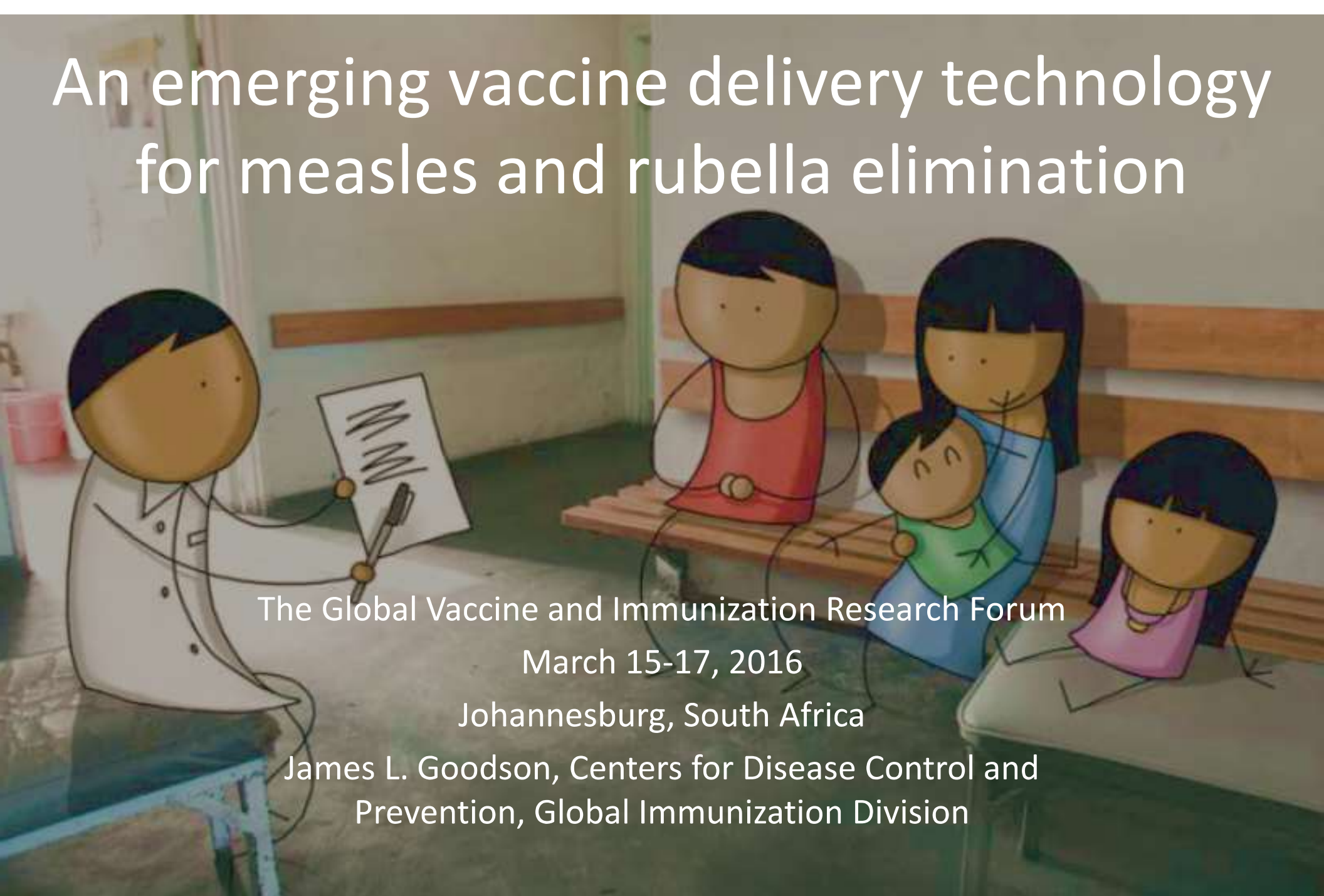


# An emerging vaccine delivery technology for measles and rubella elimination



The Global Vaccine and Immunization Research Forum

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Johannesburg, South Africa

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Prevention, Global Immunization Division

# Outline

- Challenges of currently-available measles and measles-rubella vaccines
- Emerging microneedle patch vaccination technology
- Crossing the translational gap

# Measles and Rubella Elimination Using Currently-available Vaccine

- ❑ Licensed in 1963 (M) and 1969 (R)
- ❑ Live virus - freeze dried powder
- ❑ Highly effective (2 doses=97%-99%)
- ❑ Vaccine provides long-lasting (lifelong) immunity
- ❑ However, current *product characteristics causing missed opportunities to vaccinate, and multiple barriers to high two-dose coverage*
  - *The key trade-offs of staying with current suboptimal delivery methods are coverage and equity!*



