# Spray Drying Adjuvanted Tuberculosis Vaccine Encapsulates Nano-emulsions Within a Dry Powder Inhalable Product

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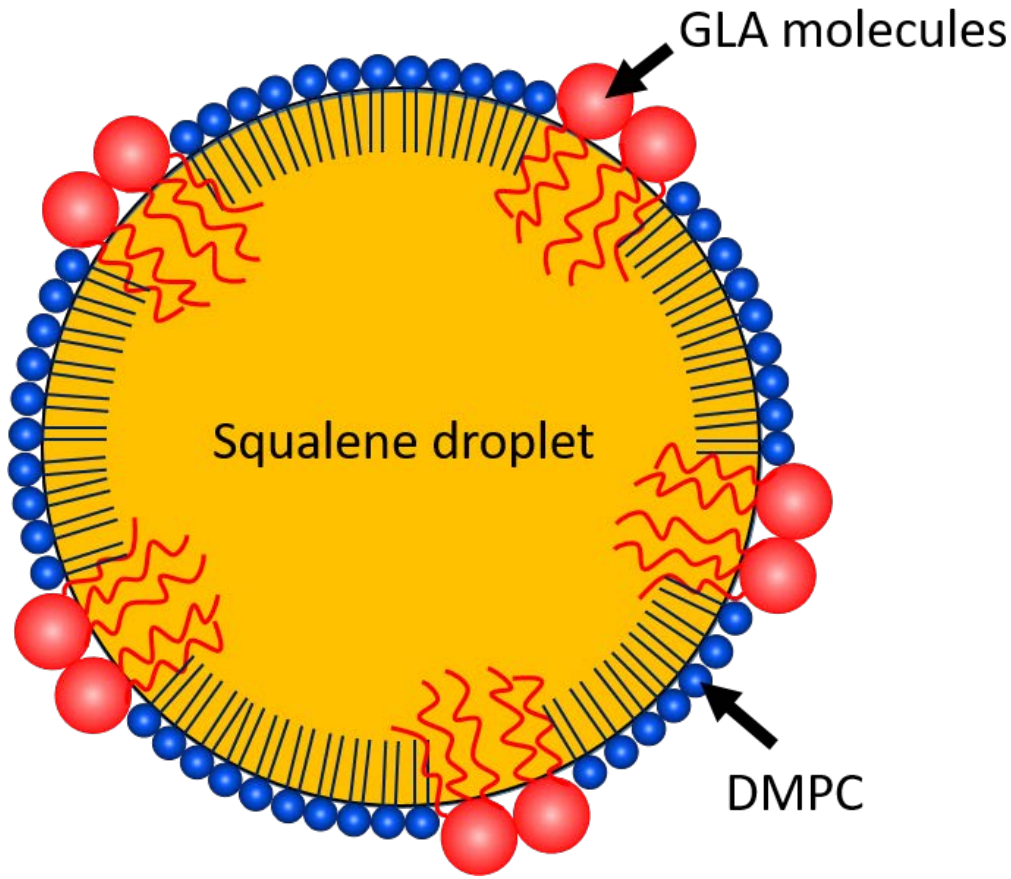
MECHANICAL ENGINEERING

# Introduction

- ID93+GLA-SE is a subunit vaccine developed by the Infectious Disease Research Institute (IDRI) to induce immunity against TB
  - The vaccine is a **nano-emulsion** where the **antigen** (ID93) is associated with the **adjuvant** emulsion droplets (**GLA**-**SE**)
  - **Liquid injectable** presentation is currently undergoing **Phase II clinical trials** [1]

- Why move to a dry powder inhalable product?
  - Eliminate the **cold-chain** requirement
  - Reduce risks associated with **needles**
  - Respiratory vaccination may also be **more efficacious** for respirable diseases [2]






[1] World Health Organization, (2018), "Global Tuberculosis Report"
[2] J. Wang *et al.* (2004), J Immunology 173: 6357-6365

Image adapted from: Anderson R. *et al*. Colloids and Surfaces B: Biointerfaces (2010) 75:123-132

# Development of an inhalable product via particle design and spray drying

A successful spray dried inhalable vaccine product must have several characteristics:

