

Nasal and Aerosol Vaccines Development



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Intranasal administration offers a truly “Needleless” solution to Vaccine delivery.

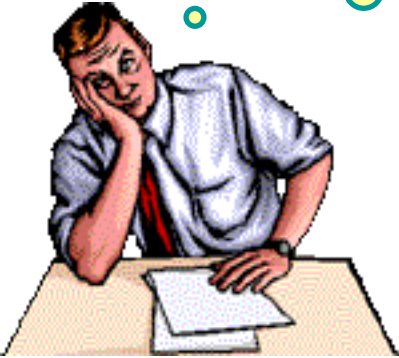


A boy trying to escape from influenza vaccination, Courtesy: CDC

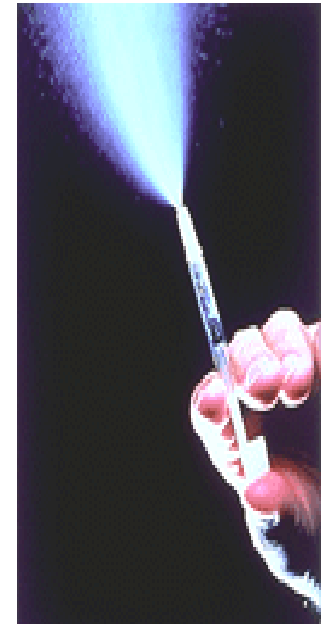


The needle free nasal vaccine may reduce the fear against vaccination.

Why Alternative Route For Vaccine Delivery System?



- **Lessons learned from Oral Polio campaigns**
- To optimize therapeutic effect of vaccine
- To optimize therapeutic dose of vaccine
- To improve patient convenience and compliance
- To control overall healthcare costs
- To target vaccine delivery



Issues Related With Injectables!



According to **Safe Injection Global Network (SIGN) 2010** meeting report

- global burden of disease from unsafe medical injections has been estimated for the year 2008 by the WHO
 - 14% of HIV infections,
 - 25% of HBV infections,
 - 8% of HCV infections and
 - 7% of infections with bacteraemia

The CDC estimates:

- 600,000 percutaneous injuries each year involving contaminated sharps in the U.S. A.
- Technological developments can increase protection.

Nasal Vaccine: Nasal Cavity

It is important to understand the immune mechanism that delivers protection

This understanding guides the design of more effective vaccines

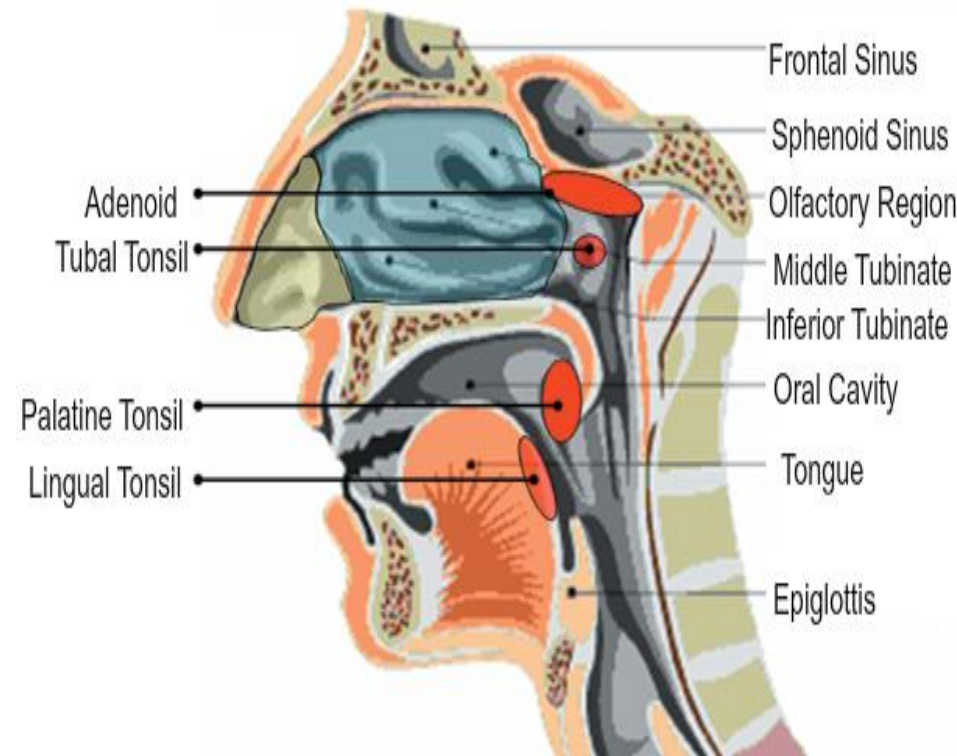


Figure 1: Sagittal section of human nasal cavity

Nasal mucosal surface area coverage:

- ◆ Larger surface area

Volume and Concentration:

- ◆ low volume - high concentration
- ◆ Volumes over 1 ml per nostril are too large and may result in runoff out of the nostril.

