The Role of Vaccine in Emergency Response

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John Fitzsimmons, Revolving Fund for vaccine Procurement, PAHO (Online)
The role of vaccine in the Zika response

Heather Deehan, UNICEF/John Fitzsimmons, PAHO/David Wood, Bernadette Murgue, WHO
Zika Industry Consultation
May 11-12, 2016
Session Objectives

• To provide an overview of PAHO’s technical cooperation and Revolving Fund

• To provide an overview of UNICEF response to health emergencies and role in rapid vaccine research and development

• To provide an overview of the WHO response to Zika and plans for vaccine
Immunization:
*a flagship program for the Americas*

- The Expanded Program on Immunization (EPI) of the Americas was created in 1977 as a **Regional Immunization Program**

- The Revolving Fund for Vaccine Procurement was launched in 1979 as a procurement mechanism for essential vaccines, syringes and other related supplies without interruption
PAHO Comprehensive Approach
Technical cooperation on immunization

Weblink: PAHO’s Regional Immunization Action Plan (RIAP) 2016-2020
### Milestones in the 39 years of the EPI in the Americas

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
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<tbody>
<tr>
<td>1977</td>
<td>PAHO’s Directing Council establishes the EPI</td>
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<tr>
<td>1979</td>
<td>Creation of the Revolving Fund</td>
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<td>1980</td>
<td>Creation of international evaluation methodology for the EPI</td>
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<td>1983</td>
<td>“Days of Tranquility”</td>
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<td>1985</td>
<td>Creation of the EPI Technical Advisory Group</td>
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<td>1985</td>
<td>Creation of the Interagency Cooperation Committee</td>
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<td>1991</td>
<td>Last indigenous case of polio in Peru</td>
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<td>1994</td>
<td>Declaration of the goal to eliminate measles</td>
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<td>1994</td>
<td>1st Region certified free of polio</td>
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<td>2003</td>
<td>1st Vaccination Week in the Americas</td>
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<td>2006</td>
<td>Launch of the Pro-Vac initiative</td>
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<td>2010</td>
<td>Directing Council resolution on strengthening the EPI (RIVS)</td>
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<tr>
<td>2012</td>
<td>1st World Immunization Week</td>
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<td>2013</td>
<td>Directing Council resolution on the principles of the Revolving Fund</td>
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<tr>
<td>2015</td>
<td>1st Region free of rubella</td>
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<td>2015</td>
<td>Directing Council resolution on the Regional Immunization Action Plan</td>
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<td>2016</td>
<td>Polio Switch</td>
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40 years of the EPI in the Americas

Close coordination with WHO to prevent and respond to epidemics
Global Evolution of the EPI, 2016

Countries with Pneumococcal Conjugate vaccine in the national immunization programme; and planned introductions in 2016

Countries with Rotavirus vaccine in the national immunization programme; and planned introductions in 2016

Countries with HPV vaccine in the national immunization programme

Countries with Influenza vaccine in the national immunization programme
Key Enablers for Success since 1977

High Level of Commitment from Member Countries
WHA & PAHO DC Resolutions

Quality Vaccines
Suppliers

The PAHO Revolving Fund
“Facilitating Access”
UNICEF Core Commitment to Children in Emergencies

Nutrition

Health

Water, Sanitation & Hygiene

Education

Child Protection
Global Emergency activities

59 countries & territories

Type of response in 2014

- Natural disasters (hydro-meteorological): 77
- Natural disasters (geo-physical): 25
- Socio-political crisis (acute economic crisis, conflict/civil unrest, human rights crisis): 68
- Health crisis (acute nutritional crisis, epidemic, influenza-human pandemic): 96
- Other humanitarian situations: 28

Responded to

294 humanitarian situations

These crises were designated Level 3 emergencies following the activation of UNICEF’s Corporate Emergency Procedure.

This map is stylised and not to scale. It does not reflect a position by UNICEF on the legal status of any country or area or the delimitation of any frontiers. The dotted line represents approximately the Line of Control agreed upon by India and Pakistan. The final position of the Line of Control is subject to the outcome of the Kashmir dispute.
Recent examples 2015

Nepal earthquakes: UNICEF emergency supply routes & response

Supplies delivered: 1,275 MT
Procurement value: $24.5M

Key supplies:
- 8,564 tarpaulins for clinics, schools and child-friendly spaces
- 30,160 tarpaulins (785,600 m2)
- 710 emergency health kits
- 1,080 midwifery kits
- 378,280 vials of vaccines (1 vial = 10 doses)
- 50 diarrhoea disease kits
- 3,500 family child kits
- 5,100 water and sanitation kits
- 12.8 million water purification tablets
- 196 water tanks (to store more than 70,000 liters of water)
- 500 squatting plates
- 9,325 early childhood development kits
- 149,648 school kits
- 5,714 recreation kits
- 12,371 cartons of ready-to-use therapeutic food (RUTF) (1 carton = 150 sachets)

Life-saving supplies to Ebola-affected countries between 4 August 2014 and 10 April 2015

UNICEF has supplied 7,994 MT of supplies to Guinea, Liberia and Sierra Leone

Guinea Supply: 3711 MT by air
Sierra Leone Supply: 4233 MT by sea

Support: Education, Information, and Water Supply

#Backtoschool

At schools reopen, UNICEF and partners are helping create a safe environment for children to stay healthy and learn. UNICEF-supported schools include hygiene kits, WASH kits to prevent the spread of infection, and thermometer to check each child’s warning signs of fever.
Use of Vaccines for Emergency and Outbreak response

- **Measles and MR**
  - 1M doses Measles and 100K doses MR

- **Oral Cholera**
  - LTA with 2 components: Preventive Campaigns and Emergency/Outbreak response

- **Yellow Fever**
  - LTA with 2 components: Routine and Emergency/Outbreak response

- **Meningococcal A, C and W containing vaccines**
  - LTA with 2 components: Routine and Emergency/Outbreak response

- **Oral Polio Vaccine** – sufficient availability to respond to outbreaks
  - IPV – recommended use in outbreak response
  - mOPV stockpile - Switch
Ebola: largest Supply response in UNICEF history

Responding to three countries with differing programmatic priorities...

- Real-time development of new PPE specifications and kits
- New suppliers identified rapidly and production scale-up
- Air co-ordination Cell jointly established as air-bridge to countries
- Financial commitments made for the pre-purchase of PPE
- Volunteer packing days
- 50 Ebola Community Care Centers – from concept to execution in 2-3 months
Moving forward

Majority of vaccines to be considered for Emergency Response

Decision Making Framework including 3 steps:

1) an assessment of the epidemiological risk posed by each potentially important VPD within a given context;

2) a consideration of the properties of each vaccine to be taken into account for the intervention;

3) prioritization of the importance of vaccination in relation to other urgent public-health interventions
A global ‘re-think’ of Health Emergencies is underway within UNICEF

UNICEF Health Emergencies Preparations Initiative 2016

- **Objective of the initiative**: Given the impact on children (directly and indirectly), UNICEF is prepared to support national government’s multi-sectoral health emergency response.

- **7 operating principles**:
  - Multi-sectoral
  - Supports national priorities & systems
  - Community-focused
  - Disease-specific Preparations
  - Continuous learning, innovation & monitoring
  - Equity lens
  - IASC & IHR based
  - Builds on existing structure, systems and strengths of UNICEF & partners

- **Activity Areas**:
  - Affirm the priority and organise ourselves
  - Disease-specific Preparations
  - Institutional Strengthening
  - Cooperation with Partners

- **Timeline**: Global level preparedness in place by 3Q2016
UNICEF Health Emergencies
Preparations
Categories

Reviewed on ongoing basis.

Compared with IHR, WHO R&D blueprint, CDC and other prioritised diseases

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**UNICEF Priority Disease Categories**

CRITERIA & PRIORITISATION RECOMMENDATION

Disease selection was based on currently available information according to the following criteria:

1. Impact on children
2. Presence on WHO pandemic/epidemic list
3. Pandemic potential
4. Morbidity, mortality and caseload
5. Socio-economic impact
6. Geography of disease in relation to national prevention/response capacity
7. Mode of transmission

The discussions resulted in the categorization of diseases into three groups as described in the table below. Diseases for which UNICEF already has strong preparedness and programmes are denoted in *italics*; guidance and tools for these diseases have previously been developed and are available for inclusion in the response ‘package’.

Categorization of diseases will be continuously reviewed and updated as necessary. At country level, categorization may be done based on national risk assessments.

<table>
<thead>
<tr>
<th><strong>DISEASE CLASSIFICATION</strong></th>
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<tbody>
<tr>
<td><strong>Category 1:</strong> Current epidemics of concern and focus diseases of epidemic/pandemic potential requiring the development of the full package of preparedness activities as detailed below.</td>
</tr>
<tr>
<td><strong>Category 2:</strong> Endemic or epidemic diseases of potential threat/changing pattern that require additional attention and capacity building with the development of a basic support package of preparedness activities as detailed below.</td>
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<tr>
<td><strong>Category 3:</strong> Epidemic diseases are of interest to UNICEF, but response will be limited to linking to existing resources as detailed below.</td>
</tr>
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<table>
<thead>
<tr>
<th><strong>Category 1</strong></th>
<th><strong>Category 2</strong></th>
<th><strong>Category 3</strong></th>
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<tbody>
<tr>
<td>Ebola, Marburg</td>
<td>Crimean-Congo Hemorrhagic Fever</td>
<td>Hantavirus</td>
</tr>
<tr>
<td>MERS, SARS, CoV</td>
<td>Lassa Fever</td>
<td>Hepatitis E</td>
</tr>
<tr>
<td>Zika, Dengue, Chikungunya</td>
<td>Leptospirosis</td>
<td>Shigellosis</td>
</tr>
<tr>
<td>Avian Influenza, Pandemic Influenza</td>
<td>Plague</td>
<td>Seasonal Influenza</td>
</tr>
<tr>
<td>Cholera</td>
<td>West Nile Virus</td>
<td>Typhoid Fever</td>
</tr>
<tr>
<td>Measles</td>
<td>Malaria</td>
<td>Measles</td>
</tr>
<tr>
<td>Measles</td>
<td>Meningitis</td>
<td>Polio</td>
</tr>
<tr>
<td>Yellow fever</td>
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</table>
UNICEF Health Emergencies Preparations
Help drive the R&D of health products that prevent, diagnose of treat priority diseases

Objectives:
- Right products available
- Reduce lead-time for development
- Identify bottlenecks
- Risk share
- Address the ‘gap’ between research and availability

