Industry Perspective on Vaccine Innovation Environment

National Vaccine Advisory Committee meeting
September 12, 2018

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Over the next decade, we may see:

**Innovative Technologies**
- New cell lines
- Platform technologies
- Skin patches
- Heat-stability tech
- Reverse genetics
- More complex regimens for difficult targets

**New Adult or Pediatric Vaccines**
- Universal influenza
- Zoster
- Norovirus
- CMV
- RSV
- Streptococcus vaccines
- Norovirus
- HIV
- New combinations of existing pediatric vaccines

**New Healthcare-acquired Infection Vaccines**
- *Clostridium difficile*
- *Staphylococcus aureus*
- Tuberculosis
- *Pseudomonas aeruginosa*
- Candida
- *Escherichia coli*
Innovative Vaccine Technologies
Cell-based vaccine
Micro-dermal delivery system
Bacteria proteins combined with influenza virus for greater efficacy
Insect cells
Reverse genetics
Skin patch
Needle-less shot
The Environment For Vaccine Development Is Broader And More Complex And Thus The Vaccine Business Has Unique Risks

**Development Risk**
- No correlates of protection for new targets
- Complexity of immune system, especially in certain populations
- Lack of burden of disease data or uncertain epidemiology leads to complicated clinical trial designs

**High Capital Needs**
- High safety bar requires large, sometimes global, clinical studies
- Finalization of manufacturing processes is complex and lengthy

**“Exit” Risk**
- Limited number of potential acquirers
- Difficult to fund “go it alone” strategy if not acquired
- Investor returns on previous vaccine investments are not always stellar

**Commercial Risk**
- Strong bargaining power of vaccine purchasers
- Uncertainty of ACIP recommendations
- Increasing vaccine hesitancy
- Key populations have insurance coverage or access issues (Medicare, Medicaid)

All of the above can make other investments more attractive
The Issue Of Opportunity Cost When Considering Preventive Vaccines Has Affected The Portfolio Decision-Making Process

- Research in HIV revolutionized R&D related to immunology
- The role of the immune system in many non-infectious diseases increased research in immune therapies for:
  - Cancer
  - Auto-immune disorders
  - ID therapies
- The technologies that stemmed from immune therapy research could be applied to both infectious disease vaccines and therapeutics, changing the way companies assessed vaccine R&D
- Investors and shareholders weigh the potential return on investment (ROI) and compare projects for investment which disadvantages preventive vaccines, especially if the market has uncertainty.
The Ecosystem for Therapeutics

- **Pre-clinical**
- **Phase I**
- **Phase II**
- **Phase III**
- **Licensure**

**Oncology**

- **High level of partnerships with Pharma through deals and acquisitions with many potential partners N= many**

Blotech R&D
Pre-clinical Phase I Phase II Phase III Licensure

Preventive Vaccines

The Ecosystem for Infectious Disease Vaccines

For small companies, partnerships with Pharma often occur much later (Phase III ready) with fewer potential partners N=6-10 companies

Biotech R&D

Valley of Death #1

Strong internal competition within the company for R&D and capital resources make for a high bar for ROI for vaccines

Large Pharma R&D

Valley of Death #2

For small companies, partnerships with Pharma often occur much later (Phase III ready) with fewer potential partners N=6-10 companies
<table>
<thead>
<tr>
<th>Trial</th>
<th>Number subjects enrolled</th>
<th>Year trial completed</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCV7</td>
<td>~38,000</td>
<td>1998</td>
</tr>
<tr>
<td>HPV4</td>
<td>~18,000</td>
<td>2004</td>
</tr>
<tr>
<td>HPV4</td>
<td>~19,000</td>
<td>2005</td>
</tr>
<tr>
<td>Rotavirus (pentavalent)</td>
<td>~70,000</td>
<td>2006</td>
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<td>Influenza high dose</td>
<td>~32,000</td>
<td>2013</td>
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<tr>
<td>PCV13 (CAPiTA) **</td>
<td>~85,000</td>
<td>2014</td>
</tr>
<tr>
<td>Dengue</td>
<td>~40,000</td>
<td>2014</td>
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</tbody>
</table>
Vaccines Present a Unique Need for High Initial Capital Plus Continuous Investment

Product Life Cycle Timeline

- Need to build for regional or global capacity
- Can be upwards of $700M to over $1B
- Can take up to 5 years for regulatory approval so need to invest during high risk R&D phase
- Biologics manufacturing often requires updates to complex processes

