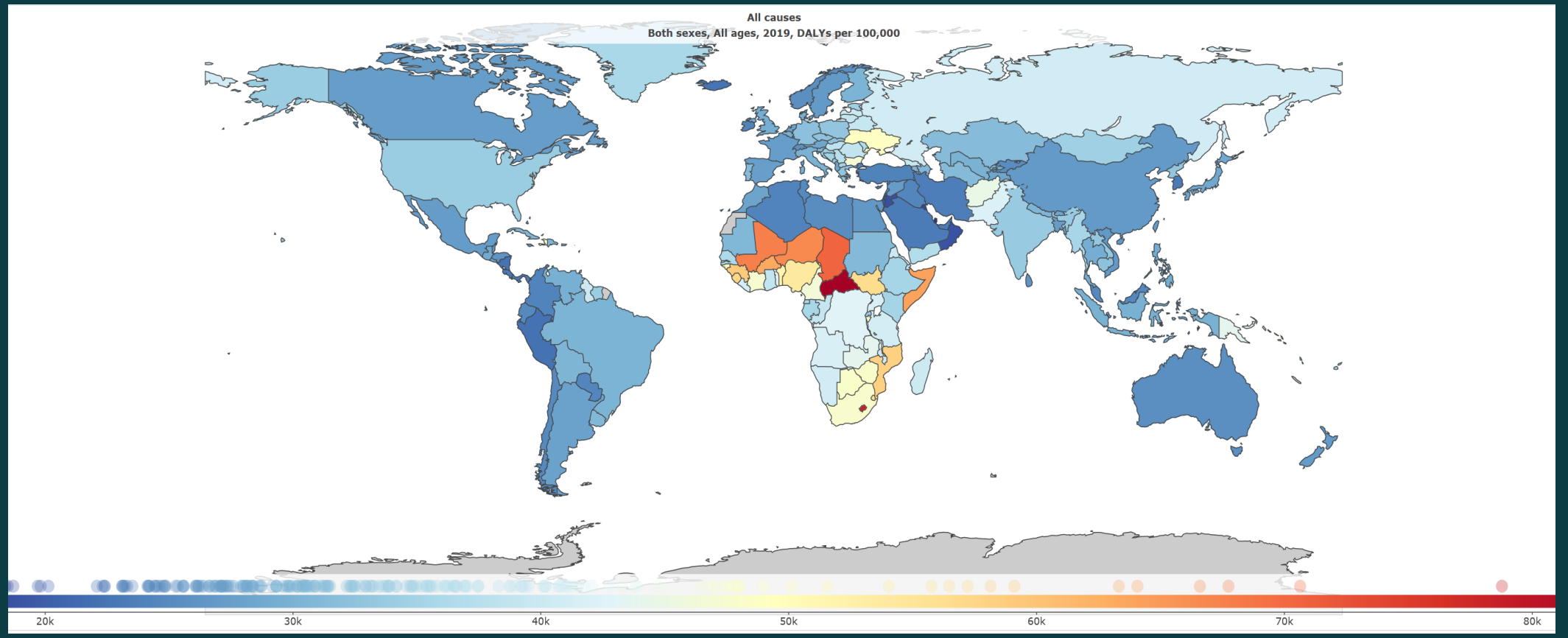
AAHI

UNIVERSITY OF ALBERTA

Motivation

- **Increasing antimicrobial resistance** to traditional antibiotics calls for renewed focus on prevention via vaccines
- **The threat of global pandemics** requires effective countermeasures that can be rapidly developed and deployed globally
- **Substantial infectious disease burden in developing countries** needs effective interventions suitable for resource-poor settings

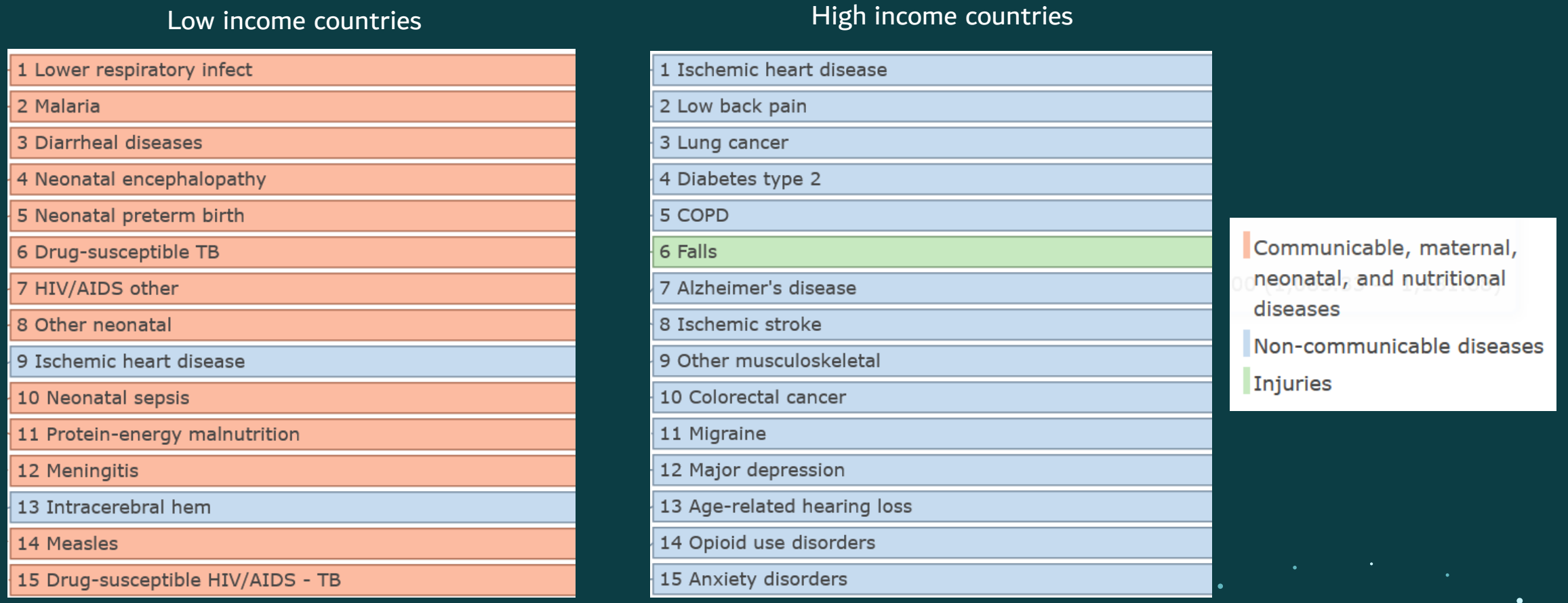
Burden of Disease



Disability Adjusted Life Years per 100000

The greatest burden of disease is in low-income countries, esp. Africa.
Interventions need to be suitable for global use.

Burden of Disease: 15 Leading Causes by Income level



Causes of disease burden are radically different in poor countries. Infectious diseases, and neonatal conditions dominate.

Goals

- **Develop temperature stable vaccines** using a platform approach to simplify the supply chain, eliminating cold chain distribution to enable global transport, storage, and delivery.
- **Use rapidly scalable manufacturing processes** to produce temperature stable vaccines with low operational costs, for more efficient responses to emerging health threats

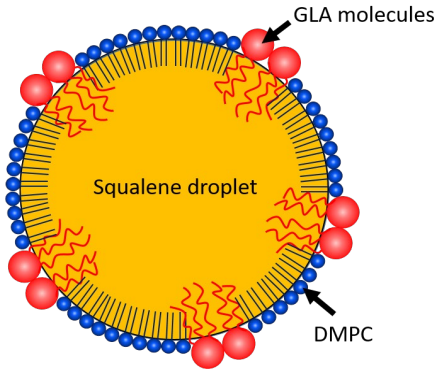
Goals

- **Prevent infection and transmission** of respiratory diseases by targeting the site of natural infection
- **Enable needle-free delivery of vaccines** to promote uptake and ease of use in resource-poor settings

Vaccine Systems

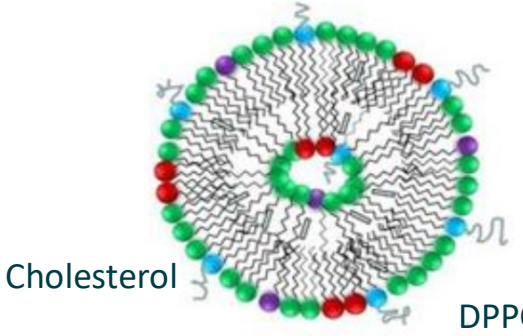
Nano-emulsion (subunit)

d ≈ 90 nm

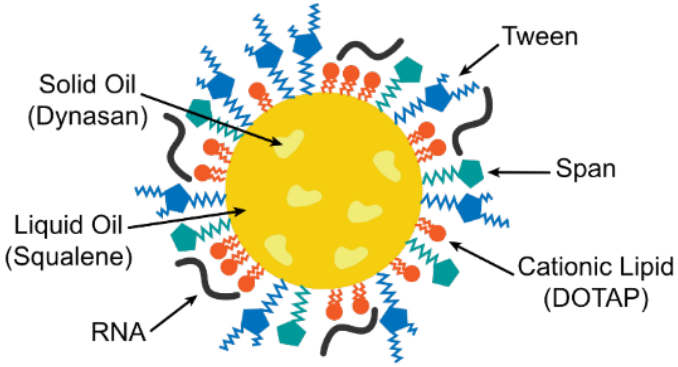


Nano-liposome (subunit)

