New Vaccine Delivery Technologies

6th Annual CUGH Conference – Mobilizing Research for Global Health
Boston, USA

Darin Zehrng
dzehrng@path.org
Senior Technical Officer and Portfolio Leader, Delivery Technologies
Vaccine and Pharmaceutical Technologies Group
March 26, 2015

PATH
A catalyst for global health
New Vaccine Delivery Technologies

Delivery devices
- Disposable-syringe jet injectors*
- Intradermal delivery devices*
- Microneedles*
- Intranasal delivery
- Aerosol/dry powder inhalation
- Electroporation

Packaging
- Prefilled syringes/compact prefilled autodisable devices*
- Blow-Fill-Seal / multi-monodose*
- Integrated reconstitution*

Formulation
- Fast dissolving tablets and gels
- Solid-dose implants

* - discussed in presentation
New Vaccine Delivery Technologies

**Delivery devices**
- Disposable-syringe jet injectors*
- Intradermal delivery devices*
- Microneedles*
  - Intranasal delivery
  - Aerosol/dry powder inhalation
  - Electroporation

**Packaging**
- Prefilled syringes/compact prefilled autodisable devices*
- Blow-Fill-Seal / multi-monodose*
- Integrated reconstitution*

**Formulation**
- Fast dissolving tablets and gels
- Solid-dose implants

* - discussed in presentation

All photos: PATH
New and Alternative Delivery Technologies

• Many new technologies are needle-free.
• Some are compatible with existing vaccine formats (e.g., vials or ampoules).
• Others are integrated with formulation (e.g., combination products).
• Improved ease of vaccine delivery, efficacy, cost-effectiveness, and safety are areas of focus.
• Developers include industry, academic, and nonprofit research groups.
Potential Public Health Benefits

- Increase vaccine access and coverage—enable community health workers to deliver vaccines.
- Improve immunogenicity.
- Reduce the need for and the number of injections.
- Reduce risk of infections/cross-contamination.
- Reduce potentially dangerous sharps waste.
Potential Public Health Benefits

- Relieve tensions and fears surrounding immunization.
- Reduce drop-out by optimizing schedules.
- Reduce health worker workload—simplified administration and reconstitution (free up time for other tasks).
- Reduce cold chain dependency through improved thermostability (heat and freeze stability) – incorporation of enhanced formulation in presentation.

Photo: PATH/Ummit Kartoglu
Photo: PATH/Debra Kristensen
Current Challenges to Vaccine Delivery

- Training and availability for health care workers.
- Resource availability for routine, supplementary immunization activity, and outbreak response.
- Appropriate vaccine management and cold chain capacity.
- Supply access (e.g., needles and syringes, safety boxes).
- Needlestick injuries to health care workers.
- Disposal of sharps waste—community needlestick injuries.
Disposable Syringe Jet Injectors

Photo: ©PharmaJet.

Photo: ©PATH.

Photo: ©PATH.
Disposable Syringe Jet Injectors (DSJIs) deliver vaccines and medicines without using needles; instead, DSJIs generate a pressurized liquid stream that penetrates through the skin to deliver injections into the tissue.
DSJI WHO Prequalification

- Prequalification requirements are based upon the International Organization for Standardization standard for jet injectors (ISO+).
- Requires device clearance through globally recognized national regulatory authority.
- PharmaJet Stratis® technology was the first DSJI to complete this process (January 2013).
Intradermal Delivery Device Categories

**Needle-based devices** (standard needle and syringe, hollow microneedles, mini-needles, ID adapters)

Disposable-syringe jet injectors

Microneedle patches
• Most vaccines are delivered via intramuscular or subcutaneous routes (0.5 ml).
• Fractional dose intradermal (ID) delivery holds potential due to the presence of Dendritic Cells (DCs) in the skin.
• ID vaccine examples:
  • Rabies post exposure prophylaxis (PEP).
  • Influenza – Fluzone® ID.
  • IPV – Global Polio Eradication Initiative (GPEI) research.
## ID Delivery Devices: Needle-based

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Device</th>
<th>Development Status</th>
<th>Image</th>
</tr>
</thead>
<tbody>
<tr>
<td>West Pharmaceutical Services, Inc.</td>
<td>ID Adapter</td>
<td>Commercialized</td>
<td>A</td>
</tr>
<tr>
<td>BD</td>
<td>Soluvia™</td>
<td>Commercialized (influenza vaccine)</td>
<td>B</td>
</tr>
<tr>
<td>Star Syringe, Ltd.</td>
<td>Star ID</td>
<td>Preclinical</td>
<td>C</td>
</tr>
<tr>
<td>NanoPass</td>
<td>MicronJet 600</td>
<td>Commercialized</td>
<td>D</td>
</tr>
</tbody>
</table>

All photos except where noted: PATH
# ID Delivery Devices: Disposable Syringe Jet Injectors

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Device</th>
<th>Development Status (for ID delivery)</th>
<th>Image</th>
</tr>
</thead>
<tbody>
<tr>
<td>PharmaJet®</td>
<td>Tropis</td>
<td>Clinical</td>
<td>A</td>
</tr>
<tr>
<td>Bioject</td>
<td>ID Pen</td>
<td>Clinical</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>Zetajet®</td>
<td>Clinical</td>
<td>—</td>
</tr>
<tr>
<td>Bioject</td>
<td>Biojector® 2000</td>
<td>Device clearance</td>
<td>D</td>
</tr>
<tr>
<td>Medical International Technologies(MIT)</td>
<td>Dart</td>
<td>Preclinical</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>H4</td>
<td>Preclinical</td>
<td>—</td>
</tr>
</tbody>
</table>

---

All photos/PATH
Comparison of Microneedle Delivery Platforms

Solid, coated, dissolving, hollow, and hydrogel.