Increasing Costs

R&D and manufacturing costs

Introduction
For Vaccines, the U.S. Market Size is Defined by CDC Recommendations

- Uncertainty over a vaccine recommendation, combined with increasing resource intensity of development, has increased the risks associated with vaccine R&D
- ACIP deliberations take into account a host of factors:
  - What populations and indications will be recommended?
  - Is the epidemiology / burden well understood?
  - Will there be public funding for the vaccine?
  - Is the intervention cost-effective? Are there pricing pressures?
  - What else is already in the market? How important is competition?
- In recent years companies have had increasing concerns regarding the consistency and predictability of the ACIP process, which raises new questions:
  - Remaining pathogens likely to need new approaches – adjuvants, novel delivery vehicles. Is there a willingness to "pay" for translation and use of new technologies?
  - What will recommendations look like for niche vaccines or those with limited use?
  - How early can companies get an indication of the potential for positive (or less positive) recommendations as part of the development process?
Global Health and Tropical Diseases Partners

TARGETS

R&D FUNDING

ACCESS

INFRASTRUCTURE

World Health Organization

unicef

Gavi

Pan American Health Organization

ClinicalTrials.gov

A service of the U.S. National Institutes of Health

The Global Fund

To Fight AIDS, Tuberculosis and Malaria

PATH
• Vaccines targeted to global diseases affecting many countries, primarily developing ones, although many of these vaccines can serve as travel vaccines in developed countries.
• R&D for these vaccines is generally funded through global public-private partnerships with the Bill & Melinda Gates Foundation, PATH, Wellcome Trust, the Global Fund and other global funding partners.
• These vaccines are vital for global public health and would normally be made available through programs like UNICEF, PAHO and Gavi or US government programs.
• Investment is required in large scale global clinical trials and manufacturing facilities in preparation for global demand.
Emerging Infectious Diseases (EID) Partners

TARGETS

R&D FUNDING

MARKET

TECHNOLOGY

Vaccine A

Vaccine B

Vaccine C

Vaccine D

Platform

New vaccines for a safer world

CEPI

World Health Organization

UNICEF

Pan American Health Organization

Gavi

BARD

Biotech
• Vaccines targeted to global diseases with pandemic or outbreak potential in multiple countries or globally.
• R&D for these vaccines is generally funded through public-private partnerships with government agencies such as the Department of Defense, NIH or BARDA or with international groups such as the Bill & Melinda Gates Foundation or Wellcome Trust.
• This is an area where new platform technologies are expected to play a key role. Platforms, such as unique cell lines, may help speed development and manufacturing; allow for fast transitions from one pathogen to another; build cross-pathogen safety profiles.
• These vaccines have a more uncertain market than other vaccines. They could be purchased by governments for stockpiles or held in late Phase 2 in the event of an outbreak.
Partnerships for New Vaccines with Commercial Markets

- Targets: CMV
- Populations: RSV, Norovirus
- New Technology: Academia to Industry, Biotech to Large Pharma
• Some of these vaccines will be targeted to specific populations or sub-sets of existing recommended populations or cover additional strains.

• Many vaccines in this category use novel technologies, such as novel adjuvants, in their development or production.

• Novel adjuvants will be used to help boost immune responses in special populations (elderly), extend the duration of immunity or reduce the number of doses needed.

• This category could include clinical activities undertaken by vaccine companies in support of maternal immunization recommendations.

• In addition, this could include new ways to improve the way vaccines are stored or delivered, for example, improved heat stability, patches, use in multiple injection technologies, nasal spray delivery, etc.
Vaccines For Combating Antimicrobial Resistance (AMR)
79% of deaths reported in 2013 CDC AMR Report are due to HAIs

These vaccines may help with prevention of infections in humans and animals
  Reduce downstream antibiotic use and further resistance
  Includes viral vaccines that could prevent antibiotic use (flu, RSV)

There is a low risk of resistance to AMR vaccines
  Prophylaxis can be widely used without generating resistance

These vaccines may demonstrate a longer duration of protection when compared to antibiotics
  Reduce recurrent infections and hospital readmissions

Vaccines are effective against susceptible & AMR strains
  Demonstrated with Hib and pneumococcal vaccines
Potential Ways to Reduce Barriers