~100 nm



Nano-structured Lipid Carrier (NLC) (saRNA)



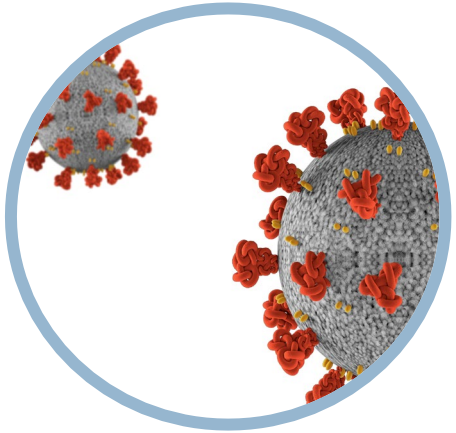
Adjuvant:	Squalene GLA (TLR 4) (Glucopyranosyl lipid adjuvant)	- GLA (TLR 4) 3M-052 (TLR 7/8) (Imidazoquinoline)	Squalene

Spray Dried Vaccine Candidates

TUBERCULOSIS

ID93 + GLA-SE

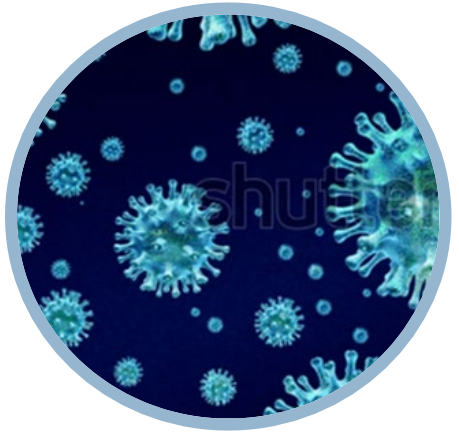
AAHI's recombinant protein ID93 and its GLA-SE adjuvant formulation is in preclinical studies in NHPs administered by inhalation and nasal delivery.



COVID-19

S2P Trimer + GLA-3M-052-LS

AAHI has established proof-of-concept of a spray dried presentation of its liposomal formulation of GLA and 3M-052, combined with an S2P trimer developed by University of Rio de Janeiro.

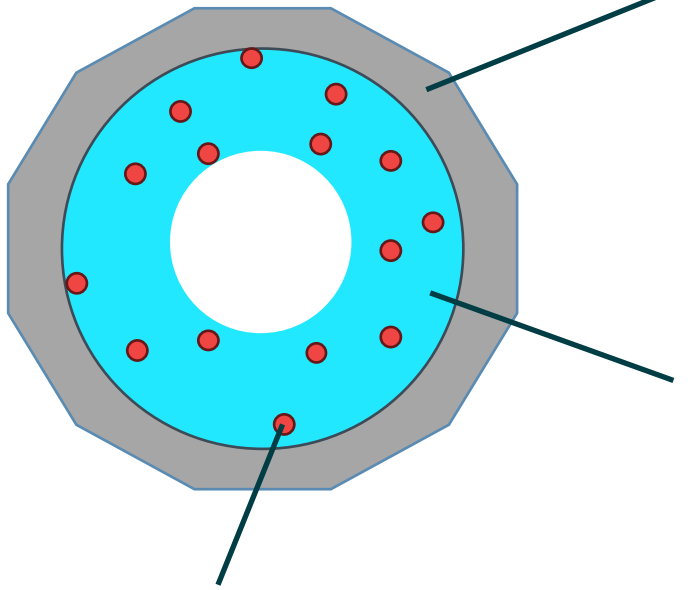


INFLUENZA

saRNA + NLC

AAHI has spray-dried an H5N1 influenza saRNA with its nanostructured lipid carrier delivery vehicle.

Design Targets



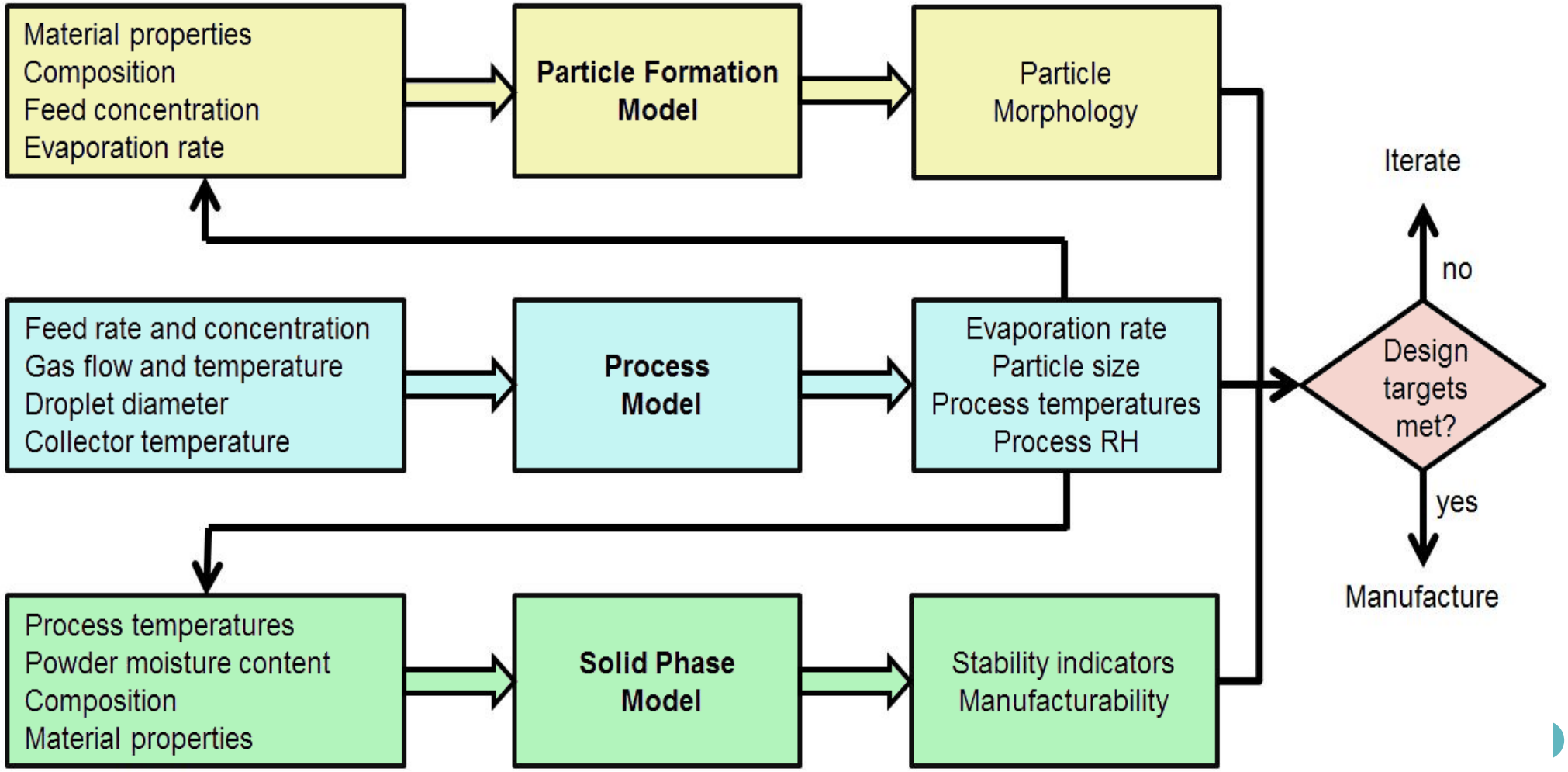
Optional Shell Former:
Leucine or trileucine