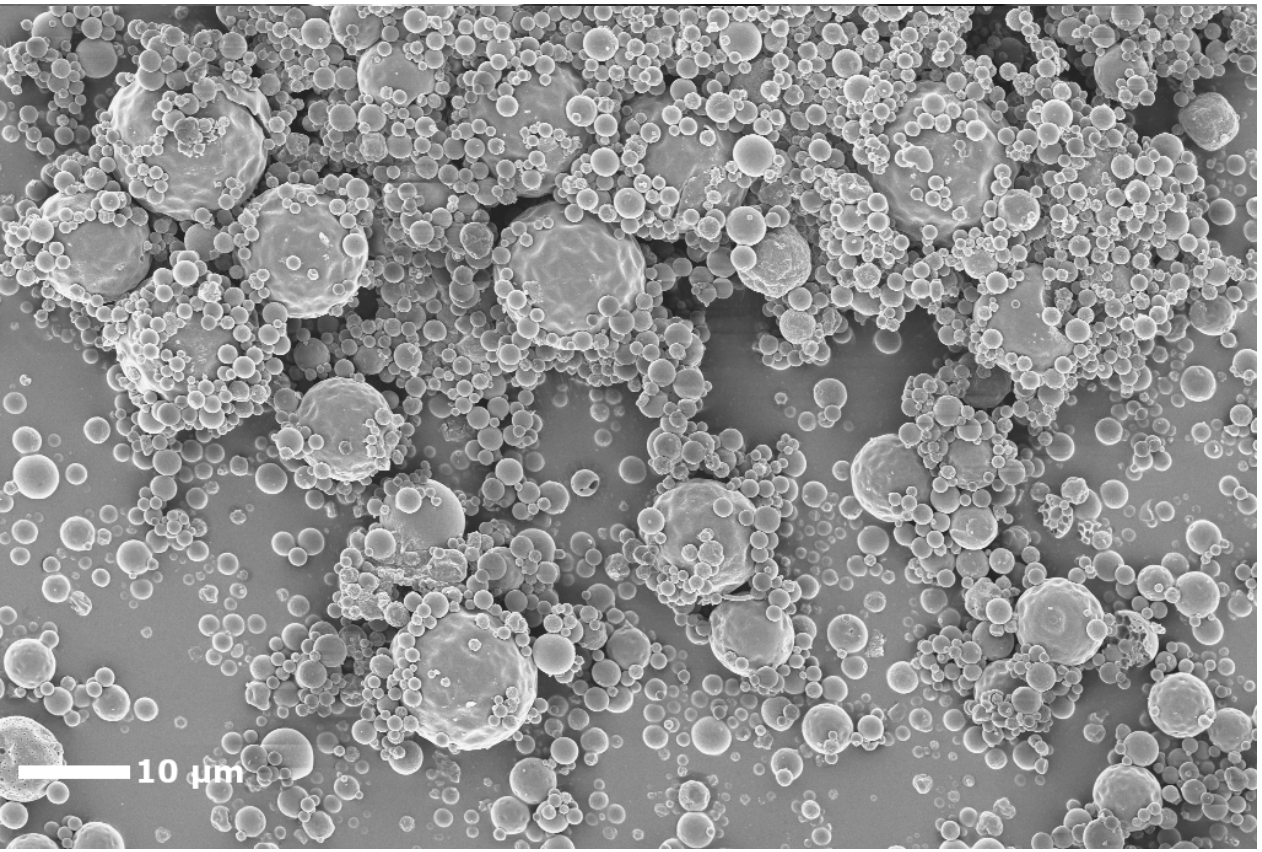
1. The microparticles must encapsulate the **nano-emulsion** droplets with a **high retention rate**

