



**World Health  
Organization**

# **2018 Annual Review of Diseases Prioritized under the Research and Development Blueprint**

## **Informal Consultation**

6-7 February 2018  
Geneva, Switzerland

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## **Meeting Report**

The meeting was organized under the WHO R&D Blueprint, which aims to reduce the time between declaration of a public health emergency and the availability of effective diagnostic tests, vaccines, antivirals and other treatments that can save lives and avert a public health crisis <http://www.who.int/csr/research-and-development/en/>



**R&D Blueprint**

Powering research  
to prevent epidemics



## Executive summary

On 6-7 February 2018, the World Health Organization held an informal consultation in Geneva, Switzerland, to review the list of priority diseases for the WHO R&D Blueprint. The R&D Blueprint focuses on severe emerging diseases with potential to generate a public health emergency, and for which insufficient or no preventive and curative solutions exist. A list of diseases that most readily meet these criteria and for which additional research and development is urgently required was agreed at an international consultation held in November 2015<sup>1</sup> and updated following a second consultation in January 2017.<sup>2</sup>

To review the list of priority diseases, the February 2018 meeting brought together experts in: microbiology of severe diseases, including virology, bacteriology and mycology; clinical management of severe infections; epidemiology, in particular during health emergencies; public health policy, including emergency response; animal health, including veterinarians expert in zoonoses from both livestock and wildlife; and anthropologists; as well as experts from defence or security sectors familiar with biological weapons. These experts made use of a tailored prioritization methodology developed by WHO and validated at an informal consultation in November 2016.<sup>3</sup> The methodology uses the Delphi technique, questionnaires, multi-criteria decision analysis, and expert review to identify relevant diseases.

The 2018 annual review determined that given their potential to cause a public health emergency and the absence of efficacious drugs and/or vaccines, there is an urgent need for accelerated research and development for:<sup>4</sup>

- Crimean-Congo Hemorrhagic Fever (CCHF)
- Ebola Viral Disease and Marburg Viral Disease
- Lassa Fever
- Middle East respiratory syndrome coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS)
- Nipah and henipaviral diseases
- Rift Valley Fever (RVF)
- Zika disease
- Disease X

Other diseases were considered during the review including: Arenaviral hemorrhagic fevers other than Lassa Fever; Chikungunya; highly pathogenic coronaviral diseases other than MERS and SARS; emergent non-polio enteroviruses (including EV71, D68); and Severe Fever with Thrombocytopenia Syndrome (SFTS). These diseases pose major public health risks and further research and development is needed, including surveillance and diagnostics. They should be watched carefully and considered again at the next annual review. Efforts in the interim to understand and mitigate them are encouraged.

<sup>1</sup> <http://www.who.int/medicines/ebola-treatment/WHO-list-of-top-emerging-diseases/en/>

<sup>2</sup> <http://www.who.int/blueprint/priority-diseases/en/>

<sup>3</sup> [http://www.who.int/csr/research-and-development/documents/prioritizing\\_diseases\\_progress/en/](http://www.who.int/csr/research-and-development/documents/prioritizing_diseases_progress/en/)

<sup>4</sup> The order of diseases on this list does not denote any ranking of priority.



## Introduction

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. The R&D Blueprint presents options to reduce the time lag between the identification of a nascent outbreak and approval of the most advanced products that can be used to save lives and stop larger crises. It focuses on severe emerging diseases with potential to generate a public health emergency, and for which no, or insufficient, preventive and curative solutions exist.

Activities under the R&D Blueprint are organized into three approaches. The second approach focuses on accelerating research and development processes. It includes work to assess epidemic threat and define a list of priority pathogens.

As an interim measure, an informal consultation was convened by WHO in December 2015 where a panel of scientists and public health experts compiled an initial list of diseases.<sup>5</sup> In light of technical developments, increased understanding of disease, or as a result of real world events, including subsequent public health emergencies, it is necessary to regularly review the list of priority diseases. This consultation was the first such review and the first use of a more robust methodology for compiling a list.

