The Promise of New Vaccine Delivery Technologies

Next-Generation Vaccine Delivery Technology Meeting
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Darin Zehrung
dzehrung@path.org
Senior Technical Officer and Portfolio Leader, Delivery Technologies
Vaccine and Pharmaceutical Technologies Group
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New and alternative delivery technologies

- Many new technologies are needlefree.
- Some are compatible with existing vaccine formats (e.g., vials or ampoules).
- Others are integrated with formulation (e.g., vaccines or adjuvants).
- There is the potential for improved thermostability out of the cold chain.
- Improved ease of vaccine delivery and safety for health care workers and the public is a key focus.
- This is through a combination of industry, academic, and nonprofit research projects.
Innovative delivery technologies of the past—smallpox

- The first half of the smallpox eradication program used high-speed jet injectors with intradermal nozzles, delivering tens of millions of doses.
- Bifurcated needles replaced jet injectors for the later half of eradication.
- Alternative delivery technologies were critical in the success of smallpox eradication.
Global Vaccine Action Plan

Strategy objective

Country, regional and global research and development innovations maximize the benefits of immunization.

- Achieve a world free of poliomyelitis
- Meet global and regional elimination targets
- Meet vaccination coverage targets in every region, country and community
- Develop and introduce new and improved vaccines and technologies
- Exceed the Millennium Development Goal 4 target for reducing child mortality

Projected benefits of vaccines worldwide: 2010 to 2020

Bill & Melinda Gates Foundation: Vaccines Work

Vaccine delivery technologies:
Potential public health benefits

• **Vaccine safety and efficacy:**
  - Improve existing vaccines.
  - Enable new vaccines to reach clinical targets.
  - Realize new routes of administration.
  - Increase efficacy in different populations.

• **Economics and vaccine availability:**
  - Drive efficiencies in immunization programs.
  - Promote schedule reduction.
  - Increase the availability of high-cost or supply-constrained vaccines.
Vaccine delivery technologies: Potential public health benefits

- **Vaccine logistics:**
  - Increase efficiency in the vaccine supply chain.
  - Eliminate the need for the cold chain.
  - Enable more rapid outbreak response.

- **Vaccine delivery:**
  - Eliminate sharps waste.
  - Reduce number of steps for vaccine preparation and delivery.
  - Increase vaccination coverage and public acceptance.
Vaccine delivery—where can innovation occur?

<table>
<thead>
<tr>
<th>Vaccine manufacturer</th>
<th>International transportation</th>
<th>Central store</th>
<th>District/regional store</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sharps disposal</td>
<td>Vaccine delivery</td>
<td>Vaccine preparation (Reconstitution/syringe filling, etc.)</td>
<td>Health center</td>
</tr>
</tbody>
</table>

 Graphics: PATH
The Complex Journey of a Vaccine

1. Raw Material Reception
   All incoming raw materials are checked for conformance with the quality specifications.

2. Bulk Antigen Manufacturing
   The active ingredient of the vaccine is manufactured. This is the most critical step in the production of high quality, safe and efficacious vaccines.

3. Formulation
   The active ingredient is mixed with other ingredients to enhance the immune response and ensure product stability.

The vaccine is filled into the final container. This could be a vial or a prefilled syringe.

The vaccine in the final container is labeled in accordance with regulatory requirements and packed, ready for shipping to the customer.

Quality assurance confirms that the product has been manufactured and tested in accordance with the correct procedures. The national regulatory authority gives the final authorization to release the product for distribution.

A vaccine undergoes up to several hundred Quality Control tests during its manufacturing journey.

### Differences of Approval Times

- **V1** = Original vaccine with no variation
- **V2** = Improved vaccine + variation(s)

- **50% of the population**
  - Up to 24 months for V2 to be approved in first group of countries
  - Up to 48 months for V2 to be approved in last group of countries

- **40% of the population**
  - Up to 6 months for V2 to be approved in middle group of countries