# Complicated Logistics --- Requires Trained Healthcare Workers and Cold Chain

- Trained, skilled healthcare workers and strict cold chain (4-8°C) requirements
- Use cold, original diluent only
  - Place diluent in refrigerator few hours before use
  - Diluent vials must not be frozen
- Requires additional needle and syringe for mixing
- Reconstitute **just before** use
- Always check expiration date and vaccine vial monitor (VVM)
  - Stage 1 or 2 = vaccine is ok
  - Stage 3 or 4 = discard vial



# Complicated Logistics --- poor thermostability and multi-dose vials

- After reconstitution
  - Very heat and light sensitive
  - Prepared vaccine should be placed in slit in foam cushion that fits over opening of vaccine carrier.
- **MUST Discard within 6 hours**
- This leads to hesitancy to open multi-dose vial for small numbers of children



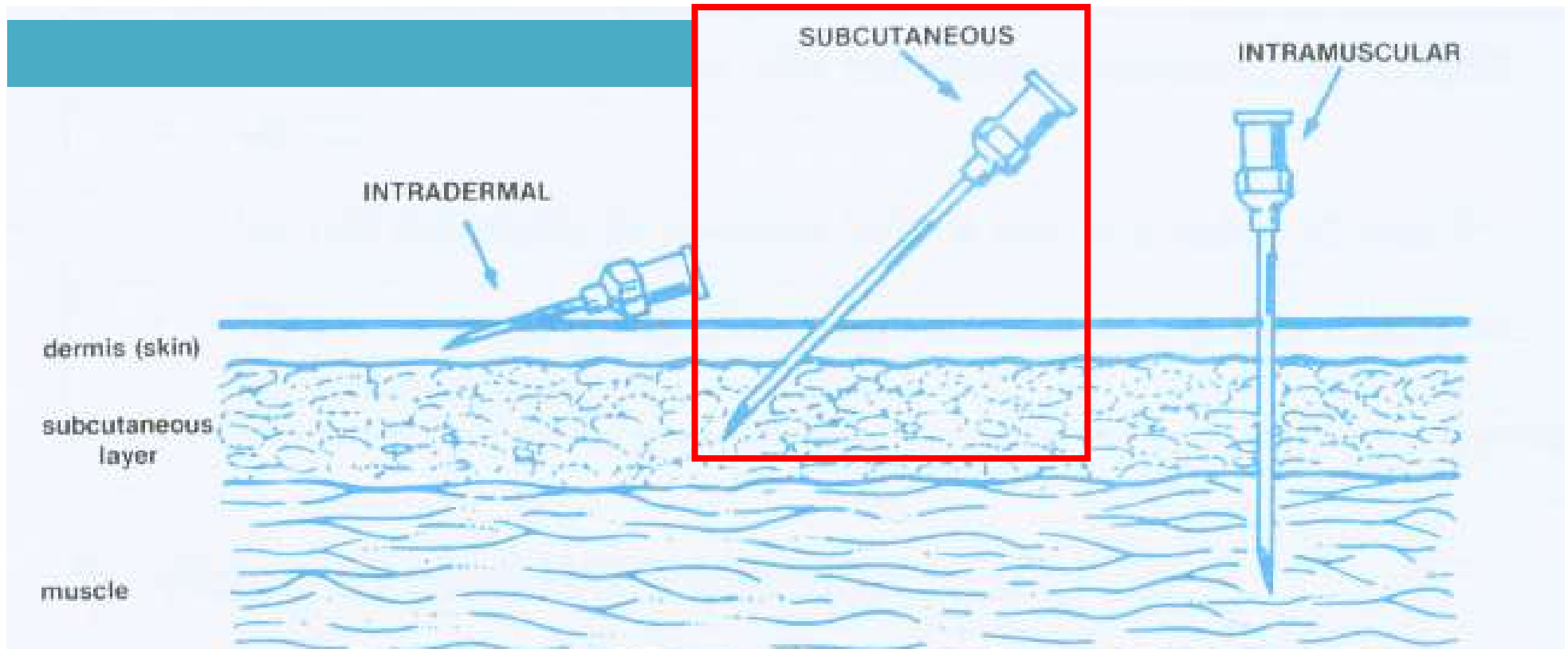
# Risk for Programmatic Errors of Currently-available MR Vaccine

- Reconstitution and handling errors lead to AEFIs, anaphylaxis and deaths
- Errors leading to AEFIs negatively impact coverage:
  - Contamination/needle sticks during procedure
  - Keeping and using reconstituted measles vaccine beyond 6 hours, sometimes kept overnight
  - Using inappropriate diluent to reconstitute the vaccine