- Continue to strengthen the consistency and clarity of the ACIP process
- Share epidemiology and burden of disease data more readily with industry to encourage prioritization and development
- Increase vaccine confidence in the U.S. and globally
- Continue to build the adolescent, maternal, adult and elderly immunization platforms, especially with regard to accessing vaccines
- Encourage the use of push and pull incentives for emerging infectious disease vaccines and vaccines targeted to antimicrobial resistant pathogens
- Continue to work with providers to encourage strong recommendations and also to alleviate business pressures

*In the end, the value of working on the development of preventive vaccines needs to be somewhat comparable to other therapeutic areas to encourage continued and increased participation by industry*
Vaccine Research & Development: The Role of Public Private Partnerships in Enabling Innovation

Annie Mo, Ph.D.
Program Officer
Parasitology & International Programs Branch
Division of Microbiology & Infectious Diseases
NIAID, NIH, DHHS

Sept. 12, 2018
NVAC Presentation
Note: These are select examples. The list of pathogens is not comprehensive.
Overcoming Vaccine R&D Huddles

- Basic Research
- Preclinical Development
- Clinical Evaluation

Limited understanding of the science to develop optimal vaccines

Challenging clinical trial design for specific populations

Converging regulatory requirements across countries

Uncertain ROI for new and improved vaccines

Information from: Encouraging vaccine innovation: promoting the development of vaccines that minimize the burden of infectious diseases in the 21st century. Report to Congress, 2017
Innovations for Vaccine R&D

Improving Existing Vaccines
(storage, coverage, effectiveness, etc.)

Developing New Vaccines
(against difficult pathogens/diseases)
Advancing Vaccine Development

Vital Research and Development Partnerships

NIH

Academia

Biotech and Pharmaceutical Companies

FDA or Other Federal Agencies

Non-profit Organizations

Other Governments or Non-Governmental Organizations

Modified from A. S. Fauci's slide
Supporting Vaccine R&D: Enabling Public Private Partnerships

- **Grants** (Solicited & Unsolicited)
- **Contracts** (Solicited)
- **Cooperative Agreements** (Solicited & Unsolicited)
Other Mechanisms for Engaging in Public Private Partnership

- Material Transfer Agreement (MTA)
- Licensing Agreement
  - Collaboration Agreement
  - Cooperative Research and Development Agreement (CRADA)
    - Non-clinical Evaluation Agreement
    - Clinical Trial Agreement
Partnerships with Private Sector to Develop Universal Influenza Vaccines

- **MSSM/GSK/NIAID VRC Chimeric HA**
  - Phase 1 DNA prime (chimeric H8/1, N1 NA) & IIV boost (chimeric H5/1, N1 NA) in healthy adults
  - Analysis of humoral NA and HA stalk-specific responses

- **RedeeFlu (M2SR LAIV)**
  - Phase 1 H3N2 M2SR prime & IIV4 boost in pediatric subjects
  - Analysis of humoral & CMI responses including NA immune responses & HA stalk-specific responses

- **M-001 Peptide Vaccine**
  - Phase II M-001 prime & seasonal IIIV3/IIV4 boost in healthy adults
  - Analysis of CMI responses

- **Imiquimod (Aldara) Topical Adjuvant**
  - Phase II: Imiquimod with H5N1 vaccine in healthy adults
  - Analysis of humoral & CMI responses
**MS/GSK/NIAID** - vaccine strategy that stimulates an immune response to conserved regions of the HA stalk region using chimeric HAs in prime-boost approach.

**Flugen** – designed to test whether H3N2 M2-deleted SR LAIV priming elicits stem, NA, CMI, sIgA boosted by QIV

**Biondvax** - repetitions of 9 conserved linear epitopes HA, NP, M1 protein that are prepared as a single recombinant protein.

**Imiquimod** – f/u to 2 clinical trials in Hong Kong – very high seroconversion rates and more robust responses to drifted variants of H1, H3 and B
A Prime/Boost Vaccine (Ad26.ZeBov/MVA-BN-FILO) for Preventing Ebola

Preclinical & Phase I, II Trials

Phase II Trials in Africa

Regulatory Submission & Stockpile

(AdVac®)
Jassen/Crucell

Oxford Vaccine Group

Bavarian Nordic
(MVA-BN® Filo)

PREVAC Consortium

Inserm

LSHTM

ALIMA

Jansen

EUAL Submission

Project BioShield
Late Stage Development & Procurement
MVA-BN: multivalent, glycoprotein from Zaire, Sudan, and Marburg

Insert: French National Institute of Health and Medical Research

Other Health Authorities

Guinea, Liberia, Sierra Leone
A Successful Public Private Partnership
-Innovation through Patenting and Licensing

1980’s

Wyeth Lederle

CRADA

Reassortant Rotavirus

1990’s

Wyeth

RotaShield
On/Off Market

2000’s

Wyeth

Non-exclusive License Agreements
to 11 Industrial Partners
in Developing Countries & US

2018

All Materials & Docs Transferred

2010’s

SERUM INSTITUTE OF INDIA PVT. LTD.

Thermostable ROTASIIIL®

Universal Immunization Programme
(India)

WHO
Pre-qualification expected
Human & Bovine

Reassortant Rotavirus
Partnerships have the potential to accelerate the translation of promising concepts into effective public health interventions.

PPP have enabled innovations at diverse stages of the vaccine R&D process.

Successful PPP require
- Aligned goals
- Leveraging comparative advantages of partners
- Shared risk, responsibility, and accountability
- Careful strategic planning
- Flexible mechanisms
Acknowledgement

Lee Hall
Barbara Mulach
Claire Schuster
Mukul Ranjan
Colleen Sico
Kimberly Taylor
Christopher Roberts
Opportunities and Resources
Public-Private Partnerships

Dr. Linda C. Lambert
Deputy Assistant Secretary
Director, Medical Countermeasures Research
Support Services
BARDA/ASPR
ASPR’s Mission

Save Lives and Protect Americans from 21st Century Health Security Threats
• Our mission is to save lives and protect Americans from 21st century health security threats.
The BARDA Model

BARDA develops and makes available medical countermeasures (MCMs) by forming unique public-private partnerships with industry partners.
Our Industry Partners

FDA Approvals, Licensures, and Clearances

- H5N1 Adjuvanted Pandemic Vaccine for Pediatrics (Q-Pan®)
- H5N1 Pandemic Vaccine w/ Adjuvant (Q-PAN®)
- Influenza Virus A/B Rapid Diagnostic (LIAT®)
- H1N1 Vaccine (Fluzone®)

Timeline:
- 2007
- 2009
- 2011
- 2012
- 2013
- 2014
- 2015
- 2016
- 2017
- 2018
- 2019

Brands:
- Sanofi
- GSK
- Cobas
- BD Veritor
- Neulasta
- Flublok
- Rapivab

Other:
- Zika Diagnostic
- C. Diff Diagnostic
Public-Private Partnerships

- BARDA considers every contract, other transactional authority, or cooperative agreement as a partnership with the company.
- BARDA brings our subject matter experts and funding to work with our partners to develop and make available medical countermeasures.
- Specific examples of PPP:
  - Centers for Innovation and Advanced Development and Manufacturing
  - Other Transactional Authority
  - CARB-X
  - DRIVe
Centers for Innovation and Advanced Development and Manufacturing (CIADMs)

- Establishment of the CIADMs was a result of the 2010 PHEMCE review – highlighting the need to expand domestic manufacturing for pre-pandemic vaccines.
Other Transactional Authority

- Antibiotics and Diagnostics

- Influenza Antivirals and Emerging Infectious Diseases

- Influenza Vaccines and Antivirals

- All Other Transactional Agreements have cost-share efforts. Meaning the company and BARDA share in the costs for development of the candidates under the portfolios.
- A private sector approach to funding and portfolio management
- Portfolio currently contains 35 candidates
- For every $1 provided by funders and alliance partners – $7-8 in private equity follow on investments
BARDA Division of Research, Innovation, and Ventures (DRIVE)  

DRIVE Mission: Driving Life-Saving Innovation  

Accelerate the research, development, and availability of transformative countermeasures to protect Americans from natural and intentional health security threats.
DRIVE-X

Initial Emphasis:

- Prevent illness from infectious exposures through early identification and action
- Save lives by solving sepsis

Future Areas:

- Create universal treatment options for broad classes of pathogens
- Ensure access to life-saving medical countermeasures for all Americans
- Transform the process by which medical countermeasures are developed (non-animal testing)
- Opioid Defense
Response Framework

**Situational Awareness/Recognize**
How do we know something is happening, an agent has entered the community?

**Identification/Characterize**
What is it, is it drug resistant, are certain subpopulations more susceptible, will it become an epidemic?

**Design**
How do we stop the spread of the disease? Drugs, vaccines, PPE, social distancing?

**Produce**
On demand manufacturing of X?

**Validate**
Methods under design are evaluated, clinical trials, non-clinical trials, epidemiology, surveillance

**Distribute**
Novel ways to get product/information to those who need it.

**Administration**
Everyone who needs X is provided X
BARDA has had a Successful Decade Based on our Successful Partnerships

Formed strong partnerships with over 200 industry partners

Supported 40 FDA licensure/approvals across 36 different medical countermeasures

Supported 27 different projects under Project BioShield, 14 products added to the Strategic National Stockpile, 8 FDA licensures

Significantly expanded domestic vaccine production capacity: 60 M doses to 600 M antigen doses for influenza

Accelerated antibacterial product development to address critical vulnerabilities
How to Contact BARDA

https://www.medicalcountermeasures.gov/home.aspx
  • Portal to BARDA: Register to request a TechWatch meeting!
  • Learn about and register for BARDA Industry Day (October 29-30, 2018)

https://www.fbo.gov/ (“FedBizOpps”)
  • Official announcements and info for all government contract solicitations

https://www.usajobs.gov/
  • Join the team!

https://www.phe.gov/about/BARDA/Pages/default.aspx
  • Program description, information, news, announcements

www.drive.hhs.gov
  • DRIVe questions
BARDAD
INDUSTRY
DAY
October 29-30, 2018
Grand Hyatt • Washington, D.C.
ONLINE REGISTRATION OPENED

National Vaccine Advisory Committee

PUBLIC-PRIVATE PARTNERSHIPS: SUCCESSES AND FAILURES IN FINANCING VACCINE INNOVATION

PATH

David C. Kaslow, M.D.
PATH Essential Medicines

CENTER FOR VACCINE INNOVATION & ACCESS
1. About PATH & CVIA (Center for Vaccine Innovation & Access)

2. PDP models

3. Another valley of death

4. Full Public Value of Vaccines (for panel discussion)
PATH—a global organization

Work in more than 70 countries. 150 million people reached each year on average.

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 potency when given

300+ million people immunized with MenAfriVac® in the African meningitis belt

310+ million children vaccinated in 6 countries with Japanese Encephalitis Virus Vaccine
With expertise in science, health, economics, technology, advocacy, and dozens of other specialties, PATH develops and scales solutions—including vaccines, drugs, diagnostics, devices, and innovative approaches to strengthening health systems worldwide.
NVAC: PUBLIC-PRIVATE PARTNERSHIPS: SUCCESSES AND FAILURES IN FINANCING VACCINE INNOVATION

Vial Vaccine Monitor

Meningitis A conjugate vaccine

RTS,S malaria vaccine

Autodisable syringe

Rotavirus vaccine

Japanese encephalitis vaccine
CVIA portfolio includes over two dozen vaccines in development and use across 17 disease targets

Portfolio snapshot current as of August 2018; does not include new/ongoing proposal development work, nor ongoing support to the Expanded Programme on Immunization in multiple countries.

**Reflects wind-down activities.
CVIA’s goal

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)
“Development” valley of death

Valley of death

1 About PATH & CVIA

2 PDP models

3 Chapter Title

4 Full Public Value of Vaccines
Product Development Partnership:

A unique, non-profit business model bringing together public, private, academic and philanthropic sectors to develop technologies for global health.

PDPs pave the way for new research on infectious diseases and accelerate the development of safe and effective vaccines, drugs and diagnostics for the most vulnerable populations as quickly and cheaply as possible.

- Sharing the risk
- Sharing the cost
Product Development Partnerships (PDPs): *Four models (at least)*

- **Assisted business case (Outbreak)**
  - Examples: Ebola, MERS, Nipah, Lassa Fever
  - Solutions:
    - Coalition for Epidemic Preparedness Innovations (CEPI)
    - BARDA
    - DARPA

- **Assisted business case (LMIC only)**
  - Examples: Cholera, Malaria, Men A, Non-typhoidal salmonella, Shigella
  - Solutions:
    - Public funding
    - Priority Review Vouchers
    - LMIC Manufacturers
    - Push & Pull mechanisms
      - GAVI financing

- **Uncertain business case (LMIC ↔ HIC)**
  - Examples: Grp A Strep, Grp B Strep, TB
  - Solutions:
    - Reverse tiered pricing
    - Push & Pull mechanisms
      - Advanced Market Commitments
      - GAVI financing