<table>
<thead>
<tr>
<th>Disease</th>
<th>Diagnostic</th>
<th>Prevention</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ebola/Marburg (v.)</td>
<td>E: RDTs (4 in 2015), labs-PCR M: ELISA,PCR</td>
<td>E-M: 4 candidate vaccines under trial for WHO PQ (Merck product – under EUAL registration)</td>
<td>E: 4-5 candidates under study, &amp; serum treatment M: Palliative care</td>
</tr>
<tr>
<td>SARS/MERS-CoV (v.)</td>
<td>SARS: Chest x-ray, ELISA, PCR, IFA MERS: PCR</td>
<td></td>
<td>MERS: antivirals being studied</td>
</tr>
<tr>
<td>Zika (v.)</td>
<td>RT-PCR (w/in 5 days of symptoms)</td>
<td></td>
<td>No cross-protection seen with new Dengue vaccines</td>
</tr>
<tr>
<td>Avian/Reproductive Influenza (v.)</td>
<td>RDT, PCR, IFA</td>
<td>Flu platform available from seasonal influenza</td>
<td></td>
</tr>
<tr>
<td>Cholera (b.)</td>
<td>Rapid dipstick (in pre-qual), PCR</td>
<td>2 vaccines WHO PQ</td>
<td>ORS, IV, antibiotics (when necessary)</td>
</tr>
<tr>
<td>Polio &amp; vDPV (v.)</td>
<td>Viral culture, Serology, RT-PCR</td>
<td>Multiple vaccines activated/inactivated, oral/injected, salk/sabin, type1-2-3; WHO PQ</td>
<td></td>
</tr>
<tr>
<td>Dengue/Chikungunya (v.)</td>
<td>D: RDT, RT-PCR, ELISA CH: PCR, ELISA</td>
<td>2 Dengue vaccines being reviewed for WHO PQ (Sanofi-2016; licensed by Brazil; Takeda-2017)</td>
<td>Palliative care</td>
</tr>
<tr>
<td>Crimea-Congo Hemorrhagic Fever (v.)</td>
<td>RT-PCR, ELISA</td>
<td>Old vaccine used in Bulgaria; candidate vaccines by Erciyes (Turkey) pending FDA review</td>
<td>Serum treatment under study in Turkey (Refik Saydam Health Institute)</td>
</tr>
<tr>
<td>Lassa Fever (v.)</td>
<td>ELISA, RT-PCR</td>
<td>Candidate vaccine under study by USAMRIID</td>
<td>Ribavirin gives potential interference</td>
</tr>
<tr>
<td>Leptospirosis (b.)</td>
<td>RDT, ELISA, PCR, Culture</td>
<td>Doxycycline is prophylaxis Vaccines avail in Cuba &amp; China</td>
<td>Antibiotics</td>
</tr>
<tr>
<td>Plague (b.)</td>
<td>RDT, PCR, ELISA, Microscopy</td>
<td></td>
<td>Antibiotics</td>
</tr>
<tr>
<td>Rift Valley fever (v.)</td>
<td>PCR, Culture, Microscopy</td>
<td></td>
<td>Palliative care</td>
</tr>
<tr>
<td>West Nile (v.)</td>
<td>PCR, ELISA</td>
<td></td>
<td>Phase 1 testing</td>
</tr>
<tr>
<td>Meningitis (b., v.)</td>
<td>PCR, Culture</td>
<td>Vaccines against groups A, B, C, C135, Y incl. in combination (Sanofi, GSK, BioManghin, Pfizer, others under licensure), WHO PQ</td>
<td>Antibiotics</td>
</tr>
<tr>
<td>Yellow fever (v.)</td>
<td>ELISA (conf. 6-10 days after illness)</td>
<td>Vaccines WHO PQ</td>
<td>Palliative care</td>
</tr>
<tr>
<td>Hantavirus</td>
<td>PCR, ELISA</td>
<td></td>
<td>Phase 2 study of</td>
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Reducing vaccine timelines: from research to availability

**Typical Vaccine Lead Time**
- **Basic Research and Development**: 10-15 years
- **Phase I: Preclinical Dev.**: 5-7 years
- **Phase II: Clinical Dev**: 2-3 years
- **Phase III: Advanced Dev**: 10+ years
- **Licensure**: Total Lead Time: 17-25 Years

**Ebola Vaccine Lead Time**
- **Basic Research and Development**: 11 years
- **Phase I: Preclinical Dev.**: 2003: Patent application
- **Phase II: Clinical Dev**: Oct-Dec 2014
- **Phase III: Advanced Dev**: March 2015: Phases II and III begin concurrently - still ongoing
- **Licensure**: August 2014: WHO declares Ebola Epidemic
- **2018 – Earliest projected WHO Prequalification and National Licensure**

**Zika Vaccine Target Lead Time**
- **Basic Research and Development**: January 2016 – March 2017
- **Phase I: Preclinical Dev.**: Q3 2017: Concurrent Phases II and III
- **Phase II: Clinical Dev**: February 2016: WHO declares Zika a Public Health Emergency
- **Phase III: Advanced Dev**: Q2 2017
- **Licensure**: 2018 – 2019: WHO Prequalification and National Licensure
UNICEF Considerations and Potential Role