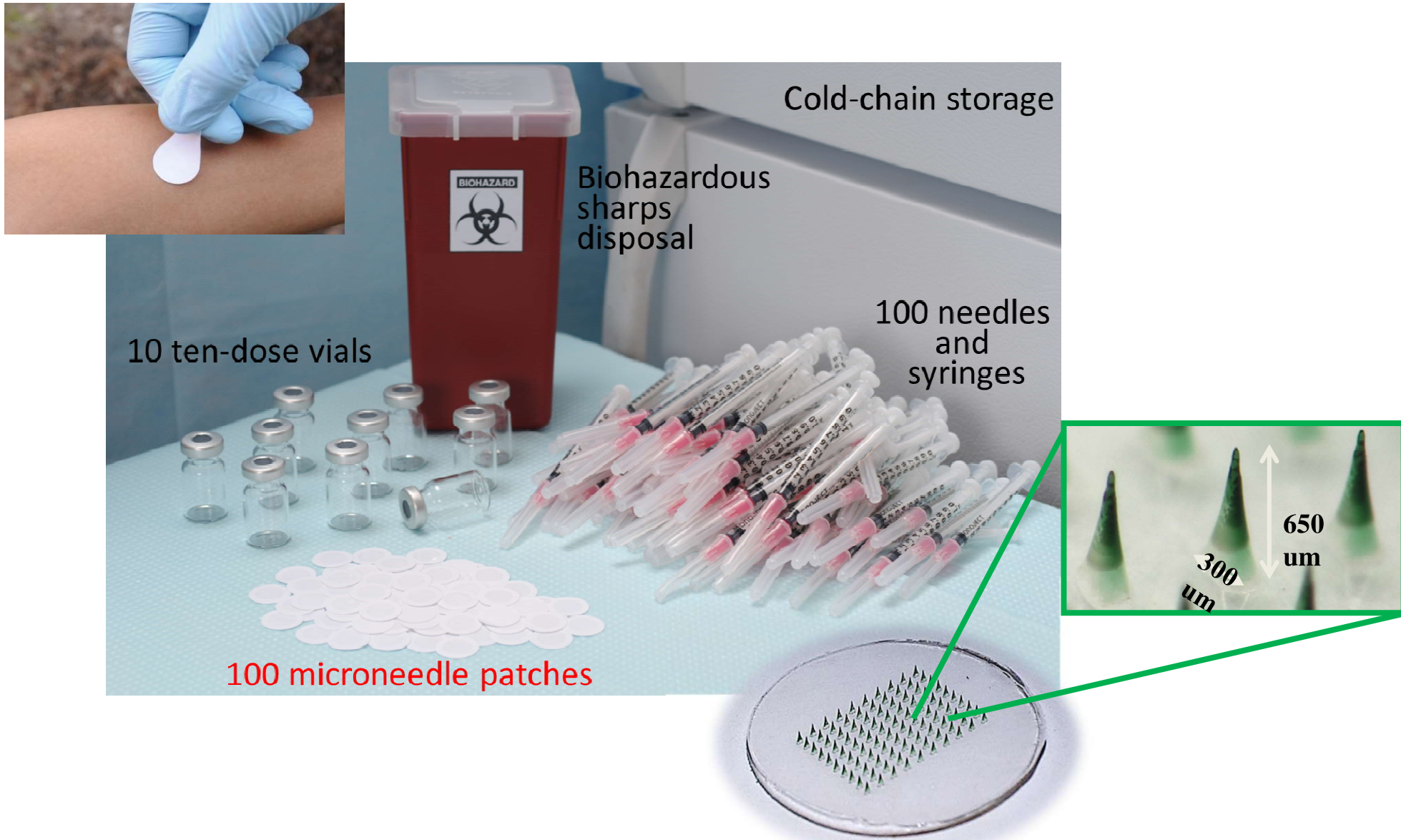
Draw 0.5 ml of reconstituted vaccine

# Subcutaneous Injection Using Hypodermic Needle Required for Currently-available MR vaccine



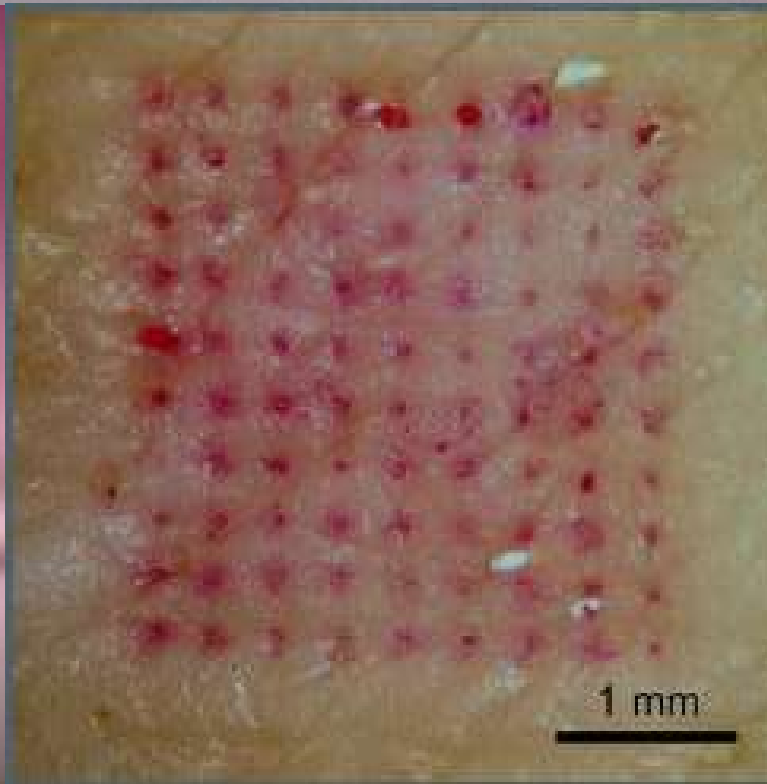
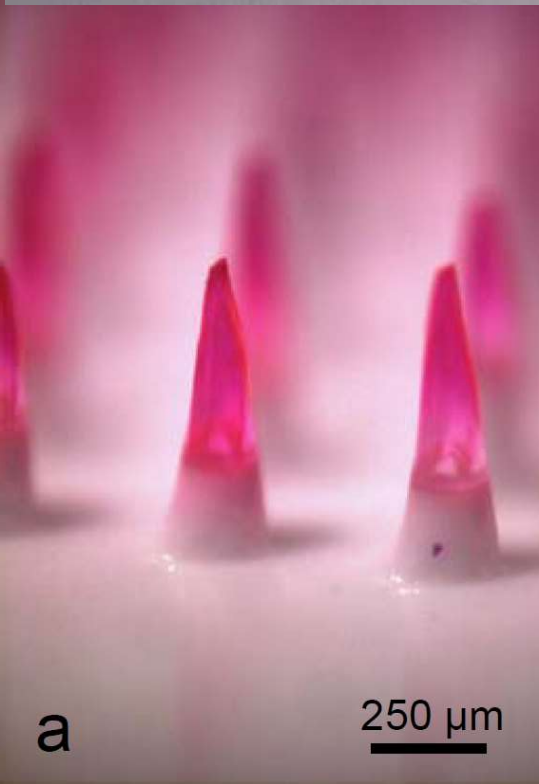
