

Research and development for potentially epidemic diseases

A blueprint for research and development preparedness and rapid research response

Report by the Secretariat

1. In January 2017, the Executive Board, at its 140th session, considered an earlier version of this report.¹ Following the Board's discussions,² and in order to provide details of new developments, paragraphs 2, 12, 17, 19 and 25 have been updated.
2. In June 2015, in response to resolution EBSS3.R1 (2015) on Ebola,³ the Secretariat started work on the development of a blueprint for research and development preparedness and response (the R&D Blueprint) for potentially epidemic diseases. The overall goal of the R&D Blueprint is to reduce delays between the identification of an outbreak and the deployment of effective medical interventions to save lives and minimize socioeconomic disruption. Areas under the Blueprint include product research and development for diagnostics, vaccines, therapeutics and vector control tools, as well as necessary and relevant research in social sciences and epidemiology.
3. The Blueprint focuses on the following areas of work: identifying priority infectious disease threats as well as gaps and priorities in research and development; improving collaboration between stakeholders; and promoting an enabling environment for the conduct of research and development during outbreaks. In addition, it aims to complement the Secretariat's efforts to foster research and development related to Type II and Type III diseases, and the specific research and development needs of developing countries in relation to Type I diseases, in line with the global strategy and plan of action on public health, innovation and intellectual property and the recommendations of the Consultative Expert Working Group on Research and Development: Financing and Coordination.⁴
4. The Blueprint was prepared with global experts from all relevant disciplines and under the guidance of an independent advisory group. The document and a description of its initial activities

¹ Document EB140/9.

² See the summary records of the Executive Board at its 140th session, second meeting, section 3, third meeting, section 3 and fourth meeting.

³ Operative paragraphs 31, 32, 33 and 34.

⁴ See documents A61/9 and A62/16, and A65/24, respectively.

were noted by the Sixty-ninth World Health Assembly in May 2016.¹ The following paragraphs provide an update on progress since then.

R&D ROAD MAPS FOR RESEARCH AND DEVELOPMENT TO ADDRESS POTENTIAL OUTBREAKS OF DISEASE DUE TO PRIORITY PATHOGENS

5. The epidemic of Ebola virus disease in West Africa in 2014–2016 and the current Zika virus outbreak have highlighted the importance of having a clear road map for research and development in place before such an event occurs in order rapidly to activate and coordinate research and development and disburse the necessary funds as soon as the need arises. To that end, the Secretariat has begun to elaborate research and development road maps for the 11 pathogens that were prioritized through an expert consultation (Geneva, 8 and 9 December 2015) as likely to cause public health emergencies in the near future. (The list will be reviewed periodically; see paragraph 16.) By defining the needed medical products, delineating actions and assigning roles, these road maps will save time and facilitate the activation and coordination of research and development.

6. Following a consultation with experts (Geneva, 10 and 11 December 2015), the Secretariat completed and published an R&D road map for the Middle East respiratory syndrome coronavirus (MERS-CoV).² The virus has grown in global importance, causing illness and death across 27 countries, and has attracted significant interest from the research and development community, with efforts to design diagnostic, preventive and therapeutic products for this pathogen and the disease it causes gaining momentum.

7. The road map for MERS-CoV research and product development is based on four strategic goals:

- establishment of a surveillance network of coronavirus laboratories as an early warning system to identify circulating species and strains in animal populations, the causes of new outbreaks of coronavirus disease in human populations, and emerging strains in all populations;
- a better understanding of the pathogenesis MERS-CoV infection, the natural history of the disease it causes, and its veterinary and human epidemiology;
- development, manufacture, testing, licensure and use of improved diagnostics, preventives and therapeutics that enable the interruption of transmission between humans and from dromedary camels to humans;
- establishment by the global donor community of a direct path for manufacturers from preclinical proof-of-concept studies to post-licensing procurement of MERS-CoV products, through initiation of a public health financial model for supporting research and product development on emerging pathogens prioritized in WHO's Blueprint process.

¹ Documents A69/29 and WHA69/2016/REC/3, summary records of Committee A, fifth meeting and seventh meeting, section 1.

² Available at <http://www.who.int/csr/research-and-development/mers-roadmap-may-2016.pdf?ua=1> (accessed 11 October 2016).

