WHO R&D Blueprint

novel Coronavirus

Human-Animal-Environment Interface Research

R&D Blueprint

Powering research
to prevent epidemics

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INTRODUCTION

As part of WHO's response to the COVID-19 pandemic, the WHO R&D Blueprint, in collaboration with the Global Research Collaboration for Infectious Disease Preparedness and Response (GLOPID-R), developed a global research roadmap to accelerate research that can contribute to containing the spread of this epidemic and to facilitate that those affected receive optimal care.

The research priorities identified at the Human-Animal-Environment Interface are listed in the document and include:

- Investigation of possible animal host ranges (including wildlife, farmed wildlife, livestock, companion animals, stray animals, pests/vermin), investigation of the potential transmission pathways between susceptible animal(s) and to humans and vice versa;
- Confirmation of the role of candidate species through virus persistence, amplification and excretion studies. Continued assessment of the role of known susceptible hosts in amplifying and maintaining the virus;
- Studies on candidate animal-human interactions, including the persistence of the virus in the environment of this interface. Continued investigation of viral persistence under a variety of environmental conditions including food processing packing and shipment modalities.

Scientific projects aiming to initiate important scientific and technical work or to facilitate on-going research of interest and identified as priority are currently supported.

RESEARCH PRIORITIES

Research priorities identified by the Working Group:

Priority Research Area 1: Investigate the origin of SARS-CoV-2 and potential ('natural' or induced by contact with humans) **animal reservoir and intermediate host** through surveillance/investigation strategies which consider:
- Serological surveillance is more likely to detect SARS-CoV-2 in animals and can guide more specific targeted virological surveillance (see also priority research area 11);
- Continued sampling of wildlife, incl. bats, and complement the banks of samples for investigation during future emergencies;
- Targeting surveillance to selected locations may improve likelihood of detection e.g. markets/farms where wildlife and other animal species (including domestic animals/livestock) are gathered, keeping in mind that animals sampled might have been infected by humans;
- Other types of animals (free ranging, feral, vermin) found in proximity to infected farms or markets (and other relevant locations) should also be considered in investigations.

Priority Research Area 2: Identify the animal reservoir and intermediate host through surveillance/investigation strategies which consider:
- Continued testing archived animal samples (serum, feces etc.) collected from recent surveillance projects in Asia;
- Continued use of biodiversity and host-phylogenetic diversity data sets to model targeting of sampling to increase likelihood of identifying range of susceptible species and potential reservoirs across Asia, Middle East and Europe.

Priority Research Area 3: investigate SARS-CoV-2 host range **and possible role of companion animals** in the epidemiology of human disease:
- Host range determination, receptor specificity/distribution in different species;
- Cell line infections and animal experimental infections to understand transmission;
- Assessment of the potential role of companion animals in the epidemiology of the disease in countries affected with human cases.

Priority Research Area 4: Investigate transmission pathways
- Investigation of the potential transmission pathways between susceptible animal(s) and to humans and vice versa;
- Continued assessment of the role of known susceptible hosts in amplifying and maintaining the virus;
- Continued investigation of viral persistence under a variety of environmental conditions including packing and shipment modalities.

Priority Research Area 5: Consolidate baseline data to inform prevention and control strategies
- Better understanding of the dynamics around illegal wildlife capture, transport, and trading, and current prevention strategies, considering:
  - Social/marketing studies on consumer demand *vis-à-vis* wild animals meat and products;
  - Existing international standards, agreements, legislation, and guidance around wildlife trade, markets etc;
  - Research to support implementation of new guidelines and standards being developed regarding animals and the environment;
  - Relevant stakeholders – NGOs, IOs, national government, public, traders, expand new partnerships.

Priority Research Area 6: Assess drivers of high-risk practices

- Further analysis of Emerging Infectious Diseases hotspots and ecological / anthropological drivers or risk factors;
- Social and economic drivers of legal and illegal activities;
- Value chains leading to human animal/wildlife/environmental exposure.

Priority Research Area 7: Develop strategies to improve preparedness and reduce risk of spill over events
- Effective coordinated surveillance approach(es) for early detection and reporting in places of animal-human interface;
- Risk communication strategies avoiding stigmatisation and other unintended consequences;
- Social and behavioural change (SBC) practices to improve hygiene practices along the food chain;
- SBC practices to implement realistic and feasible strategies including markets improvements to encourage a high level of compliance with hygienic and other universally adopted standards at traditional markets;
- Determination of optimal strategies to manage wild animal farming and to stop illegal transportation and trading of captured animals.

