WHO R&D Blueprint

Processes and methods for prioritization of diseases
The vision the Blueprint is a world in which our R&D response to PHEIC caused by emerging pathogens is faster and more effective than ever before and in which we are able to ensure that a continuous effort aiming to accelerate the results of research but also adapt to the scientific, logistical and social challenges that are specific to epidemics.
In May 2015, the Sixty-Eighth World Health Assembly:

...welcomed the development of a blueprint, in consultation with Member States and relevant stakeholders, for accelerating research and development in epidemics or health emergency situations where there are no, or insufficient, preventive, and curative solutions, taking into account other relevant work streams within WHO.
The R&D Blueprint seeks to create an enabling environment through which all actors, through increased funding, data sharing and partnerships, can drive change in the public health landscape to provide an elevated level of global impact.

This new environment will reduce the time it takes for new medical technologies to reach developing countries in a public health crisis.
Core approaches

A. Improving coordination & fostering an enabling environment

B. Accelerating Research & Development processes

C. Developing new norms and standards adapted to the epidemic context

- a. Assessing epidemic threat & defining priority pathogens
- b. Developing R&D roadmaps to accelerate evaluation of diagnostics, therapeutics & vaccines
- c. Outlining appropriate regulatory & ethical pathways
Priority diseases

There’s an urgent need for R&D for:

- Arenaviral hemorrhagic fevers (including Lassa Fever)
- Crimean Congo Haemorrhagic Fever (CCHF)
- Filoviral diseases (including Ebola and Marburg)
- Middle East Respiratory Syndrome Coronavirus (MERS-CoV)
- Other highly pathogenic coronaviral diseases (such as Severe Acute Respiratory Syndrome, (SARS))
- Nipah and related henipaviral diseases
- Rift Valley Fever (RVF)
- Severe Fever with Thrombocytopenia Syndrome (SFTS)
- Zika

(The order of diseases on this list does not denote any ranking of priority.)
Other areas of substantial output

Other pathogens were considered & a wide range of additional relevant R&D initiatives encouraged

1. Emerging flaviviruses (such as Kyasanur Forest Disease or Usutu);
2. Emerging Bunyaviruses (such as Oropouche);
3. Emerging Alphaviruses (such as Chikungunya & Mayaro virus);
4. Rickettsia;
5. Plague;
6. Hantaviral diseases;
7. Chandipura virus disease.

• Cross-cutting R&D to address multiple diseases
• One-Health approach
• Anti-microbial resistance
A robust methodology was needed

Reporting lacked detail… Unclear how criteria were developed… Potential sources of bias and mitigations are not reported. The publication was not peer-reviewed and it is unclear if any other review took place… Delphi scoring was limited to one round. Did not meet all of the key communicable disease facets. 95% confidence intervals used to aid discussion of discrepancies in scoring.
Timeline
Activities undertaken to-date

May 2015 – WHO international consultation on Blueprint

December 2015 – WHO informal consultation on priority diseases

Early 2016 – Blueprint team develops methodology outline

May 2016 – SAG reviews methodology outline

Summer / Autumn 2016 – Detailed methodology developed

December 2016 – Informal consultation reviews & validates methodology

January 2017 – Annual review of list of priority diseases
Overview of the prioritization process

All possible diseases & pathogens → List of contenders for prioritization → Prioritized list of diseases & pathogens

- Landscape analysis
- Delphi process
- Triaging list of diseases to be considered
- Ranking the diseases
- Assessing confidence in the prioritized list
- Ranking the long list of diseases & pathogens
- Promoting the prioritized list
- Post-prioritization activities

New disease
- Decision instrument
- Emergency prioritization exercise

Routine reviews

19 September 2017 | R&D Blueprint – prioritization of diseases
**Decision instrument for new diseases**

WHO becomes aware of a novel public health threat relevant to the R&D Blueprint.