UNICEF will operate at the global, regional, countries and community level to:

- Define priorities
- Undertake disease specific preparation based on established priorities
- Strengthen institutional response by mapping existing analytics and data, identifying gaps and strengths
- Drive Research and Development and availability of vaccines
- Collaborate and engage with key partners, streamlining preparedness and response activities

UNICEF will do this by:

1) Develop Target Product Profile with the leadership of WHO
2) Convene Industry and Partners
3) Develop Demand and Procurement Forecasting for UNICEF countries
4) Contracting – pull mechanisms and market incentives for vaccines
Overview of Vaccines in the Zika Response
WHO response to Zika, 2016

1 Feb: PHEIC microcephaly & neurological disorders

14 Feb: strategic response framework
Zika: Some urgent research needs

- Natural history of the illness in humans
- Clinical complications
- Are neurologic complications new?
- Routes of transmission/acquisition
- Full confirmation of all vectors involved
- Immunopathology
- Development and availability of diagnostic tests
- Preventive and control countermeasures
WHO response to Zika

- 1-2 March: Zika research meeting, PAHO/WHO, Washington
- 7-9 March: Zika R&D meeting, GVA
- 14–15 March: Vector Control Advisory Group meeting, GVA
- 14-15 March: Consultation for the EUAL procedure for Diagnostics
- 17–19 March: Management of Zika complications, GVA
- 17–18 March: Harmonization of study protocols, Recife
- 25-26 April: Zika summit, Paris
- May: finalization of harmonization process, Colombia
- 6-7 June: Regulatory consultation on Zika vaccines
Zika R&D priorities
WHO consultation, 7-9 March 2016

- Multiplex diagnostics (Zika, Dengue, Chikungunya)
- **Inactivated Zika vaccines for women of child-bearing age**
- Repurposing molecules
- Animal models
- Innovative vector control measures
- Regulatory issues
- Data sharing and sample sharing
Zika response: what has been achieved

- Diagnostic: Product pipeline → EUAL process → TPP
- Vaccine: Product pipeline → Draft TPP
- Therapeutics: Product pipeline
- Vector control: Product pipeline
• Continued landscaping of vaccine candidates
• Target product profile for emergency and epidemic use
  – 1st draft ready, public consultation ongoing
  – Consultation on regulatory considerations: 6-7 June, 2016
  – Final TPP in June
• EUAL process: Epidemic use of vaccines & accelerated licensure strategies
What has been achieved?

Initiated the process to communicate on ongoing research and open access resources during PHEIC, using ZIKA open access approach and publication of technical notes and peer review papers for Zika.

Convened a series of expert consultations.

Fostered discussions on the Blueprint among members of the Scientific Advisory Group.

Informed discussion on the Blueprint at the Executive Board and bilateral discussions and international meetings including but not limited to representatives of Member States.
Meeting: *Designing a Vaccine Efficacy Trial during epidemics, Chamonix, 24-25 March 2016*

**Aim and Objectives**

(i) To strengthen global collaboration and communication between disease content experts, epidemiologists, statisticians and modellers

(ii) To outline methodologies to use dynamic models along with simulation to design vaccination strategies and to design clinical trials to study them

(iii) To propose a work plan and collaborative approaches leading to the design of models and evaluation of trial designs for top priority highly infectious pathogens listed by WHO

**NEXT STEPS**
Meeting: **Good Participatory Practices**, Montreux, 12-13 May 2016

**Aim and Objectives**

(i) To provide trial funders, sponsors, and implementers with systematic guidance on how to effectively engage with stakeholders in the design and conduct of prevention and treatment trials for emerging pathogens.

(ii) To develop Good Participatory Guidelines to implement research in emergency settings
Conclusions

- Zika outbreak as an important testing ground for the Blueprint strategy
- Improved WHO’s ability to coordinate Zika-related R&D
- The lack of committed R&D financing remains an ongoing concern
Thank you