Glass Stabilizer:
Trehalose

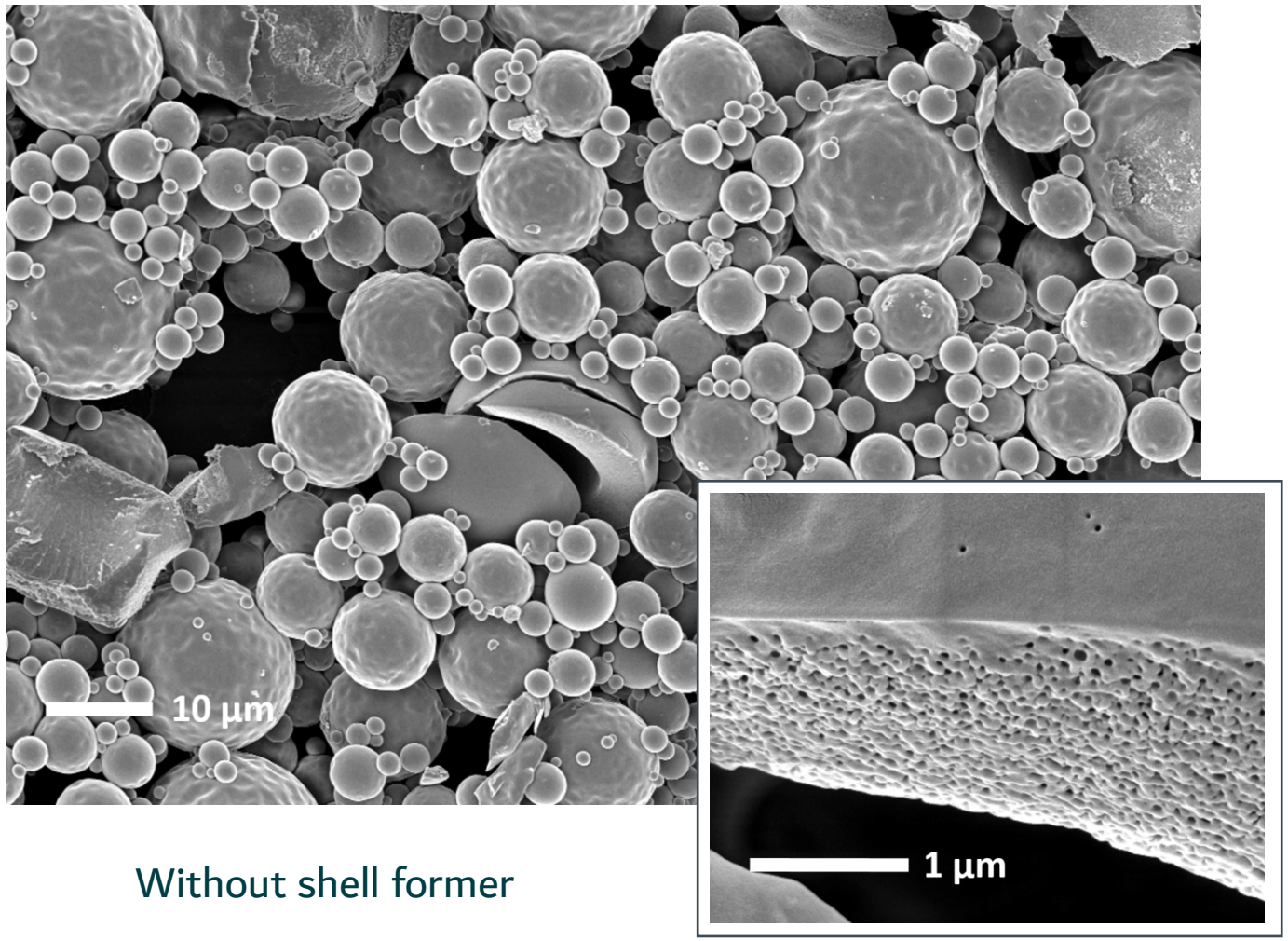
Vaccine Nanostructures
(Emulsion droplets, liposomes, carrier particles, virus)

- Physical and biochemical stability (25°C)
- Minimal processing loss
- Flexible dose
- Particle size for nasal delivery and animal studies
- Compatible with inexpensive, single-use devices
- Straightforward regulatory strategy
- Low development risk and clear path to scale-up

In-silico Design Accelerates Product Development

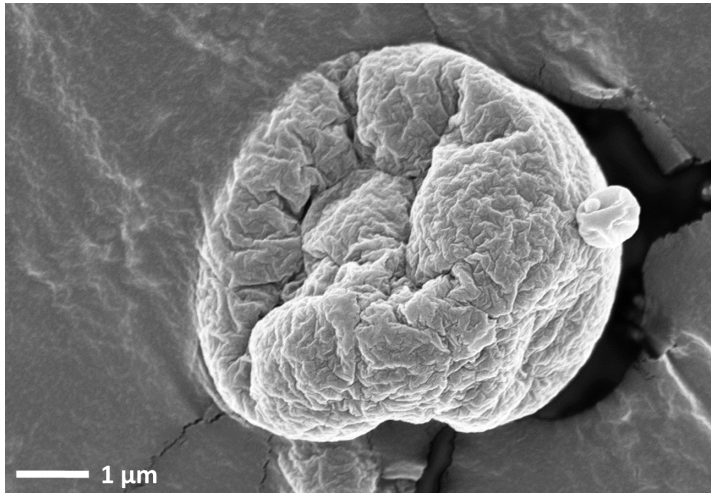


Morphology: TB Vaccine



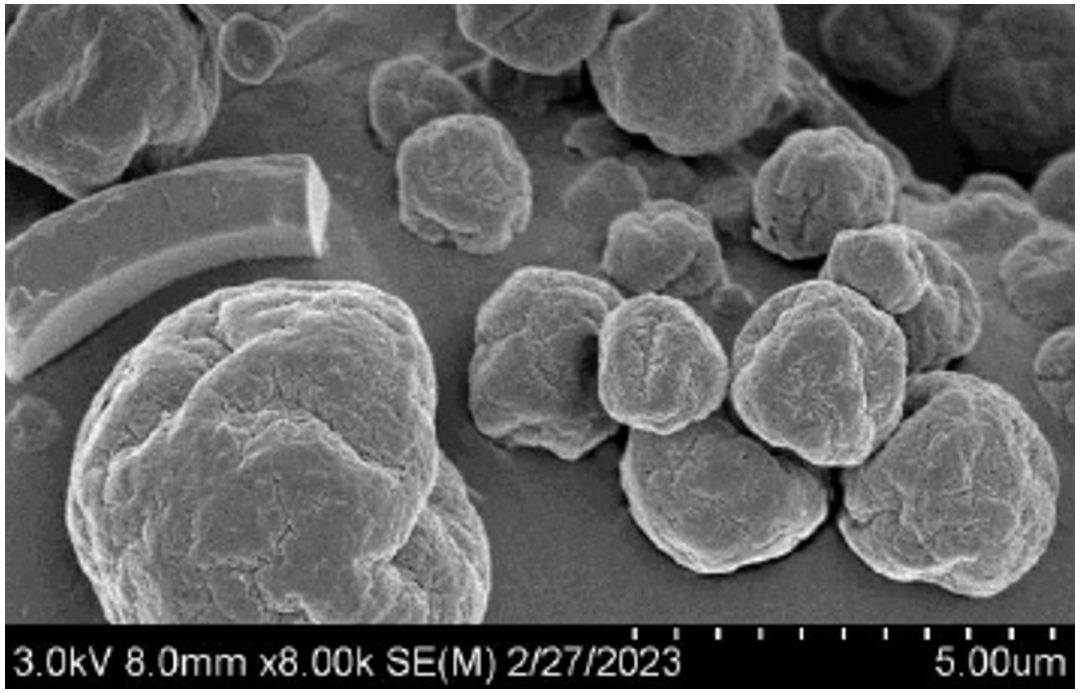
Without shell former

Small particle size for mouse studies.
With added trileucine shell.