**Step one:** Microneedles are applied.

**Step two:** Pharmaceutical is released.
# ID Delivery Devices: Microneedle Patches

<table>
<thead>
<tr>
<th>Developer</th>
<th>Device</th>
<th>Development Status</th>
<th>Patch type</th>
<th>Components</th>
<th>Image</th>
</tr>
</thead>
<tbody>
<tr>
<td>Georgia Institute of Technology</td>
<td>__</td>
<td>Preclinical</td>
<td>Dissolvable</td>
<td>Patch (potentially no applicator needed)</td>
<td>A</td>
</tr>
<tr>
<td>(Georgia Tech)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Corium</td>
<td>MicroCor®</td>
<td>Preclinical</td>
<td>Dissolvable</td>
<td>Patch and integrated applicator</td>
<td>B</td>
</tr>
<tr>
<td>Vaxxas / University of Queensland</td>
<td>Nanopatch™</td>
<td>Preclinical</td>
<td>Solid coated</td>
<td>Patch and applicator</td>
<td>C</td>
</tr>
</tbody>
</table>

Photos:
- A: Georgia Tech
- B: Corium
- C: Vaxxas
## Parenteral Prefill Technologies

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Device</th>
<th>Development Status</th>
<th>Image</th>
</tr>
</thead>
<tbody>
<tr>
<td>BD®</td>
<td>Uniject</td>
<td>Market available</td>
<td>A</td>
</tr>
<tr>
<td>BD®</td>
<td>Hypak</td>
<td>Market available</td>
<td>B</td>
</tr>
<tr>
<td>Gerresheimer</td>
<td>Gx RTF®</td>
<td>Market available</td>
<td>C</td>
</tr>
<tr>
<td>Taisei Kako Co., Ltd</td>
<td>ClearJect™ (COC polymer)</td>
<td>Market available</td>
<td>D</td>
</tr>
<tr>
<td>Rommelag</td>
<td>BFS for injection</td>
<td>In development</td>
<td>E</td>
</tr>
<tr>
<td>Angela Brevetti</td>
<td>Secureject®</td>
<td>Market available</td>
<td>F</td>
</tr>
</tbody>
</table>

![Device Images](A,B,C,D,E,F)
Parenteral Prefill Technologies: Uniject

Uniject is a compact pre-filled autodisable device**

*Uniject is a trademark of BD. **PATH website. Available at: http://www.path.org/our-work/uniject.php.
Blow-fill-seal (BFS)

Technology:
- Plastic containers formed, filled, and sealed in a continuous process.
  - *Equipment manufacturers*: Rommelag, Weiler Engineering, Angela Brevetti.
- Widely used for pharmaceuticals; determined to be technically compatible with live attenuated influenza and rotavirus vaccines.
## Oral Prefill Technologies

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Device</th>
<th>Development Status</th>
<th>Image</th>
</tr>
</thead>
<tbody>
<tr>
<td>BD®</td>
<td>Uniject DP</td>
<td>Market available</td>
<td>A</td>
</tr>
<tr>
<td>Rommelag</td>
<td>BFS</td>
<td>Market available</td>
<td>B</td>
</tr>
<tr>
<td></td>
<td>BFS MMD</td>
<td>In development</td>
<td>C</td>
</tr>
<tr>
<td>Lameplast</td>
<td>Tube</td>
<td>Market available</td>
<td>D</td>
</tr>
</tbody>
</table>

Photos: PATH/Patrick McKern

PATH 3D-printed prototype.
Technology example: Multi-mono-dose

Multi-mono-dose (MMD):

- A conjoined strip of single-dose containers with a single label and Vaccine Vial Monitor (VVM).
- Separating a single container from the strip opens the container.
- Formed using BFS or other plastic container technologies.
# Reconstitution Technologies

<table>
<thead>
<tr>
<th>Manufacturer</th>
<th>Device</th>
<th>Development Status</th>
<th>Image</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vetter</td>
<td>Lyo-Ject</td>
<td>Market available</td>
<td>A</td>
</tr>
<tr>
<td>Eulysis</td>
<td>SVS</td>
<td>In development</td>
<td>B</td>
</tr>
<tr>
<td>LyoGo</td>
<td>LyoGo</td>
<td>In development</td>
<td>C</td>
</tr>
<tr>
<td>LyoTip</td>
<td>LyoTip</td>
<td>In development</td>
<td>D</td>
</tr>
</tbody>
</table>

![Image A](Photo: ©Vetter.)

![Image B](Photo: ©Eulysis.)

![Image C](Photo: Lyogo)

![Image D](Photo: ©LyoTip.)
Key Considerations – Vaccine Delivery Technologies

• Integrate new technology early in vaccine development process.

• Ensure alignment with generic Preferred Product Profile (gPPP) for vaccines – pursue consultation with WHO.

• Confirm programmatic suitability for WHO prequalification.

• Estimate device costs (cost of goods, cost per delivered dose).

• Assess potential cold chain impact.

• Confirm human factors/healthcare worker usability.
Thank you

Darin Zehring
Senior Technical Officer
Portfolio Leader, Delivery Technologies
Vaccine and Pharmaceutical Technologies Group
dzehring@path.org