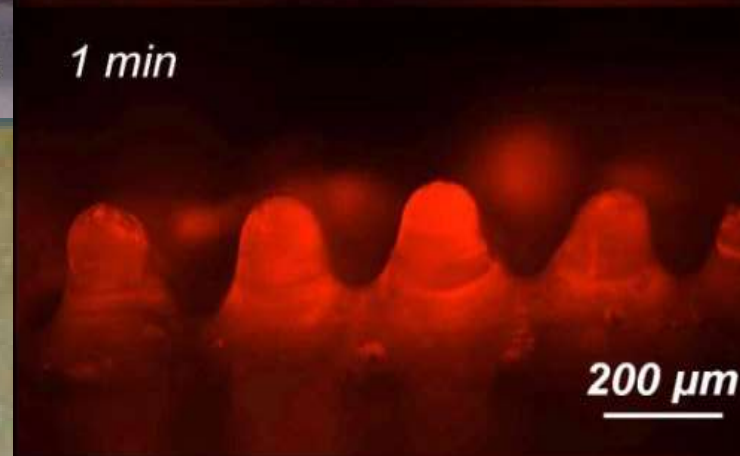
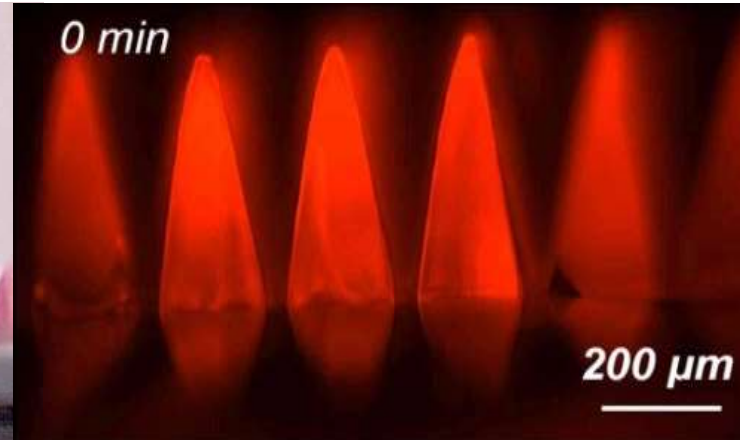
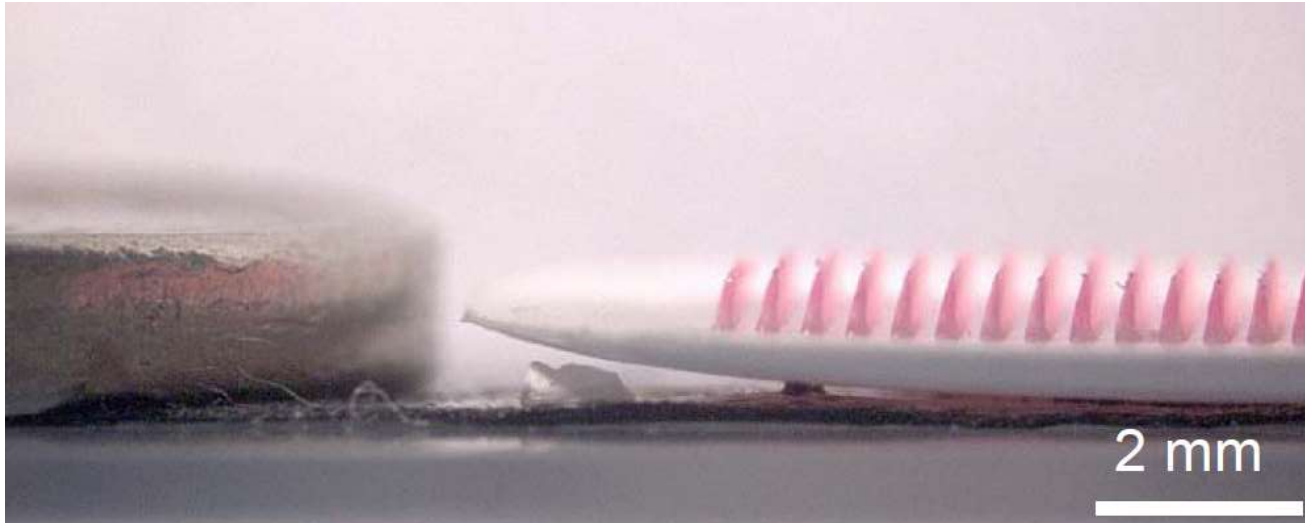
- Improper hypodermic injection technique AEFIs
- Injection pain caused by hypodermic needles can be a deterrent for vaccination acceptance

# Emerging Vaccine Delivery Technology – Vaccine Patch





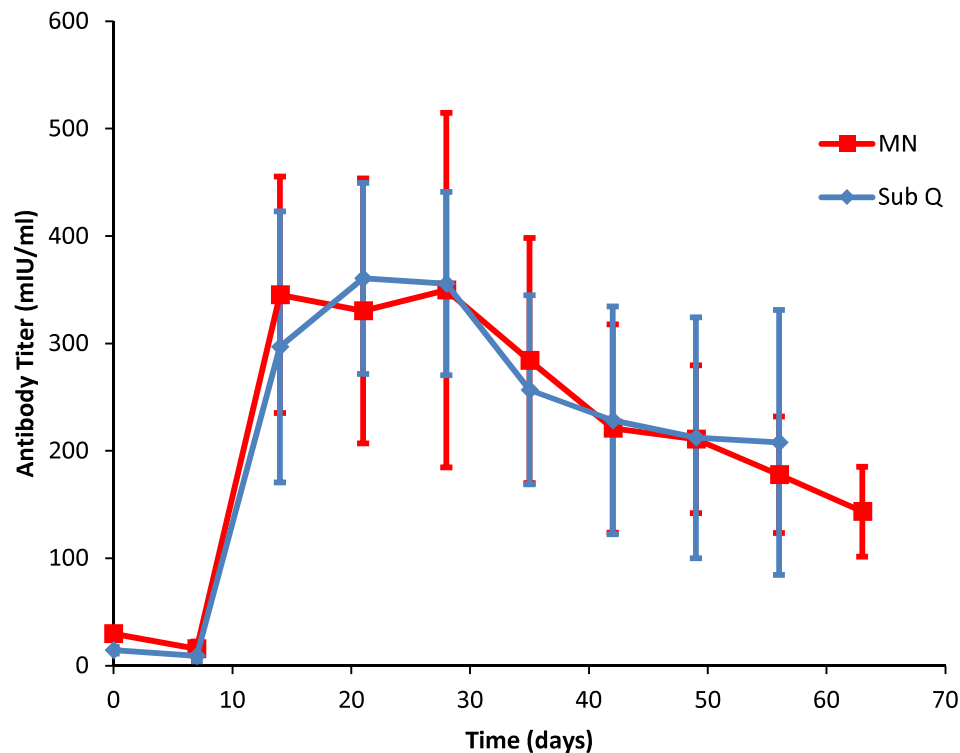
# Dissolving microneedles Deliver Vaccine to the Skin Using a Simple Patch