Priority Research Area 8: Analyse behavioural risks
- Identify communities with high levels of exposure to bats and other key animals if identified as risk factors - analyse risk behaviours;
- Test samples from wildlife and people in these communities for serological evidence of SARS-COV-2 and other CoV spillover.

Priority Research Area 9: Improve knowledge surrounding the wildlife trade
- Characterise the wildlife trade value chain globally and regionally and how it is linked with hotspots of Emerging Infectious Diseases;

- Policy/social research to regulate wildlife trading – innovation (cameras, drones etc), collaboration with social scientists, law enforcement/ behaviour/demographic patterns;
- Study of economic impact of removing (captured and/or farmed) wildlife from markets and market closures;
- Analyses of the social impacts and economic analyses of different degrees of limiting wildlife trade for food: 1) complete ban; 2) partial ban (select species); 3) regulating and testing animals; 4) promoting only farmed wildlife as a source of food.

Priority Research Area 10: Improve knowledge on wildlife trade operations
- Wildlife capture vs. production: Scenario analysis of whether or not farming wildlife reduces the risk of SARS-CoV-2 emergence, amplification and transmission as compared to wild caught wildlife;
- Wildlife consumption: Survey of public to assesses knowledge, attitudes, and practices around wildlife consumption, geographic variation, and changing consumer demographics to develop risk reduction strategies;
- Adjust research/risk communication existing in this area relating to other zoonotic diseases (e.g. zoonotic influenza, Nipah, SARS, neglected zoonosis, etc.) and the breeding, keeping, selling and consumption of livestock.

Priority Research Area 11: Diagnostics
Serology
- A fit for purpose serology test for use in different species as a powerful tool in surveillance for SARS-CoV-2 in animals (the utility of serology was demonstrated in SARS-CoV and Hendra virus investigations);
- Adaptation and validation of current SARS-CoV-2 serology test used in humans to animal systems.

RT-PCR
- Continued strengthening of RT-PCR platforms adapted to animal systems;
- Adaptation of RT-PCR tools need to be fit for purpose, e.g. for initial screening of animal surveillance samples, sensitivity will be more important than specificity, therefore for RT-PCR screening tools, primers which span the whole subgroup of SARS-related viruses can be used (with both SARS CoV and SARS CoV-2 as positive controls). RT-PCR which are more specific to SARS Cov2 could be used to differentiate viruses when samples are positive on screening.

Other tests
- Virus neutralization, pseudo particle VN, surrogate particle VN, and other tests may also be useful for detection in animal samples.

Currently, 13 research projects have been selected for support, which are summarized below.

SUPPORTED RESEARCH PROJECTS

INVESTIGATION IN ANIMAL POPULATIONS

Preliminary Assessment for New Wildlife SARS-CoV-2 Reservoir Establishment

Ecohealth Alliance, New York, USA, & Liberia, Côte d'Ivoire, Egypt, Jordan, Indonesia, Georgia

Objective: To improve understanding of the origin, spread and transmission of SARS-CoV-2 and the risk associated with the establishment of animal reservoirs, especially in a large variety of bats species from different part of the world

Activities:

- Serological testing of archived samples of dozens of species of bats from different part of the world (Liberia, Côte d'Ivoire, Egypt, Jordan, Indonesia and Georgia);
- Training of national partners on serological tests (surrogate virus neutralisation) and capacity building in countries.

References
Tan CW, Chia WN, Chen MI, Hu Z, Young BE, Tan YJ, Yi Y, Lye DC, Anderson DE, Wang LF. A SARS-CoV-2 surrogate virus neutralization test (sVNT) based on antibody-mediated blockage of ACE2-spike (RBD) protein-protein interaction.

Surveillance for spillover event and maintenance of SARS-COV-2 and other emergent virus in hematophagous bats population in Amazon Region.

PANAFTOSA, Rio de Janeiro - Brasil

Objective: To understand the risk of amplification and establishment of a reservoir of SARS-CoV-2 in blood-feeding bats in the Amazon.

Activities:

- Collection and sampling of vampire bats *(Desmodus rotundus)* in an area of high transmission of COVID-19 and frequent attack on humans;
- Molecular identification and virus isolation;
- Development of a guide for the surveillance of vampire bats for SARS-CoV-2.