- **Compelling business case (HIC → LMIC)**
  - Examples: CMV, Hib, HPV, PCV, RSV, Rota
  - Solutions:
    - Tiered pricing
    - Push & Pull mechanisms
      - Advanced Market Commitments
      - GAVI financing
Developing products for low resource settings: *Principles of global access*

**A clear link to mission**
Collaborations with private sector must lead to positive impact in low resource settings on:

- Availability
- Accessibility
- Affordability
- Acceptability

**With recognition of private sector needs**
To apply their development, manufacturing, and distribution strengths toward innovative technologies that, in the absence of PATH involvement, would not be a private-sector priority

- Sustainability

1 About PATH & CVIA
2 PDP models
3 Another valley of death
4 Full Public Value of Vaccines
Case Study: RTS,S/AS01E (Mosquirix®): 30+ years in development
**What:** Product Development Partnership established in 2001 by GlaxoSmithKline (GSK) and PATH.

**Why:** To develop a vaccine that will protect infants and children residing in malaria endemic regions of sub-Saharan Africa from clinical disease and severe malaria resulting from *Plasmodium falciparum* infection.

Consistent with the 2015 Landmark goal from the Malaria Vaccine Technology Roadmap (circa 2006 and 2013)

“By 2015, develop and license a first-generation malaria vaccine that has a protective efficacy of more than 50% against severe disease and death and lasts longer than one year.”
Efficacy of the RTS,S/AS01E in a Phase 3 multicenter safety, efficacy and immunogenicity trial in two age categories

Vaccine efficacy over 12 months following the first 3 doses in 5–17 months and 6–12 weeks of age at first vaccination

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>5-17 months</th>
<th>6-12 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>% VE against all clinical malaria episodes (with 95% CI)</td>
<td>51.3% (47.5–54.9)</td>
<td>32.9% (26.3–38.9)</td>
</tr>
<tr>
<td>% VE against severe malaria (with 95% CI)</td>
<td>44.5% (23.8–59.6)</td>
<td>38.5% (7.8–59.0)</td>
</tr>
</tbody>
</table>

As published in Malaria vaccine: WHO position paper
WHO WEEKLY EPIDEMIOLOGICAL RECORD, NO 4, 29 JANUARY 2016
RTS,S is indicated for active immunisation of children aged 6 weeks up to 17 months against malaria caused by *Plasmodium falciparum* and against hepatitis B.

- The use of RTS,S should be based on official recommendations considering *Plasmodium falciparum* malaria epidemiology in different geographical areas.
- Vaccination in children from 6 weeks up to 17 months of age (at first dose): Three doses, each of 0.5 ml, should be given at monthly intervals. A fourth dose is recommended 18 months after the third dose.

“...it is important that established protective measures, for example insecticide-treated bed nets, continue to be used in addition to the vaccine.”

RTS,S “should not be used for the prevention of hepatitis B in settings where prevention against malaria caused by *P. falciparum* is not sought.”

RTS,S crossed the valley of death
Additional steps for vaccine uptake in LMICs

- WHO’s Strategic Advisory Group of Experts (SAGE) informs WHO global policy recommendations and strategies
- WHO Prequalification (PQ)
  - Programmatic suitability (PSPQ criteria)
- Financing provides the mechanism for procurement, GAVI, PAHO Revolving Fund or in ministries of finance
WHO recommends further evaluation of RTS,S/AS01 in a series of pilot implementations, addressing several gaps in knowledge, before considering wider country level introduction.

- Feasibility of administering 4-dose schedule
- Impact on all-cause mortality (including gender-specific mortality)
- Further assess causal relationship to excess cases of meningitis and cerebral malaria
- Evidence of any adverse effects of vaccine implementation on other malaria control measures
Mind the gap: jumping from vaccine licensure to routine use

Failure to tackle this implementation phase with the same commitment shown to the licensure phase will pose greatest risk for vaccines developed mainly for the world’s poorest people (eg, malaria, typhoid, haemorrhagic fevers). Thus, implementation assessments must become the third component of the core vaccine evaluation tripod, joining safety and efficacy. The essential value of this third phase has not been fully appreciated…

*Katherine L O’Brien, Fred Binka, Kevin Marsh, Jon S Abramson
“Mind the gap”: A second “valley of death”?