**Has the pathogen or disease (in current form) already been reviewed by a prioritization exercise?**

- **Y:**
  - Has something changed?
    - **Y:**
      - **Is there a substantial disease or pathogen programme at WHO?**
        - **N:** Report to the programme
        - **Y:**
          - **Either disease & pathogen characterization data or...**

- **N:**
  - **Review past decisions:**
    - **N:**
      - **Either disease & pathogen characterization data or...**
    - **Y:**
      - **Is the disease highly transmissible?**

**Is medical countermeasure available or ineffective?**

- **Y:**
  - **Is the disease causing high morbidity or frequently causing high morbidity?**

- **Y:**
  - **Is there a risk of spillover across the human-animal interface?**

- **Y:**
  - **Is the disease demonstrating unusual patterns, arising rapidly, or otherwise pose a risk to other nations?**

- **Y:**
  - **Is the disease having a significant societal impact?**

**For factors which may be relevant when considering these questions see Prioritization Criteria (Part I Section E)**

- **Y:**
  - **Are local resources likely to cope?**

- **N:**
  - **Convene a sub-group of the Prioritization Committee to run an emergency prioritization to determine provisional status**

- **N:**
  - **"Don't know" to any**

- **N:**
  - **"Yes" to any**

- **N:**
  - **"No" to all**

- **No further action required**

19 September 2017 | R&D Blueprint – prioritization of diseases
Methodology for Prioritizing Severe Emerging Diseases for Research and Development

Background

At the request of its 194 Member States in May 2015, the World Health Organization (WHO) convened a broad coalition of experts to develop an R&D Blueprint for Action to Prevent Epidemics. This methodology is based on an expert review of the most advanced products that can be used to deal with emerging and re-emerging diseases, and for which no, or insufficient, preventive and curative solutions exist. The expert review was guided by the following principles:

1. Ensuring evidence-based analysis and thorough prioritization processes.
2. Developing evidence-based guidelines for the evaluation of diagnostics, therapeutics, and vaccines.
3. Identifying gaps in regulatory and ethical pathways.
4. Identifying the best global strategies to foster rapid and coordinated disease outbreak response.

Methodology

The methodology was defined by the principles outlined above. The World Health Organization (WHO) convened an expert panel to evaluate the burden of emerging and re-emerging diseases. The methodology was designed to prioritize diseases based on scientific evidence and public health impact. The panel reviewed a list of candidate diseases and identified those with the highest potential impact on global health. The methodology was designed to be flexible and adaptable to changing circumstances.

1. An annual prioritization exercise to review and update the list of prioritized diseases and pathogens.
2. A separate process for dealing with new diseases or pathogens, including those that present a new threat to global health.
3. Regular reviews to ensure that the methodology remains relevant and effective.

The methodology was reviewed by an expert panel of global health leaders and endorsed by the World Health Assembly in May 2015. The methodology is designed to be flexible and adaptable to changing circumstances.
Prioritization criteria
Factors used to prioritize diseases

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Weights</th>
</tr>
</thead>
<tbody>
<tr>
<td>Human transmissibility</td>
<td>32%</td>
</tr>
<tr>
<td>Medical countermeasures</td>
<td>21.90%</td>
</tr>
<tr>
<td>Severity</td>
<td>14.65%</td>
</tr>
<tr>
<td>Human/animal interface</td>
<td>9.42%</td>
</tr>
<tr>
<td>Other contributing factors</td>
<td>9.42%</td>
</tr>
<tr>
<td>Public health context of the affected area</td>
<td>6.13%</td>
</tr>
<tr>
<td>Potential social impacts</td>
<td>4.18%</td>
</tr>
<tr>
<td>Evolutionary potential</td>
<td>2.28%</td>
</tr>
</tbody>
</table>
Prioritization Committee

Regionally & gender diverse experts in:

- Microbiology of severe pathogens
- Clinical management of severe infections
- Epidemiology
- Public health policy
- Animal health
- Anthropology
- Bioethics
- Biological weapons
Relative scoring
Indicative results

A) Final ranking by using the geometric average

B) Final ranking by using the arithmetic average

C) Final ranking by using Smart Vaccines
Confidence indicators

- Other studies
- Discordance intervals
- Multi-scenario sensitivity analysis
  - Removal of weightings
  - Suppression of highly weighted criteria
  - Changing weight of criteria (All +20% & +50%)
- Repetition with another scoring tool
Conclusions

• WHO developed its own methodology to prioritize diseases of relevance to Blueprint
• Built upon best practice
• Corrects earlier methodological shortcomings
• Balances need for repeatable methodology with expert input
• Fully publicly available
• Process to update methodology (next update 2018)
• Robust confidence in results produced