INNOVATION FOR IMMUNIZATION

PATH Center for Vaccine Innovation and Access (CVIA)

David C. Kaslow, MD
Mitundu Community Hospital
Malawi

Lusitana Taziona
5-months old
23 April 2019

1st child in the world to receive malaria vaccine through routine immunization
Phase 3 Study

Pilot Implementation

[Map of Africa with logos of organizations involved in the studies]
Phase 3 Study

Pilot Implementation

Partnership
Global team of 1,500+ working across 70+ countries

- 7+ billion vaccine vials with Vaccine Vial Monitors (VVMs) to ensuring vaccines potency when given
- 6+ billion autodisable syringes used to deliver single use (Soloshot) vaccines
- 310+ million children vaccinated in 6 countries with Japanese Encephalitis Virus Vaccine
- 300+ million people immunized with MenAfriVac® in the African meningitis belt

Pathway to Global Health

- Malaria vaccine
- Rotavirus vaccine
Global team of 1,500+ working across 70+ countries

Innovation

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Malaria vaccine

Rotavirus vaccine
Next decade of vaccine

https://stm.sciencemag.org/content/11/497/eaaw2888.full
Next decade of vaccine

Health Equity

Mind the Gap

https://stm.sciencemag.org/content/11/497/eaaw2888.full
PATH's mission is to advance health equity through innovation and partnerships.
1. Why and what is CVIA?
2. Innovations needed to overcome barriers
3. An assumption-based framework
Why a Center for Vaccine Innovation and Access (CVIA)?

To fix John Snow’s pump without the “invisible hand” of Adam Smith

Cholera outbreak
Soho, London (1854)

The Theory Of Moral Sentiments
(Part IV, Chapter I)
Product Development Partnerships: Non-profit business model bringing together public, private, academic and philanthropic sectors to develop vaccines for public markets in low resource settings

Circa 2008

- Sharing the risk
- Sharing the cost

Translation R&D gap (aka First Valley of Death)

Industry standard cross-disciplinary product teams: Project teams cluster into four Diseases Areas supported by six Functional Areas in a typical balanced matrix with ≈175 staff.
PATH’s Vaccine & Immunization scope: Vaccine innovation and partnership from development, introduction, and improvement to impact.

- **Cutting-edge research to tackle the toughest global health problems**
- **Better data to reach more kids**
- **Progression of vaccine development and introduction to impact for low- and lower middle-income countries**
  - Discovery
  - Preclinical
  - Proof-of-Concept
  - Proof-of-Efficacy
  - Registration
  - WHO policy & PreQual.
  - Proof-of-Effectiveness/Implementation
  - Financing & Procurement
  - Uptake

- **Solving with a country-centered approach**
- **Strengthening immunization in primary health care**
**PATH CVIA Portfolio:** Over two dozen vaccines in development and use across 17 disease targets

![Diagram of vaccine development stages and disease targets]

*Portfolio snapshot current as of June 2019; does not include new/ongoing proposal development work in dengue, Zika, or Ebola, nor ongoing support to the Expanded Programme on Immunization in multiple countries.*

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**Enteric and Diarrheal Diseases:** Rotavirus, ETEC/Shigellosis, Polio, Typhoid

**Malaria:** Malaria, Pertussis, Influenza, Group B Strep

**Respiratory Infections and Maternal Immunization:** Yellow Fever, Respiratory syncytial virus, Nipah

**Zoonotic, Emerging, and Sexually Transmitted Diseases:** Human papillomavirus, Japanese encephalitis, Nipah, Yellow Fever

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*Portfolio snapshot current as of June 2019; does not include new/ongoing proposal development work in dengue, Zika, or Ebola, nor ongoing support to the Expanded Programme on Immunization in multiple countries.*
1  Why and what is CVIA?
2  Innovations needed to overcome barriers
3  An assumption-based framework
Addressing three apparent gaps across the product cycle for vaccines

Progression of vaccine development and introduction to impact for low- and lower middle-income countries

<table>
<thead>
<tr>
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Translation R&D gap
(aka First Valley of Death)

[Image](http://www.nature.com/news/2008/080611/full/453840a.html)

Late Stage & Introduction gap
(aka Second Valley of Death)

[Image]

Coverage & Equity gap

[Image]


https://www.nature.com/articles/d41586-018-07758-3

https://stm.sciencemag.org/content/11/497/eaaw2888.full
**Innovation for Immunization in the late stage and introduction gap?**

Progression of vaccine development and introduction for public markets in LMICs

- **Discovery**
- **Preclinical**
- **Proof-of-Concept**
- **Proof-of-Efficacy**
- **Registration**
- **WHO policy & PreQual.**
- **Proof-of-Effectiveness/Implementation**
- **Financing & Procurement**
- **Uptake**

**Translation R&D gap** (aka First Valley of Death)

**Late Stage & Introduction gap** (aka Second Valley of Death)

**Coverage & Equity gap**


Path


https://www.nature.com/articles/d41586-018-07758-3
https://stm.sciencemag.org/content/11/497/eaaw2888.full
Late stage development is the most labor- and cost-intensive phase of vaccine development

70% of the total R&D budget

https://stm.sciencemag.org/content/11/497/eaaw2888.full
Late stage development and introduction is also CAPEX-intensive

Ave. cost of Phase 1 for CMC **USD12M** Total costs can range from **USD200M - 500M**