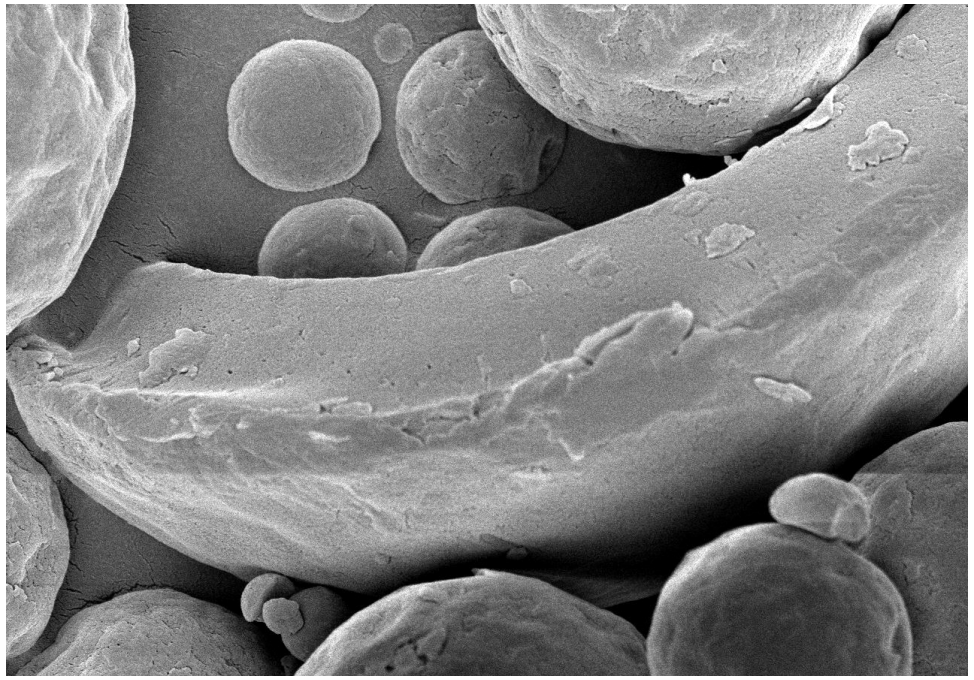


Morphology GLA-3M-052 COVID Vaccine

With 1% trileucine



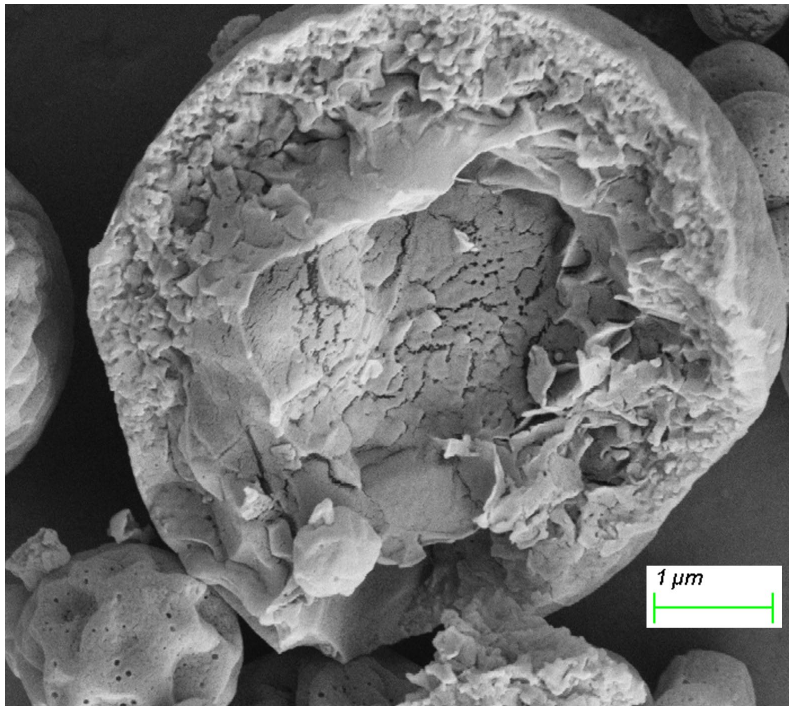
Without shell former (trehalose only)



