WHO R&D Roadmap
Rift Valley Fever
Rapid Scoping Document

Highlights Summary - Core Experts Meeting
Thursday and Friday, 9-10 May 2019
OIE HQ, Paris, France
Rift Valley Fever Rapid Scoping Document Meeting
9-10 May 2011, OIE HQ, Paris, France

Background

The WHO R&D Blueprint is a global strategy and preparedness plan that allows the rapid activation of R&D activities during epidemics. Its aim is to fast-track the availability of effective tests, vaccines and medicines that can be used to save lives and avert large scale crisis. The R&D Blueprint works on the basis of a list of identified priority diseases. These are diseases that pose a public health risk because of their epidemic potential and for which there are no, or insufficient, countermeasures. For each of those diseases an R&D roadmap is developed, as a concise, comprehensive document laying down a vision and strategic goals to accelerated R&D efforts and align them around well-identified public health priorities. The R&D roadmaps encompass basic research through to late-stage development, licensure and early use of products. They will serve as a collaborative framework to underpin strategic goals and research priority areas so as to accelerate the development of diagnostics, therapeutics and vaccines to prevent and control severe emerging diseases due to priority pathogens. Where relevant, target product profiles (TPPs) and generic protocols are also developed through broad and open consultations with leading experts and other stakeholders.

Rift Valley Fever (RFV) has been identified as one the WHO priority diseases for which accelerated basic and applied research as well as product development would be beneficial. The RFV roadmap should describe a clear statement of desired goal and the specific pathway for reaching it, while clearly outlining RFV R&D targets, pathways, priorities and timeframes. However, before moving forward with the formal road mapping process, the R&D Blueprint has been asked to develop a rapid scoping document (in particular gaps to be addressed by the R&D roadmap and research priorities for earlier implementation).

Public Health England (PHE - now replaced by the UK Health Security Agency and Office for Health Improvement and Disparities - UKHSA) and WHO are co-leading this exercise, in collaboration with the World Organization for Animal Health (OIE) and the Food and Agricultural Organization of the UN (FAO), under the tripartite FAO-OIE-WHO Memorandum of Understanding (MoU) regarding cooperation to combat health risks at the animal/human ecosystems interface in the context of the “One Health Approach”. RFV (with a few other agents) is one of the Blueprint priority pathogens that fits, and is best addressed through, the One Health approach, due to the environmental, animal and human determinants of its epidemiology and impact, as well as its diverse effects on livelihood, economy (domestic markets and international trade) and human health. Given the nature of the disease, developing the R&D roadmap as a joint strategy - with appropriate participation from agencies with responsibility for human and animal health and the environment - was deemed the best way forward to build support to effective national or regional research plans and response capabilities and to minimize the risk of outbreaks and socio-economic impact of disease.¹

Between 9 and 10 May 2019, an informal meeting of core experts from the four organizations (FAO², OIE, PHE now UKHSA and WHO), with the participation of Wellcome Trust and DFID³, was convened at the OIE headquarters in Paris with the goal of discussing and developing a first draft of the rapid scoping of essential information (including the identification of key priorities) for RVF. The draft resulted from the analysis of all information and data identified and compiled through the baseline situation analysis (BSA), a systematic approach to map and assess where the critical gaps and advances in ongoing research and product-development initiatives are. This first draft document will be further discussed and agreed with a taskforce of internationally recognized subject-matter experts (SMEs), including scientists from the most affected countries, with specific expertise in RVF and in one or more R&D areas.

² Representatives from FAO were not able to attend the meeting.
³ Representatives from DFID were not able to attend the meeting.
The Paris meeting served as a key opportunity to start obtaining insights on the status of science; share information, experiences, and practices; review and evaluate the need, development status, and future prospects for RVF medical countermeasures; agree on the roadmap vision indicating the way forward; build consensus on preliminary strategic goals; determine an outline for research priorities; and agree on the next steps (timelines, taskforces, meetings and venues), while generating strong buy-in and commitment for the formal R&D roadmap development.