The first valley of death

A second valley of death?


1 About PATH & CVIA
2 PDP models
3 Another valley of death
4 Full Public Value of Vaccines (for panel discussion)
If we build it, will anyone want to use it???

Favorable value proposition as driver of vaccine development and access
Traditional \textit{v} Full Public Value of Vaccines

\textbf{FPVV approach also based on:}
- Disease reduction directly and indirectly by reducing:
  - Vaccine preventable disease incidence
  - All cause mortality
  - Under 5 mortality
  - Long-term sequelae
  - Pathogen transmission
  - Anti-microbial resistance
- Reducing frequency and size of outbreaks
- Stabilizing health systems
- Social and economic benefits
- Equity, access, affordability, acceptance and sustainability
- Protecting against financial risk

\textbf{Traditional approach based on:}
- Efficacy (individual direct benefit) \& effectiveness (direct and indirect health benefits)
- Risk/safety profile (individual)
- Cost-benefit analysis

Traditional Direct Risk/Benefit v Full Public Value

- Health
  - Direct
  - Indirect

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

- Individual
  - Traditional Direct Risk/Benefit

- Population
  - Full Public Value
Create alignment across a range of stakeholders, with respect to global health priorities
Provide a resource to effectively advocate for development and introduction of vaccines
Inform investment decisions at all stages of development and implementation
Accelerate suitability for and accessibility of vaccines to LMICs

Full Public Value Proposition as driver of sustainable vaccine development and access
PATH
Leveraging Public-Private Partnerships to Move the Needle in Product Development

Biotechnology Company Perspective

National Vaccine Advisory Committee
September 12, 2018

Timothy Cooke, Ph.D.
Chief Executive Officer, NovaDigm Therapeutics

Biotechnology Industry Representative, National Vaccine Advisory Committee, 2015-2019
Member, Incentives for Vaccines Working Group, PACCARB 2017
Member, Biotechnology Innovation Organization (BIO)
- Antimicrobial Resistance Working Group
- Vaccines Policy Advisory Committee
Advisory Board, CARB-X
Disclosure Statement

Timothy Cooke has the following affiliations:

Chief Executive Officer, Board Director and shareholder in NovaDigm Therapeutics, a company developing vaccines against *Candida* and *Staphylococcus aureus*.

Consultant to Ology Bioservices, a contract development and manufacturing organization.

Consultant to Fina Biosolutions, an R&D service organization focused on polysaccharide conjugate vaccines.
Biotechs developing infectious disease vaccines

• These biotechs would not exist without public-private partnerships
  – Especially uncertain/unattractive markets (biodefense, pandemic, global health)

• New biotechs cannot attract investors without robust commercial markets
  – Need to maintain/expand Big Pharma interest in infectious disease vaccines

• Historical venture-capital model for creating biotechs under severe stress
  – High costs of vaccine development (especially Phase 2 to 3 transitions)
  – Consolidated industry reduces acquisition opportunities (4 dominant pharmas)
  – ID vaccines (and antibiotics) have relatively low pricing expectations
  – Investments are relative and are going elsewhere (e.g., immuno-oncology, orphan)
Venture Capital Funding

Venture capital funds

$ invested

Institutional investors
Pension funds, endowments, insurance cos., foundations, etc.

$ invested

$ returned

“Private” biotech companies

$ returned if and when private company gets acquired

Governments NGOs

$ objectives
Venture Capital Funding

- **Venture capital funds**
  - $ invested
  - $ returned

- **Institutional investors**
  - Pension funds, endowments, insurance cos., foundations, etc.
  - $ returned

- **Individual investors**
  - $
  - $

- **“Public” biotech companies**
  - initial public offering (IPO)
  - objectives
  - $

- **“Private” biotech companies**
  - $ returned if and when private company gets acquired
  - $ invested

- **Governments NGOs**
  - $ objectives
“Big Pharma” and biotech infectious disease vaccine pipeline

Pipeline adapted from PhRMA Pipeline Oct 2017 and updated Feb 2018
(n = 132 candidates from US, EU, Japan, Korea, Canada, Australia)
Startup biotech to marketed vaccines
Only 7 companies over 20 years

• Crucell – acquired marketed products from Berna (2005)
• Valneva – Ixiario®/Japanese encephalitis (2009)
• Bavarian Nordic – Imvamune®/small pox (2010 US sales)
• Protein Sciences* – Flublok®/seasonal influenza (2016)
• PaxVax* – VaxChora®/cholera (2016)
• Dynavax – Heplisav®/hepatitis B (2017)