Rugose particles improve dispersibility

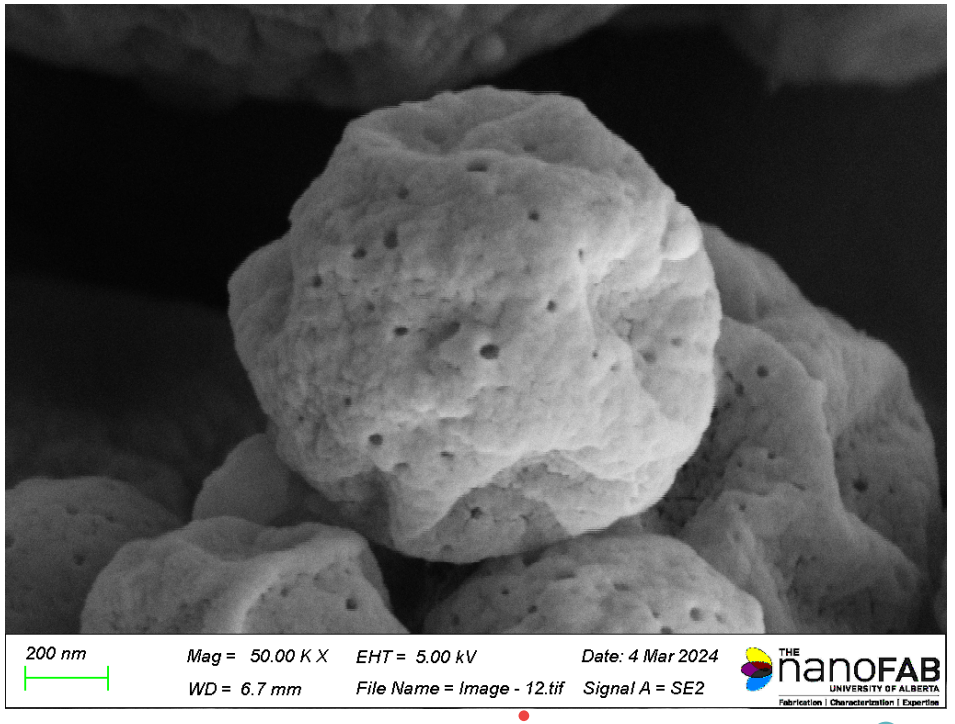
Morphology saRNA Influenza Vaccine

Interior structure



With 20% leucine

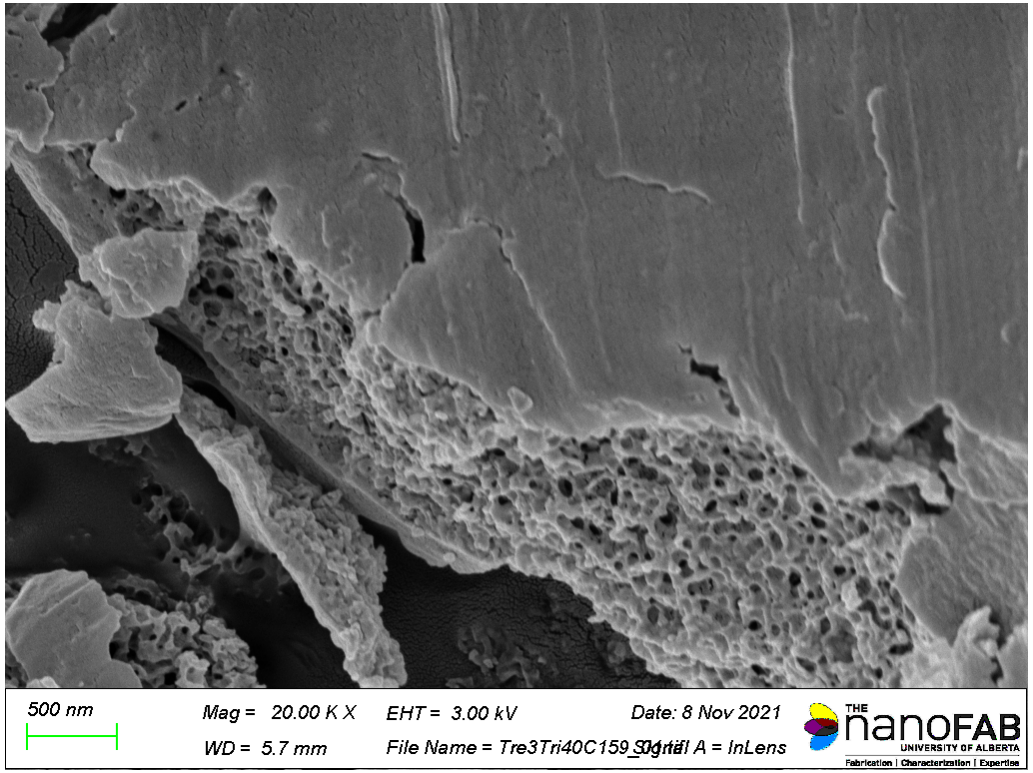
Surface structure



Physical Stability

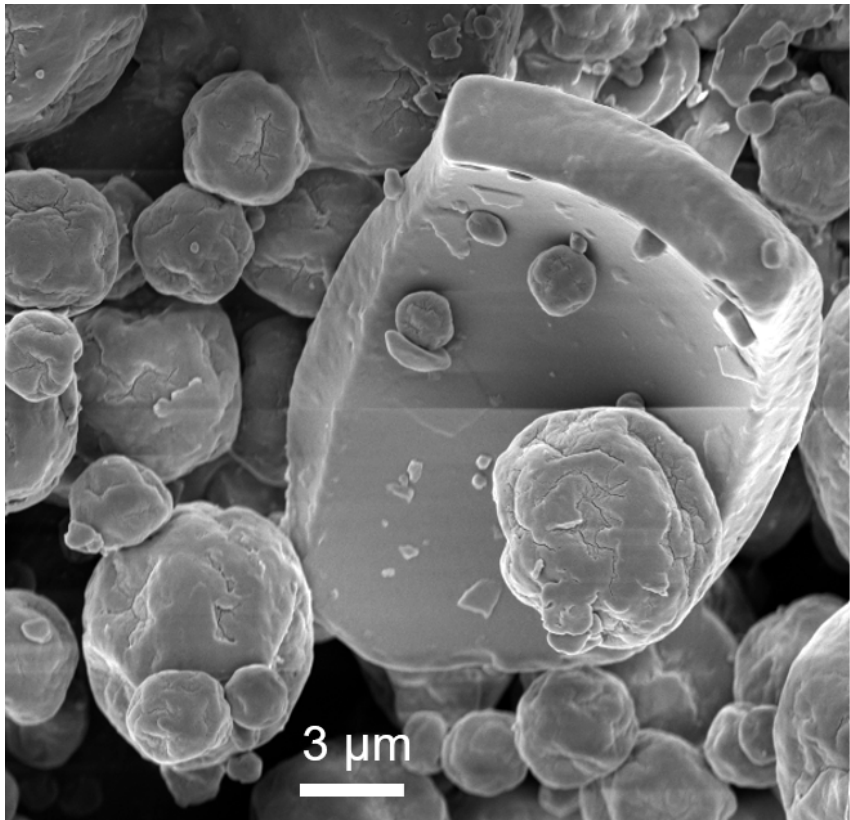
No morphological changes
No solid phase changes
(verified by Raman spectroscopy)

