Leveraging Innovation to Improve Patient Access & Global Health

CASSS
Well Characterized Biological Products

David Robinson
Bill & Melinda Gates Foundation
WE ENVISION A WORLD WHERE EVERY PERSON HAS THE OPPORTUNITY TO LIVE A HEALTHY, PRODUCTIVE LIFE
ALL LIVES HAVE EQUAL VALUE
OUR GLOBAL REACH AND PRESENCE

2016 active grantees: 1,500+
2016 grant payments: $4.3B
2016 employees worldwide: 1,400+

Trust endowment: $40B

Locations:
- Seattle
- Washington, D.C.
- India
- Nigeria
- Ethiopia
- South Africa
- China
- Europe and Middle East Office
OUR VACCINE & ANTIBODY PORTFOLIO

<table>
<thead>
<tr>
<th>Program Area</th>
<th>R&amp;D / Pre-clinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Licensure</th>
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<tbody>
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<td>EDD</td>
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<td>Other</td>
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Distribution of Portfolio by Program Area

Distribution of Portfolio by Vaccine Type

- Live/Inactivated Viral
- rProtein
- Antibody
- Conjugate Vaccines
- Conjugate Vaccine
- mAb
- Inactive Bacterial
- rProtein
- Viral Vector
- Other
GLOBAL NUMBER OF DEATHS OF CHILDREN UNDER AGE FIVE

Drivers of progress

Improvments in
- Maternal education
- Income growth
- New drugs, vaccines and other health innovations

Driven by
- Increases in donor spending

Numbers of deaths (millions)

https://www.globalgoals.org/goalkeepers, accessed May 1, 2018; www.healthdata.org; IHME accessed 13MAY2018
GLOBAL NUMBER OF DEATHS OF CHILDREN UNDER AGE FIVE

If we progress

If we regress

https://www.globalgoals.org/goalkeepers, accessed May 1, 2018; www.healthdata.org; IHME accessed 13MAY2018
WHAT ROLE CAN INNOVATORS IN TECHNOLOGY AND REGULATORY PLAY

• Increase coverage by making vaccination easier
  • Reduce number of injections that a child needs to receive
• Increase access by reducing the cost of vaccination
  • Lower the capital costs of new facilities
  • Improve the accuracy of potency assays to reduce the overfill
• Enable the adoption of new technologies
  • Close regulatory interactions with technical developers
  • Streamlining and harmonizing regulatory policies across the globe
REDUCING THE NUMBER OF INJECTIONS VIA PULSATILE RELEASE FOR MULTI-DOSE VACCINES

Cup-Shell Microparticles
McHugh, Janklevec, Langer
MIT

Atomic-Layer Deposition,
Garcea, Randolph
Weimer
U. C. Boulder

https://www.colorado.edu/research/report/2016-17/shot-arm
Kevin J. McHugh et al. Science 2017;357:1138-1142
MAKING VACCINE SUPPLY AND ADMINISTRATION EASIER

MAPS could enable house-to-house campaigns if:

- More thermostable
- Delivered by lower-skilled health-care worker
- Non-inferior immunogenicity
- Appropriate cost

Image and description of MAP

<table>
<thead>
<tr>
<th>Grantee</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>“Peel-and-stick”</td>
<td>Dissolving MAP with audible force-feedback indicator</td>
</tr>
<tr>
<td>Micron Biomedical</td>
<td></td>
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<tr>
<td>Nanopatch</td>
<td>Coated polymer MAP with single-use spring applicator</td>
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<tr>
<td>Vaxxas</td>
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<tr>
<td>Mimix</td>
<td>Dissolving MAP made of silk protein with audible force-feedback indicator</td>
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</tbody>
</table>

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REDUCING COSTS VIA MODULAR FACILITIES, PROCESS INTENSIFICATION AND PROCESS INTEGRATION

• **ULTRA** uses strain engineering and process intensification to reduce costs for making recombinant **protein based vaccines**
  - Targeting manufacturing costs of $0.15 per dose

• **NevoLine™** uses compact bioreactor and membranes for semi-continuous production of **viral vaccines**
  - Prototype compact enough to fit in isolator enabling production of sIPV
  - First microfacility will be built and installed in 2018

• **Just** uses design database to optimize **antibodies** for manufacturability and process intensification to reduce manufacturing costs and facility footprint & cost
  - HIV broadly neutralizing antibodies optimized for high productivity and formulation at high concentrations required for subcutaneous administration

**Viral Vaccines:**

- **NevoLine™**

**Just**

**mAbs:**

**NevoLine™** uses compact bioreactor and membranes for semi-continuous production of viral vaccines

- Prototype compact enough to fit in isolator enabling production of sIPV
- First microfacility will be built and installed in 2018
Some of the more labile, and difficult to assay, vaccines have overages of nearly ten-fold to account for the uncertainty of the potency assays and loss of potency upon storage.

Investing in technologies to increase the precision of potency assays and improve thermostability for vaccines.

Potential to reduce overage and reduce costs.

**T.L. Schofield / Biologicals 37 (2009) 387–396**
CAN TAKE A LONG TIME TO GET NEW PRODUCTS, AND NEW TECHNOLOGIES, APPROVED AROUND THE GLOBE

Data gathered in 2014

Source: BMGF Regulatory Strategy study

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Phase 1: Accelerate access to quality medicines in LICs by having optimized regulatory systems through which a quality dossier can proceed to decision at the NRA level in half the time required. In 2012, phase 2: expand impact.
The Foundation has partnered with NIIMBL to set up a collaboration for global health

Our Mission

The NIIMBL mission is to accelerate biopharmaceutical manufacturing innovation, support the development of standards that enable more efficient and rapid manufacturing capabilities, and educate and train a world-leading biopharmaceutical manufacturing workforce, fundamentally advancing U.S. competitiveness in this industry.

How we want to work together:

- Collaborate to de-risk technologies of mutual interest to global health and broader biopharmaceutical industry
- Introduce global health challenges to NIIMBL membership of academics, pharmas and biotech
- Joint funding of priority programs through RFP call
- Partner on solutions for workforce development and regulatory engagement
TECHNOLOGIES ARE ONLY ONE ELEMENT OF ACCELERATING DEVELOPMENT: HOLISTIC UNDERSTANDING IS REQUIRED

1. Materials sourcing for supply chain development (clinical trials, reg. submission)
2. Tech transfer and process validation – Bulk, formulation, and analytical manufacturer considerations
3. Talent and capability building at facility (engineering, QA/QC, line operations)
4. Vaccine-specific workforce development
5. Regulatory oversight – NRA capability building, PV and PQC oversight
6. Local infrastructure (transport, utilities)
7. Government buy-in and support (including policy)
8. Health sciences infrastructure and support (technical service providers, plant design, air and water handling)
9. Vaccine procurement systems

Central / Network level considerations

Need to ensure a well trained workforce

Need appropriately staffed and skilled National Regulatory Authorities

Ensuring continued high quality is our number one priority!