* Private biotech companies
Venture capital funded to acquisition
Pace of acquisitions has slowed over last 5 years

<table>
<thead>
<tr>
<th>Date</th>
<th>Company</th>
<th>Acquirer</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>May 2008</td>
<td>Iomai</td>
<td>Intercell</td>
<td>$190M</td>
</tr>
<tr>
<td>July 2008</td>
<td>Acambis</td>
<td>Sanofi Pasteur</td>
<td>$546M</td>
</tr>
<tr>
<td>Mar 2011</td>
<td>Crucell</td>
<td>J&amp;J Janssen</td>
<td>$2,400M</td>
</tr>
<tr>
<td>Oct 2012</td>
<td>LigoCyte</td>
<td>Takeda</td>
<td>$60M upfront + milestones</td>
</tr>
<tr>
<td>May 2013</td>
<td>Inviragen</td>
<td>Takeda</td>
<td>$35M upfront + $215M milestones</td>
</tr>
<tr>
<td>May 2013</td>
<td>Okairos</td>
<td>GSK</td>
<td>$325M</td>
</tr>
<tr>
<td>June 2013</td>
<td>Isconova</td>
<td>Novavax</td>
<td>$30M</td>
</tr>
<tr>
<td>Sept 2013</td>
<td>Medicago</td>
<td>Mitsubishi Tanabe</td>
<td>$357M</td>
</tr>
<tr>
<td>Feb 2015</td>
<td>GlycoVaxyn</td>
<td>GSK</td>
<td>$212M</td>
</tr>
<tr>
<td>Aug 2017</td>
<td>Protein Sciences</td>
<td>Sanofi Pasteur</td>
<td>$650M upfront + $100M milestones</td>
</tr>
<tr>
<td>Aug 2018</td>
<td>PaxVax</td>
<td>Emergent</td>
<td>$270M</td>
</tr>
</tbody>
</table>

6 acquisitions/3 years
3 acquisitions/5 years
Venture capital funded to initial public offering
ID vaccine-focused biotechs had difficulty becoming public companies

• Strong opportunity for biotech initial public offerings 2013-2017
• 179 IPOs for drug development biotechs in US
• 19 IPOs infectious disease companies (11%)
• 2 IPOs ID vaccine companies (1%)
  – Argos Therapeutics & Genocea Biosciences in 2014
• 3 biotechs acquired public companies to become publicly traded
  – VBI Vaccines in 2014, Altimmune & Vaxart in 2017
Venture capital funding for US drug development biotechs
Venture capital funding for US drug development biotechs

[Graph showing US VC Funding for Drug Development Biotechs, with data points for oncology, rare diseases, infectious diseases, and ID vaccine from 2008 to 2017.]
Venture capital funding for US ID vaccine biotechs

Dave Thomas & Chad Wessel, BIO Emerging Therapeutic Company Investment and Deal Trends, 2008-2017 & unpublished data

Modernna has a broad mRNA-based platform technology with a pipeline of 9 ID vaccines, 5 oncology candidates and 7 other therapeutic candidates (July 2018).

PaxVax is focused on ID vaccines (acquired by Emergent Aug 2018)

There are about 20 “Other” private biotechs
Biotechs developing infectious disease vaccines

• Public-private partnerships are more important than ever to mitigate VC and public investor funding gaps for biotechs
  – NIH, DoD, Gates, PATH, CEPI and CARB-X play important roles usually up to Ph2
  – Transitioning from Phase 2 to 3 requires “BARDA-scale” funding (≥$100M)

• Need commercially successful infectious disease vaccines
  – Maintain/expand Big Pharma interest in funding internally and acquiring biotechs
  – Success stories for investors in ID vaccines (venture capital, institutional, individual)

• Need government policies that can support vaccine use & development
  – Expand coverage and reimbursement for existing vaccines (esp. adult, adolescent)
  – Lower development cost/risk (regulatory innovation, ACIP predictability)
Public biotechs with clinical-stage/marketed ID vaccines

Government intervention has been successful in sustaining biotechs

The two most valuable public ID vaccine biotechs are Emergent BioSolutions (anthrax vaccine) and Bavarian Nordic (smallpox vaccine). Their value was driven largely by government intervention through BARDA.