

Considerations on monitoring SARS-CoV-2 in animals

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COVID-19 is a reminder of the importance of the One Health approach. COVID-19 is an emerging infectious disease caused by the SARS-CoV-2 virus, which most likely emerged from an animal source and, through human-to-human transmission and adaptation, resulted in a pandemic.

BACKGROUND

Computational predictions and the results of laboratory research and field studies have demonstrated that a broad range of animal species are susceptible to infection with SARS-CoV-2 with varying clinical manifestations. Natural infections in companion animals, animals in zoos and aquaria, animals farmed for fur, and free-ranging wildlife have occurred following spillover of ancestral strains and of variants of SARS-CoV-2 from infected humans.

Currently, the human population is maintaining SARS-CoV-2 with occasional spillover occurring from people into animals. SARS-CoV-2 infection in some animals, e.g., white-tailed deer and mink, has resulted in animal-to-animal transmission. The findings of multiple spillovers followed by onward transmission in free-living white-tailed deer provide evidence for potential establishment of non-human reservoirs of SARS-CoV-2. It is unknown whether inter-species transmission between multiple susceptible species in the same locality may enable the long-term maintenance of SARS-CoV-2 within an ecosystem.

The evolution of SARS-CoV-2 and the emergence of new variants in humans (or potentially animals) may alter the host range of SARS-CoV-2 as well as other characteristics, with implications for its epidemiology and for risk assessment. The implications of viral evolution and emergence of variants at the human-animal-environment interface are not well understood and further research is needed.

There is little evidence of SARS-CoV-2 spillback into humans except in the case of contact with infected farmed mink and hamsters. Several mink farm workers in close contact with large numbers of infected mink, and a pet store worker and a customer in close contact with infected Syrian hamsters have been infected following animal-to-human transmission. In general, the risk of animals spreading currently circulating lineages of SARS-CoV-2 to people is considered to be low, whilst the consequences may vary depending on the context. Although significant for global human health, SARS-CoV-2 appears to have had a limited and local impact on animal health, with the notable exception of mink where infections in mink farms have caused significant outbreaks in multiple countries with varying morbidity and mortality in affected animals. Infections in companion and zoo animals have also been reported with varying morbidity and mortality. We also know that companion animals can be infected without showing any signs of illness.

To fully understand the implications of SARS-CoV-2 at the human-animal-environment interface it will be necessary to monitor SARS-CoV-2 infections in animals.

In January 2022, the WHO IHR Emergency Committee for COVID-19 issued a temporary recommendation: Real-time monitoring and data sharing on SARS-Cov-2 infection, transmission and evolution in animals will assist global understanding of the virus epidemiology and ecology, the potential for evolution of new variants in animal populations, their timely identification, and assessment of their public health risks.

PURPOSE

The purpose of this document is to provide **high-level considerations on monitoring SARS-CoV-2 in animals to support risk assessment and risk management at the human-animal-environment interface, and to provide examples of situations in which animal populations may be monitored for SARS-CoV-2 infections.**

The considerations aim to promote the principles of **multisectoral coordination and transparency when studying SARS-CoV-2 at the human-animal-environment interface.**

- The following general considerations are intended to be **non-prescriptive** and seek to cover a broad range of human and animal interactions.
- These are **not surveillance guidelines** aimed at specific objectives such as early warning or detecting the presence/absence of disease with a prescribed level of confidence.
- The **target audience is broad**, and includes policy makers, researchers, scientific writers, and other interested parties, including the general public.

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01 Reasons for monitoring SARS-CoV-2 in animals

Risk assessment

Widespread SARS-CoV-2 infections in animals and the continual evolution of the virus raise a number of questions, including:

- What is the full host range of SARS-CoV-2?
- Once introduced to animals, what is the potential for onwards transmission to other animals or to humans?
- Will animal reservoirs become established?
- Will new variants emerge as a result of infections in animals?
- What are the potential implications of animal infections for human and animal health?
- How will these risks change as new variants emerge?

The answers to these questions are complex and are influenced by the dynamic interactions between host, virus, and environmental factors that continue to evolve.

A process of ongoing risk assessment at the human-animal-environment interface is needed to better understand the following risks and how they change over time:

- The susceptibility of different wild and domestic animal species to infection (especially in the natural setting) with SARS-CoV-2,
- Transmission dynamics of the SARS-CoV-2 within susceptible animal populations and to other susceptible species, including humans,
- The consequences of SARS-CoV-2 infection, including clinical presentation, virus shedding, and viral evolution.

