Sustainable Influenza Vaccine Manufacturing Capacity Worldwide: Establishing an Adjuvant Hub

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Program Lead, BARDA International Influenza Vaccine Manufacturing Capacity Building Program

8th Meeting with International Partners on Prospects for Influenza Vaccine Technology Transfer

March 18, 2015
BARDA Multifaceted Approach to Building Sustainable Capacity

GOAL: Enhance sustainable influenza vaccine production capacity worldwide
BARDA International Program is Designed for Synergy

- **Grants to Manufacturers (WHO)**
- **CMC and Clinical Technical Support (PATH)**
- **Adjuvant Hub (IDRI)**
- **Biomanufacturing Training (BTEC, Onsite)**

Goal: increase the use of scalable mfg technology
Adjuvant Hub for Influenza Vaccines

Christopher Fox
8th WHO International Partners Meeting
Sao Paulo, Brazil, March 17-18, 2015
Infectious Disease Research Institute

• Founded in 1993
• 120 employees (93 in R&D, 37 PhDs)
• Funders include BARDA, NIH, BMGF, DARPA, PATH, WHO, M.J. Murdock Charitable Trust, Eli Lilly & Co., American Leprosy Missions, GSK, and other Public Private Partnerships
• Annual budget for 2014 ~$23 million

Headquartered in state-of-the-art research facility in Seattle’s global health hub.
IDRI’s Stable Emulsion (SE)

- Designed for 1:1 v:v mixing with vaccine
- Manufactured by microfluidization
- ~100 nm particle size, low polydispersity
- Particle size stability >5 years at 5°C
- Multiple cGMP batches produced
- Phase III clinical testing
Preclinical and Clinical Expertise

- Two IDRI employees formerly worked in Influenza Division of CDC
- Extensive adjuvanted vaccine testing in mice, ferrets, etc.
- Experienced regulatory/clinical team

### IDRI Influenza Clinical Experience

<table>
<thead>
<tr>
<th>Sponsor/Partner</th>
<th>Disease Area</th>
<th>Adjuvant Formulation</th>
<th>Status</th>
<th>Phase and (Number of Subjects)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Immune Design/IDRI</td>
<td>Seasonal influenza</td>
<td>SE, GLA-SE</td>
<td>Complete</td>
<td>Phase 1 (58)</td>
</tr>
<tr>
<td>Immune Design/Protein Sciences</td>
<td>Pandemic influenza</td>
<td>GLA-SE</td>
<td>Complete</td>
<td>Phase 1/2 (220)</td>
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<tr>
<td>Immune Design/Novavax</td>
<td>Pandemic influenza</td>
<td>GLA-SE</td>
<td>Complete</td>
<td>Phase 1 (169)</td>
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<tr>
<td>DARPA/IDRI</td>
<td>Pandemic influenza</td>
<td>GLA-AF</td>
<td>Complete</td>
<td>Phase 1 (43)</td>
</tr>
<tr>
<td>Protein Sciences</td>
<td>Pandemic influenza</td>
<td>SE</td>
<td>Complete</td>
<td>Phase 2 (240)</td>
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<tr>
<td>Protein Sciences</td>
<td>Pandemic influenza</td>
<td>SE</td>
<td>Planned</td>
<td>Phase 3</td>
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</tbody>
</table>

Ferret challenge
IDRI Adjuvant Hub Services

- Supply cGMP and/or research-grade SE adjuvant to DCVMs for preclinical and clinical development
- Provide on-site technical support for physicochemical compatibility testing (adapted to account for adjuvant effects)
  - SRID, particle size, deglycosylated SDS-PAGE, visual appearance, etc.
- Support design and implementation of preclinical and clinical studies of adjuvanted influenza vaccines
  - HI, MN assay technical support
  - Regulatory support
  - Mouse study technical support
  - Ferret challenge study technical support
  - GLP toxicology study technical support
  - Clinical trial operational and technical support
Compatibility of Cantacuzino Institute’s H5N1 Vaccine with SE

<table>
<thead>
<tr>
<th>Batch</th>
<th>Particle Size T=0 (Z-avg, nm)</th>
<th>Particle Size T=8hrs (Z-avg, nm)</th>
<th>Particle Size T=24hrs (Z-avg, nm)</th>
<th>HA content T=0 (µg/ml)</th>
<th>HA content T=8hrs (µg/ml)</th>
<th>HA content T=24hrs (µg/ml)</th>
<th>pH antigen</th>
<th>pH antigen-adjuvant mix</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antigen alone</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>36.4</td>
<td>35.5</td>
<td>37.7</td>
<td>7.2</td>
<td>-</td>
</tr>
<tr>
<td>1</td>
<td>106.2</td>
<td>105.7</td>
<td>105.9</td>
<td>37.9</td>
<td>36.4</td>
<td>40.3</td>
<td>7.2</td>
<td>7.0</td>
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<tr>
<td>2</td>
<td>109.7</td>
<td>105.7</td>
<td>105.4</td>
<td>37.5</td>
<td>34.2</td>
<td>38.5</td>
<td>7.2</td>
<td>7.1</td>
</tr>
<tr>
<td>3</td>
<td>107.2</td>
<td>107.4</td>
<td>108.4</td>
<td>33.3</td>
<td>36.6</td>
<td>35.5</td>
<td>7.2</td>
<td>7.0</td>
</tr>
</tbody>
</table>
Key Elements of IDRI Adjuvant Hub

**Vaccine Manufacturer**
- Has established split vaccine antigen (ready for Phase 1)
- Indicates interest to IDRI or BARDA
- Visits IDRI for initial training
- Acquires any needed equipment/supplies (critical equipment includes particle sizer [DLS], and standard lab supplies/reagents for SRID, HI, MN assays)

**IDRI**
- Distributes research-grade adjuvant and visits DCVM for assay training
- Provides operational/technical support for preclinical studies
- Provides cGMP adjuvant and operational/technical support for toxicology and clinical studies
- Maintains communication and provides technical guidance
Acknowledgments

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  • Sheng Li
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  • Tom Warf
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• IDRI Key Scientists
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  • Neal Van Hoeven (HI/MN/Preclinical)
  • Lakshmi Jayashankar (HI/Clinical)
  • Erik Laursen (cGMP manufacture)

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