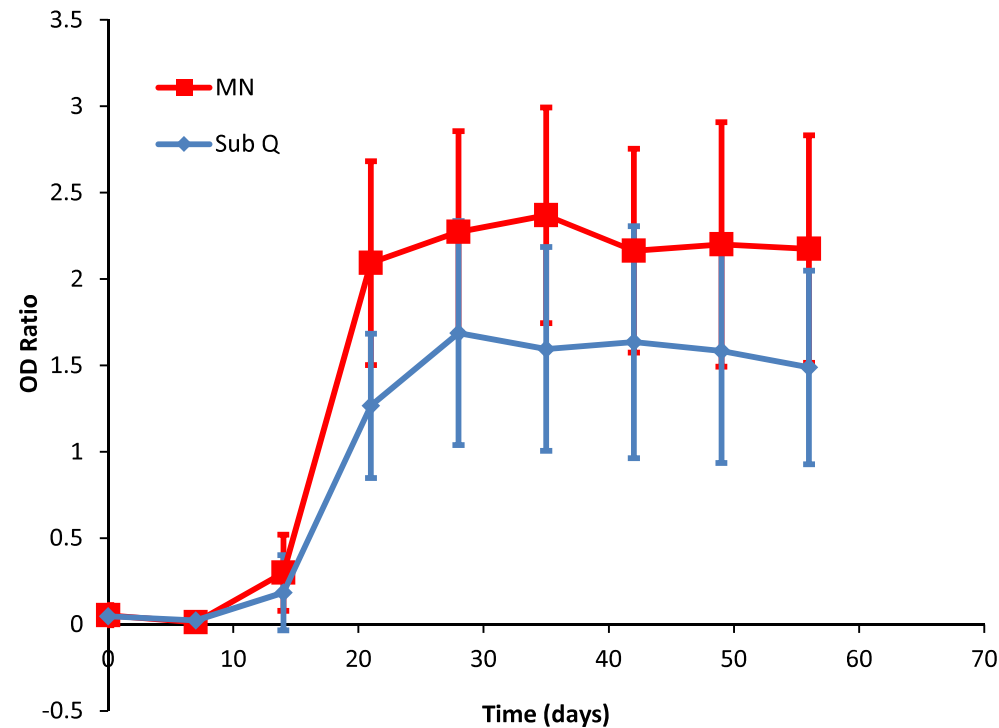
# MR Immunogenicity– We have Preclinical Proof of Concept

MR microneedle patch vaccination is thermostable and immunogenic in non-human primates

### Measles IgG Response

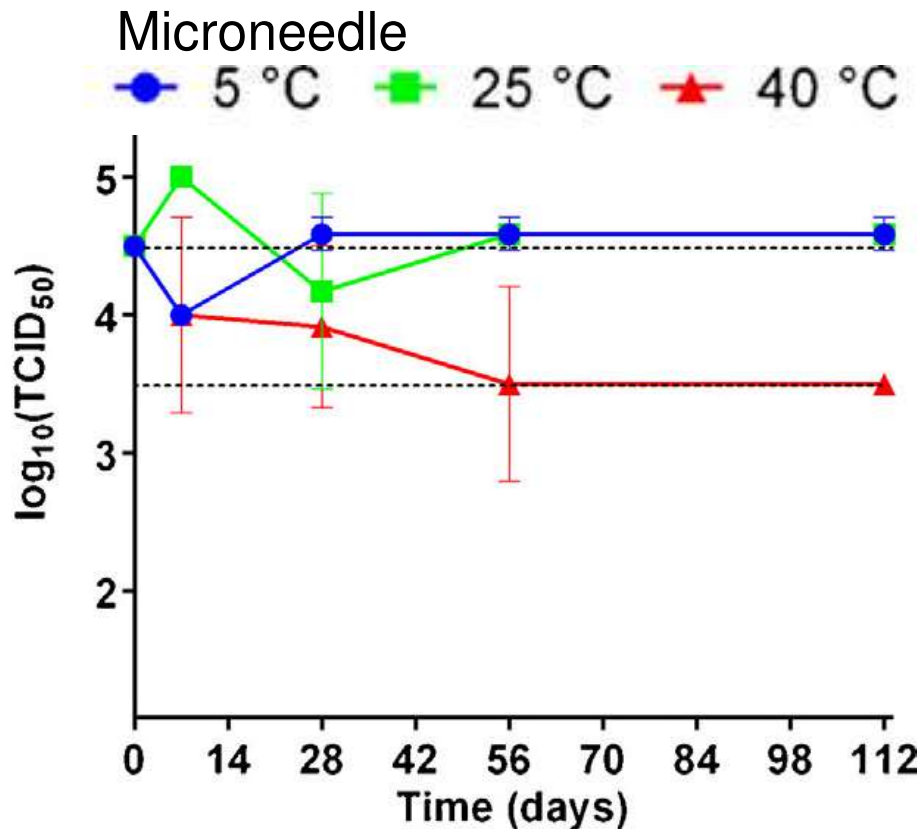


### Rubella IgG Response



Measles vaccine microneedle patch has shown full potency for almost **4 months at 5°C and at 25°C** and < 10-fold decrease in potency after almost **4 months at 40°C**

# Thermostability Results



The dashed line represents the range between 100% titer retention and a 10-fold loss of titer

- Measles vaccine microneedle patch\*
  - full potency for almost **4 months at 5 °C and at 25 °C**
  - < 10-fold decrease in potency after almost **4 months at 40 °C**
- Increased thermostability will increase coverage\*\* and population immunity (house-to-house mass campaigns, immunizations at health posts without cold chain, RI outreach to hard-to-reach populations, reduce invalid doses and loss of potency and efficacy when exposed to high ambient temperatures.

\*Reference: Chris Edens, Marcus L. Collins, James L. Goodson, Paul A. Rota, Mark R. Prausnitz. Measles vaccination of non-human primates using a microneedle patch. *Vaccine*. 2015; [doi:10.1016/j.vaccine.2015.02.074](https://doi.org/10.1016/j.vaccine.2015.02.074).

\*\*Reference: Karp C, Lans D, Esparza J, et al. Evaluating the value proposition for improving vaccine thermostability to increase vaccine impact in low and middle-income countries. *Vaccine*. 2015;33(30):3471-3479.

# Advantages of Vaccination Using an Intradermal Patch for MR Vaccination

- **Immunogenicity**
  - evidence in macaques, potential dose-sparing
- **Thermostability**
  - reduced or no cold chain requirement
- **Single-dose presentation**
  - no reconstitution, minimal wastage, reduces missed opportunities!
- **Administration by minimally-trained personnel**
  - enables house-to-house campaigns
- **No sharps waste**
  - no sharps disposal, no sharps injuries, biodegradable material
- **Small package size**
  - single-dose, simplified storage, reduced cold chain storage volume, transportation and disposal
- **Cost-effective**
  - similar to that of lyophilized vials, reduced shipping costs



# Potential Game Changer for MR Elimination and Eventual Eradication

Potential to increase population immunity and coverage through both routine and mass vaccination campaigns.



# ...However, there are challenges to be overcome

- Funding needed to start human CTs
- Significant investment in manufacturing infrastructure will be needed post CT Phase I
- Complex product development partnerships
  - Unclear product development pathway to licensure and implementation
  - Demand forecast is needed to assess potential return on investment

# Work ongoing

- WHO convened a workshop with developers, regulators, manufacturers, funders in Dec 2015 to assess MAP status and discuss product development strategies
- Target product profile for MR/MAP defined by VPPAG delivery technologies working group
- Field acceptability studies are planned

# Phase 1 clinical trial of influenza vaccination using a microneedle patch --- interim results\* show excellent safety and immunogenicity

- Currently being conducted by Georgia Tech and Emory University in 100 human subjects
- **Seroconversion** after vaccination using microneedle patch as strong or stronger than vaccination by intramuscular injection
- **Safety** profile of microneedle patch and intramuscular vaccination similar
- **Reactogenicity** to microneedle patch very mild and transient
- **Subject preference** strongly favors microneedle patch



# Achieving a World without Measles through Innovation



# Thank you!



**World Health  
Organization**

Organisation mondiale de la Santé

# Weekly epidemiological record Relevé épidémiologique hebdomadaire

12 FEBRUARY 2016, 91th YEAR / 12 FÉVRIER 2016, 91<sup>e</sup> ANNÉE

No 6, 2016, 91, 61–72

<http://www.who.int/wer>

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## Meeting of the International Task Force for Disease Eradication, November 2015

The 24th meeting of the International Task Force for Disease Eradication (ITFDE) was convened at the Carter Center, Atlanta, GA, USA, on 10 November 2015 to discuss the potential eradicability of measles and rubella.<sup>1</sup>