## Disease prioritization methodology

In order to ensure the list of diseases prioritized under the R&D Blueprint is as accurate as possible, WHO has developed a comprehensive methodology. This is based upon established best practice and practical national experiences in compiling similar lists. The resulting methodology also specifically addressed criticism of earlier attempts to prioritize diseases.

The general approach and key prioritization criteria (Annex A) to be used in the prioritization process were identified at the December 2015 consultation<sup>6</sup>. These were subsequently expanded by WHO and an outline of the eventual methodology was presented to, and validated by, the R&D Blueprints Scientific Advisory Group (SAG) in May 2016.

Following input from the SAG, the methodology was further developed through: the inclusion of specific disease scenarios: a series of sub-criteria to explore different factors that could affect the relevance of a disease to R&D Blueprint objectives; and a semi-quantitative weighting of the prioritization criteria. WHO also developed the tools for Multi-Criteria Decision Analysis (MCDA) through a custom implementation of an Analytic Hierarchy Process (AHP), developed in collaboration with field leaders in these tools. This was then supplemented by online questionnaires to gather data from participants.

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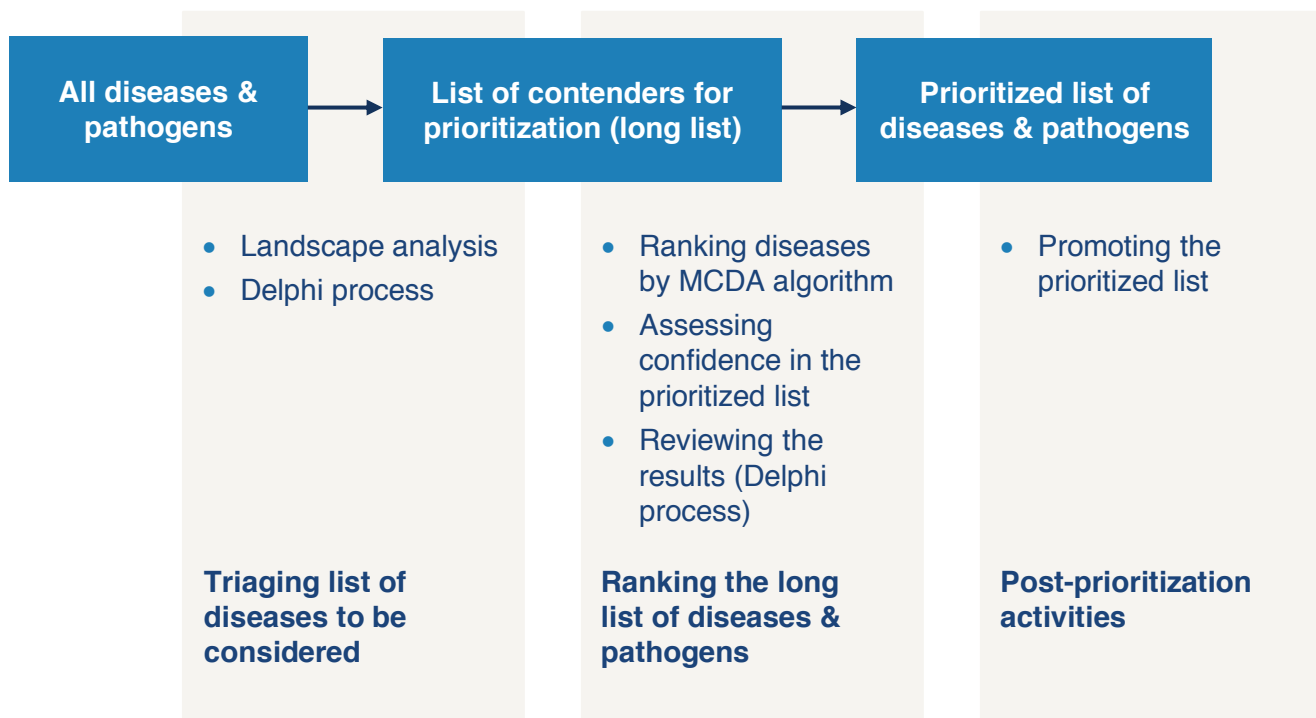
<sup>5</sup> <http://www.who.int/medicines/ebola-treatment/WHO-list-of-top-emerging-diseases/en/>

