World Health Organization

WHO R&D Blueprint

COVID-19

WHO COVID-19 at the Human-Animal Interface Pillar

Achievements

February 2020 – April 2021

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R&DBlueprint

Powering research
to prevent epidemics

Contents

1. Overall Summary

As part of WHO's response to the COVID-19 pandemic, the WHO Research and Development (R&D) Blueprint was activated to improve coordination between scientists and global health professionals, accelerate the research and development process, and develop new norms and standards to learn from and improve upon the global response. In collaboration with the Global Research Collaboration for Infectious Disease Preparedness and Response, in February 2020 the WHO R&D Blueprint developed a global research roadmap to accelerate research that can contribute to containing the spread of this epidemic and to facilitate receipt of optimal care by those affected. Animal and environmental research on the virus origin, and management measures at the human-animal interface (HAI) is one of the pillars of the WHO COVID-19 R&D Blueprint, which is supported by a group of international experts convened by WHO in the COVID-19 AHI R&D Expert Group (see Annex 1).

2. Aim

Three primary objectives for HAI research were identified:

> Objective 1: to identify animal source and route of transmission (hosts, any evidence of continued spillover to humans and transmission between animals and humans).
>
> Objective 2: to improve understanding of socioeconomic and behavioural risk factors for spillover and transmission between animals and humans (identify the risks linked to trade and consumption of potentially infected animal species and the communities or occupational groups more at risk across different interfaces).
>
> Objective 3: To design and test suitable risk reduction strategies at the human-animal environment interface, accordingly (limit infection in high risk areas and for at risk populations and the public).

The global research roadmap also includes detailed knowledge gaps and research priorities identified by the HAI pillar. The WHO COVID-19 HAI R&D Expert Group worked in concert with the WHO Secretariat, the OIE Ad-hoc group on COVID-19 and the human-animal -ecosystem interface, the OIE advisory group for animal health surveillance during the COVID-19 events, the FAO experts and other COVID-19 research pillars and working groups, with the purpose of facilitating coordination and collaboration of research and innovation, and boosting synergy in the field of human-animal interface during the response to the COVID-19 pandemic.

Research priorities and questions

Progress made on the research areas described in the global research roadmap were reviewed in July 2020 and, taking into consideration new knowledge gaps identified during the course of the pandemic, the COVID-HAI R&D Expert Group reviewed the need for research needs, which are included in the following areas:

- Identification of animal host(s) regionally and any evidence of continued spillover to humans
- Improved understanding of socioeconomic and behavioural risk factors for spillover
- Design and test of sustainable risk reduction strategies:

These needs are covered by the 11 priority research areas identified.

1. Investigate the origin of SARS-CoV-2 and potential 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 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.

- **<u>Priority Research Area 5:</u> 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 including new partnerships.

- **<u>Priority Research Area 6:</u> 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.

- **<u>Priority Research Area 7:</u> Develop strategies to improve preparedness and reduce risk of spillover 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 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.

- **<u>Priority Research Area 8:</u> 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.

- **<u>Priority Research Area 9:</u> 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 assess 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: Diagnostic**

  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.

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HAI research projects according to the R&D Blueprint roadmap objectives

Many studies have been initiated by members of the WHO COVID-19 HAI R&D Expert Group, in line with the objectives for HAI research identified in the R&D Blueprint global research roadmap and the related research priorities areas and questions. The tables below present summaries of these projects, including the types of study, objectives, leading institution and related publications so far. It is by no means a comprehensive list of all the studies the members of the group have contributed to. It encompasses most of the studies that relate to the objectives set out by the group when this list was assembled, and members contributed to it until February 2021.

Priority Research Area 1: Investigate the origin of SARS-CoV-2 and potential animal reservoir and intermediate host

Project	Institution	Objectives	Link to publication
Serological investigation of SARS-CoV-2 related coronavirus infection in animals, South East Asia/Thailand	Duke-NUS Medical School, Singapore & Thai Red Cross- Health Science Centre, Thailand	To detect infection with SARS-CoV-2 related Coronaviruses in various animal species through serological survey of archive and fresh sample of animals (bats, pangolins, monkeys, cat, dog, goat, cow, rodents, deer, slow loris, gibbon, civet, otter, tiger, snake)	https://www.nature.com/articles/s41587-020-0631-zhttps://www.nature.com/articles/s41467-021-21240-1?fbclid=IwAR2-OB_e_eVnQOSsKMjb9Mptv-0a2RRyUy7THUXLQeoOcreAu7KffmRpNcc