**Highlights**

**Overall scope**

- RVF could be the perfect example of a tripartite partnership to move from One Health as a concept (“a collaborative and comprehensive way to address, when relevant, animal and public health problems”) to a concrete project; more and more stakeholders, including donors, recognize the importance of such an approach and it is an additional asset to countries;
- RFV can be the next success story – following the steps of Rabies and zoonotic tuberculosis;
- RFV has been chosen by the Coalition for Epidemic Preparedness Initiative (CEPI) as one of their priority disease for human vaccine development; one of the objectives of the rapid scoping document exercise is to give CEPI direction for the development of their request for proposals (RFPs);
- R&D landscaping, priority setting, and guidance tools generated ahead of crises play a critical role in shaping and accelerating research during outbreaks;
- Coordinating and facilitating research during outbreaks will in turn bring critical experience in informing contributions to response plans and adjusting priorities;
- Supporting sustainable efforts towards capacity building in countries at risk is an absolute component of the R&D activities;
- Building on the early post-outbreak momentum is imperative to support the development of regional and national plans;
- Important to understand how to address and run the parallel themes of human and animal health; are these to be considered two sub-sets in the roadmap? There should be a common vision with separate goals and strategies for animal and human – roles and responsibilities need to be defined amongst the 4 organizations engaged in this exercise;
- End point of the roadmap is to prevent and control outbreaks - roadmaps are designed to provide directions for product development so that medical countermeasures (MCMs) are available in the affected countries in an affordable way and in a timely manner;
- The R&D Blueprint is coordinating and overseeing the roadmapping process, but this is done in collaboration with partners;
- The roadmap is looking not only to technical tools but also to best strategies to control the disease; the roadmap includes an implementation phase; together with the roadmap as a tool, also critical are the national research plan and the ownership countries have and the business case that gets generated;
- When research is integrated into the response the benefit is tangible and discussions on the ethics of doing research during outbreaks subsequently die down;
- Operational research is part of the roadmap – when we define the research priority areas; WHO is now working with GOARN on this very aspect;

**Vaccines**

- Vaccines section of the BSA: example from Rabies: good progress comes when a single strategy “One Health” is managed, the message was quite clear for the entire community; this is possible with clear roles and responsibilities amongst the different partner organizations. Focusing on the more attractive single strategy (i.e. save human lives) may not be the best way forward for a disease like RVF;
- Today, it is very difficult to have a vision of what should be done to decrease the burden of disease in humans; today, for example we do not know whether we need to vaccinate wild animals; we do not know what would be the effectiveness of a vaccine in the field; we do not know enough about the epidemiology of the disease; we need to allow a number of different approaches in the roadmap and progress in parallel on different fronts;
Regarding vaccines, it may be good to have a combination vaccine: one that can be combined with a vaccine that is used on a high priority basis (e.g. pestis in sheep or Brucella);

A clear aim is critical: eradicate RVF or prevent cases in humans? In the second instance the strategy will be to target animals for example;

Need to understand what will be the driver to convince farmers to vaccinate their animals – would the farmers perceived the same risks and the impact of economic loss of livestock? If one human is infected, that means we have between 500 to 1000 animal infected – RVF is first and foremost an animal disease with an impact on human health, with an impact on farmers, hence local/national economies;

From the BSA: human vaccine: A need for a new vaccine? For what target population? Those in contact with potentially infected animals/animal products? Or all age groups in the area of an outbreak? Various novel vaccine candidates evaluated in rodent models. Promising results with: ChAdOx1-GnGc and Sindbis replicon expressing Gc, Gn and Nsm; no data in NHP model, no clinical data to date;

Anything anti-mosquito vaccine? In this case there are many mosquitos that can amplify and transmit the disease, therefore a vaccine against mosquito is complicated; virus resistance in the mosquitos is for some of the mosquitos, not all;