<sup>6</sup> <http://www.who.int/csr/research-and-development/meeting-report-prioritization.pdf?ua=1>

The entire methodology, its supporting models and attendant tools were reviewed at a dedicated consultation held in Geneva, Switzerland in November 2016.<sup>7</sup> The meeting validated a general approach, endorsing a system of annual reviews, biennial methodology reviews, supplemented as necessary with emergency reviews (Figure 1). The annual reviews use a combination of rounds of the Delphi technique, questionnaires and MCDA to review and update the R&D Blueprint's priority list of diseases. Following their revision in light of feedback, insights and recommendations received at the meeting, the tools and models were subsequently validated via a silence procedure in January 2017. The resulting methodology was published online.<sup>8</sup>

After its first full implementation, WHO carried out an assessment of the prioritization methodology.<sup>9</sup> This assessment demonstrated: (a) the ranking produced was robust across different sensitivity scenarios; (b) similar group ranking was generated using three different approaches; and (c) the criterion “availability of medical countermeasures” had very little impact on the final ranking despite a high weight. As a result, the prioritization criteria and sub-criteria were updated. Furthermore, to address possible biases, WHO developed a more comprehensive procedure for input from regional offices and expanded the range of experts proposing diseases for inclusion and participating in the annual review. The updated methodology will undergo a comprehensive review later in 2018.

**FIGURE 1: Overview of the annual prioritization exercise**



<sup>7</sup> [http://www.who.int/csr/research-and-development/documents/prioritizing\\_diseases\\_progress/en/](http://www.who.int/csr/research-and-development/documents/prioritizing_diseases_progress/en/)

<sup>8</sup> <http://www.who.int/csr/research-and-development/RDBlueprint-PrioritizationTool-19Feb2017.pdf?ua=1>