GLA-SE TB Vaccine



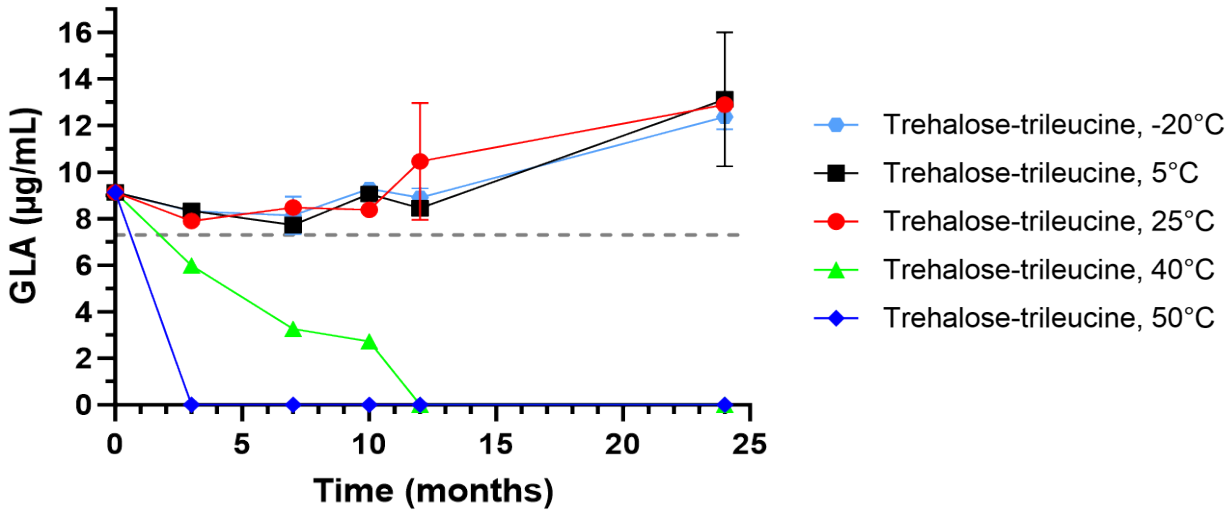
After 2 years storage at 40°C

GLA-3M-052 COVID Vaccine
After 10 months storage at 40°C



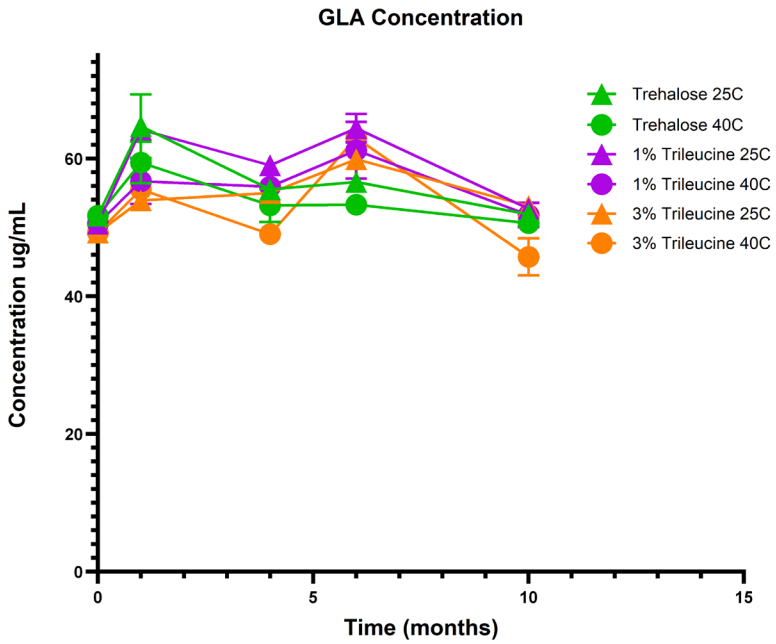
Adjuvant Stability - GLA

GLA-SE TB Vaccine



Stable for 2 years at 25°C

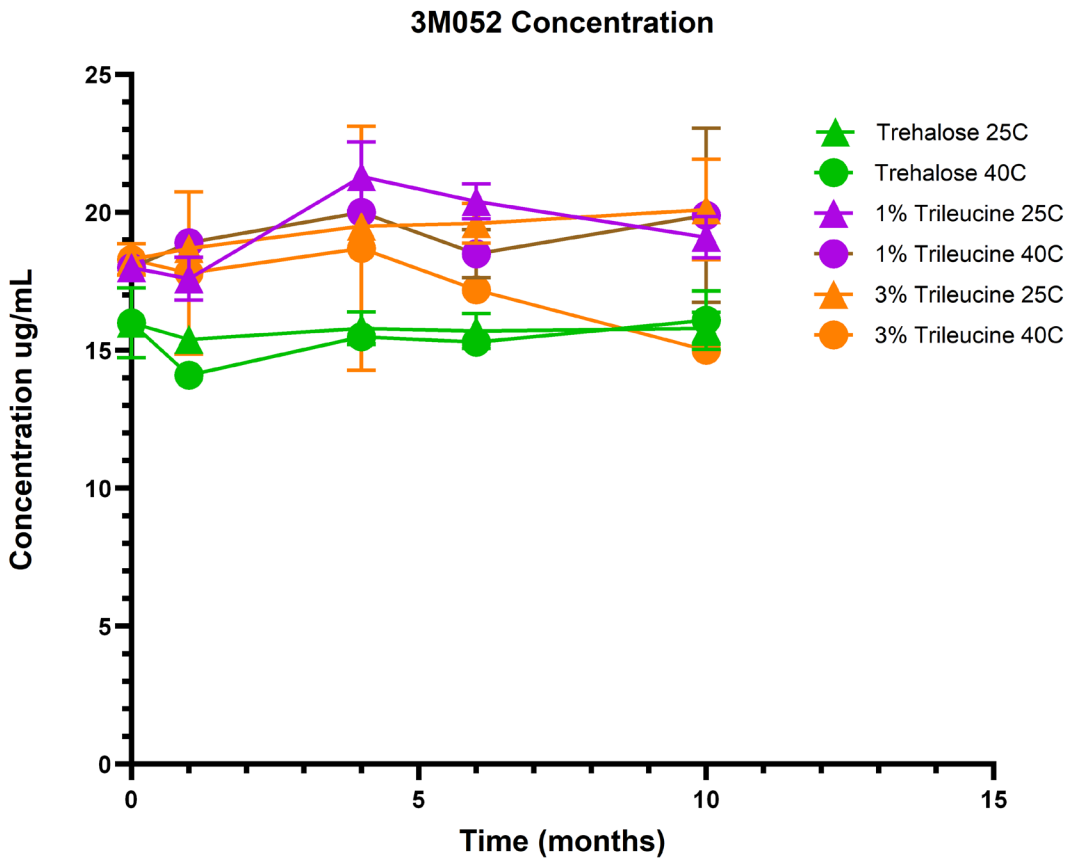
GLA-3M-052 COVID Vaccine



Stable for 10 months at 40°C

Adjuvant Stability – 3M-052

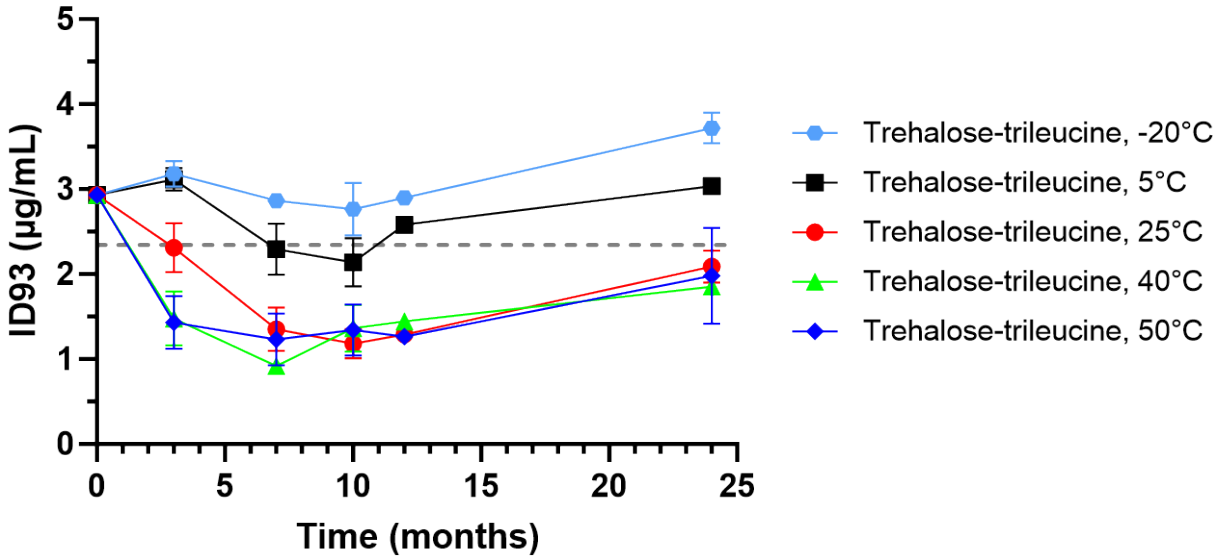
GLA-3M-052 COVID Vaccine



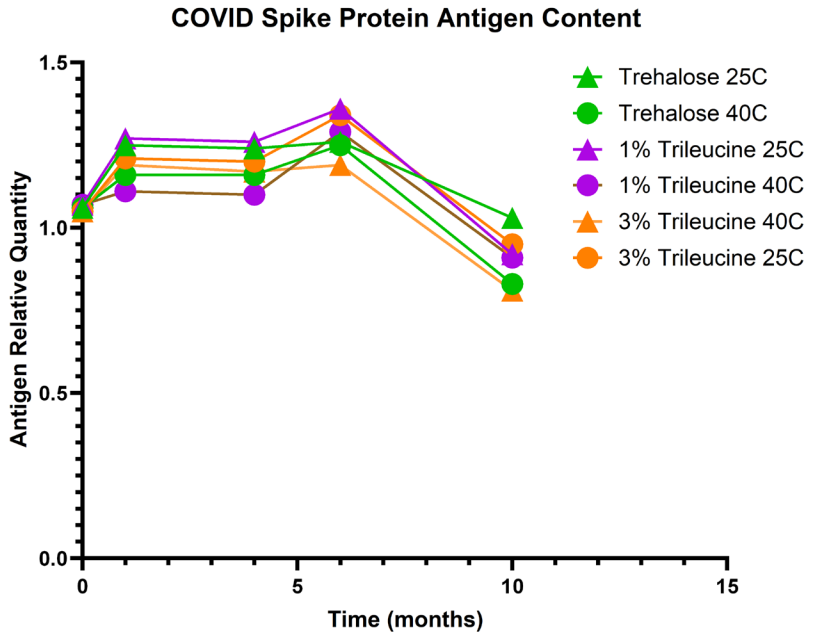
Stable for 10 months at 40°C

Antigen Stability

GLA-SE TB Vaccine



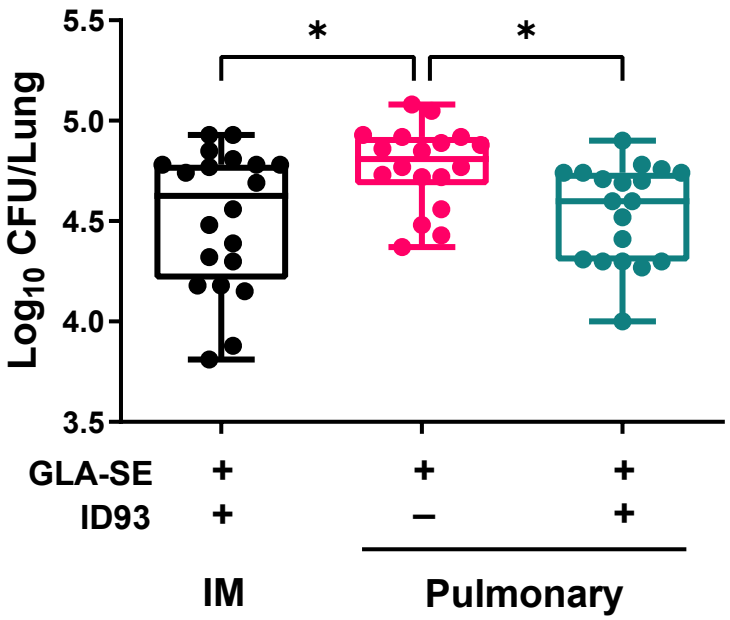
GLA-3M-052 COVID Vaccine



Dry Powder Vaccine Efficacy

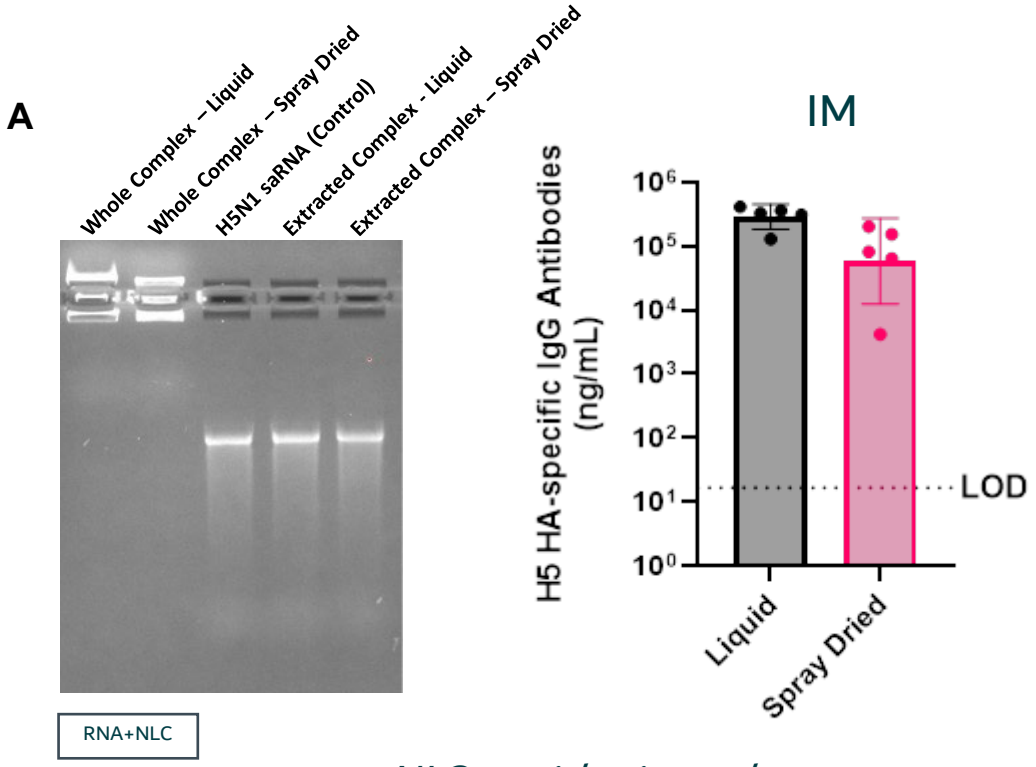
GLA-SE TB Vaccine
Lung Bacterial Burden

Mouse



Comparable efficacy of pulmonary and IM delivery.

