SARS-CoV-2 (Severe acute respiratory syndrome-related coronavirus 2)

Biosafety Advisory

February 29, 2020*

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Summary of recent changes

- Update to the name of the novel coronavirus and the disease it causes to reflect current nomenclature.

- Reporting to the Canadian Food Inspection Agency (CFIA) should the coronavirus disease COVID-19 be detected in animals.
- Separate sections for recommended biosafety measures for diagnostic activities and biosafety requirements for *in vitro* and *in vivo* activities.

This biosafety advisory is being provided by the Public Health Agency of Canada (PHAC) to assist clinical, diagnostic, and research laboratories in implementing proper biosafety procedures to handle samples that may contain SARS-CoV-2 (previously referred to as 2019-nCoV, the novel coronavirus that originated in the province of Hubei, China). SARS-CoV-2 is responsible for the outbreak of COVID-19, which began in China in December 2019. This advisory is based on currently available scientific evidence as of February 29, 2020 and is subject to review and change as new information becomes available. SARS-CoV-2 has been classified as a Risk Group 3 (RG3) human pathogen by the Centre for Biosecurity.

This document is intended to support local risk assessments (LRAs). [1] Laboratories receiving specimens from patients under investigation for COVID-19 must be aware that improper handling of these specimens poses a risk of exposure or infection, which could seriously impact the health of personnel and the community.

Background

The first reports of COVID-19 surfaced in the province of Hubei, China in December 2019. [2] The novel coronavirus SARS-CoV-2 has been identified as the causative agent and its genetic sequence is publicly available to inform the development of diagnostic tests and support vaccine development research. [3], [4] Common symptoms of COVID-19 in humans include fever and

respiratory symptoms (e.g., cough, shortness of breath, breathing difficulties). [5] In more severe cases, infection can cause pneumonia and can be life-threatening. [6] While a number of countries have reported travel-associated cases of COVID-19, there are multiple cases of COVID-19 resulting from human-to-human transmission as evidenced by cases in individuals who have not traveled to affected areas. [7], [8], [9] The World Health Organization's (WHO) website provides information on the number of confirmed cases.

Epidemiological studies have linked many COVID-19 cases in the earlier stages of the outbreak in the province of Hubei, China to a large seafood and live animal market, suggesting a possible zoonotic origin of their infection. [10] The World Organization for Animal Health (OIE [Office International des Epizooties]), which provides guidance for Veterinary Authorities, indicates that SARS-CoV-2 is an emerging pathogen and that detection in an animal should be reported to the OIE through the national Veterinary Authority, which for Canada, is the Canadian Food Inspection Agency (CFIA). [11] Individuals are asked to immediately notify the CFIA if COVID-19 is detected in an animal. Should new information result in the classification of SARS-CoV-2 as an emerging animal pathogen, this advisory will be updated to include the CFIA's regulatory perspective. Until such time, the oversight of activities with SARS-CoV-2 remains under the PHAC's purview.

Biosafety recommendations for diagnostic activities

A pathogen (e.g., SARS-CoV-2) in a primary specimen (i.e., in its natural environment) is excluded from the Human Pathogens and Toxins Act (HPTA) and is therefore not regulated by the PHAC as long as the pathogen

has not been cultivated or intentionally collected or extracted (e.g., concentrated, cultured). Primary specimens will generally contain lower concentrations of pathogens than found in cultures (i.e., propagated pathogens). Examples of primary specimens include sputum, blood, plasma, feces, and tissues that are collected directly from patients. Diagnostic specimens from naturally exposed animals (i.e., not resulting from *in vivo* studies) are also considered primary specimens.