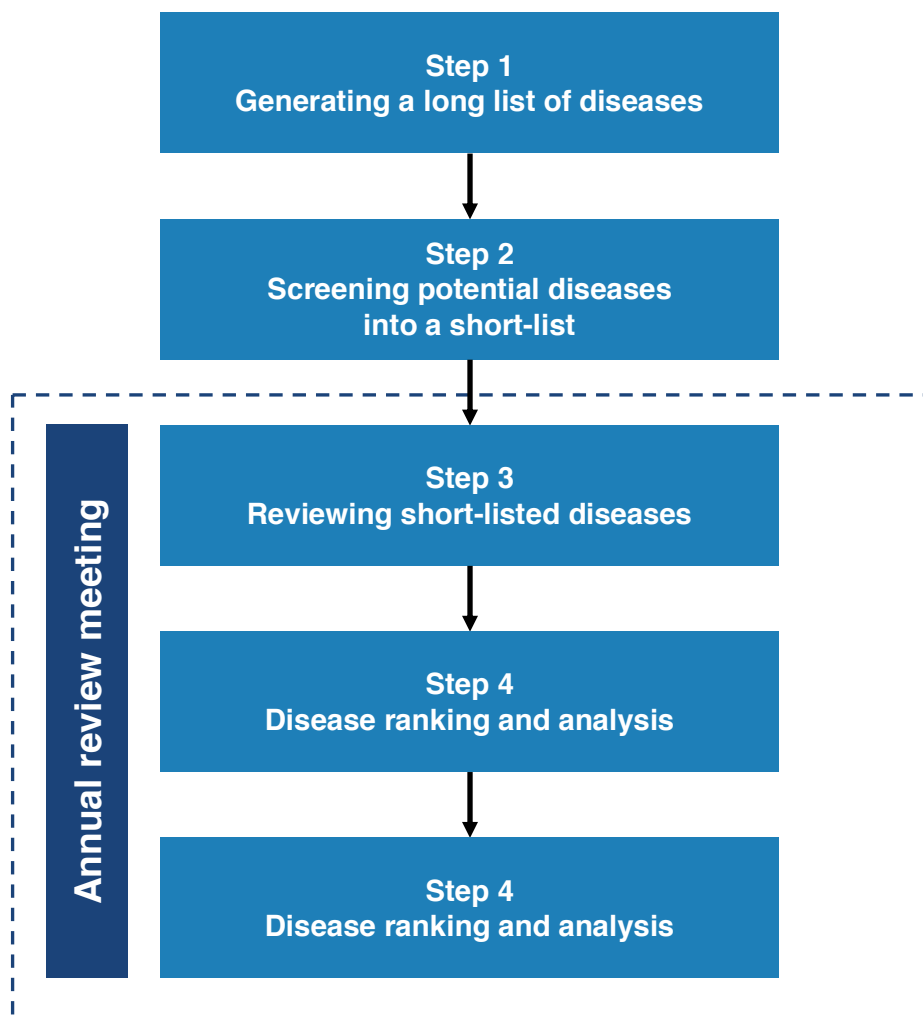
<sup>9</sup> Publication pending

## Updating the list of priority diseases

In accordance with the published methodology and the findings of the assessment of its implementation, the February 2018 meeting brought together experts in: microbiology of severe diseases, including virology, bacteriology and mycology; clinical management of severe infections; epidemiology, in particular during health emergencies; public health policy, including emergency response; animal health, including veterinarians expert in zoonoses from both livestock and wildlife; anthropologists, bioethicists, and other relevant social sciences; as well as experts from defence or security sectors familiar with biological weapons. Collectively, these experts formed the Prioritization Committee (Annex B). Some, or all of them, might also be called on prior to the next annual review should an emergency prioritization exercise be warranted.

The 2018 annual review followed a five step process (Figure 2). The first two steps were carried out prior to the 2018 review meeting and the remaining three steps formed the basis of the work of the meeting (Annex C).

**FIGURE 2: The five-step annual process to review diseases prioritized under the WHO R&D Blueprint**





## Generating a long list of diseases

According to the published methodology, diseases on the preceding list from January 2017, as well as any that had been forwarded via the Blueprint's tool for addressing new diseases were to be automatically included in the comprehensive review to be conducted at the annual meeting. As a result, the nine diseases on the 2017 priority list were automatically included on the shortlist. No disease had been identified using the Blueprint's tool for new diseases.

Over 90 experts were asked to propose additional diseases to be considered in the 2018 review. These experts included those proposed by each of the WHO regional offices as well as all the experts involved in the prioritization process since 2015. Between August and December 2017, each expert was requested to propose two diseases relevant to the Blueprint. Expert proposals were compiled into a long-list by 13 December 2017:

1. Aflatoxicosis
2. Alphaviruses
3. Anthrax
4. Candida auris
5. Chandipura virus
6. Chikungunya
7. Cholera
8. Endemic Kaposi Syndrome
9. Kyasanur Forest disease
10. Leishmaniasis
11. Mayaro
12. Necrotising cellulitis/fasciitis
13. Emerging non-Polio enteroviruses
14. Oropouche
15. Plague
16. Sindbis
17. South American Hemorrhagic Fevers
18. Usutu
19. West Nile Virus disease
20. Zoonotic brucellosis

## Screening potential diseases into a short-list

In order to identify which diseases from the long-list should be considered alongside the nine forwarded from the 2017 review, the same external experts (those recommended by the WHO regional offices and those to have participated in past prioritization exercises) were asked to identify up to 5 of the proposed diseases they felt were most relevant to the scope of the Blueprint.

The top scoring diseases were: Chikungunya, Plague, Non-polio / emerging enteroviruses, Cholera, West Nile Virus and Leishmaniasis. The short-list for the 2018 annual review included:

- Arenaviral hemorrhagic fevers (including Lassa Fever)
- Chikungunya
- Cholera
- Crimean-Congo Hemorrhagic Fever
- Filoviral diseases (including Ebola and Marburg)
- Leishmaniasis
- MERS-CoV
- Other highly pathogenic coronaviral diseases (such as SARS)
- Nipah and related henipaviral diseases
- Emerging non-polio enteroviruses
- Plague
- Rift Valley Fever
- Severe Fever with Thrombocytopenia Syndrome
- West Nile Virus
- Zika



In advance of the annual review meeting a background document was compiled summarising each of these diseases. Contributions for this document were produced by disease specific experts involved in the prioritization process and a consultant commissioned by WHO. Information compiled for each disease covered its discovery, epidemiology, transmission, clinical course, as well as details of relevant surveillance and public health control measures.

## Reviewing short-list diseases

The review of the short list diseases had two components. Following concerns raised during the short-listing process, the list was reviewed for its relevance to the scope of the Blueprint. Each disease was then discussed in turn to highlight factors which might justify its inclusion in the priority list.

Participants were reminded that some diseases fell outside the scope of the blueprint, in particular if there were already major control initiatives, or extensive R&D pipelines, or existing funding streams, or established regulatory pathways. During the course of the meeting, it was determined that four of the short-listed diseases were outside the scope of the Blueprint: cholera was determined to have a major control initiative through which any research and development efforts might be more appropriately channelled; Leishmaniasis is already prioritised as a neglected tropical disease and any research and development efforts might be more appropriately channelled through this forum; via a closed ballot a simple majority and over two-third majority of participants determined West Nile Virus and plague respectively were outside of the scope of the Blueprint. As a result, these four diseases were removed from the short-list.

Each of the diseases on the short-list, including those ultimately deemed to be outside the scope of the Blueprint, was discussed in turn. Each was introduced by an expert. There were then opportunities to share insights, seek clarifications, or explore relevant unpublished data. During the debate on arenaviruses, a consensus was reached to single out Lassa Fever under the 2018 review. Lassa Fever had previously been used as an example of relevant arenavirus. The virus family was to be captured elsewhere in the report as warranting further research and development. The remaining diseases were passed into the scoring process.

## Disease ranking and analysis

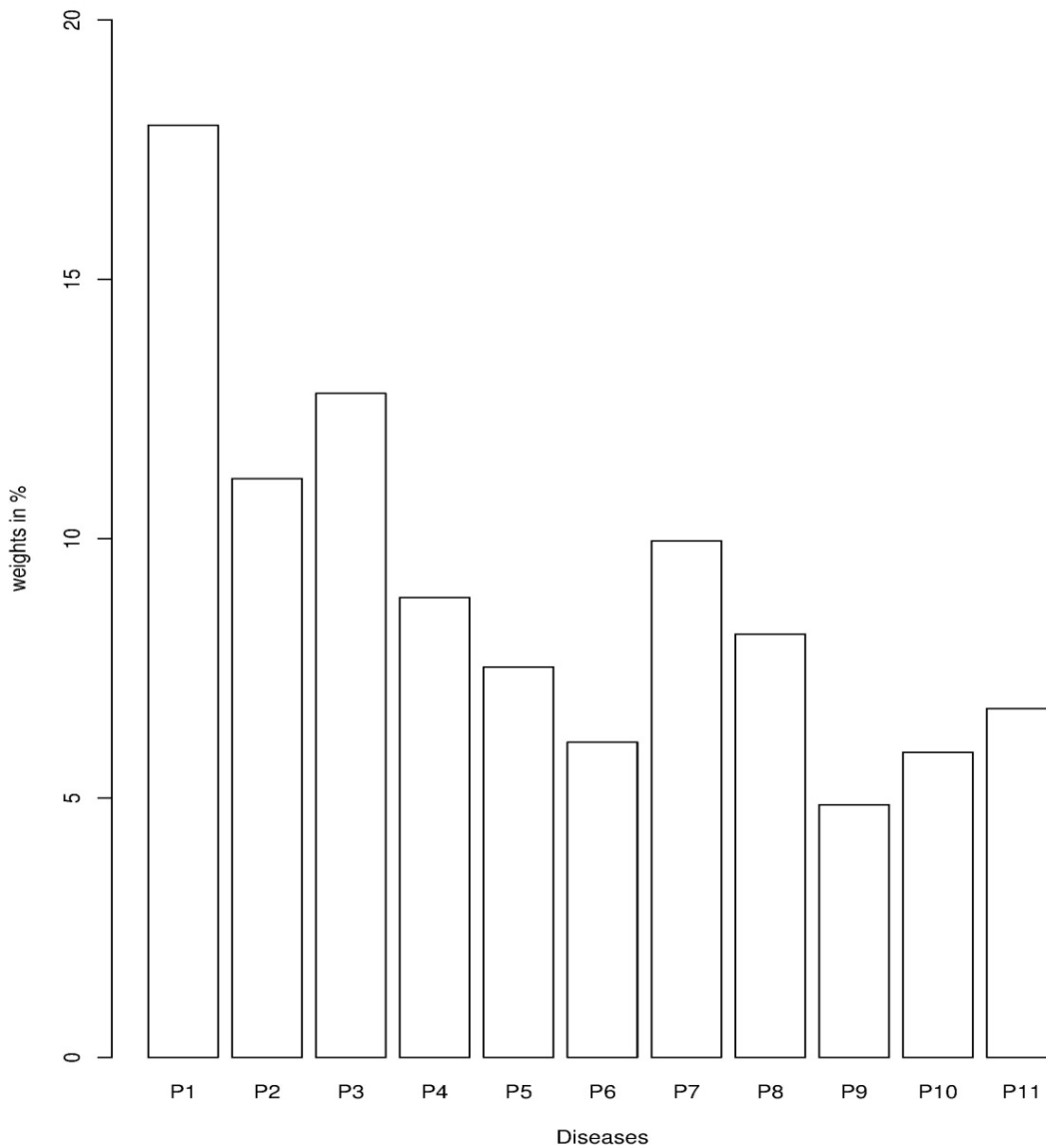
Participants used the online surveys tool developed by WHO to compare how the remaining short-listed diseases corresponded with 29 factors of 7 different criteria contained in the prioritization methodology. The results were analysed using the AHP MCDA approach detailed in the prioritization methodology. WHO presented a summary overview of the results. This included, for each criterion, a representation of the score for each disease broken down by individual sub-criteria.

During a discussion of the results, participants identified ways in which they fit expectations (for example high scores in for human-to-human transition for those diseases known to spread rapidly). They also discussed unexpected results, where scores were higher or lower than expected.

The Prioritization Committee then examined overall scores for each of the diseases (Figure 3).



**FIGURE 3: Overall scores for diseases analysed using MCDA during the 2018 annual prioritization review showing discordance intervals**



Participants noted that these results could not be used directly to rank the short-listed diseases. The results were used, however, to identify a sub-set of the four lowest scoring diseases (Chikungunya, Rift Valley Fever, non-Polio enteroviruses, and Severe Fever with Thrombocytopenia Syndrome). Participants agreed that additional consideration was warranted as to whether these diseases should be prioritised under the Blueprint.



## Generating the list of priority diseases

During a review of the four lowest scoring diseases, participants made cases for both including them and removing them from the priority list. A consensus quickly emerged that Rift Valley Fever should remain on the list of priority diseases. Despite a thorough exchange of views amongst participants, there was no consensus as to what should be done with the other three diseases. There was broad recognition that they were relevant to the scope of the Blueprint and that additional research and development was necessary but there was disagreement as to whether they should be prioritised to the same degree as the other diseases being considered. As a result, an agreement was reached they should be captured in the report of the meeting in such a manner as to stress the importance of continued research and development but without including them in the priority list. It was noted that one of these diseases, Severe Fever with Thrombocytopenia Syndrome, had been included on the list in 2017 and experts which had been present during that review recalled that it had been the lowest scoring disease to have made the list. Equally a second disease, Chikungunya, was also considered during the last review and was the highest scoring disease not to make the priority list. Several participants present at both 2017 and 2018 reviews suggested that had such a category been used last year both of these diseases would likely have been in it already. The third disease, emerging non-Polio enteroviruses, had not been on the long-list of diseases considered in 2017.

As a final step, participants discussed the most appropriate terminology to capture the diseases reviewed. Some minor changes were made to terms used previously. There was agreement that the list should contain diseases (as opposed to pathogens). There was also an effort to focus on specific diseases, rather than families of pathogens. For example, the entry 'filoviral diseases (including Ebola and Marburg)' was changed to read 'Ebola Viral Disease and Marburg Disease'. There was also agreement to group closely related diseases. For example, separate entries for MERS and SARS were combined into a single entry.

## The 2018 list of diseases to be prioritized under the R&D Blueprint

The 2018 annual review determined that given their potential to cause a public health emergency and the absence of efficacious drugs and/or vaccines, there is an urgent need for accelerated research and development for:<sup>10</sup>

- Crimean-Congo Hemorrhagic Fever
- Ebola Viral Disease and Marburg Viral Disease
- Lassa Fever
- MERS and SARS
- Nipah and henipaviral diseases
- Rift Valley Fever
- Zika disease
- Disease X

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<sup>10</sup> The order of diseases on this list does not denote any ranking of priority.



A number of additional diseases were discussed and considered for inclusion in the priority list, including: Arenaviral hemorrhagic fevers other than Lassa Fever; Chikungunya; highly pathogenic coronaviral diseases other than MERS and SARS; emergent non-polio enteroviruses (including EV71, D68); and Severe Fever with Thrombocytopenia Syndrome. These diseases pose major public health risks and further research and development is needed, including surveillance and diagnostics. They should be watched carefully and considered again at the next annual review. Efforts in the interim to understand and mitigate them are encouraged.

Although not included on the list of diseases to be considered at the meeting, monkeypox and leptospirosis were discussed, and experts stressed the risks they pose. There was agreement on the need for: rapid evaluation of available potential countermeasures; the establishment of more comprehensive surveillance and diagnostics; and accelerated research and development and public health action.

Several diseases were determined to be outside of the current scope of the Blueprint: dengue, yellow fever, HIV/AIDS, tuberculosis, malaria, influenza causing severe human disease, smallpox, cholera, leishmaniosis, West Nile Virus and plague. These diseases continue to pose major public health problems and further research and development is needed through existing major disease control initiatives, extensive research and development pipelines, existing funding streams, or established regulatory pathways for improved interventions. In particular, the meeting heard of a need for improved diagnostics and vaccines for pneumonic plague and additional support for more effective therapeutics against leishmaniosis.

**The meeting also agreed:**

- For many of the diseases discussed, as well as many other diseases with the potential to cause a public health emergency, there is a need for better diagnostics.
- Existing drugs and vaccines need further improvement for several of the diseases considered but not included in the priority list.
- Any type of pathogen could be prioritised under the Blueprint, not only viruses.
- Necessary research includes basic/fundamental and characterization research as well as epidemiological, entomological or multidisciplinary studies, or further elucidation of transmission routes, as well as social science research.
- The value, where possible, of developing countermeasures for multiple diseases or for families of pathogens.

The impact of environmental issues on diseases with the potential to cause public health emergencies was discussed. This may need to be considered as part of future reviews.

The importance of the diseases discussed was considered for special populations, such as refugees, internally displaced populations, and victims of disasters.

The value of a One Health approach was stressed, including a parallel prioritization processes for animal health. Such an effort would support research and development to prevent and control animal diseases minimising spill-over and enhancing food security. The possible utility of animal vaccines for preventing public health emergencies was also noted.

Although anti-microbial resistance is addressed through specific international initiatives the possibility was not excluded that in the future, a resistant pathogen might emerge and appropriately be prioritized.



## Annex A: Prioritization criteria

The 2015 WHO Consultation for Prioritization of Pathogens identified nine prioritization criteria. These were revised and reordered during the 2016 methodology review. One criteria was removed following the assessments of its first use. The current prioritization criteria are:

- Human transmission;
- Severity or case fatality rate;
- The human/animal interface;
- Other factors (including the pathogens geographic range, shared epidemiological and/or genotypic characteristics with pathogens that pose an epidemic threat, the absence of robust protective immunity, a high risk of occupational exposure, or connections with biological weapons programmes);
- Public health context of the affected area;
- Potential societal impacts;
- Evolutionary potential.



## Annex B: The 2018 Prioritization Committee

### **Chantal Reusken**

Erasmus University  
Netherlands

### **Joshua Obasanya**

Nigeria Centre for Disease Control  
Nigeria

### **Stefano Messori**

World Organization for Animal Health  
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### **Pedro Vasconcelos**

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Brazil

### **Annie Wilkinson**

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### **Devendra Mourya**

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### **Gail Carson**

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### **David Brett-Major**

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### **Albert Icksang Ko**

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### **Yazdan Yazdanpanah**

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### **Peter Horby**

Oxford University  
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### **Miles Carroll**

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United Kingdom



**Inger Damon**

Centers for Disease Control and Prevention  
USA

**Jimmy Whitworth**

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United Kingdom

**Hilary Marston**

National Institute of Allergy and Infectious  
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USA

**Cathy Roth**

Department for International Development  
UK

**Supaporn Wacharapluesadee**

Chulalongkorn University  
Thailand

**Pierre Rollin**

Centers for Disease Control and Prevention  
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**Melissa Willis**

Biomedical Advanced Research and  
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USA

**Alfonso Rodriguez-Morales**

Fundación Cenit  
Colombia

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**Observers**

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**Farah Al-Shorbaji**

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**Sameera Suri**

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**Massinissa Si Mehand**

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**Piers Millett**

Consultant  
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**Pierre Gsell**

WHO/FWC  
Switzerland



## Annex C: Agenda for the WHO R&D Blueprint Annual Review of Priority Diseases

World Health Organization, Salle C, Geneva, 6-7 February 2018

### 6 February 2018

**Chair of the morning sessions: Miles Carroll**

**8.30-9.00 Welcome Coffee**

**9.00-9.45 Opening session**

Welcome remarks: WHO

Introduction to the R&D Blueprint (WHO): Ana Maria Henao Restrepo

**9.45-10.30 Session 1: Establishing the short list of diseases**

Overview of meeting objectives and of the prioritization process: Piers Millett

Discussion to ensure the short list of diseases meets the scope of the Blueprint

10.30-11.00 Coffee Break

**11.00-12.30 Session 2: Discussion of diseases in the short list**

12.30-13.30 Lunch

**Chair of the afternoon sessions: Cathy Roth**

**13.30-15.00 Session 3: Discussion of diseases in the short list (Cont.)**

15.00-15.30 Coffee break

**15.30-17.00 Session 4: Completion of the prioritization survey**

### 7 February 2018

**Chair of the morning sessions: Peter Daszak**

**8.30-9.00 Welcome Coffee**

**09.00-09.15 Opening by Peter Salama, Deputy Director General, WHO/WHE**

**09.15-10.30 Session 5: Presentation of survey results and sensitivity analysis**

10.30-11.00 Coffee break

**11.00-12.30 Session 6: Discussion of discordant results**

12.30-13.30 Lunch

**Chair of the afternoon sessions: Inger Damon**

**13.30-15.00 Session 7: Establishing the final list of priority diseases**

15.00- 15.30 Coffee Break

**15.30-17.00 Closing Session**

Review of exercise and feedback to improve the process

Closing remarks and next steps (WHO)

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