Alternative models for influenza vaccine R&D financing

Third WHO consultation on Global Action Plan on Influenza Vaccines (GAPIII)
Nov 15-16 2016

John-Arne Røttingen, interim CEO of CEPI
Influenza – the need for vaccines

• Influenza vaccines are pivotal for both prevention of seasonal epidemics and for pandemic preparedness

• Importance of influenza vaccines applies equally across High Income Country (HIC) and Low and Middle Income Country (LMIC) regions

• However:
  • Limited efficacy of seasonal vaccines (antigenic drift and shift; limited cross-protection across virus subtypes; short duration of immunity)
  • Improved, yet constrained manufacturing capacity and time to scale-up for pandemic vaccines
    • Rapid response manufacturing platforms are limited (egg-based, cell-based, recombinant vaccine technologies)
    • Maintaining production capacity is expensive
  • Lacking a universal influenza vaccine that provides long-lasting immunity against a broad spectrum of divergent influenza viruses
Influenza vaccines – a large market

- Traditionally a commercially rather unattractive global enterprise due to low profit margins and barriers to entry

Today:
- A stable market of ~ USD 4 billion (in annual sales) for seasonal vaccines
- A global vaccine production capacity of ~ 1.5 billion seasonal and ~6.4 billion pandemic doses
- ~ 100 influenza vaccine candidates in the pipeline
- Faster response capabilities due to manufacturing platform technology improvements (e.g. cell-based vaccines, antigen-sparing adjuvanted vaccines, recombinant vaccines)
- Ongoing sharing of influenza viruses and data

Driving factors/initiatives:
- Industry-driven investment initiatives / partnerships
- Global Action Plan for Influenza Vaccines
- BARDA Pandemic Influenza Strategy
- Pandemic Influenza Preparedness Framework
- Pandemic Influenza Vaccine procurement schemes (e.g. EU Joint Procurement Agreement)

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Current R&D financing and incentive mechanisms

Push mechanisms

- Direct investments and acquisitions (seasonal, pandemic) (Industry)
- Advanced Development Partnerships (seasonal, pandemic) (BARDA, Industry)
- Capability transfer to LMICs (pandemic) (BARDA, Industry)
- Idle capacity sustainment (pandemic) (BARDA)

Pull mechanisms

- GISRS vaccine virus selection (seasonal) (WHO)
- Stockpiles (pandemic) (BARDA)
- Advance Purchase Commitments (pandemic) (Governments)
- Joint Vaccine Procurement (pandemic) (EU)
Challenges with current R&D financing mechanisms

• Significant costs and risks in influenza vaccine development
  • A lengthy and costly business of failure: over a decade and at least USD 1 billion to bring new products to launch with 5% chance of success at start
  • Particular technical and regulatory challenges with novel-antigen, novel-platform, broad spectrum use vaccines
• Insufficient virus data sharing due to competition and disincentives for collaboration in the market of seasonal vaccines
• Misalignment of R&D incentives between a stable market of seasonal vaccines and an uncertain market for pandemic or universal vaccines – challenge for market transition
• Rapid R&D response capabilities nurtured by too limited public funding (almost only BARDA)
• Manufacturing capacity patchy and costly for pandemic vaccines – market failure (in particular for LMICs)
• Global access to influenza vaccines in the event of a pandemic is not guaranteed
Why are alternative R&D financing mechanisms needed?

• Due to
  • Market failure (Pandemic vaccines)
  • Market transition failure (New seasonal or Universal vaccines)

• To mobilize new resources and complement the current menu of reward mechanisms to incentivize influenza vaccine R&D

• To incentivize a smooth and sustainable shift of R&D efforts and knowhow from a relatively stable market of current seasonal vaccines to a more uncertain market of pandemic and novel universal vaccines, through:
  • better risk and benefit sharing arrangements between industry and society
  • reduced supply shortages and more equitable access provisos to underserved populations
  • Improved technical and institutional platforms to improve speed of R&D response
  • More collaborative and transparent partnership models for novel R&D and data sharing

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What kind of R&D financing mechanisms are needed?