2. The microparticles must **stabilize** the **biologic components** ID93 and GLA at **room temperature**

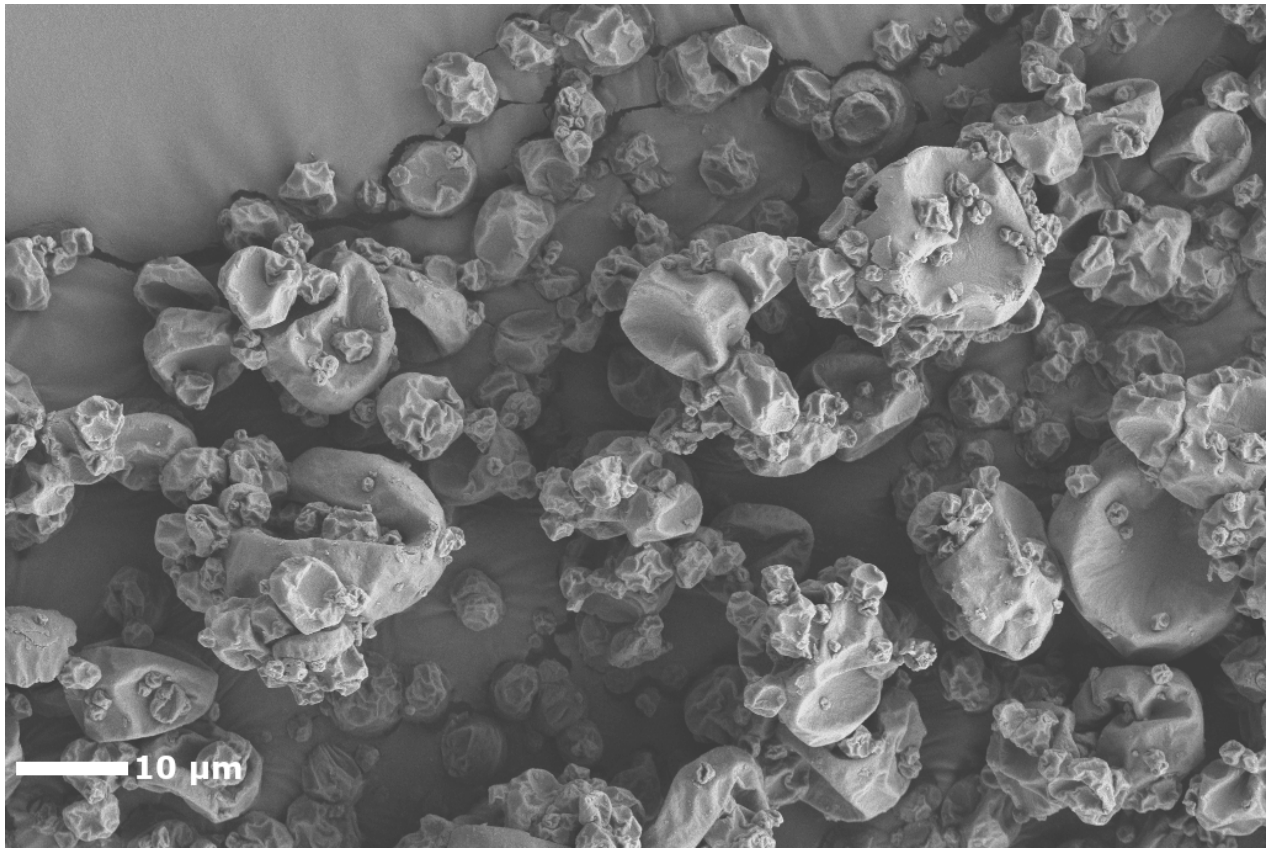
3. The primary particle size must be within an **inhalable range** (MMAD 2-5 µm)

4. The dry powder must be **easily dispersible**

# Spray drying vaccine with trehalose encapsulates the nano-emulsion droplets within an amorphous trehalose matrix, addition of trileucine as a dispersibility enhancer to the formulation generates rugose particles

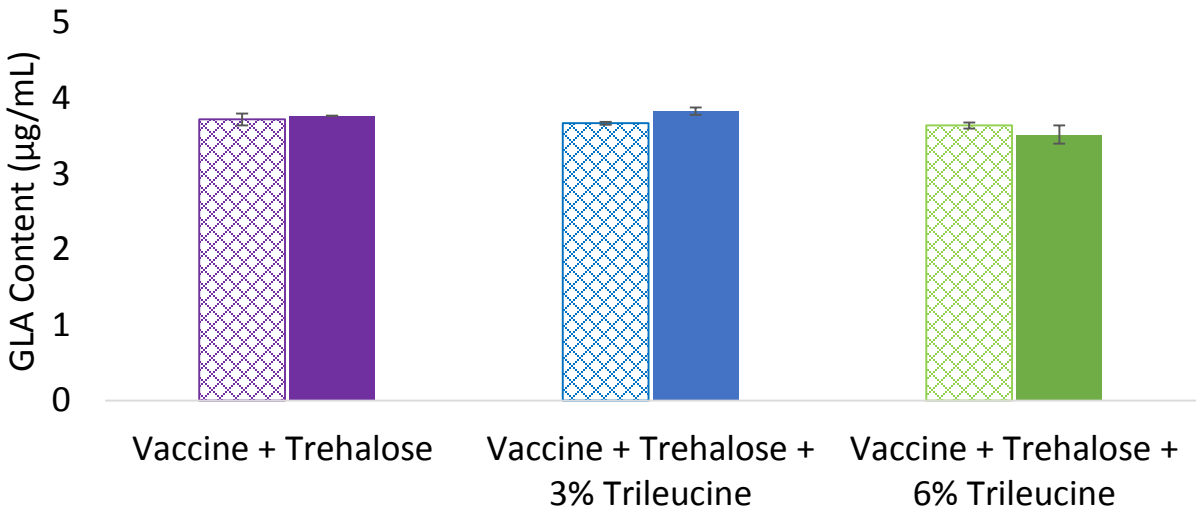


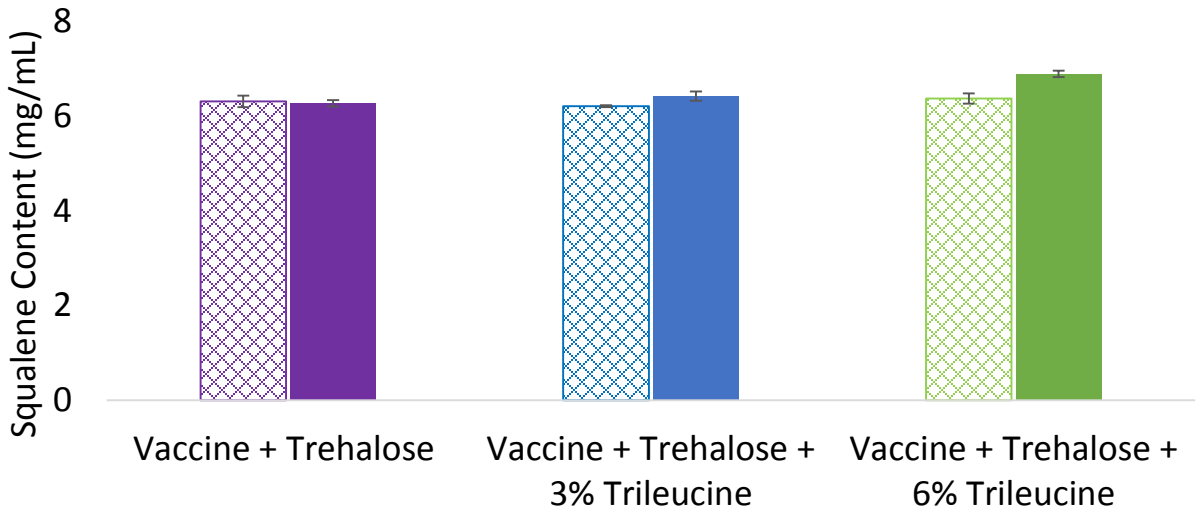

Vaccine + Trehalose

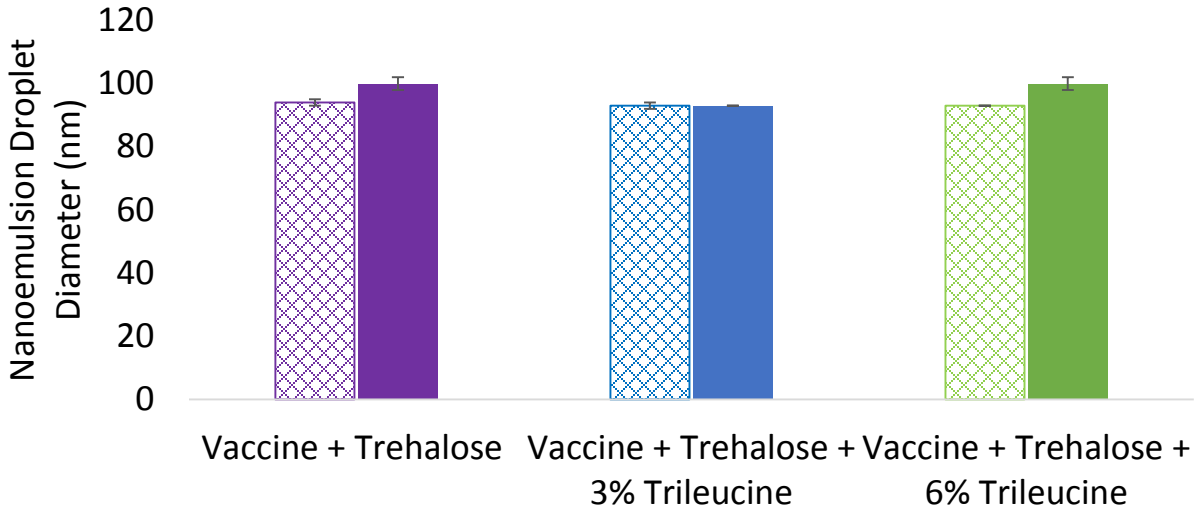


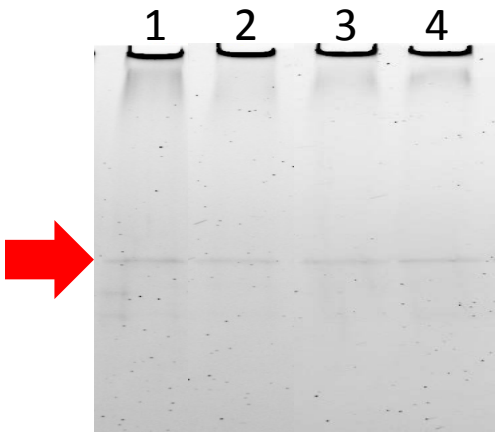

Vaccine + Trehalose + Trileucine

# Comparison of chemical properties of the liquid vaccine to reconstituted spray dried powder show that vaccine integrity is preserved



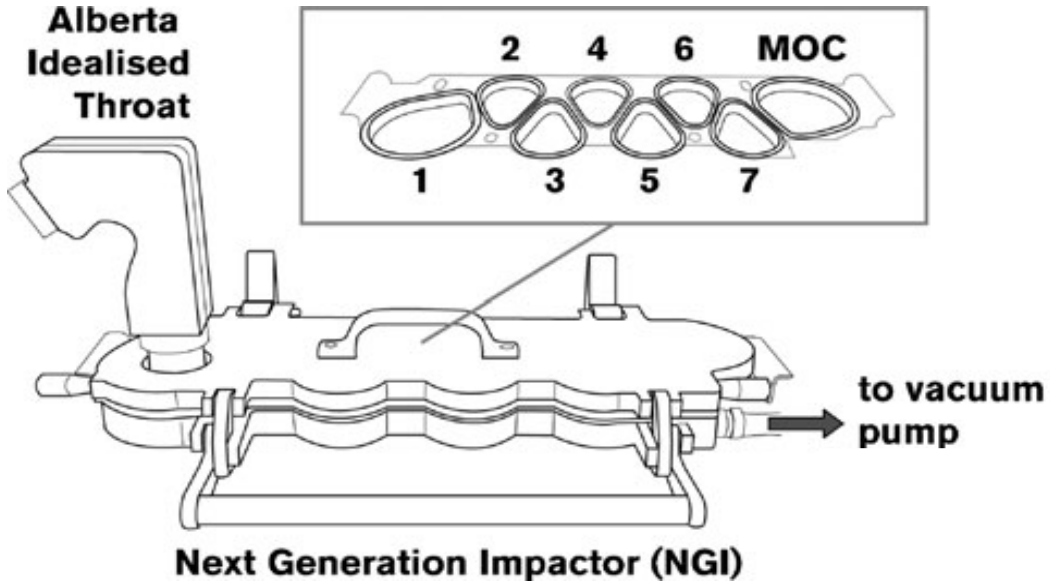




Lane 1 – Vaccine + Trehalose
Lane 2 – Vaccine + 3% Trileucine
Lane 3 – Vaccine + 6% Trileucine
Lane 4 – ID93 + GLA-SE control