R&D BLUEPRINT ACTIVITIES ON ZIKA VIRUS

8. Following the declaration on 1 February 2016 that the recent cluster of microcephaly cases and other neurological disorders reported in Brazil, following a similar cluster in French Polynesia in 2014, constituted a Public Health Emergency of International Concern, the Secretariat used the Blueprint framework to trigger rapidly a series of research and development actions. Initial activities included the mapping of existing research and product development for Zika virus infection. On the basis of the findings, the Secretariat convened 130 experts from 27 countries for a consultation (Geneva, 7–9 March 2016) in order to identify gaps in knowledge and agree on a plan for accelerating product development.

9. As a result of the consultation, the Secretariat prioritized research and development activities for diagnostics, vaccines and vector-control measures. In April 2016, WHO and UNICEF jointly published target product profiles for diagnostic tests for Zika virus infection, specifying the desired features for these assays to facilitate development and manufacture.¹

10. The Emergency Use Assessment and Listing procedure established during the Ebola virus disease outbreak to accelerate quality assessments of new products was opened to candidate in vitro diagnostics for Zika virus infection in early February 2016. To date, more than 20 such diagnostic tests have been submitted for WHO's assessment and listing, and one has been listed as appropriate for international procurement. It is expected that more tests will be submitted for assessment to regulatory agencies and WHO in the coming months as many diagnostic companies are developing new products. The Secretariat will continue to use existing regulatory and laboratory capacity to maximum advantage in order to facilitate the Emergency Use Assessment and Listing procedure.

11. In June 2016, the Secretariat convened regulators and vaccine developers for an initial discussion of regulatory considerations of Zika virus vaccines (Geneva, 6 and 7 June 2016). A target product profile for vaccines aimed at protecting against Zika virus infection and associated congenital syndrome vaccines for emergency use as an outbreak response was issued in July 2016.²

12. WHO and the Wellcome Trust jointly organized a meeting (London, 5–7 October 2016) to discuss how best to capitalize on the commonalities of mosquito-borne viral diseases in order to define common research approaches for the development of products to combat these diseases. The latest information on Zika vaccine development was reviewed at a consultation co-organized by WHO and the United States National Institutes of Health (Bethesda, Maryland, United States of America, 10 and 11 January 2017).

PLATFORM TECHNOLOGIES

13. In the absence of market-driven research and development, platforms for sharing technologies have the potential to strengthen research and development efforts, including those in low- and middle-income countries. In October 2015, the Secretariat launched a public consultation on ideas for potential platforms to support development and production of health technologies for the infectious diseases with epidemic potential prioritized by WHO. The main requirement was that these solutions

¹ Available at <http://www.who.int/csr/research-and-development/zika-tpp.pdf> (accessed 11 October 2016).

² Available at http://www.who.int/csr/research-and-development/who_zika_vaccine_tpp.pdf (accessed 11 October 2016).

be sufficiently flexible to enable expedited development and manufacture of candidate products for clinical trials (in months rather than years).

14. The initiative was open to international organizations, government agencies, non-profit organizations, for-profit companies and academic institutions. The scope of health products considered included vaccines, therapeutics (medicines and blood products), diagnostics and enabling technologies. The platforms had to apply to three or more pathogens prioritized by WHO.

15. Candidate products emerging from this process should be affordable for use in populations at risk. Proposals that resulted in a strategic geographical distribution of platform production sites were especially welcome. Additionally, a goal of the consultation was the encouragement of the submission of proposals that include significant participation by entities in developing countries.

16. By the closing date of 5 February 2016, 35 proposals had been received. After an initial screening and a technical workshop led by an ad-hoc advisory group of experts, six most-promising proposals were identified: three vaccine platforms, one for diagnostics, one for immunotherapy and one covering all product streams. The six proposals were presented to potential funders and interested Member States during a second technical workshop (Geneva, 21 July 2016).

REVISION OF EPIDEMIC THREATS AND THE LIST OF PATHOGENS PRIORITIZED BY WHO

17. Consultations were held in December 2016 to fine-tune the prioritization methodology. Based on the revised tool, the WHO's list of pathogens for priority research and development was reviewed and updated on 24 and 25 January 2017. The 2017 list of pathogens contains the infectious agents for the following diseases: Lassa fever and other severe arenaviral haemorrhagic fevers; Crimean-Congo haemorrhagic fever; filoviral diseases (including Ebola virus disease and Marburg haemorrhagic fever); Middle East respiratory syndrome (MERS); other highly pathogenic coronaviral diseases (such as severe acute respiratory syndrome (SARS)); Nipah and related henipaviral diseases; Rift Valley Fever; severe fever with thrombocytopenia syndrome; Zika virus disease; and any new disease "X" identified by the decision instrument. Experts highlighted that Chikungunya virus disease continues to warrant further research and development. It is of note that the list of R&D Blueprint priority diseases only includes pathogens for which there are no medical countermeasures available, and excludes pandemic influenza.