- New **methods** and **sources** of financing (= resource mobilization mechanisms)
- Offering **incentives** to encourage shift from focus of current market (= reward mechanisms)
- Through tailored **partnership models** with a common mission based on collaborative principles of risk and benefit sharing
What kind of R&D financing mechanisms are needed?

Classification of financing mechanisms

Reward mechanisms = methods of payment
- Direct (or cash) payments
  - Front-loaded
  - Back-loaded
  - Recurring manner
  - Full or partial reimbursement
  - Unconditional or milestone based

Indirect rewards
- Knowledge
- Predictability of revenue
- Access to markets

Resource mobilization mechanisms = methods of fund raising
- Private sector funding sources
- Governments, citizen philanthropists

- Unconditional or milestone based
Resource mobilization examples from global health R&D beyond just vaccines

<table>
<thead>
<tr>
<th>SOURCES</th>
<th>INDICATIVE EXAMPLES</th>
</tr>
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<tbody>
<tr>
<td>• Governments / citizens / philanthropists</td>
<td>• ODA and national health R&amp;D budgets</td>
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<td>• Earmarked taxes and fees / e.g. airline ticket tax</td>
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<td>• Various consumer voluntary contributions</td>
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<td>• Private giving campaigns</td>
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<td>• Pooled funding through management and coordination intermediaries e.g. PDPs,</td>
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<td>• Pledge / guarantee backed debt/equity financing / e.g. IFFIm, GHIF</td>
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<tr>
<td>• Private sector</td>
<td>• Retained earnings / re-invested business revenue</td>
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<td>• In-kind contributions / e.g. in PDPs, in IMI, in GHIT Fund, etc.</td>
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<td></td>
<td>• Various debt/equity financing instruments</td>
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### Reward mechanisms examples from global health R&D beyond just vaccines

<table>
<thead>
<tr>
<th>PAYMENTS</th>
<th>INDICATIVE EXAMPLES</th>
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<tbody>
<tr>
<td>• Direct</td>
<td>• Grants</td>
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<td>• Various end-product and milestone prizes</td>
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<td></td>
<td>• Procurement</td>
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<td>• Risk-sharing loans</td>
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<td></td>
<td>• Venture capital</td>
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<tr>
<td></td>
<td>• Private sector patent buy-outs / buy-backs</td>
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<tr>
<td></td>
<td>• Risk/cost sharing through PDPs</td>
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<tr>
<td></td>
<td>• Incubators / accelerators</td>
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<tr>
<td></td>
<td>• Advance Market Commitments</td>
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<tr>
<td>• Indirect</td>
<td>• Liability protection</td>
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<td></td>
<td>• Volume guarantees</td>
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<td></td>
<td>• R&amp;D tax credits and relief programmes</td>
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<tr>
<td></td>
<td>• Regulatory and legislation</td>
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<tr>
<td></td>
<td>• Tiered pricing schemes</td>
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<td></td>
<td>• Patent pools</td>
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Lessons from CEWG?
(Consultative Expert Working Group on Research and Development: Financing and Coordination)

Balancing innovation and access by complying with following criteria:

• Delinkage of the price of the final product from the cost of the R&D
• Utilize collaborative approaches, especially open knowledge innovation approaches
• Utilize licensing approaches that secure access to final products
• Continuously strive to mobilize new sources of financing
• Foster effective and efficient coordination mechanisms amongst existing organizations/initiatives
• Strengthen capacity for R&D and production, including through technology transfer, in LMICs
What could such mechanisms look like?

**CEPI** is one ambitious new public-private partnership between governments, industry, philanthropy, academia, civil society, and other global health stakeholders.