**Disease epidemiology**

- A better understanding is needed on how much RVF there is across Africa (endemicity, epidemics and cycles) and what proportion of domestic animals is affected regularly, whether there are areas where RVF is a much bigger problem than in other areas, and how much economic loss;
- Human are used as sentinels to detect disease in animal;
- The starting point is to estimate the burden and the cost of the disease;
- The RVF “belt” is due to El Nino, domestic and localized flooding and their meteorological cycles;
- Important to understand RVF ecology and geography: what, where and when. There is a need for an integrated One Health strategy from forecasting to outbreak response, more collaboration at the human-animal interface and strong buy in from affected countries;
- For RVF there are still numerous unanswered questions (e.g. What is the true RVF burden? How is the disease transmitted? How to detect outbreaks earlier? In animals/humans; How can outbreaks be better prevented? Controlled? Can effective mosquito control measures be implemented? Is there a way to improve the treatment of affected individuals?);
- The Holstein cow is highly susceptible to RVF compared to other traditional breeds that can much better resist – need to balance the benefits in terms of resistance;
- Some local breeds of pigs in Africa are resistant – genetically engineering a breed to make it resistant? Ethical aspect and acceptability of this procedures will certainly be an issue;

**Treatments**

- In terms of treatment: ribavirin was used in Saudi Arabia – however almost all the people treated developed severe neurological sequelae;

**Diagnostics**

- Concern raised on how to manage the surveillance data, by bringing diagnostics to the field; and how the information would reach the national level and the decision-makers;
- An issue to be considered will be the cost of collecting and sending samples – for the animal side;
- Diagnostics need a concept of use to give them value;
- From the BSA: Innate immunity seems to play a major role in protection; very limited data available on the adaptive responses to RVFV infection in humans and very limited immunology data available to support the feasibility of a human vaccine and guide its development. Diagnostics gaps: (1) how to provide access to rapid testing in rural areas?; (2) adequate performance of available assays?; (3) DIVA for veterinary vaccines;
Cross cutting

- Various tools most likely needed: Sustained efforts towards early detection and control of RVF outbreaks; Novel technologies for better access to diagnostics and/or reliably forecasting outbreaks; Promoting local communities as first line of defence; Developing effective mosquito control measures (feasible?); Improved veterinary vaccines with safety for pregnant animals, DIVA capacity, low cost, needle-free...; A human vaccine to protect veterinarians, slaughterhouse workers and farmers; Stimulators of innate immunity may offer a novel approach for prophylaxis; Access to treatment for those with severe disease. Novel therapies do not necessarily need to be virus-specific;
- Need to think how the social sciences (that need to be carried out for the different MCMs) will be incorporated into the roadmap; then there is the business case side and the economic side that should be built into the roadmap as well and elevated;

OIE resources and plans

- OIE is planning on organizing a meeting later this year on Innovative Approaches in Emergencies Management and RVF will be one of the topic covered;
- OIE standards on RVF: Chapter 8.15. Infection with Rift Valley fever virus; and Chapter 3.1.18. Rift Valley fever (infection with Rift Valley fever virus); OIE promotes standards for implementing diagnosis, the basis for the appropriate diagnostics tests and criteria that should be followed for vaccines to be registered and licensed and requirement for commercial production; OIE provides principles to developers; there is a similar procedure to the WHO PQ for diagnostics kits validation but not for vaccines; OIE does not specifically promote the use of commercial tests;
- OIE is meeting with NASA to discuss forecasting;
- OIE does not have any vaccine bank for RVF vaccine; a proposal was discussed in 2016 to revise the status of the RVF vaccines in preparation of a possible institution of a RVF vaccine bank; OIE recently published a strategic paper on vaccines bank;
## Agenda