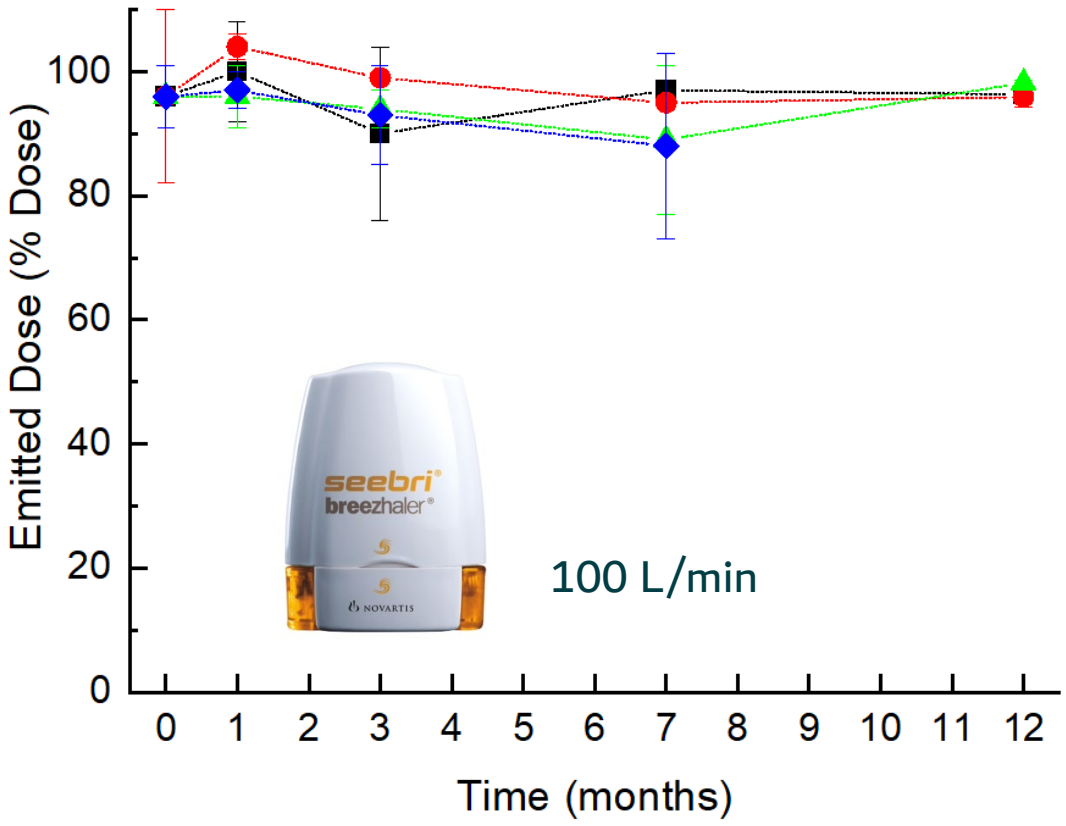
saRNA Influenza Vaccine

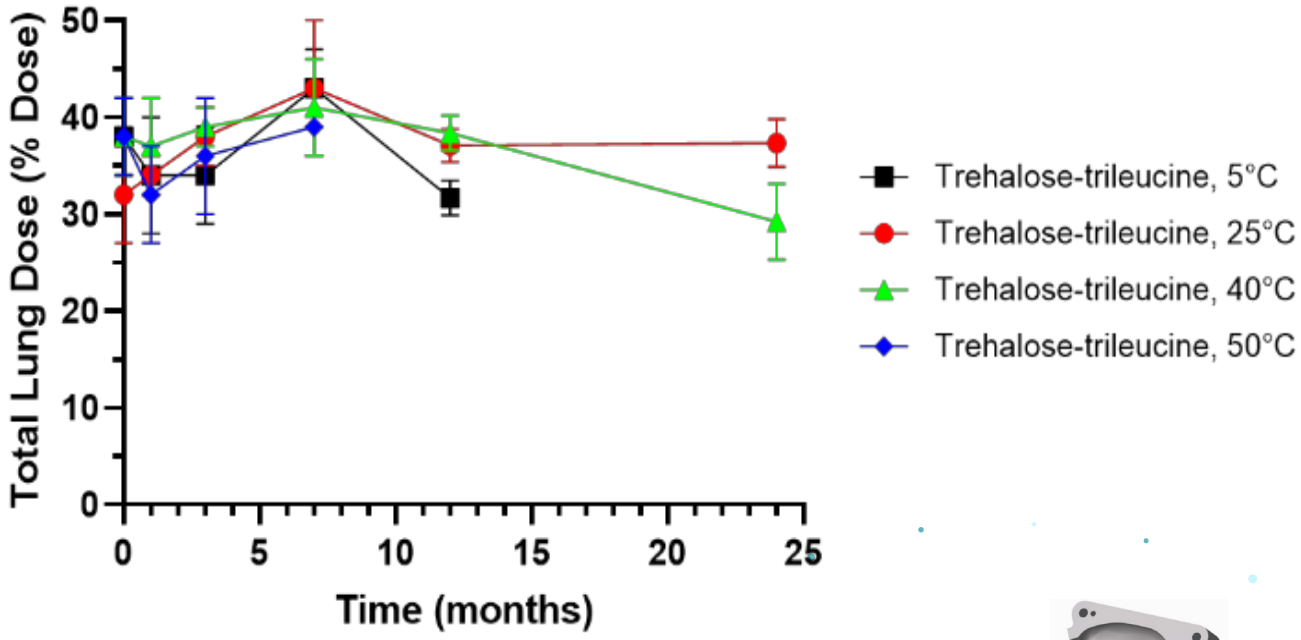


NLC particle size and immunogenicity retained after spray drying and reconstitution.

Aerosol Performance

GLA-SE TB Vaccine
Surrogate test in passive DPI



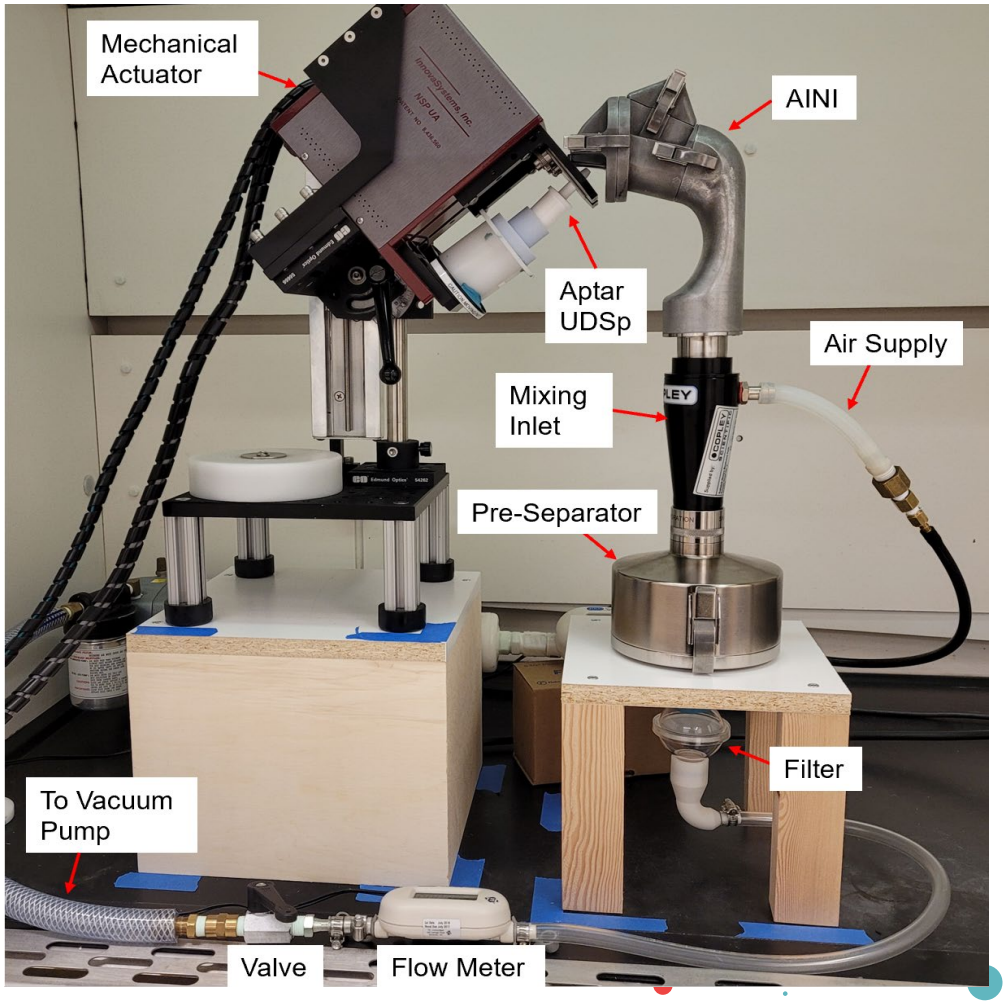


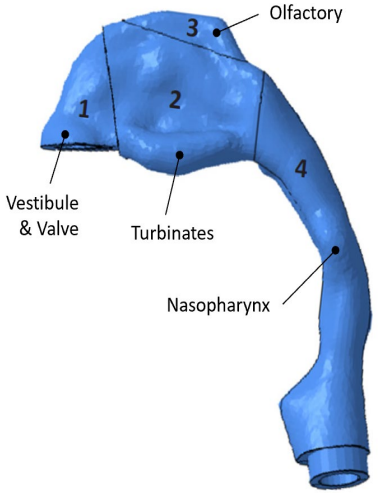
Alberta
Idealized
Throat

Test Procedures for Dry Powder Nasal Devices

- Repeatable automated actuation
- Deposition testing in idealized nasal geometry