Risk management / case management

Active surveillance may be warranted to support disease management options where there is a risk to animal health, human health, or biodiversity.

FOR EXAMPLE, surveillance to inform risk management when susceptible animal species are kept in (large) groups and where there has been a risk of exposure to SARS-CoV-2. Notably, it is known that the introduction of SARS-CoV-2 to mink farms represents a significant risk for both animal and public health. Therefore, active surveillance of mink and other susceptible animals farmed for fur is recommended to ensure early detection of infection and rapid implementation of containment measures.



Mink breeding farm exterior in rural Denmark

02 General considerations for monitoring SARS-CoV-2 in animals

Design and coordination

In general, justification for monitoring the occurrence of SARS-CoV-2 in animals includes situations where the results will inform decision making, animal/population management, or public health response, or further the body of knowledge on the transmission or control of the virus.

The purpose of the study should be clearly defined and should inform study design. Fit for purpose study designs are needed, for instance, to: detect presence of infection in individual animals or at population level; estimate prevalence of infection; assess the possibility for persistence of infection at population level; etc.



White-tailed deer

The design and implementation of studies to monitor SARS-CoV-2 in animals should involve all relevant stakeholders including public health services, national Veterinary Services, wildlife authorities, the environmental sector, citizens (e.g., farmers, pet owners, zookeepers, hunters, hikers), etc.

Before undertaking a study, it is important for One Health partners across sectors to consider and agree on communications messages and actions should there be positive results. Actions on positive findings may not be needed, but if any action is taken (including communication on the findings) it should be proportionate and based on risk.

To make efficient use of resources, it may be advantageous to take an opportunistic approach to sampling. For example, to test samples that have been collected for other monitoring studies (e.g., disease surveillance or other health or environmental studies) or to collaborate with hunters or with rodent/pest control services.

Coordination and collaboration between groups carrying out related studies can improve the overall impact of studies and the efficient use of resources.

Existing evidence from natural infections and results from laboratory infection studies and in silico experiments may be useful in informing field-based studies. Susceptibility of one species may suggest that a closely related species is also susceptible, but it should be noted that this is not always the case and empirical evidence should be prioritized in these cases. Results of transmission studies may indicate the potential for infection to become established at population level. Information about routes of viral shedding may support decisions on the samples to be collected.

It should be noted that the evolution of SARS-CoV-2 and the emergence of new variants may affect host range, transmission potential, pathogenesis, and route of viral shedding. When interpreting field findings and results of laboratory infection studies it is important to pay attention to the particular strain used in the study or detected in the field.

When conducting studies in the field, it is important to collect information on the local ecosystem. This will provide information on direct or indirect contact with humans and other animals or disease vectors.

Risk-based sampling targeted towards specific locations, species, and times of year may increase the likelihood of detecting presence of infection, though it should be noted that randomized sampling better support other evaluations such as prevalence studies.

Collecting samples

Samples may be collected from live animals, dead animals, and/or the environment.

Consideration should be given to the public health and animal health and welfare implications associated with handling and sampling of animals.

Sampling should be done by competent personnel trained in the correct use of personal protective equipment, and chain of custody of samples should be maintained.

Depending on the type of test, samples may include single or combinations of oropharyngeal, nasal, and rectal swabs, urine, faeces and blood. When collecting and taking samples from animals, care should be taken to avoid cross-contamination from the environment or from infected humans or other animals.

Testing of samples

The most appropriate diagnostic tool(s) or combination of tools (serology, antigen detection, PCR etc.) should be selected according to the purpose of the study.

Broad serological surveillance is more likely to detect exposure to SARS-CoV-2 in animals than virological surveillance alone (virological surveillance only presents a narrow time window of virus or nucleic acid recovery from an infected host). In many instances serological studies can inform more specific targeted virological surveillance.

Temporal changes in antibody levels may elucidate transmission patterns within and between populations.

Genetic sequence data provide information which is essential for risk assessment, comparative analyses, and epidemiological investigation. Wherever possible, viruses detected in animals should be sequenced and whole genome sequences should be deposited in publicly available databases without delay.

The laboratory should use a validated test, appropriate to the purpose of testing, and consider the sensitivity and specificity which may vary across different species. If a private laboratory tests animal samples, close communication and coordination should be maintained with the Veterinary Authority.

If real-time RT-PCR is used for detection and borderline PCR cycle threshold (Ct) values are obtained, further validation and confirmatory testing may be required.

Dissemination of results

Positive results in animals (*c.f. case definition in Section 5 of this document*) should be reported to the national Veterinary Authorities and Public Health Authorities and other relevant One Health partners (e.g., wildlife authority).

WOAH Members are required to report all occurrences of SARS-CoV-2 in animals (*c.f. definition in Section 5 of this document*) to WOA as an emerging disease.

Whole genome sequences should be deposited in publicly available databases without delay.

03 Considerations for risk assessment

The following examples may be reasons for monitoring SARS-CoV-2 in animals to assess risk at the human-animal-environment interface. For each reason some key considerations have been highlighted.

Assessment of the full host range of SARS-CoV-2

- Studies should be informed by existing field findings and results of animal infection studies and computational predictions.
- New SARS-CoV-2 variants may have a different host range, pathogenesis, transmission potential and viral shedding patterns.

Assessment of potential for onwards transmission to other animals

- Studies should be informed by existing field findings and results of animal infection studies and computational predictions.
- Consider sampling animals within the same epidemiological risk group.
- Take into account the level of direct or indirect contact between animals and a human or animal population in which SARS-CoV-2 is or has recently been circulating. Indirect contact may include contact with human waste.

Assessment of potential for onwards transmission to humans

- Consider the level of direct or indirect contact between animals and a human or animal population in which SARS-CoV-2 is or has recently been circulating. Indirect contact may include contact with human waste.
- Coordinate closely with the public health services on design of studies and on sampling, testing, and sharing of data including genomics data.

Assessment of risk of establishment of non-human animal reservoirs

- If animals are susceptible and efficient transmission between animals is demonstrated, assessments of risk of establishment of the species as a non-human reservoir may be warranted.
- Longitudinal studies are needed to further investigate the temporal trends in establishment of reservoirs.

Assessment of risk of emergence of new variants as a result of infections in animals

- It is essential that whole genome sequences of SARS-CoV-2 from clinical samples and isolates recovered from animals or their environment are generated and shared. Whole genome data should be shared without delay in publicly available databases to allow comparative analyses.

Potential implications of SARS-CoV-2 animal infections for animal health

- It should be important to collect and report data on clinical signs from field findings and animal infection studies.
- Reporting of atypical clinical signs and mortality in known susceptible hosts, including companion animals and wildlife species is encouraged.
- Reporting of evidence of infection of any domestic livestock species is required.

04 Considerations for risk management

The rationale for monitoring SARS-CoV-2 in animals for risk management should include considerations on the risk of infection of animals, the risk of exposure to other susceptible animals or humans, the consequences of exposure, and actions taken on positive findings.

Sampling and testing of different categories of animals should be based on risk assessment, considerations include:

Companion animals

- The likelihood of exposure to a source of SARS-CoV-2 (human, animal or environment)
- The likelihood of transmission to companion animal(s)
- Level and intensity of contact with humans and other animals
- Susceptibility of different animal species to infection with circulating strains of SARS-CoV-2
- The likelihood of companion animals spreading infection to other households through contact with other companion animals or directly with humans in other households



Syrian hamster

Table 1: Criteria to Guide Evaluation and Laboratory Testing for SARS-CoV-2 in Animals

Adapted from a version initially developed collaboratively by the Centers for Disease Control and Prevention and the US Department of Agriculture, USA. It provides epidemiological risk factors and clinical features that can guide decisions on the testing of animals for the purpose of case management.

Criteria	Epidemiological Risk	AND Clinical Features
A	Animal with history of exposure to a person or animal suspected or confirmed to be infected with SARS-CoV-2.	Animal is asymptomatic; OR
B	Animal with exposure to a known high-risk environment (i.e., where human cases or animal cases have occurred), such as a residence, facility, or vessel (e.g. nursing home, prison, cruise ship).	Animal has clinical signs suspicious of SARS-CoV-2 infection.*
C	Threatened, endangered or otherwise imperilled/rare animal in a rehabilitation, sanctuary or zoological facility with possible exposure to SARS-CoV-2 through an infected person or animal.	Animal is asymptomatic; OR Animal has clinical signs suspicious of SARS-CoV-2 infection.*
D	Animals in a mass care or group setting (e.g., farm, animal feeding operation, animal shelter, boarding facility, zoo, or other animal holding) including companion animals, livestock, and other species, where their exposure history to people with COVID-19 is unknown.	A cluster of animals show clinical signs suspicious of SARS-CoV-2 infection.*
E	Farmed mink (<i>Neovison vison</i>). Farmed mink refers to mink bred or raised in captivity for their fur and other by-products.	Animals are asymptomatic; OR One or more animals have clinical signs suspicious of SARS-CoV-2 infection.*

NOTE: Veterinarians are encouraged to consider other, more common, causes of illness in animals and use their clinical judgement when deciding whether or not to test animals for SARS-CoV-2. All decisions to test an animal should be made in coordination with relevant public health and animal health officials.

* For more information on clinical signs see section 4. Some animals have been infected with SARS-CoV-2 without showing clinical signs. Therefore, there may be instances when asymptomatic animal(s) may be tested based on veterinary clinical and/or public health judgement.

- The likelihood of companion animals spreading infection to other contact animals (e.g. breeding establishments, pet shops, gatherings, colonies, stray animals, free ranging)
- The likelihood of spread through trade and movement
- Potential consequences of exposure (human infection and illness; vulnerable individuals or groups; disease spread; establishment of animal reservoirs; high risk settings; genetic variants)

Farmed animals

- The likelihood of exposure to a source of SARS-CoV-2 (human, animal or environment)
- The likelihood of transmission to the farmed animals
- Susceptibility of different animal species to infection with circulating strains of SARS-CoV-2
- The likelihood of virus amplification in susceptible species e.g., contact between animals and size of epidemiological groups
- The likelihood of spread through trade and movement
- Potential consequences of exposure (human infection and illness; animal infection and illness; animal production; disease spread; economic; establishment of animal reservoirs; genetic variants)



American mink (Hinton, Alberta)

Wildlife

- The likelihood of exposure to a source of SARS-CoV-2 (human, animal or environment)
- The likelihood of transmission to the wild animal(s)
- Susceptibility of different wild animal species to infection
- The likelihood of infection of other wildlife following release of captive wild animals to the field
- Translocation of wildlife from one location to another
- The likelihood of infection of endangered and threatened species
- Potential consequences of exposure (human infection and illness; wildlife morbidity and mortality; risk to conservation efforts/biodiversity; biodiversity loss; disease spread; establishment of new wildlife reservoirs; genetic variants)

Zoos (or zoological collections)

- The likelihood of exposure to a source of SARS-CoV-2 (human, animal or environment)
- The likelihood of transmission to zoo animal(s)
- Susceptibility of different animal species to infection

- The likelihood of infection of endangered and/or threatened species
- The likelihood of moving infection between zoos or zoological collections
- Consequences of exposure (human infection and illness; disease spread; risk to conservation/biodiversity; biodiversity loss; economic; genetic variants)

Animal gatherings and group animal settings

- The likelihood of exposure to a source of SARS-CoV-2 (human, animal or environment)
- The likelihood of transmission to the animal(s)
- Susceptibility of different animal species to infection
- The likelihood of introducing infection to gathered animals
- The likelihood of animal-to-animal transmission at the gathering (e.g. temporary, permanent, resident animals or visitor animals)

- The likelihood of further spreading infection through dissemination of contact animals
- Consequences of exposure (human infection and illness; disease spread; amplification of infection; risk to animal health; establishment of reservoirs; genetic variants)

Urban peri-domestic animals

- The likelihood of exposure to a source of SARS-CoV-2 (human, animal or environment)
- The likelihood of transmission to the animal(s)
- Susceptibility of different animal species to infection
- The likelihood of animal-to-animal transmission
- The likelihood of further spreading infection
- Consequences of exposure (human infection and illness; disease spread; amplification of infection; risk to animal health; establishment of reservoirs; genetic variants)

The actions to be taken on positive or negative findings should be based on risk, be proportionate, and be carefully planned for using a One Health approach, before sampling and testing of animals for SARS-CoV-2.

05 Case definitions

SARS-CoV-2 clinical signs in animals

Several animal species have been proven to be susceptible to infection with SARS-CoV-2 either through natural and/or by experimental infection. However, current evidence suggests clinical signs may include but are not limited to nasal discharge, ocular discharge, respiratory distress, coughing, vomiting or diarrhea (frequently), and should be considered in epidemiological investigations. Clinical signs in animals may also vary with different strains of SARS-CoV-2. Some animals may be infected and not show clinical signs.

Case definitions (may evolve with future information)

The following are suggested case definitions that can be adapted to local contexts.

Suspected case

SARS-CoV-2 infection can be suspected in an animal if:

- Animal has clinical signs suggestive of SARS-CoV-2 infection (described above) and all other likely differential diagnostic aetiologies have been effectively ruled out by a veterinarian. AND
- Animal has an epidemiological link with a confirmed human COVID-19 patient, SARS-CoV-2 infected animal or suggestive case history indicating potential exposure.

Confirmed case

The following defines a laboratory confirmed case of SARS-CoV-2 infection in an animal (with or without clinical signs):

- Viral nucleic acid has been identified in a sample* taken directly from an animal, giving cause for suspicion of previous association or contact with SARS-CoV-2, by:
 - Targeting at least two specific genomic regions at a level indicating presence of infectious virus; OR
 - Targeting a single genomic region followed by sequencing of a secondary target OR
 - SARS-CoV-2 has been isolated from a sample* taken directly from an animal

* Samples for virus detection and viral nucleic acid are preferably nasal swab, oropharyngeal swab, nasal washing, tracheal swab and/or a rectal sample may be taken, or a faecal sample may be used in situations where direct sampling is not possible due to risks to the animal or testing staff; or from internal organs collected post-mortem.

06 Reporting to WOA

The purpose of collecting and sharing information at international level is to better understand SARS-CoV-2 epidemiology with a view to informing risk assessment, risk management and risk communication.

In accordance with Chapter 1.1. of the *Terrestrial Animal Health Code*, confirmed cases should be notified as an emerging disease to WOA through the World Animal Health Information System (WAHIS). As per Article 1.1.5 of the *Terrestrial Animal Health Code*, Members are encouraged to report any other relevant information, such as experimental studies or prevalence surveys, to the WOA World Animal Health Information and Analysis Department as a summary report to information.dept@woah.org. Members should send reports in a timely manner to facilitate early warning.

Particular attention should be given to providing information on the 'Description of the population affected' that should focus on additional data at the outbreak level (i.e. clinical signs of the animals), and on the 'Epidemiological comments' that should provide information at the event level (an 'event' includes all epidemiologically related outbreaks (i.e. animal population survey, sampling information)).

WOAH strongly encourages Members to share whole genome sequences of SARS-CoV-2 isolates from animals in public available sequence databases without delay to allow comparative analyses.

WOAH-WAHIS uses a standardised template. However, in order to capture the additional information which is critical to our understanding of emerging diseases, Members are also encouraged to fill in the free text boxes available, giving particular consideration to:

- i. Zoonotic potential
- ii. Description of the population affected by the outbreak. (As per definition of the *Terrestrial and Aquatic Animal Health Code*, an outbreak is defined as 'the occurrence of one or more cases in an epidemiological unit.')
- iii. Source of the outbreak or origin of infection
- iv. Epidemiological comments about the event
- v. Information about the strain of SARS-CoV-2 detection
- vi. Information about the whole genome sequence of the virus including the name of database where the sequence was submitted and the accession number.

07 Communication

Communication of test results and finding mutations or variants in animals should be timely.

Communication to the public should aim to avoid inappropriate measures being taken against domestic or wild animals which might compromise their welfare or health or have a negative impact on international trade or biodiversity, if misinterpreted.

Information about animal infections should be based on evidence and complement public health risk communication messages.

08 Further information

Further information on current knowledge about SARS-CoV-2 in animals can be found on the WOAHP website: <https://www.woah.org/en/what-we-offer/emergency-and-resilience/covid-19/>

Further information on the public health aspects of COVID-19 can be found on the WHO website: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>

Further information on animal health surveillance can be found in the WOAHP *Terrestrial Animal Health Code*: https://www.woah.org/en/what-we-do/standards/codes-and-manuals/terrestrial-code-online-access/?id=169&L=1&htmfile=chapitre_surveillance_general.htm

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