SUSCEPTIBILITY OF ANIMALS & VIRUS EVOLUTION

Risk assessment for coronaviruses in domestic and captive animals in close contact with humans

ARC-Onderstepoort Veterinary Research (ARC-OVR), Onderstepoort, South Africa

Objective: To improve knowledge about the potential of recombination of SARS-CoV-like viruses from pools of different species and the risk for increased transmission to humans.

Activities:

- Experimental challenge of pigs and investigation of disease progression through RT-PCR;
- Investigation of the immune response of infected pigs generated using a transcriptomic approach;
- Estimation of the risk of potential SARS CoV-2 spread in animal populations with close interactions with humans; Identification of potential high risk areas in South Africa; monitoring of sentinel animals.

SARS-CoV-2 variation, from genotype to phenotype

Erasmus MC - Department of Viroscience. University Medical Center Rotterdam

Objective: : To improve our understanding of the evolution, spread and transmission of SARS-CoV-2 during the pandemic with a focus on the role of interspecies transmission events and possible establishment of new reservoirs of the virus in animals

Activities:

- Analyse of the genomic diversity of SARS-CoV-2 throughout the pandemic in the population as a whole, and particularly in animals. . Sample will be tested on in vitro and in vivo models that allow rapid characterization of novel variants in different animal models;
- Assessment of mutations to phenotypic changes affecting pathogenicity or transmissibility;
- Advices to Public Health Authorities on the potential consequences of genomic and phenotypic changes for zoonotic disease risk, potential for reservoir establishment, and possible impact of genetic changes on diagnostics, therapeutics, and vaccine development.

SARS-CoV-2 EvoZOOne / SARS-CoV2 evolution and zoonotic potential assessment.

ANSES Nancy Laboratory for Rabies and Wildlife, France

Objective: To assess the specificity of available serological tools for serological diagnostic in animals living closed to humans, explore the diversity of strains of coronavirus in circulation and describe their genetic characteristics, and test the susceptibility of certain of these animals species.

Activities:

- Focus is on cats, dogs, rodents (Cricetidae, Microtus, Arvicola, Ondatra, rabits) , Mustelidae (minks from all French farms, Weasel), birds (chicken, turkey, duck, fattened duck), foxes, and wild boars;
- Analysis Screening by Elisa (protein N), Positive confirmation with Luminex (proteins S1, S2, N, trimeric S and RBD) or seroneutralisation; qRT-PCR & Full genome characterization (NGS) on qRT-PCR positive samples;
- Cell culture models complement this study (cats, dogs, rabbits, poultry, pigs).
- Full and deep genome sequencing will be performed and eventual mutations or recombinations will be detected.

Requirements and consequences of SARS-CoV -2 infection in animals
Kansas State University, USA

Objective: To determine the expression pattern of host proteins involved in SARS-CoV-2 infection, monitor mutations, assess the susceptibility of deer and cattle to SARS-CoV-2 and evaluate the spread and persistence of SARS-CoV-2 in the animal environment.

Activities:

- The co-expression of ACE2 and TMPRSS2 (necessary for efficient SARS-CoV-2 infection of cells) is investigated in respiratory and gastrointestinal tissues from young and old pigs, cattle, deer, dogs and cats using in situ hybridization and/or immunohistochemistry;

- A variety of permanent cell lines derived from livestock and wildlife species are infected at different MOIs and the development of mutations is determined by next generation sequencing;

- Deer and cattle are infected and the development of SARS-CoV-2 mutations is monitored;

- Analysis of the contamination of the immediate environment of infected animals.

VIRUS DETECTION

Canine olfaction for COVID-19 screening

Veterinary School of Maison Alfort, France, Faculté de Médecine, Beirut, Lebanon ; Dubai University, Emirates ; University of Buenos Aires, Argentina; University of Recife, Brazil; U.N.A.M., Mexico; University of Sonora, Mexico; Catholic University of Santiago, Chile; University of Adelaide, Australia; Liege and Gent Universities, Belgium; University of Windhoek, Namibia; Madrid University, Spain

Objective: Consolidation and extension of the dog-based screening program,

Activities:

- Increased number of dogs trained;
- Assessment of the efficiency of detection of infected persons in retirement houses and mass gathering environments
- Evaluation of possible interactions with chronic diseases and other respiratory viruses

BEHAVIOUR OF SARS-CoV-2 IN THE FOOD ENVIRONMENT

Persistence and particulate behavior of SARS-COV2 in environmental water matrices
ANSES, Laboratory for Hydrology – Nancy

Objective: To assess the persistence and particulate behavior of SARS-COV2, through in vitro research.