- **10%**
  - V2 ready to replace V1

Autodisable and reuse-prevention syringe pricing—baseline technologies

<table>
<thead>
<tr>
<th>Autodisable (AD) syringes</th>
<th>Type</th>
<th>Total awarded quantity (units)</th>
<th>Weighted average price per unit (USD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5 mL AD syringe</td>
<td>For immunization injections of all 0.5ml dose vaccines</td>
<td>1,158,000,000</td>
<td>$0.0396</td>
</tr>
<tr>
<td>0.1 mL AD syringe</td>
<td>For immunization injections of BCG vaccine</td>
<td>440,000</td>
<td>$0.0410</td>
</tr>
<tr>
<td>0.05 mL AD syringe</td>
<td>For immunization injections of BCG vaccine</td>
<td>84,000,000</td>
<td>$0.0463</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Syringe, re-use prevention (RUP), 2 mL</th>
<th>Long-term arrangement fixed-unit prices based on incoterm FCA port/airport of origin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supplier name</td>
<td>Product type</td>
</tr>
</tbody>
</table>
| Helm Medical GmbH                     | Syringe, RUP, 2 ml, with fixed needle/BOX—100                                       | $4.25
Vaccine preventable outbreaks 2008 – 2013

Measles Cases
- 134,042 DR Congo 2011
- 129,285 China 2008
- 77,000 Malawi 2010

Rubella Cases
- 39,122 Poland 2013
- 10,102 Japan 2013
- 24,272 Romania 2012

Cases of Whooping Cough by Individual outbreaks
- 13,046 Australia New South Wales 2011
- 5,923 USA Washington 2012
- 5,270 USA California 2012

Number of Cases 2008-2013 by Country
- 109,299 Nigeria
- 202,810 China
- 169,082 DR Congo
- 95,048 Malawi
- 47,454 USA
- 32,929 South Africa
- 29,902 India
- 20,715 Australia
- 18,638 France
- 14,541 UK

Vaccine-preventable disease outbreaks
2008 – 2014 (all)

http://www.cfr.org/interactives/GH_Vaccine_Map_
Temperature sensitivity of vaccines

- **Heat sensitivity**: Most sensitive
- **Freeze sensitivity**: Not sensitive, Least sensitive, Most sensitive

Vaccines to the left of the line are not damaged by freezing.

**Vaccine formulation**
- Freeze dried
- Liquid, no adjuvant
- Liquid, with alum adjuvant

*The diluent for MenA PS-PCV contains alum adjuvant and is freeze sensitive.*
Current challenges to vaccine delivery

• Training and availability for health care workers.
• Routine, supplementary immunization activity, and outbreak response.
• Appropriate vaccine management.
• Supply access (e.g., needles and syringes, safety boxes).
• Needlestick injuries to health care workers.
• Disposal of sharps waste—community needlestick injuries.
Unsafe injections in developing and transitional countries – 2010*

- Total number of injections: 16.3 billion
- Number of injections per person per year: 2.88
- Reuse rate: 5.5%
- Infections resulting from unsafe injections:
  - Hepatitis B: 1.7 million.
    - 2.6 % of all new cases.
  - Hepatitis C: 315,000
    - 6 % of all new cases.
  - Human immunodeficiency virus (HIV): 35,000.
    - 1.3 % of all new cases.

*New data from WHO on the burden of disease from unsafe injections. WHO (Selma Khamassii) personal communication February 2014
Last-mile logistics involve unreliable cold chain
Value-added product attributes

- **Enhanced thermostability** (heat and freeze protection) enables supply logistics and distribution at or beyond the cold chain.

- **Compact, low-weight packaging** minimizes product volume and reduces space requirements.

- **Increased potential for fractional dosing** reduces supply and delivery costs.

- **Ease of use** is improved within different delivery scenarios (routine immunization or mass campaign).

Value-added product attributes (continued)

- **Simplified product preparation** reduces the number of steps and requirements, helping to ensure effective delivery.

- **Autodisable features** prevent reuse and potential disease transmission.

- Innovative materials (including primary container, secondary, and tertiary packaging) **minimize environmental impact, the risk of needlestick injury, and unsafe medical waste.**

- **Improved patient/parent acceptance** increases willingness for vaccination.

Questions to consider

• What are the outstanding public health needs?
• What are the biggest challenges in the development of new vaccine technologies?
• How should product attributes be prioritized?
• What are important trends to consider?
• What are the barriers to introduction?
• How should global stakeholders prioritize potential solutions?
• How can industry- and public-sector investment be best focused?
Thank you

Darin Zehrung
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