Responding to the calls of several high-profile panel and expert reports to **address critical R&D gaps** for pandemic preparedness and global health security, **CEPI** will proactively **develop new vaccines for priority emerging infectious diseases (EIDs)** to stop future outbreaks before they become public health emergencies.
Ebola: Timing of phase III trials

- **Start stability study**: 1 Jan
- **Ebola: Timing of phase III trials**: 9 months
  - Guinea working group formed
  - WHO High level meeting: 23 Oct
  - Extension to Sierra Leone: 1 Sept
  - WHO Ethics Report: 11 Aug
  - Ring design decided: 5 Nov
  - Vaccine choice: 5 Feb
  - Vaccination initiated: 23 Mar
  - WHO Consultation on Ebola Vaccines: 29-30 Sept
  - Protocols / Financing: Dec-Jan
- **90 rings**
- **9 months**
- **6 months**

- **6 months**
  - 7 Aug: Last randomized ring vaccinated
  - 31 Jul: Preliminary results
  - 20 Jul: Interim analysis
  - 11 Aug: WHO Ethics Report
  - 5 Nov: Ring design decided
  - 5 Feb: Vaccine choice
  - 23 Mar: Vaccination initiated
Coalition for Epidemic Preparedness Innovations
CEPI – January – November 2016

High Level Meeting Davos 21 January

Task Team Meeting Meeting, Oslo 6-7 April

Task Team Teleconferences

Leadership Group Meeting Washington DC 17 May

Interim CEO appointed Interim board constituted Business Plan presented to stakeholders

Core Group and Leadership Group Teleconferences

First CEPI interim board meeting London, 31 August

CEPI soft launch Media coverage

G7 Health ministers’ side event, Kobe, 10 September

UNGA side event on health emergencies, NY, 19 September
CEPI - Vision

Vaccines contributing to preventing outbreaks from becoming humanitarian crises
CEPI - Mission

To *prioritize, stimulate, finance* and *co-ordinate* vaccine development against emerging infections with epidemic potential, especially in cases where market incentives alone do not achieve this.
Timely vaccine development – objectives for efficient global R&D preparedness

<table>
<thead>
<tr>
<th>1. “Just in Case” – Preparedness</th>
<th>Advance vaccine candidates through late preclinical studies to proof of concept and safety in humans during non-epidemic periods</th>
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<tbody>
<tr>
<td>2. “Just in Time” – Response speed</td>
<td>Validate and sustain technology platforms to support the rapid development of vaccines in known and unknown pathogen emergencies</td>
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</tbody>
</table>

- Live attenuated virus vaccines
- Whole killed virus vaccines (other forms of protein-particulate vaccines)
- VLP (Virus-Like-Particle) vaccines, other non-living technologies (e.g., liposomes)
- DNA/RNA vaccines
- Self-Amplifying-Material (SAM®)
# CEPI’s Gap-Filling Role

**CEPI role as a facilitator**

**CEPI role as a funder**

**Significant focus by others**

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<table>
<thead>
<tr>
<th>Phase</th>
<th>1 Discovery</th>
<th>2 Development/Licensure</th>
<th>3 Manufacturing</th>
<th>4 Delivery/Stockpiling</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Current Stakeholders</strong></td>
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<td></td>
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<tr>
<td>Academia</td>
<td>Industry</td>
<td>Industry</td>
<td>GAVI</td>
<td></td>
</tr>
<tr>
<td>Governments</td>
<td>National Governments</td>
<td>BARDA</td>
<td>UNICEF</td>
<td></td>
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<tr>
<td>WT/NIH</td>
<td>Regulators</td>
<td>CMOs</td>
<td>PAHO</td>
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<tr>
<td>GLOPID-R</td>
<td>Bill and Melinda Gates Foundation</td>
<td>Regulators</td>
<td>National Governments</td>
<td></td>
</tr>
<tr>
<td>Industry</td>
<td>BARDA/DTRA etc.</td>
<td>National</td>
<td>WHO</td>
<td></td>
</tr>
<tr>
<td>Regulators</td>
<td>WHO</td>
<td>Governments</td>
<td>Industry</td>
<td></td>
</tr>
<tr>
<td>Biotech</td>
<td>Biotech</td>
<td>WHO</td>
<td>Pandemic Emergency Facility</td>
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<tr>
<td>IMI / EC</td>
<td>PDPs</td>
<td>GHIF</td>
<td>(World Bank)</td>
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</table>