Particle size:

- ◆ Particle size 10-50 microns adheres best to the nasal mucosa.
- ◆ Smaller particles (nebulized) pass on to the lungs, larger particles form droplets and run-out of the nose.

Intranasal (IN) Vaccine Administration

- IN delivery route has several advantages:

- It is painless
- Mimics natural route of infection
- Its easy and convenient
- Cell mediated immune response
- Humoral response
- Specific intranasal IgA
- The nose is a very easy access point for medication delivery
- No special training is required to deliver the medication
- No shots are needed
- It eliminates any risk of a needle stick



Nasal Vaccine: Induction of adaptive immune responses

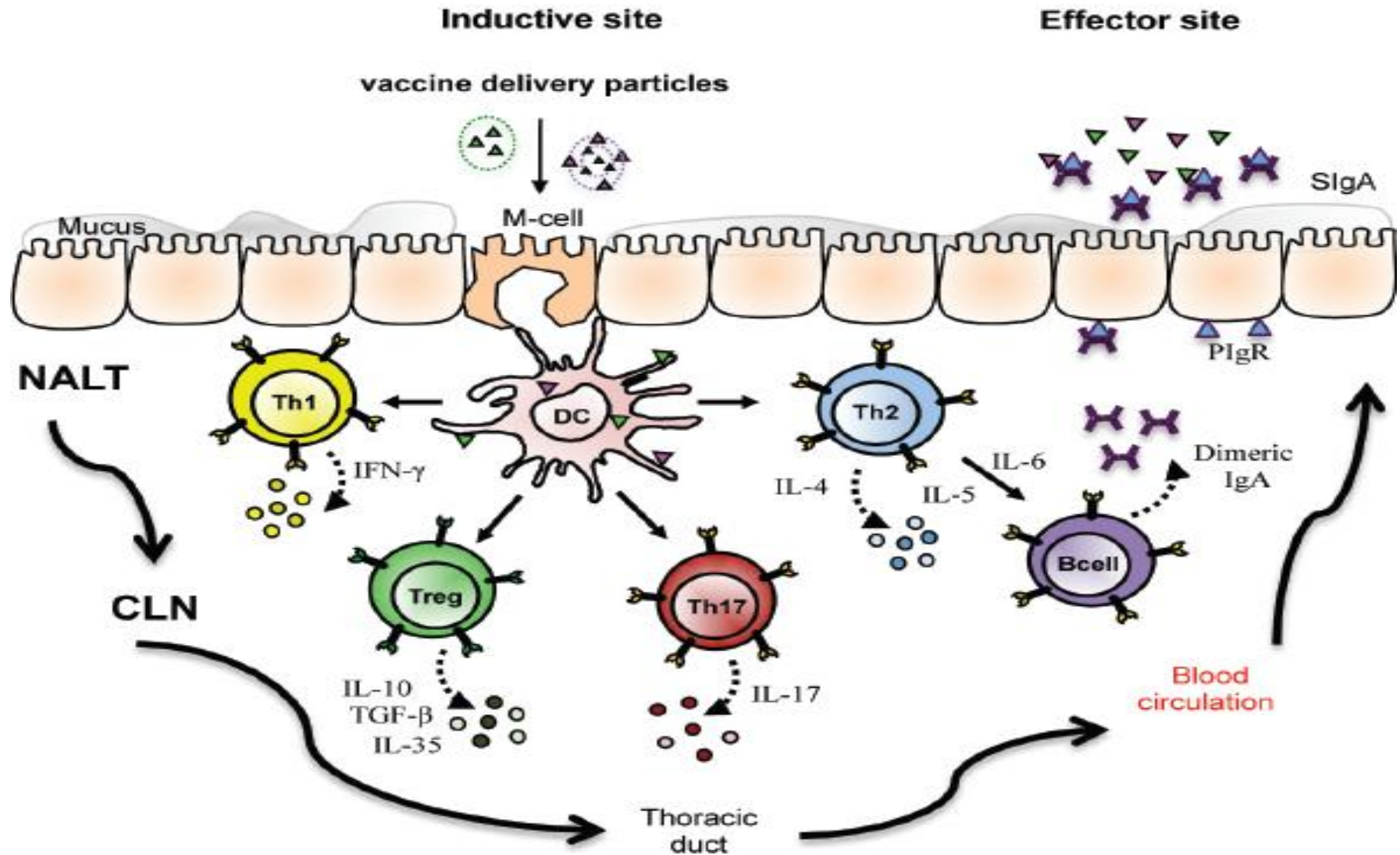
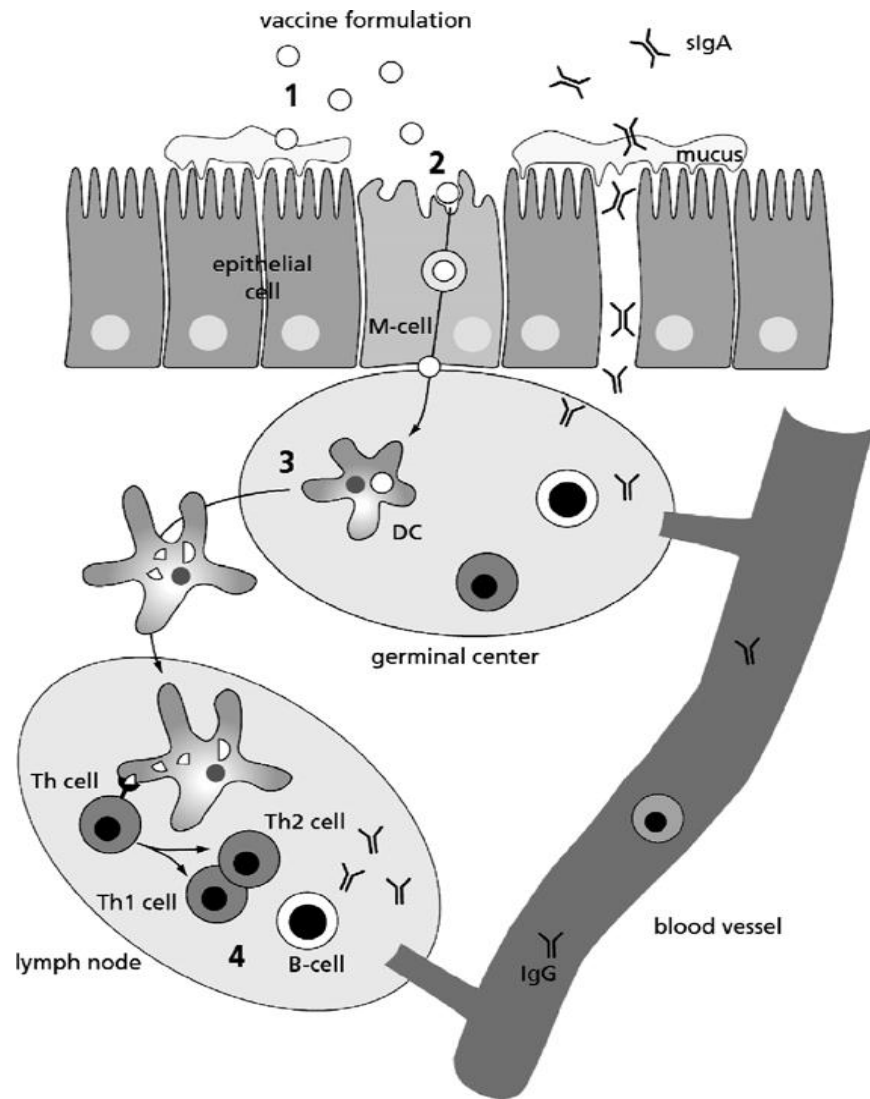


Figure 2: Nasopharynx-associated lymphoid tissue (NALT), follicular associated epithelial (FAE), Dendritic cells (DCs), villous microfold (M)-cells, T-cell receptor (TCR), cervical lymph nodes (CLN), polymeric immunoglobulin receptor (PIgR)

A Roadmap for Successful Nasal Vaccine Delivery



- Prolonging the nasal residence time (muco adhesion).
- M-cell targeting (antigen uptake by M-cell transport).
- Delivery to and subsequent activation/maturation of dendritic cells (DC).
- Induction of cytotoxic T-lymphocyte immune responses.
- Nanostructure-based vaccines major elements should constitute:
 - 1) Carrier, 2) Antigen and 3) Adjuvant

Figure 3: Schematic overview of the consecutive steps towards successful nasal vaccine delivery: (1) mucoadhesion; (2) antigen uptake by M-cell transport; (3) delivery to and subsequent activation/maturation of DC; (4) induction of B-cell and T-cell responses. DC = dendritic cell, M-cell = microfold cell, Th cell = helper T cell.

Nasal Vaccines

1

**Measles Dry
Powder
(Inhalable)
Vaccine**

2

**Measles Aerosol
Vaccine**

3

**Live Attenuated
Influenza Vaccine
(LAIV)**

1) Measles Vaccine : Dry Powder (Inhalable)

Carbon Dioxide Assisted Nebulization with a Bubble Dryer®

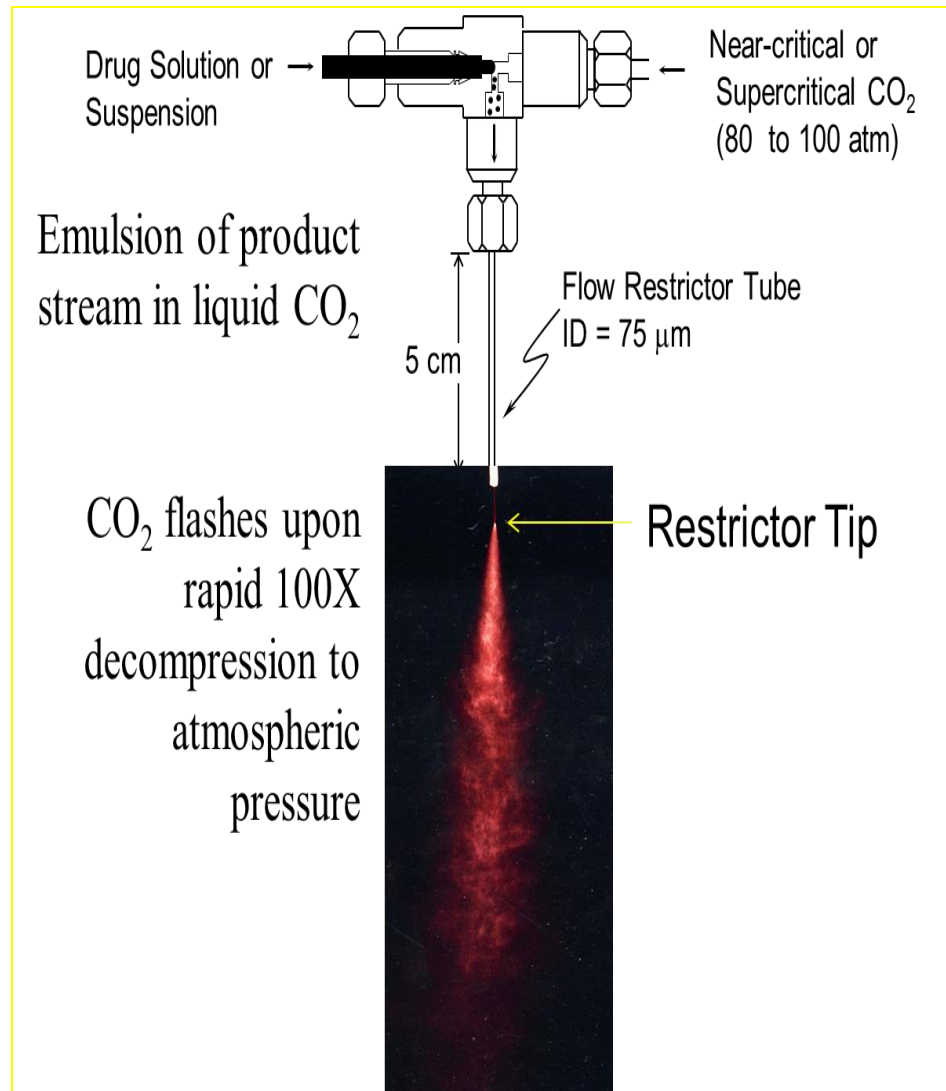


Figure 4: Carbon Dioxide Assisted Nebulization with a Bubble Dryer®

Measles Vaccine : Dry Powder (Inhalable)

PuffHaler

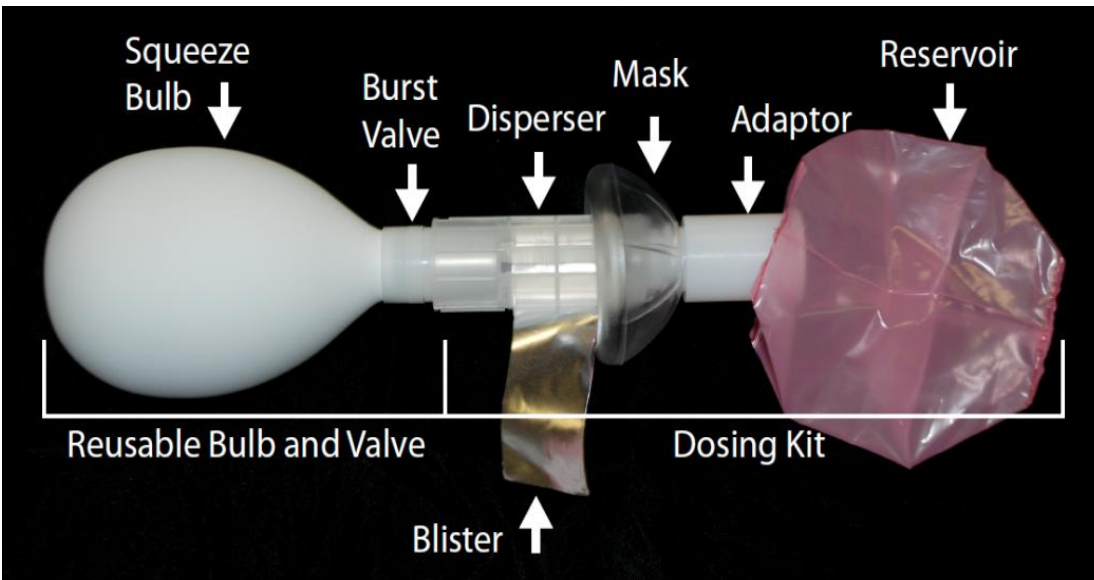
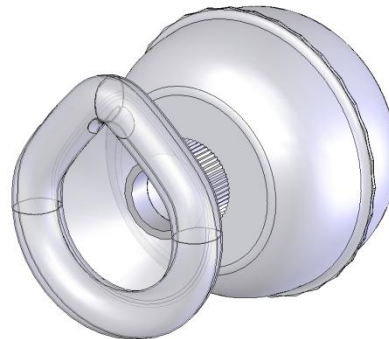
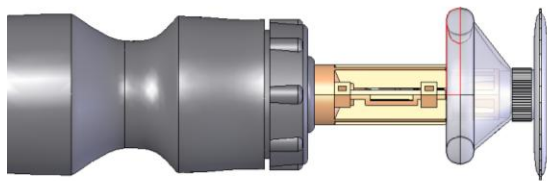


Figure 5: Puffhaler



Adaptive spacer design for adult and children - Configured at time of use

Solovant™ devices



Figure 6: Solovant™ device

Measles Vaccine : Dry Powder (Inhalable)

Status:

- ✓ Validation
- ✓ Technology transfer
- ✓ Bench testing
- ✓ Animal immunogenicity
- ✓ Animal Toxicity
- ✓ Phase 1 in healthy adults

Benefits:

- Non injectable, easier to administer
- No waste disposal
- Competitive cost per dose

Challenges:

- Need data from Phase II and III clinical trials to further assess immunogenicity and safety
- Resources to complete clinical development
- Scale up of manufacturing

Technology Availability:

Probability of technology availability for program use in the next 10 – 20 years if not sooner



2) Measles Aerosol Vaccine : Respiratory delivery of the currently available freeze dried measles vaccine

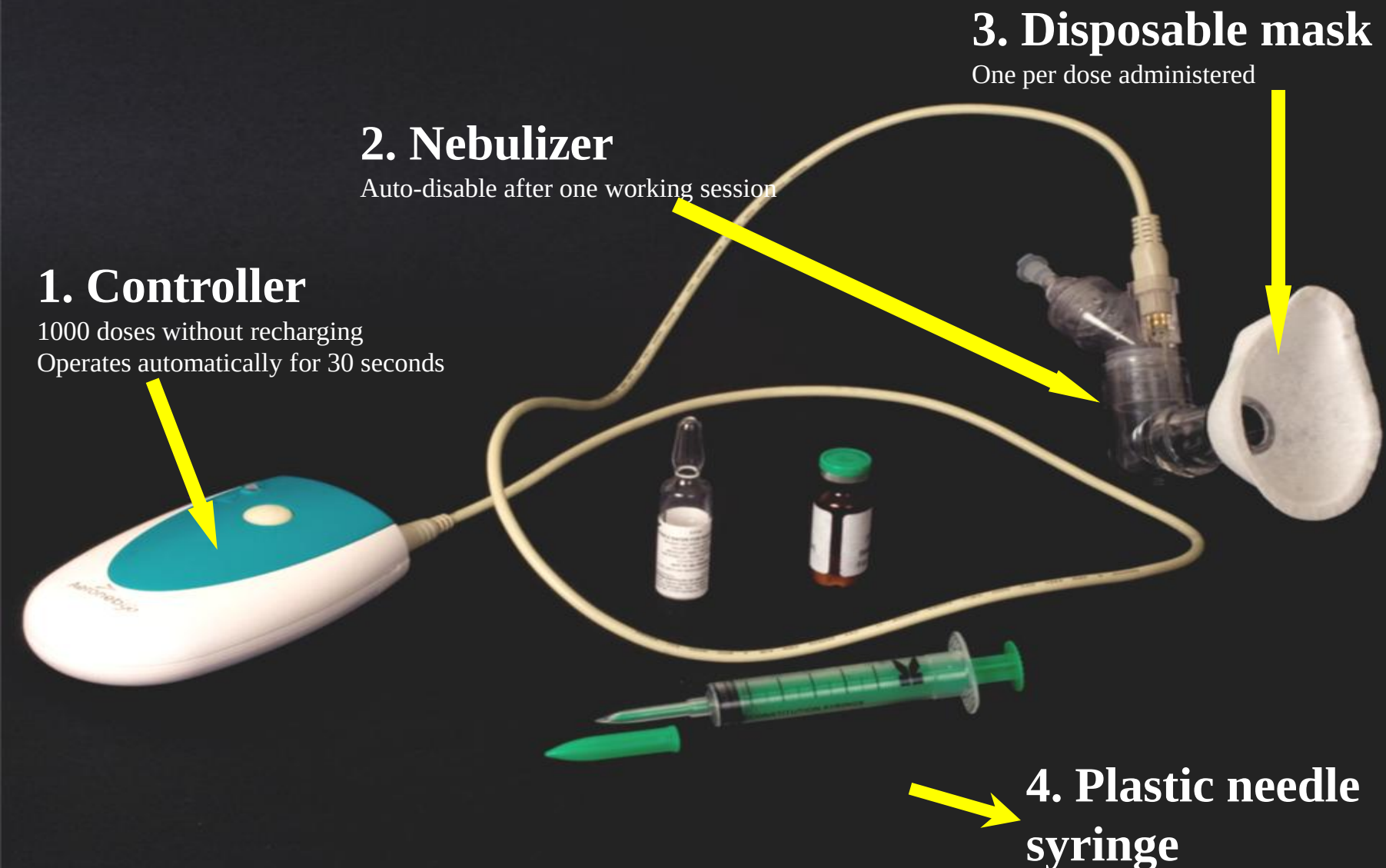
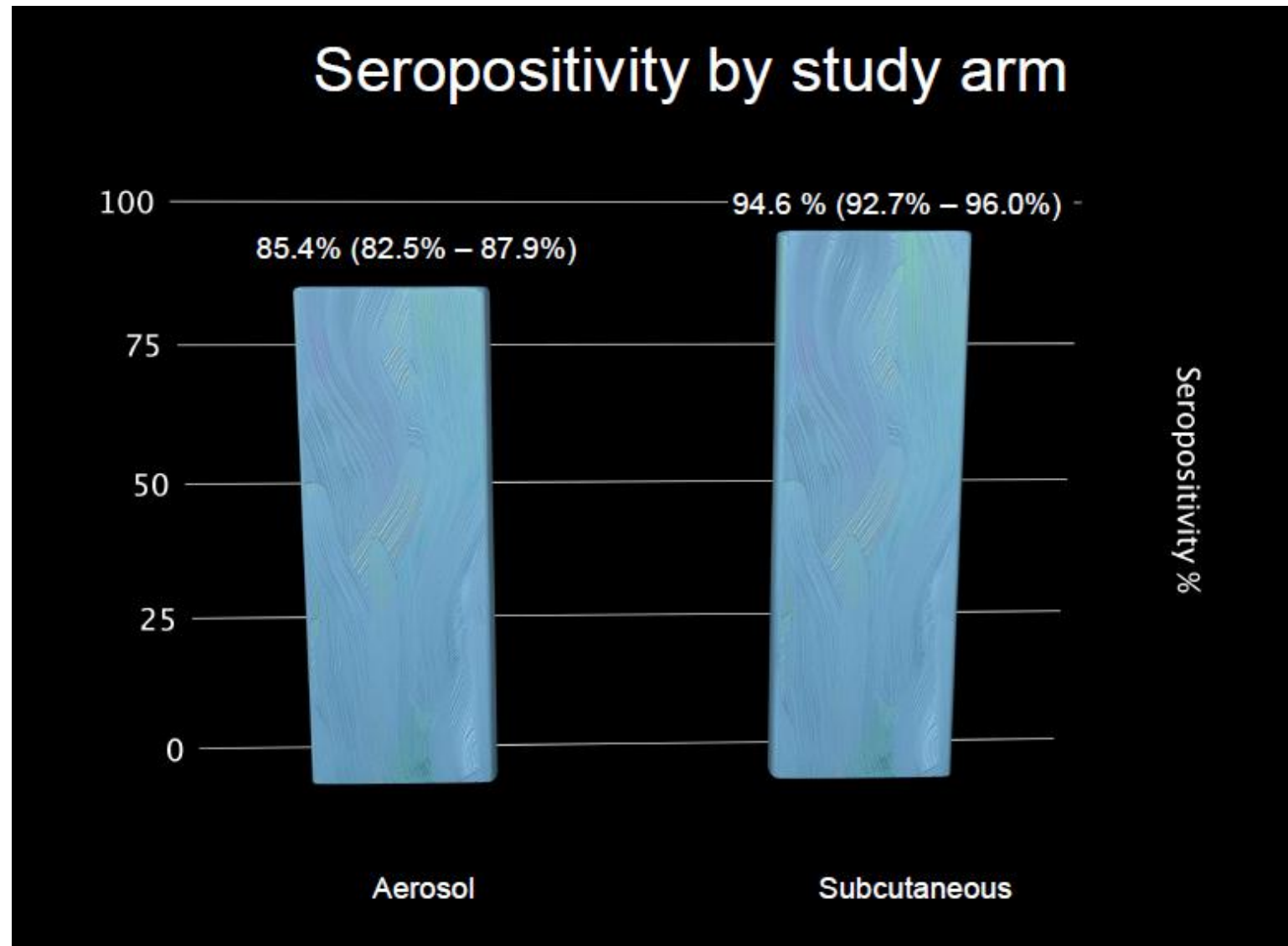