STAKEHOLDER COORDINATION

18. The Secretariat is leading efforts to better coordinate research and development activities during epidemics by establishing frameworks for research oversight and management at the national level and global mechanisms for fruitful collaboration. To that end, it has completed the mapping of all relevant global stakeholders by their areas or diseases of interest and current participation in collaborative networks. A database of research preparedness resources has been created and will be integrated into WHO's Global Observatory on Health Research and Development. A guidance document on good participatory practices in a research context as related to prioritized diseases is being finalized.

19. In addition, a set of principles for a global collaboration framework were discussed at a high-level meeting being jointly organized by WHO, the Wellcome Trust and Chatham House, the Royal Institute of International Affairs (London, 10 November 2016). A template for a coordination framework to streamline global stakeholder collaboration is being drafted and will be discussed during the first meeting of the Blueprint Global Coordination Mechanism in London on March 28, 2017.

20. Since 2015, the Secretariat has participated as an observer in the Global Research Collaboration for Infectious Disease Preparedness. This global network brings together organizations that fund research in order to facilitate an effective research response within 48 hours of a significant outbreak of a new or re-emerging infectious disease with pandemic potential. This collaboration allows WHO to inform network members of priority research and development activities during an outbreak.

21. In September 2016, WHO signed a memorandum of understanding with the Coalition for Epidemic Preparedness Innovations, a new public–private partnership that aims to finance and coordinate the proactive and expedited development of new vaccines to prevent and contain infectious disease epidemics. The memorandum of understanding provides the basis for collaborative and mutually strengthening efforts within the broad scope of the R&D Blueprint.

SHARING OF DATA AND SAMPLES

22. Sharing of data and samples is crucial for informed research and development efforts and for ensuring equitable access to potential new products, especially during epidemics. Agreements that foster such sharing, include scientists from countries at risk and facilitate governance of multiparty collaborations are effective tools.

23. Following an initial expert consultation on data sharing (Geneva, 1 and 2 September 2015), the Secretariat has advanced the discussion on this issue through the R&D Blueprint. It is also developing global norms for sharing data and results, and elaborating mechanisms for collaboration and data sharing during public health emergencies.

24. The Secretariat has initiated a process to reach consensus on principles for open-access repositories of biological samples (bio-banks), including the development of a virtual resource linking national bio-banks through an information-sharing platform. The principles for a shared system of governance and decision-making are currently being elaborated.

25. A Material Transfer Agreement capacity-building tool has been prepared in order to inform negotiations at country level on sharing biological samples. WHO in collaboration with the Institut Pasteur held a consultation on 16 December 2016 on options to deal with key issues relating to material transfer agreements in the context of a public health emergency. The aim is to finalize such a capacity-building tool during the second quarter of 2017 through consultations with various stakeholders, with subsequent conversion into an electronic web-based application to support partners engaging in negotiations of such agreements.

REGULATORY CAPACITY

26. Building capacity to design and conduct clinical trials for vaccines and therapeutics for emerging disease threats in developing countries is part of the Blueprint's plans to create enabling environments for research and development during emergencies and to ensure that national actors and scientists in countries at risk can function as equal partners in international efforts. The Secretariat has outlined a clear set of steps to inform exchanges on trial designs for prioritized diseases, and to assess each design in terms of methodological robustness and feasibility. The next step will be the development of generic protocols for the prioritized diseases to ensure consistent approaches among all stakeholders in a given research and development effort.

27. During the outbreak of Ebola virus disease, WHO outlined regulatory pathways for product evaluation in public health emergencies and supported joint clinical trial reviews of candidate products. WHO's Expert Committee on Biological Standardization, at its recent meeting (Geneva, 17–21 October 2016), considered preliminary guidelines on the quality, safety and efficacy evaluation of Ebola virus disease vaccines. Further efforts to strengthen national, regulatory and ethics bodies to respond to public health emergencies are underway.

ACTION BY THE HEALTH ASSEMBLY

28. The Health Assembly is invited to note the report.

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