Diagnostic and clinical activities with primary specimens that do not involve the cultivation, collection, or extraction (i.e., isolation) of SARS-CoV-2 (e.g., clinical chemistry studies, urinalysis, hematology and serology testing, fixation of tissues) are not regulated under the HPTA and there are no requirements with which facilities must comply to handle such specimens. It is still recommended that, at minimum, good microbiological laboratory practices be followed in work areas where primary specimens are handled. [12] Routine practices and universal precautions are also recommended in laboratories where primary specimens that may contain SARS-CoV-2 are handled. [13]

As more information on SARS-CoV-2 becomes available, it may be determined that there is a higher risk associated with certain types of primary specimens or specific diagnostic activities. [14] To reduce the risks of exposure, it is recommended for diagnostic and clinical activities with primary specimens that may result in the inadvertent extraction of live-virus to be conducted in a facility that meets the biosafety recommendations described in Table 1.

Table 1: Biosafety recommendations for diagnostic activities

Diagnostic Activities	Minimum Recommended

Diagnostic Activities	Minimum Recommended
Non-propagative diagnostic activities that do not result in the concentration or extraction of SARS-CoV-2 Example of these activities include, but are not limited to: • clinical chemistry studies, urinalysis, and hematology and serology testing (e.g., analysis with automated platforms); • visual examination of inactivated specimens or tissues (e.g., formalin-fixed); • visual examination of bacterial and fungal cultures; • routine staining and microscopic analysis of heat- or chemically-fixed smears; • assays with virus-inactivated specimens; and • preparation of specimens for packaging and distribution to diagnostic laboratories for additional testing.	**Routine practices and Universal precautions**
Non-propagative diagnostic activities that may inadvertently concentrate or extract SARS-CoV-2 Examples of these activities include, but are not limited to: • concentration of samples prior to inactivation (e.g., centrifugation of a bronchoalveolar lavage sample); and • sample preparation for nucleic acid extraction, molecular testing of nucleic acids, and antigen and antibody assays.	**CL2** [1]

	Diagnostic Activities	Minimum Recommended
1	Containment Level 2 (CL2) with the additional biosafety recommendations in Table 2.	

Where non-propagative diagnostic activities may result in the inadvertent concentration or extraction of SARS-CoV-2, it is recommended that facilities meet the minimal applicable requirements for CL2, as specified in the Canadian Biosafety Standard (CBS), and implement the recommendations specified in Table 2. Facilities where diagnostic and clinical activities with primary specimens do not pose a risk of concentrating or isolating SARS-CoV-2 may also implement the precautions recommended in Table 2 based on their LRA (i.e., as usually performed for specimens that may contain an RG3 human pathogen) for activities that may generate aerosols (e.g., preparation of smears for microscopic analysis, inoculation of bacterial or fungal culture media). Table 2 provides recommended precautions that may be implemented in any work place where activities with primary specimens from patients under investigation for COVID-19 are performed.

Table 2: Additional biosafety recommendations

Recommended precautions for diagnostic activities involving primary specimens from patients under investigation for COVID-19
• A lab coat, gloves, and eye protection are worn when handling primary specimens. • Centrifugation of primary specimens is carried out in sealed safety cups, or rotors, that are loaded/unloaded in a biological safety

cabinet (BSC) or other primary containment device.

- A certified BSC, or other primary containment device, is used for procedures that may produce infectious aerosols (e.g., pipetting [e.g., adding lysis buffer], preparing aliquots, diluting specimens, vortexing).
- Respiratory protection (that provides a level of filtration of 95% or greater [e.g., N95]) is worn where aerosol generating activities cannot be contained within a BSC or other primary containment device.
- Samples that are handled within a BSC or other primary containment device are moved to an analytic equipment (e.g., polymerase chain reaction [PCR] equipment) within a secondary closed container (e.g., gasketed, plates sealed with tape or flexible film).