**Thursday 9 May 2019**

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<th>Time</th>
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<tr>
<td><strong>SESSION 1: INTRODUCTIONS AND OVERVIEWS</strong></td>
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<tr>
<td>09:30 – 09:45</td>
<td>Opening Remarks</td>
<td>Monique Eloit, OIE DG</td>
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<tr>
<td>09:45 – 10:00</td>
<td>Welcome and Introductions of Core Experts</td>
<td>Tim Brooks</td>
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<td>10:00 – 10:15</td>
<td>One Health Approach Context (FAO, OIE and WHO)</td>
<td>Stefano Messori</td>
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<td>10:15 – 10:45</td>
<td>Overview of the WHO R&amp;D Blueprint</td>
<td>Marie-Pierre Preziosi</td>
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<td>10:45 -11:00</td>
<td>Discussion</td>
<td>All</td>
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<tr>
<td>11:00-11:30</td>
<td><strong>Coffee &amp; Tea</strong></td>
<td>Pierre Formenty &amp; Mamoudou Djingarey</td>
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<tr>
<td>11:30 – 12:00</td>
<td>WHO Progress status on Rift Valley Fever activities</td>
<td>Stefano Messori</td>
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<tr>
<td>12:00-12:15</td>
<td>OIE Standards on Rift Valley Fever</td>
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<td>12:15 – 13:00</td>
<td>Overview of the WHO Baseline Situation Analysis on RVF, focusing on gaps and research priorities</td>
<td>Martine Denis</td>
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<td>13:00 – 14:00</td>
<td><strong>Lunch</strong></td>
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<tr>
<td>14:00 - 14:45</td>
<td>Outline of the RVF roadmap and Draft RVF vaccine TPP</td>
<td>Amanda Semper &amp; Marie-Pierre Preziosi</td>
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<td><strong>SESSION 2: RVF SCOPING DOCUMENT</strong></td>
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<td>15:00 – 16:00</td>
<td>Status of RVF medical counter measures and vector control (and working session)</td>
<td>Tim Brooks</td>
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<td>16:00 – 16:15</td>
<td><strong>COFFEE and TEA</strong></td>
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<tr>
<td>16:15 – 18:00</td>
<td>Status of RVF medical counter measures (and working session) cont’d</td>
<td>Pierre Formenty</td>
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<td>18:00</td>
<td><strong>End of Day</strong></td>
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Friday 10 May 2019

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<tr>
<td>09:00 – 09:30</td>
<td>Recap from Day 1</td>
<td>Amanda Semper, Pierre Formenty &amp; Mamoudou Djingarey</td>
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<tr>
<td>09:30 – 10:30</td>
<td>Finalization of the rapid scoping document</td>
<td>Marie-Pierre Preziosi</td>
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<tr>
<td>10:30 – 10:45</td>
<td>COFFEE and TEA</td>
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<tr>
<td>10:45 – 11:30</td>
<td>Finalization of the rapid scoping document (cont’d)</td>
<td>Tim Brooks</td>
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SESSION 3: NEXT STEPS – FORMAL R&D ROADMAP DEVELOPMENT

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<tr>
<td>11:30 – 13:00</td>
<td>Roadmap process and design: ‘animal’ vs. ‘human’ centred objectives, List of experts, Taskforce, Timelines and Venues</td>
<td>Tim Brooks, Stefano Messori and Marie-Pierre Preziosi</td>
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<td>13:00</td>
<td>END OF THE MEETING</td>
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Provisional List of participants

CDC – US Centres for Disease Control and Prevention
- Stuart Nichol*

DFID – UK Department for International Development
- Cathy Roth*

FAO – Food and Agricultural Organization of the United Nations
- Ahmed Eldriissi*
- Ylma Makonnen*

OIE – World Organisation for Animal Health
- Daniel Donachie
- Glen Gifford
- Keith Hamilton*
- Stefano Messori
- Gregorio Torres

PHE – Public Health England now replaced by the UK Health Security Agency and Office for Health Improvement and Disparities - UKHSA)
- Tim Brooks
- Amanda Semper

Wellcome Trust
- Josie Golding

WHO – World Health Organization
- Virginia Benassi
- Martine Denis
- Mamoudou Harouna Djingarey*
- Pierre Formenty
- Marie-Pierre Preziosi

*unable to attend