- **Translation R&D gap**
- **Late Stage & Introduction gap**
- **Coverage & Equity gap**

**Discovery** | **Preclinical** | **Proof-of-Concept** | **Proof-of-Efficacy** | **Registration** | **WHO policy & PreQual.** | **Financing & Procurement** | **Uptake**
---|---|---|---|---|---|---|---

**Review**

The complexity and cost of vaccine manufacturing – An overview

Stanley Plotkin\(^a\), James M. Robinson\(^b,c\), Gerard Cunningham\(^a\), Robyn Iqbal\(^d\), Shannon Larsen\(^a\)

doi:10.1016/j.vaccine.2017.06.003

**Major cost drivers that impact on COGS***

- Development
- **Facilities & Equipment CAPEX**
- Consumables/raw materials
- Direct Labor
- Overhead
- Licensing/Regulatory and commercialization

See also: [https://docs.gatesfoundation.org/Documents/Production_Economics_Vaccines_2016.pdf](https://docs.gatesfoundation.org/Documents/Production_Economics_Vaccines_2016.pdf)

*Cost of Goods Sold
Innovation in the **Late Stage & Introduction Gap** to address three **barriers**:

- **Biological**
  - Many *but certainly not all* of the biological and technical gaps and uncertainties should have been addressed before entering into late stage development

- **Technical**
  - Current exception are **implementation evidence** gaps

- **Human-controlled**
  - Funding
  - Political Will
  - Stakeholder Alignment
  - Regulatory-Policy-Financing Pathway
1. Why and what is CVIA?
2. Innovations needed to overcome barriers
3. An assumption-based framework
Key assumption:

*It's not just about the money*
“Innovations” to overcome human-controlled barriers beyond just funding: ABCs

• **Acceptable** innovative approaches and tools to reduce late stage development costs and accelerate the pathway to licensure, (i.e. CHIMs, adaptive trial designs, regulatory acceptable biomarkers, including those that bridge from first-in-class to next generation candidates)

• **Binding alignment** across the regulatory-policy-financing pathway continuum—what evidence is needed when to make seamless transitions and accelerate the process?
  - Aligning profiles:
    - Target Product (licensure) Profiles
    - Target Policy Profiles (?)
    - Target Financing Profiles (?)

• **Country-based** activities including understanding demand, creating the required infrastructure and workforce capacity, and building community acceptance
Key assumption: “One size” won’t fix all cases
Four Vaccine Business Cases

**Compelling—Uncertain—Assistance—No**

- **Compelling business case (HIC → LMIC)**
  (e.g., HBV, HiB, HPV, PCV, RSV, Rota)
  Solutions:
  - Tiered pricing
  - Push & Pull mechanisms

- **Uncertain business case (LMIC ↔ HIC)**
  (e.g., Grp A Strep, Grp B Strep, TB)
  Solutions:
  - Reverse tiered pricing
  - Push & Pull mechanisms

- **Assistance-dependent business case (LMIC only; Outbreak)**
  (e.g., LMIC: Cholera, Malaria, Men A, Shigella; Outbreak: Ebola, MERS, Nipah, Lassa Fever)
  Solutions:
  - Public funding
  - Priority Review Vouchers
  - LMIC Manufacturers
  - Push & Pull mechanisms

- **No Assistance-dependent**

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The Theory Of Moral Sentiments

* (Part IV, Chapter I)
When no one owns it, everyone pays—who owns it?
Single v multiple entities?

Translation R&D gap


Late Stage & Introduction gap

Coverage & Equity gap

Pathogen-specific?
(Pneumo ADIP, Rota ADIP, Hib Initiative)

A single entity?
Key assumption:

A favorable and sustainable value proposition for all key stakeholders
**Value** as a critical vaccine attribute to optimally achieve strategic goal

<table>
<thead>
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<th>Goal</th>
<th>Sustainable, sufficient supply of safe, effective, affordable essential vaccines of international quality to meet global public health needs</th>
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<td>Critical Attributes</td>
<td>Quality</td>
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### Regulatory

### Policy and Implementation

**Value as Driver of Vaccine Product Development**

**Typical stakeholders include:**
- Public and private funders and donors;
- Developers (large pharma, biotech and academic) and manufacturers;
- Global and national policymakers including WHO;
- National/global advocacy groups including in countries with high disease burden.

**Other stakeholders:**
- Households;
- Third-party payers;
- Government (e.g. MoH, MoF, MoD);
- Donors;
- Innovators;
- Society as a whole.

From: WHO Public Health Value Proposition: DRAFT Template
Finding the optimal balance of value for all key stakeholders

Global Access Principles

- Accessibility
- Availability
- Affordability
- Acceptability

Sustainability

Favorable and sustainable value proposition
Traditional Direct Risk/Benefit v Full Public Value

- **Health**
  - Direct
  - Indirect

- **Non-health** (Societal/Economic)
  - Direct
  - Indirect

| Individual | Traditional Direct Risk/Benefit |
| Population |                                      |
Key assumption:

Public sector championship required (political will)
Creates alignment across a range of stakeholders, with respect to global health priorities

Provides a resource to effectively advocate for development and introduction of vaccines

Informs rapid, disciplined investment decisions at all stages of development and implementation

Increases the likelihood of suitability for and access and sustainability of vaccines to LLMICs

Full Public Value of Vaccines as driver of sustainable vaccine development and access