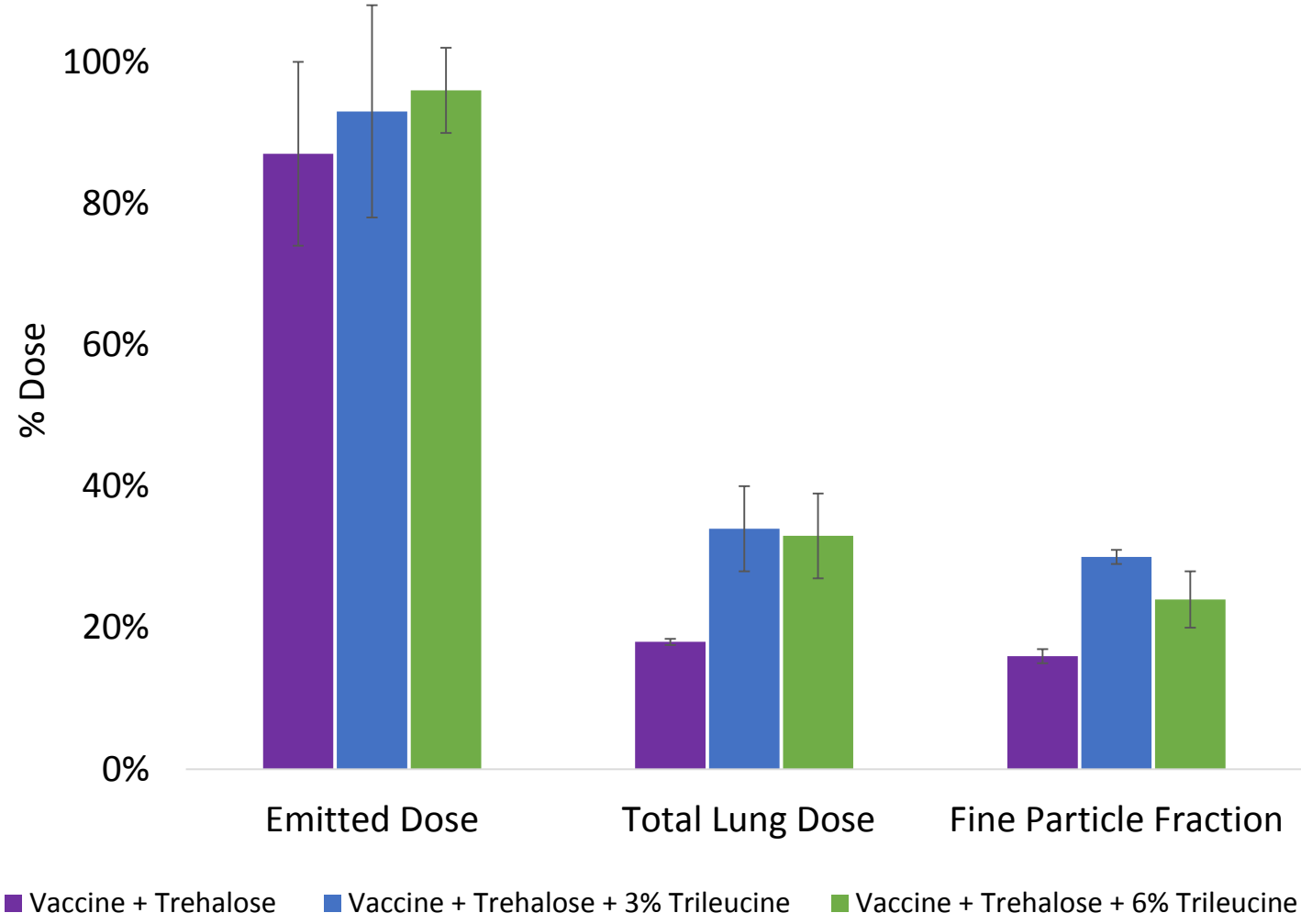


Liquid formulation ■ Reconstituted powder

# Produced powders are compatible with dry powder delivery




- Aerosol performance of powders was tested by stimulating inhalation through a dry powder inhaler
- Definitions:
  - Emitted Dose: % of dose emitted from low-resistance DPI
  - Total Lung Dose: % of dose past mouth-throat
  - Fine Particle Fraction: % of dose <5 µm

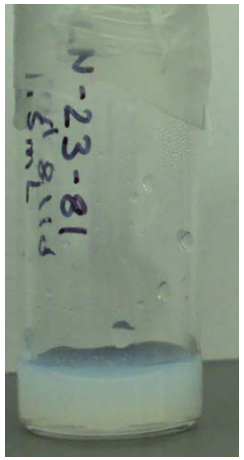



Results shown are the average of triplicates, standard deviation is represented as error bars