### Measles eradication

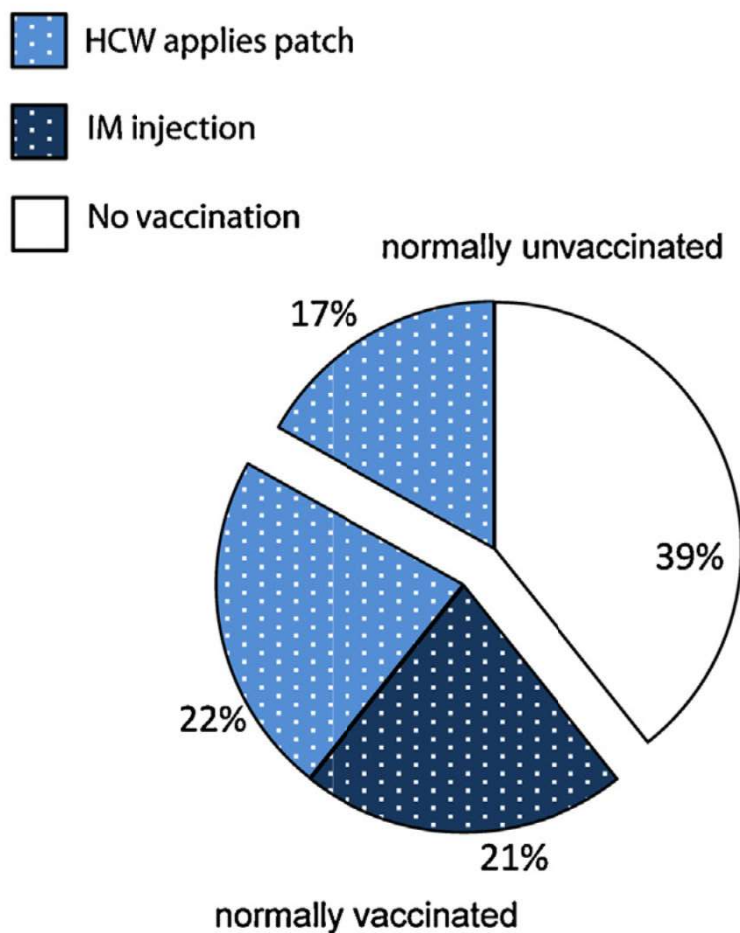
## Réunion du Groupe spécial international pour l'éradication des maladies, novembre 2015

La 24<sup>e</sup> réunion du Groupe spécial international pour l'éradication des maladies (ITFDE) a été convoquée au Centre Carter à Atlanta en Géorgie (États-Unis d'Amérique), le 10 novembre 2015, pour évoquer l'éradication possible de la rougeole et de la rubéole.<sup>1</sup>

### Éradication de la rougeole

- ITFDE reiterated measles eradication is technically feasible and should be done
- **Resources are needed for research/innovation; including for vaccine patches**
- Measles elimination efforts have been “greatly overshadowed in magnitude of resources and political commitment by GPEI”
- As polio ends, countries should adapt infrastructure and resources developed for polio eradication to measles and rubella eradication

# Acceptability of Vaccine Patches



- When participants were offered the choice of seasonal flu vaccination using a microneedle patch or conventional IM injection, intent to vaccinate increased overall from 44% (CI: 34%–54%) to 61% (CI: 50%–70%).
- This 17 percentage point increase in expected vaccination coverage overall due to offering a microneedle patch.
- Considering the normally vaccinated participants, 51% expressed a preference for the microneedle patch; the remainder preferred IM injection.
- Among the normally unvaccinated participants, 30% (CI:19%–44%) expressed willingness to get vaccinated if offered the microneedle patch, and all of these participants preferred the microneedle patch over IM injection.

# Strict Requirements for Storage of Currently-available MR Vaccine

- **Must be kept in cold chain to retain its potency**
  - Long-term storage: freeze at  $-15^{\circ}$  to  $-25^{\circ}\text{C}$  for 1-2 years
  - Health facility storage: refrigerate at  $2^{\circ}$  to  $8^{\circ}\text{C}$  up to 24-36 months (depends on manufacturer)
- **After reconstitution, becomes extremely heat- and light-sensitive**
  - Loses 50% potency in 1 hour at  $20^{\circ}$  to  $25^{\circ}\text{C}$
  - **MUST discard within 6 hours** or at the end of vaccination session, whichever comes first

# Challenges of Currently-available MR vaccine for elimination strategies (1)

- Routine Immunization:
  - An “Original EPI Vaccine”, suboptimal packaging and thermostability
  - Multi-dose vials (20-dose, 10-dose and 5-dose) identified as a major cause for *missed opportunity for timely vaccination!*\*
    - Reluctance of vaccinators to open a vial when only a few children present --- this problem is magnified when stocks are low.
    - Fear of wastage – since must discard open vial after 6 hours
    - Near the end of vaccination sessions, reluctance to open another vial for remaining few children
    - Batching of children – asking mothers to come back another time
    - MR vaccine not available every day, but only weekly or monthly
    - Leads to delayed vaccination and invalid doses
  - Multiple injection visits also can be a deterrent

# Challenges of Currently-available MR vaccine for elimination strategies (2)

- Mass vaccination:
  - House-to-house strategy was key to success of smallpox and polio eradication --- for identifying, mapping, and reaching communities in remote areas and those not accessing routine immunizations.
  - BUT, hypodermic injectable MR vaccines make house-to-house strategy for MR campaigns and outbreak response very difficult, and rarely used.
    - Requires trained health workers (a limited resource in some settings) to handle and deliver vaccination
    - Requires careful reconstitution and sharps disposal
    - Strict cold chain requirements

# Vaccine Medical Waste – not a small problem



- E.g., a measles SIA in West Africa in 2001
  - 17 million children vaccinated
  - 300 metric tons of injection waste
- Reuse of needles and/or syringes and accidental needle-sticks can cause transmission of blood-borne pathogens and disease
- Must be buried or incinerated—environmental concerns