Project	Institution	Objectives	Link to publication
Molecular and serological investigation of SARS-CoV-2-related coronavirus in humans and animals in Thailand from archived samples before COVID-19 pandemic	Chulalongkorn University, Thailand	Investigation on circulation SARS-CoV-like virus in South east Asia before the pandemic through serological testing and molecular analysis of archived biological samples of bats, macaques and humans with unexplained fever or pneumonia collected in 6 locations in Thailand between 2016 to 2019	https://onehealthoutlook.biomedcentral.com/track/pdf/10.1186/s42522-021-00039-6.pdf
WHO-convened Global Study of Origins of SARS-CoV-2: China Part. Joint WHO-China Study	WHO-led Joint International Team	Early source tracing through review of morbidity surveillance and mortality data, viral genome analysis, testing of any available stored samples for SARS-CoV-2, and through retrospective search for potential cases in China in 2019, leading up to the Wuhan market outbreak.	https://www.who.int/publications/i/item/who-convened-global-study-of-origins-of-sars-cov-2-china-part
WHO-convened Global Study of Origins of SARS-CoV-2: China Part. Joint WHO-China Study	WHO-led Joint International Team	To detect infection with SARS- related COVs in various animal species through serological survey of wildlife, livestock and poultry from 31 provinces in China, including bats in Hubei Province.	https://www.who.int/publications/i/item/who-convened-global-study-of-origins-of-sars-cov-2-china-part
WHO-convened Global Study of Origins of SARS-CoV-2: China Part. Joint WHO-China Study	WHO-led Joint International Team	Source tracing through a mapping of activities and items traded at the Huanan market, sampling and testing of the environment and animal products sold at the Huanan market for SARS-COV-2 and trace back investigation on the supply chains of animal products to Huanan market.	https://www.who.int/publications/i/item/who-convened-global-study-of-origins-of-sars-cov-2-china-part

Priority Research Area 2: Identify the animal reservoir and intermediate host

Project	Institution	Objectives	Link to publication
Preliminary assessment for new wildlife SARS-CoV-2 reservoir establishment	Ecohealth Alliance, USA	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 parts of the world	
Surveillance for spillover event and maintenance of SARS-COV-2 and other emergent virus in hematophagous bats population in Amazon Region.	PANAFTOSA - Brasil	To understand the risk of amplification and establishment of a reservoir of SARS-CoV-2 in blood-feeding bats in the Amazon.	
WHO-convened Global Study of Origins of SARS-CoV-2: China Part. Joint WHO-China Study	WHO-led Joint International Team	Analysis of available SARS-related COV genome sequences from animals to predict possible reservoir species and intermediate hosts.	https://www.who.int/publications/i/item/who-convened-global-study-of-origins-of-sars-cov-2-china-part

Priority Research Area 3: investigate SARS-CoV-2 host range and possible role of animals in the epidemiology of human disease

Project	Institution	Objectives	Link to publication
Exposure of humans or animals to SARS-CooV-2 from wild, livestock, companion and aquatic animals	FAO	This Qualitative Exposure Assessment provides a comprehensive review of available scientific evidence and assessment of exposure risk from different wild or domestic animal species. Results can inform country-level risk assessment and provide the evidence base for targeted SARS-CoV-2 investigations in animals and mitigation options.	http://www.fao.org/3/ca9959en/CA9959EN.pdf

Project	Institution	Objectives	Link to publication
SARS-CoV-2 EvoZOOne / SARS-CoV2 evolution and zoonotic potential assessment.	ANSES Nancy Laboratory for Rabies and Wildlife, France	To assess the specificity of available serological tools for serological diagnostics in animals living close to humans; explore the diversity of strains of coronavirus in circulation and describe their genetic characteristics, and test the susceptibility of certain of these animal species. Focus is on cats, dogs, rodents (Cricetidae, Microtus, Arvicola, Ondatra, rabits), Mustelidae (minks, weasel), birds (chicken, turkey, duck, fattened duck), fox, and wild boar	
Requirements and consequences of SARS-CoV -2 infection in animals	Kansas State University, USA	To determine the expression pattern of host proteins involved in SARS-CoV-2 infection, monitor mutations, assess the susceptibility of deer and sheep to SARS-CoV-2 and evaluate the spread and persistence of SARS-CoV-2 in the animal environment.	https://www.biorxiv.org/content/10.1101/2021.04.07.438866v1.fullhttps://www.mdpi.com/2076-0817/10/2/227
SARS-CoV-2, from genotype to phenotype	ERASMUS MC, The Netherland	The purpose of this assignment is to gain in depth understanding of the evolution, spread and transmission of SARS-CoV-2 during the coming phase of the pandemic with a focus on the role of interspecies transmission events, and possible establishment of new reservoirs of the virus in animals	

Priority Research Area 4: Investigate transmission pathways

Project	Institution	Objectives	Link to publication
GLEWS+ Risk assessment - SARS-CoV-2 in animals used for fur farming	FAO, OIE, WHO	This assessment assessed the overall risk of introduction and spread of SARS-CoV-2 within the fur farms, the spillover from fur farm to humans and the transmission of SARS-CoV-2 from fur farm animals to susceptible wildlife populations. It is based on information from 36 countries in Africa, Asia, Europe, South and North America, where animals of the families Mustelidae, Leporidae and Canidae are commercially farmed for fur or which have documented export of fur. These families include the known susceptible fur species (e.g.: minks, rabbits and raccoon dogs).	https://www.who.int/publications/i/item/WHO-2019-nCoV-fur-farming-risk-assessment-2021.1