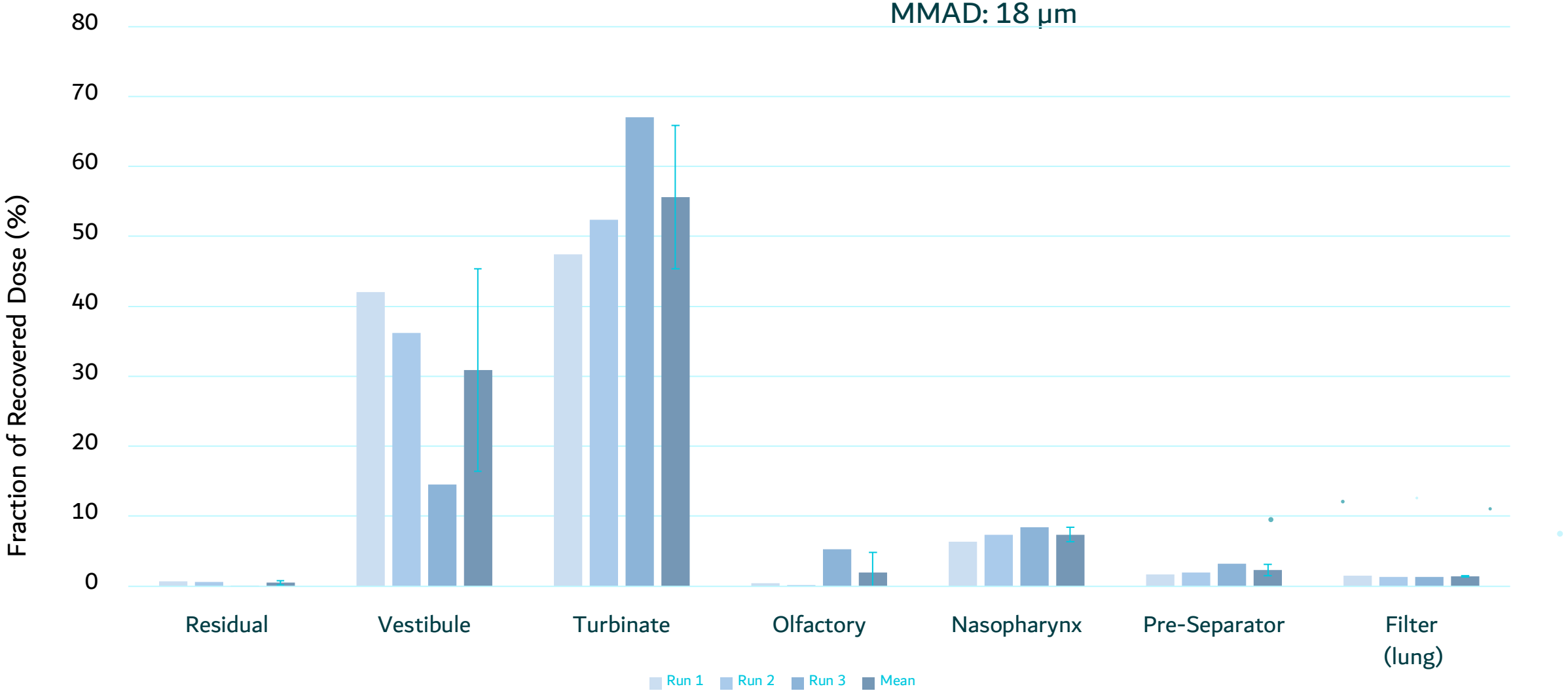
UDS active nasal delivery device / Commercial version





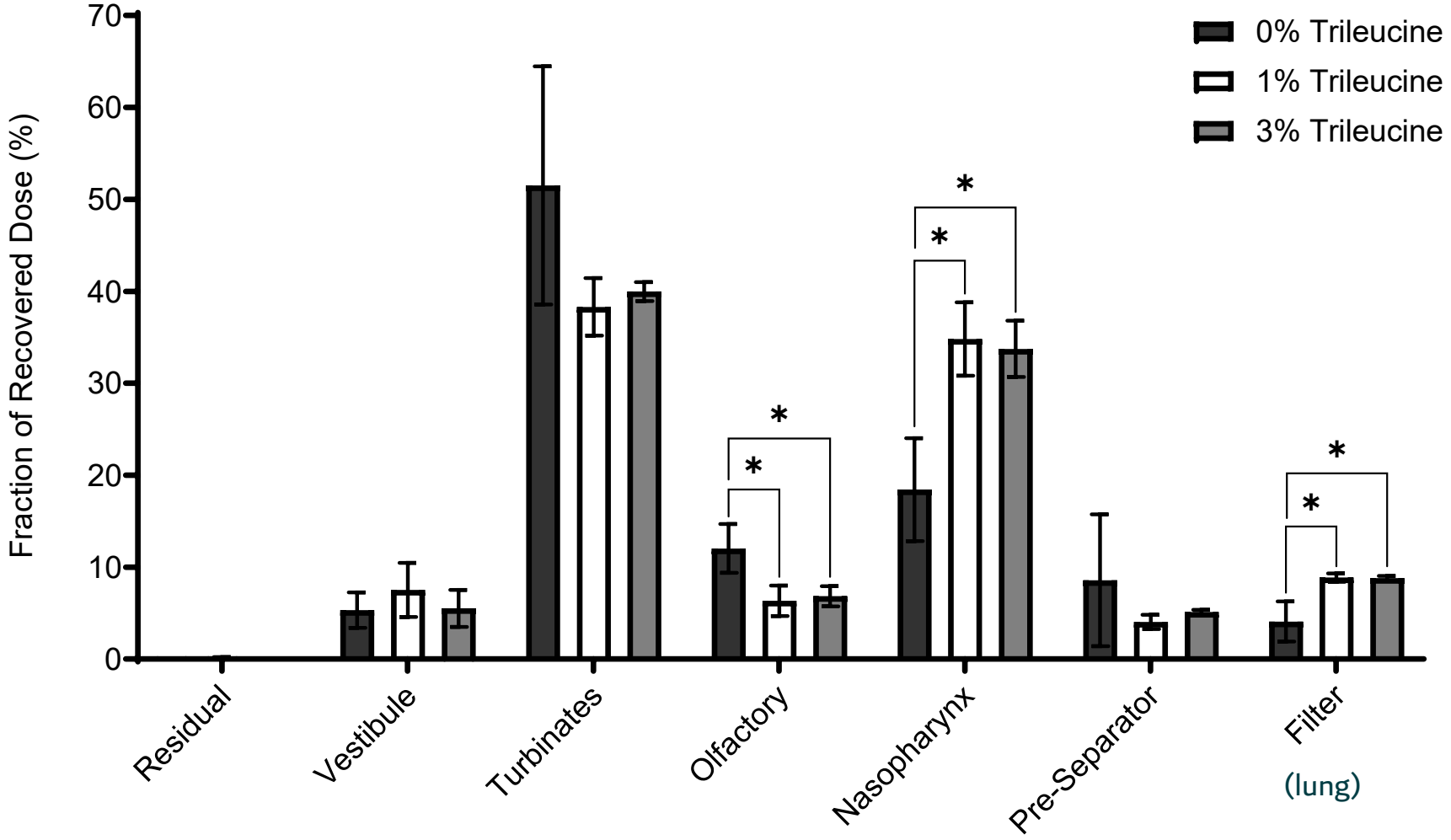
Deposition Pattern

GLA-SE TB Vaccine for non-human primate study
MMAD: 18 µm



Deposition Pattern

GLA-3M-052 COVID Vaccine with intermediate particle size
MMAD: ~9 µm



Conclusions

- The dry powder platform based on spray dried trehalose particles with an optional protective shell is compatible with a variety of adjuvanted vaccine systems and vaccine types
- The platform provides negligible manufacturing loss, outstanding thermostability, and robustness
- Particle size and deposition patterns can be adjusted for different targets in human and animal models
- Several inexpensive single-use delivery devices exist that enable needle free delivery
- Spray drying can be scaled up to manufacturing rates necessary for pandemic response
- Development is aided by predictive models and can make use of existing GMP infrastructure from respiratory therapeutics
- Ready to move from technology development to product development