Based on the currently available scientific evidence, chemical disinfectants that are effective against enveloped viruses are suitable for decontamination of SARS-CoV-2 (i.e., when they are used according to manufacturer's recommendations). Such effective disinfectants include sodium hypochlorite (bleach), 70% ethanol, 0.5% hydrogen peroxide, quaternary ammonium compounds, and phenolic compounds. It is possible other biocidal agents may be less effective (e.g., 0.05-0.2% benzalkonium chloride, 0.02% chlorhexidine digluconate). [15]

Biosafety requirements for *in vitro* and *in vivo* activities

The following table summarizes the appropriate minimum containment requirements for laboratories where SARS-CoV-2 is intentionally handled. Unless exempted under the Human Pathogens and Toxins Regulations (HPTR), all *in vitro* and *in vivo* activities with SARS-CoV-2 are to be performed in accordance with a Pathogen and Toxin Licence issued under the HPTA and in a facility that meets the minimum applicable requirements for Containment Level 3 (CL3), as specified in the CBS. [16] *in vivo* activities include experimentally exposing an animal to SARS-CoV-2 and the subsequent handling of these animals, and specimens obtained from them, in a research setting.

Table 3: Canadian containment level requirements for SARS-CoV-2

Activities with SARS-CoV-2	Minimum Containment Level Required
Non-propagative *in vitro* activities Examples of these activities include, but are not limited to: • procedures with human or animal primary specimens to intentionally concentrate or isolate SARS-CoV-2 for research purposes (e.g., ultracentrifugation of a sample).	**CL3**

1 Work in small animal containment zones (SA zones) must meet the applicable requirements in the CL3 column of the CBS and work in large animal containment zones (LA zones) must meet the applicable requirements in the CL3-Ag column of the CBS.

Activities with SARS-CoV-2	Minimum Containment Level Required
Propagative *in vitro* activities Examples of these activities include, but are not limited to: • culturing specimens (e.g., propagated virus); • preparatory work for *in vivo* activities; and • processing a culture (i.e., propagated or cultivated) known to contain SARS-CoV-2 for packaging and distribution to laboratories.	**CL3**
***in vivo* work activities** Examples of these activities include, but are not limited to: • preparing inoculum; • inoculating animals; and • collecting specimens from experimentally infected animals.	**CL3** [1]

1 Work in small animal containment zones (SA zones) must meet the applicable requirements in the CL3 column of the CBS and work in large animal containment zones (LA zones) must meet the applicable requirements in the CL3-Ag column of the CBS.

Many of the requirements in the CBS are risk- and performance-based and, as such, are dependent on an LRA being performed. Based on the risks associated with *in vitro* and *in vivo* activities taking place with SARS-CoV-2, additional biosafety measures may also be applicable at CL3. Facilities are to conduct an LRA for the activities to be undertaken with SARS-CoV-2 to

determine the appropriate risk mitigation measures (CBS R4.1.8), and update the LRA and mitigation measures as new information becomes available.

Should new information result in a change in risk group classification or the publication of a biosafety directive, such information will be reflected in the ePATHogen - Risk Group Database. [17]

Transportation

The transportation of SARS-CoV-2 specimens is subject to the Transportation of Dangerous Goods Regulations, which include the packaging requirements stipulated in the standard CAN/CGSB-43.125.

Samples of SARS-CoV-2 specimens must be assigned to:

- UN2814, if they meet Category A criteria (i.e., propagated virus);
- UN3373, if they meet Category B criteria (i.e., patient/primary specimens); and
- UN3291, if the clinical waste contains Category B infectious substances (or it has low probability of containing virus).

For more information, contact Transport Canada at TDG-TMD@tc.gc.ca or TDGMOC-TMDContenants@tc.gc.ca, or visit the Transport Canada Transportation of Dangerous Goods website or the Transport Canada Shipping Infectious Substances bulletin.

In the event of an emergency involving dangerous goods, call CANUTEC at 1-888-CANUTEC (226-8832), 613-996-6666 or *666 on a cellular phone.

Contact information

Further biosafety information may be obtained:

- from the PHAC website;
- by phone at 613-957-1779;
- by fax at 613-941-0596; or
- by email: phac.pathogens-pathogenes.aspc@canada.ca

Further information on reportable and immediately notifiable diseases may be obtained:

- by email: cfia.notification-notification.acia@canada.ca.

References and resources

Footnotes

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