Priority Research Area 5: Consolidate baseline data to inform prevention and control strategies

Project	Institution	Objectives	Link to publication
Development of an impedance based cell assay to quantify infectious particles of SARS-CoV-2	ANSES, France	Development of a new method to quantify infectious particles of SARS-CoV-2 and evaluate virus persistence during food processing	
Persistence and particulate behaviour of SARS-COV2 in environmental water matrices	ANSES, France	Quantification of SARS-CoV-2 persistence and infectivity in water and water matrices	

Project	Institution	Objectives	Link to publication
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	University College of Dublin, Ireland.	To explore the presence and genetic of SARS-CoV-2 in selected food matrices and in food processing environments	

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

Project	Institution	Objectives	Link to publication
COVID 19 and food safety: guidance for competent authorities responsible for national food safety control systems	FAO WHO	This guidance aims to ensure the effectiveness of a reduced food safety inspection programme in mitigation of risk; and temporary measures that can be introduced to contain widespread food safety risks and reduce serious disruption to national food safety programmes.	https://www.who.int/publications/i/item/WHO-2019-nCoV-Food_Safety_authorities-2020.1

Priority Research Area 7: Develop strategies to improve preparedness and reduce risk of spillover events

Project	Institution	Objectives	Link to publication
Improve preparedness and reduce risks of spillover events along the food value chain.	PANAFTOSA, Brasil	To reduce the risk of spillover events along the food value chain in the Americas	

Priority Research Area 8: Analyse behavioural risks

Project	Institution	Objectives	Link to publication
Pilot project in Dakar market.	WHO AFRO Regional office	To reduce the risk of transmission of pathogens in traditional markets	
Keeping food markets working	Global Alliance for Improved Nutrition (GAIN)	The objective of this projects are to i) better understand the specific contexts and risks to public health in traditional markets, and how to mitigate these, ii) propose options for improved participation in the policy environment, iii) develop communication approaches about the mitigation measures.	https://www.gainhealth.org/impact/our-response-covid-19/practical-guidance-keep-markets-open-and-safe

Priority Research Area 9: Improve knowledge surrounding the wildlife trade

Project	Institution	Objectives	Link to publication
A rapid review of evidence on managing the risk of diseases emergence in the wildlife trade	OIE	The purpose of this project was to gather, assess and present evidence from peer-reviewed literature to inform the process for developing guidance to reduce risk of disease emergence through wildlife trade, also considering the impact on biodiversity.	https://www.oie.int/fileadmin/Home/eng/Internationa_Standard_Setting/docs/pdf/WGWildlife/OIE_review_wildlife_trade_March2021.pdf

Priority Research Area 10: Improve knowledge on wildlife trade operations

Project	Institution	Objectives	Link to publication
Reducing public health risks associated with the sale of live wild animals of mammalian species in traditional food markets	OIE, WHO, UNEP	The purpose of this document is to provide guidance for food safety and other relevant authorities to reduce the risk of transmission of COVID-19 and other zoonoses in traditional food markets, where live animals are sold for food. The document is also relevant for other utilizations of wild animals, requiring an approach that is characterized by conservation of biodiversity, animal welfare and national and international regulations regarding threatened and endangered species.	https://cdn.who.int/media/docs/default-source/food-safety/ig--121-1-food-safety-and-covid-19-guidance-for-traditional-food-markets-2021-04-12-en.pdf?sfvrsn=921ec66d_1&download=true

Priority Research Area 11: Diagnostic

Project	Institution	Objectives	Link to publication
Consideration for sampling, testing and reporting of SARS-CoV-2 in animals	OIE	The purpose of this document is to provide high level considerations on sampling, testing, and reporting of SARS-CoV-2 in animals.	https://www.oie.int/fileadmin/Home/eng/Our_scientific_expertise/docs/pdf/COV-19/Sampling_Testing_and_Reporting_of_SARS-CoV-2_in_animals_final_7May_2020.pdf

Project	Institution	Objectives	Link to publication
Canine olfaction for COVID-19 screening	Veterinary School of Maison Alfort, France, & NOSAIS consortium	To assess the capacity of trained dogs to detect specific odours associated with infection with SARS-CoV-2 and be used to screen potentially infected persons in various environmental contexts.	https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0243122

Contribution of the following project(s)

- SARS-CoV-2 EvoZOOne / SARS-CoV2 evolution and zoonotic potential assessment (Cf priority Research Area 3): assessment of the specificity of available serological tools for diagnostic in animals living closed to humans

Annex 1. Members of the WHO COVID-19 HAI R&D Expert Group

Member	Affiliation
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