- Adhering to **equitable access** principles of affordable pricing and availability of vaccines by priority populations in emergencies
- Securing industry participation through **predictable pathways** and risk/benefit sharing arrangements and handling of liability through **indemnification**
- Supporting **data sharing** and **sample sharing** mechanisms, and long-term development of **regional capabilities** for epidemic vaccine preparedness
Organizational Setup: Startup Phase

- Founding Partners include the Gates Foundation, Wellcome Trust, Department of Biotechnology of India, Government of Norway, and World Economic Forum
- Independent legal entity, existing as an international non-profit association under Norwegian law
- Interim Secretariat is hosted by the Norwegian Institute of Public Health under a service agreement
- Flexible arrangement, can transition into other institutional and governance arrangements
- Decisions about its permanent organizational structure and governance made by the CEPI Interim Board during the interim phase
- SAC advises on scientific matters and JCG coordinates CEPI’s activities with other stakeholders
CEPI’s Funding Needs

Preliminary cost-modeling estimates 5-year costs for advancement of **10 WHO Blueprint EID vaccine candidates** to the end of clinical phase II development at between **US$600M and US$3.7B**, depending on the complexity of the technology used, pilot manufacturing requirements and other manufacturing cost variants, and stockpiling needs.

CEPI is seeking multi-year donor contributions to an **initial investment pool of US$1B (2017-21)** to advance **late-stage development of 4 to 6 vaccine candidates** against 2 to 3 priority EIDs to the end of clinical phase II development, and save countless lives and billions of dollars.
CEPI Financing Model

CEPI will use a multi-source financing model to satisfy its core resource needs.

Four financing principles

1. Broad-based
2. Long term, predictable
3. Complementary and new financial resources
4. Fit-for-purpose funding
CEPI Partnership Models

VACCINE INDUSTRY
- **Aligned contributions** from industry and other R&D partners, including staff support, access to IP, and use of vaccine production lines that will significantly reduce CEPI’s overall costs and production timelines.

INTERNATIONAL INVESTORS
- **Direct investor contributions** through multi-year grants and innovative financing mechanisms like IFFIm, which will complement indirect support through alignment on domestic R&D investments and regulatory policies.

DEVELOPING COUNTRIES
- **CEPI’s Solidarity Fund** will channel tiered, equitable contributions from affected countries that will benefit from CEPI’s ‘insurance policy’ against future pandemics emergencies. Solidarity Fund partners will also contribute and benefit through advance coordination on clinical trial arrangements.
CEPI – Investing together
A risk sharing mechanism

• We do not know where the next outbreak will hit
• We do not know which pathogen it will be
• Resources/investments are constrained and limited
• In finance terms we need to:
  • Collateralize and securitize investments
  • Share risks

• National health systems are risk sharing mechanisms (i.e. UHC)
• For global health security we need global risk sharing mechanisms across countries to
  • Prevent, detect and respond to outbreaks
  • Invest in R&D for biomedical countermeasures

• “Pay as you go” will be costly and will not solve the problem!

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Conclusions

- Increasing risk of pandemic influenza outbreaks carrying significant public health and economic burden

- Influenza vaccines are pivotal for both prevention of seasonal epidemics and of pandemic preparedness

- Need for new influenza vaccines: limited efficacy of seasonal vaccines, constrained manufacturing capacity and time to scale-up for pandemic vaccines, and lack of a universal influenza vaccine

- A stable market for seasonal vaccines creates barriers to developing novel pandemic and universal vaccines, which are characterized by highly uncertain markets

- Public funding is too limited: WHO, BARDA, EU – pioneers in push/pull incentives for better influenza vaccine preparedness

- A balance of access and innovation principles is key for fostering societally and globally acceptable R&D financing mechanisms, as demonstrated by CEWG

- CEPI is an example of a global institutional mechanism example with responsibility to incentivize vaccine R&D preparedness through new funding sources and flexible use of incentives but adhering to global access and risk/benefit sharing principles