Image (left) adapted from: Hoe S. *et al*. Pharm Res (2014) 31: 449-465

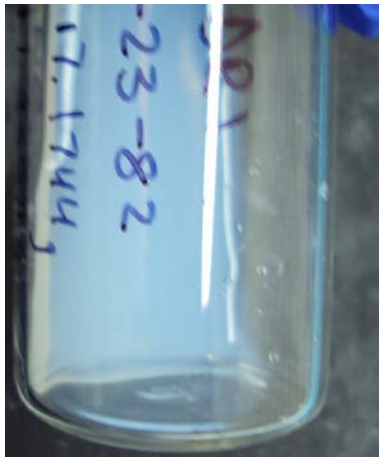
# Conclusions

- Spray drying encapsulates an adjuvanted tuberculosis vaccine within an inhalable dry powder product
  - **Nano-emulsions** can be spray dried into a dry powder with **high encapsulation efficiency**
  - **Actives are stabilized** within an amorphous glass matrix
  - Resulting powder with **dispersibility enhancer** has **reasonable aerosol performance**



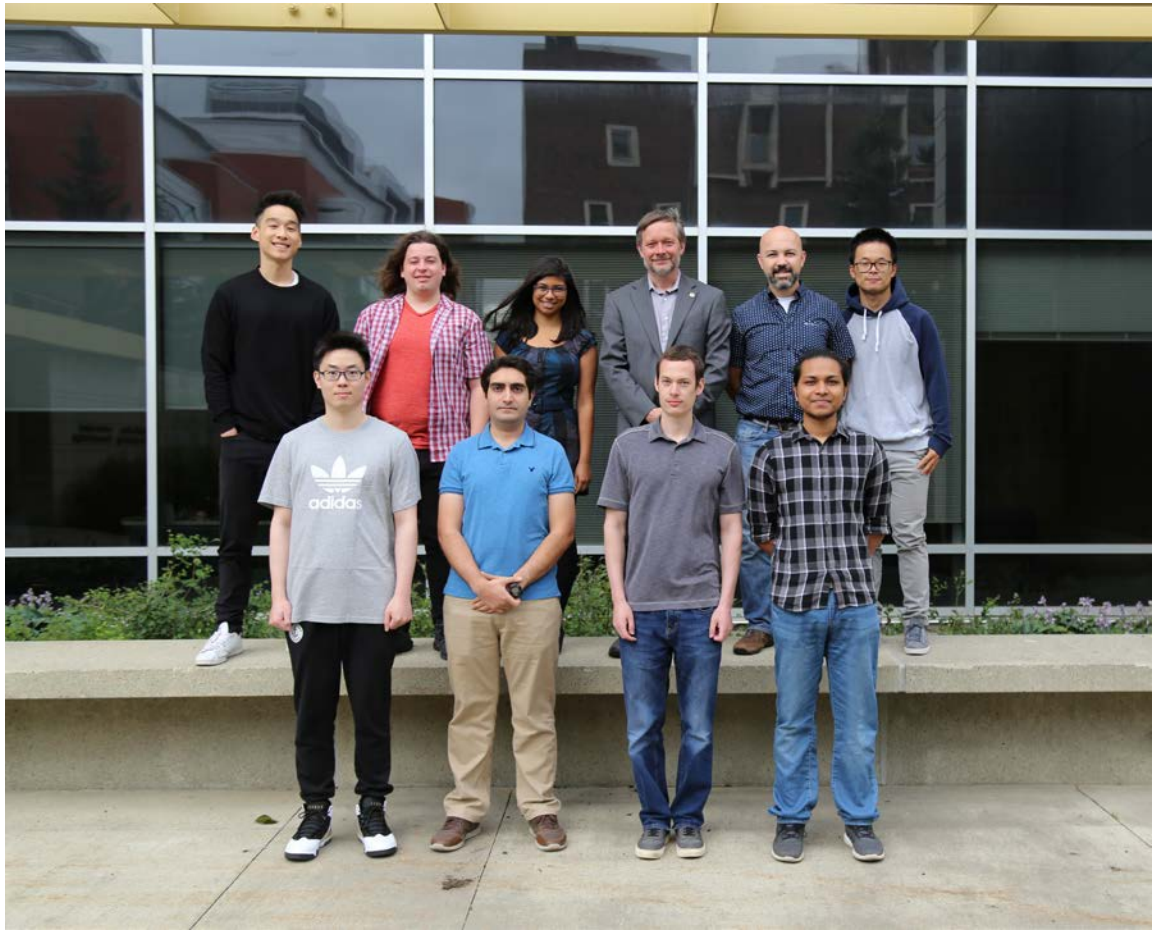

Liquid Feedstock

Spray Dried Powder




Reconstituted Formulation

# Acknowledgements



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