Figure 7: Components of Measles aerosol vaccine .



Measles Aerosol Vaccine :

Status:

- ✓ Bench testing
- ✓ Animal immunogenicity
- ✓ Animal Toxicity
- ✓ Phase 1 in healthy adults
- ✓ Phase II/III in adults
- ✓ Usability and acceptability
- ✓ Cost and ICEA



Benefits:

- Non injectable, easier to administer
- No waste disposal
- Similar cost per dose

Challenges:

- Need demonstration studies with MR to further document benefits
- Resources to conduct demonstration studies

Technology Availability:

- Could be available in 3-5 years time if funding for trial and demonstration studies with MR recommended by SAGE were conducted

40 children vaccinated



Injectable route



Aerosol route

3) Live Attenuated Influenza Vaccine:

History of LAIV:

- 55 years of experience in Russia
- Microgen manufactures the vaccine
- 14 years of experience in United States
- MedImmune manufactures the vaccine

Russian experience

- Proven safety and efficacy.
- No evidence of either genetic reversion or mutations
- Herd protection— particularly with children.
- Mucosal as well as systemic immunity.
- Protects (substantially) in face of antigenic drift.
- Immediate level of protection (7 days).

Live Attenuated Influenza Vaccine:

Components of LAIV:

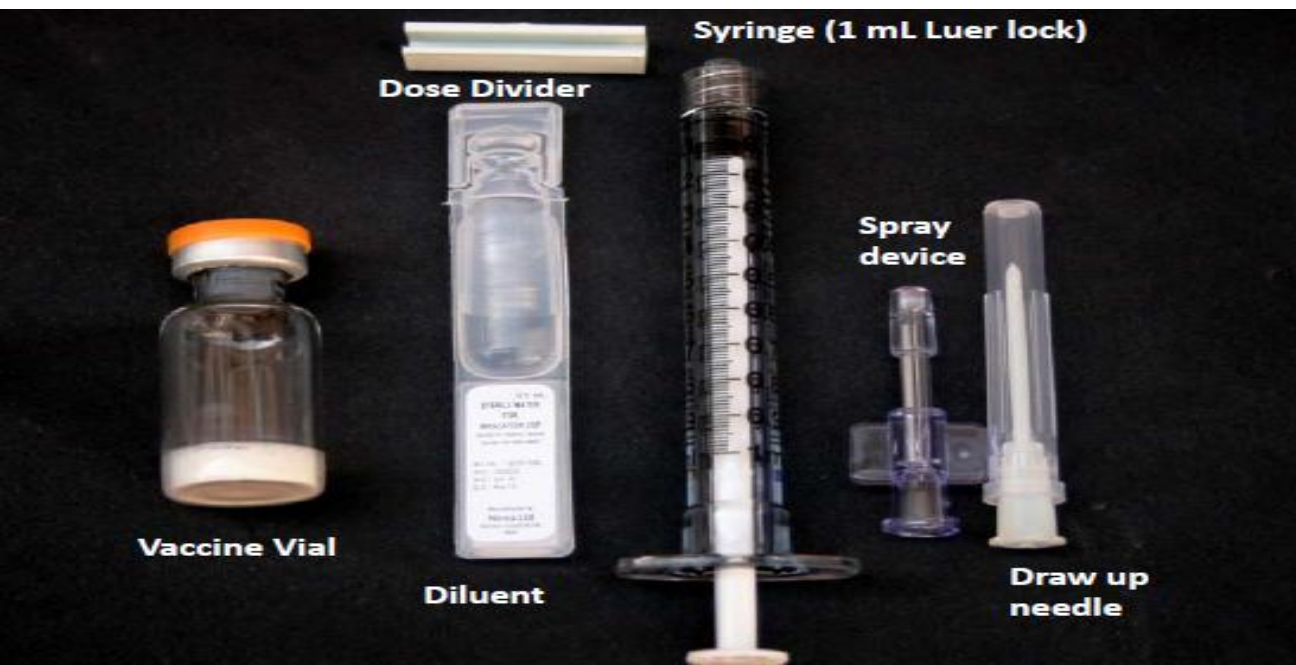
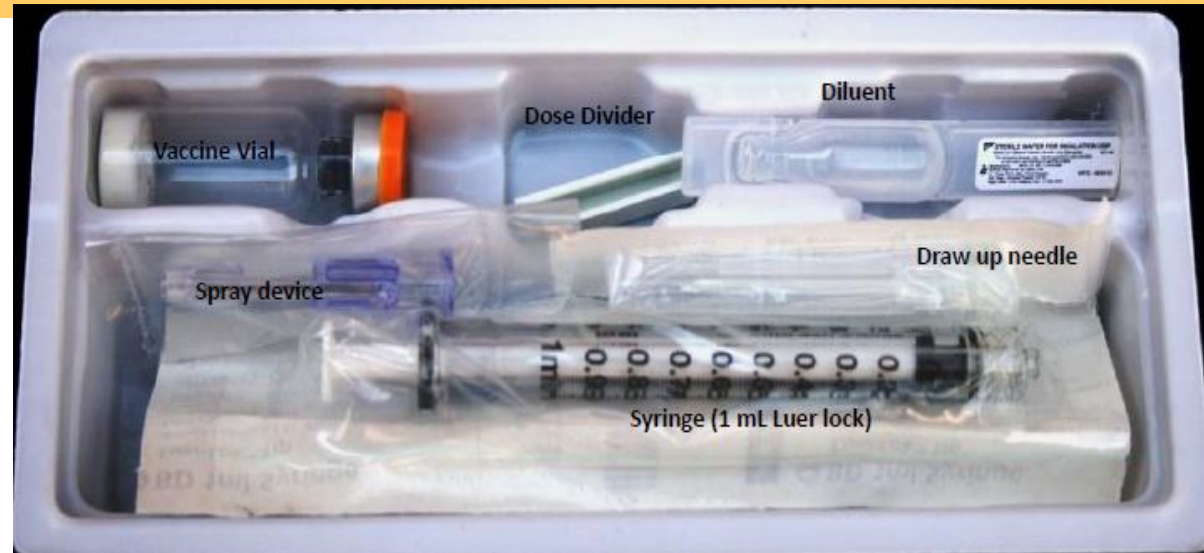


Figure 8: Components of LAIV .

Live Attenuated Influenza Vaccine:

Administration of LAIV:

- Each lyophilized vaccine vial is reconstituted using 0.5 ml of sterile water for inhalation using 1 ml syringe and plastic needle
- A dose of 0.5 ml is administered as 0.25 ml per nostril using 1.0 ml syringe and a spray device
- administered with subject in an upright position with head tilted behind
- The sprayer device creates a fine spray that primarily deposits the vaccine in the nose and nasopharynx.



Figure 9: Administration of LAIV .

Live Attenuated Influenza Vaccine (LAIV):

Potential advantages of LAIV:

- SIIL's Seasonal Live Attenuated Influenza vaccine is a single dose Lyophilized vaccine.
- The vaccine has an intranasal route of administration.
- Mimics natural route of infection
- Serum antibodies
- Cell mediated immune response
- Specific intranasal IgA
- Painless
- Herd immunity
- Protection against drifted viruses

- The flu vaccine for children is given as a single dose of nasal spray squirted up each nostril. Not only is it needle-free (a big advantage for children), the nasal spray works even better than the injected flu vaccine.
- The nasal spray is more effective than the injected flu vaccine, especially in young children, which is why children are being routinely offered the nasal spray rather than the flu jab.

Acknowledgements



Thank You