Activities:

- Quantification of SARS-CoV infectivity in water and water matrices through cell culture and Real-time RT-PCR and cell culture (conducted in BSL 3 laboratory);
- Analysis of physic-chemical characteristics in relation with the persistence of the virus. The presence of microbiological flora will also be addressed.

Development of an impedance based cell assay to quantify infectious particles of SARS-CoV-2
ANSES, Laboratory for Food Safety (Maisons-Alfort and Boulogne-sur-Mer), France

Objective: Development of a new method to quantify infectious particles of SARS-CoV-2 and evaluate virus persistence during food processing

Activities:

- Cellular impedance to detect infectious particles of SARS-CoV-2 in different cell lines is evaluated, by recording in real-time Cell Index with the xCELLigence system;
- Assessment of the correlation between infected cell impedance kinetic and quantity of virus;
- Application to the assessment of infectivity of SARS-CoV-2 in waters of different origins and food samples.

Investigating presence of SARS-CoV-2 in selected foods and food production environments using qPCR and whole virus genome sequencing: comparative analysis with globally available sequences to uncover phylogenetic relationships and potential transmission routes
UCD-Centre for Food Safety, University College Dublin, Ireland.

Objective: To explore the presence and genetic of SARS-CoV-2 in selected food matrices and in food processing environments

Activities:

- Detection in selected food (raw meat; selected vegetables and fruits) and in food processing environments (taps; door handles; refrigerator handles; smear samples from air conditioning units and other locations considered high-touch);
- Characterisation of positive samples comparative genome analysis

REDUCED RISKS DURING FOOD PROCESSING

COVID-19 in the WHO European Region and its impact on food safety in 15 Euro Countries
WHO EURO Regional Office

Objective: Development of a publication targeting policy-makers and food safety authorities in countries to illustrate the overall impact of the COVID-19 pandemic on food safety in EURO.

Activities:

- Review of existing literature on the impact of COVID-19 on food systems in general and food safety control systems in particular;

- Collection of examples from selected Member States through telephone interviews with food safety managers. Proposed countries: Central Asia (Tajikistan, Uzbekistan, Kyrgyzstan), Caucasus (Georgia, Azerbaijan), Balkan (Albania, Serbia, Bosnia & Herzegovina), East Europe (Ukraine, Republic of Moldova), EU (Denmark, Germany / Netherlands, Poland, Spain / Italy, Hungary

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Pilot project in Dakar market.
WHO AFRO Regional office

Objective: To reduce the risk of transmission of pathogens in traditional markets

Activities:

- information and awareness workshop for decision-makers and local authorities in charge of market;

- Establishment of a multisectoral committee for the Project (officially approved);

- Mapping of main markets in the Department of Dakar and selection of one pilot market;

- Survey among sellers and consumers on hygiene practices; Sampling and analysis of samples;

- Development and implementation of an Action Plan which includes i) awareness and educational materials adapted to local context, ii) food control repository , iii) development of communication material, iv) training on good practices for stakeholders (sellers, buyers, wholesalers and market administrators, control officers), v) Organization of awareness campaigns for consumers.

Improve preparedness and reduce risks of spillover events along the food value chain.
PANAFTOSA, Rio de Janeiro - Brasil

Objective: To reduce the risk of spillover events along the food value chain in the Americas

Activities:
- To improve risk-based inspection in food producing plants (FPP):
    - Development of an inspection guide to assess the risks associated with COVID-19 in FPP.
    - Online training of risk-based inspection in FPP including COVID-19 tracking
    - Deployment of food inspection blitzes to assess the presence of COVID-19 in FPP.
- To strength capacities of food traditional markets of Latin America countries (LAC):
    - development of a diagnostic tool assessing capacity/infrastructure and legislative framework of traditional markets in LAC in relation with risks associated with COVID-19
    - Assessment report and recommendation to prevent spillovers in traditional food markets in LAC.
    - Development of a guide on biosafety in traditional markets to spillovers.
- To develop a risk communication plan for emerging food safety zoonotic incidents: