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Biosafety Guidelines for COVID-19 Specimens in Biobanks

Somayeh Parichehreh-Dizaji[1] and Vahid Haghpanah[1,2]

In late December 2019, the first report of pneumonia with unknown etiology was announced to the World Health Organization (WHO) representative office in China. This is officially known as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the disease has been abbreviated as ''COVID-19'' by the WHO.[1] The Advisory Committee on Dangerous Pathogens (ACDP) found COVID-19 to be an HG3 pathogen.[2]

The outbreak is currently predicted to intensify and is the world's leading public health issue, due to the financial implications and even the manufacture of COVID-19 vaccines and medicines in the next few months. The selection, evaluation, and study of COVID-19 biological samples are a significant part of the immediate international efforts. Biobanking plays an important role in the diagnosis, treatment, and improvement of study quality.[3]

Since COVID-19 is highly infectious, safety in the preparation, handling, transport, and storage of human biospecimens is essential.[4] Some scientific research bodies have issued guidelines for this purpose. Among them is the US Centers for Disease Control and Prevention (CDC) that has disseminated general and detailed health recommendations for the processing and handling of SARS-CoV-2 samples to this end.[5] In addition, the WHO has provided recommendations and procedures for laboratories regarding secure sample processing and transportation, disinfection methods, and laboratory health highlights and correct biological safety cabinets during the COVID-19 pandemic.[6–8] Scientists at the University of California, San Francisco (UCSF), have also released their biobank guidelines for all activities related to the handling and storage of biospecimens with the extension of COVID-19, which are publicly available.[9] Some of the webinars on biobanking are also hosted by the International Society for Biological and Environmental Repositories (ISBER) to share experiences and information from biobanks at various points along the COVID-19 pandemic. In addition, knowledge is learned from past and current epidemics and how the biobanking and analysis industry approaches this new threat.[10]

According to available guidelines for the COVID-19 biospecimens, precautions must be made in connection to the collection, handling, and storage of all samples, and staff should be provided with personal protective equipment (PPE). Moreover, ethical issues should also be considered for this purpose.[6] All safety procedures for a range of human samples, including nasopharyngeal swabs, saliva, urine, blood, feces, cerebrospinal fluid, cancer tissue, and even specimens with an unknown condition related to COVID-19, should be well-thought-out in compliance with the published guidelines at all stages, including shipping, processing, sample storage, and waste disposal.[2,4,8] Table 1 presents a brief overview of available safety guidelines for collecting, processing, and storage of COVID-19 samples. Refer to the referenced websites to access free full text and more details of the updated data, outlined in this document.

Furthermore, the SARS-CoV-2 pandemic makes biobanking a significant and immediate issue for other scientific fields, such as cancer. Potentially infectious specimens that are collected during the outbreak of COVID-19 should be stored in separate freezer units, away from other collections, to decrease the chance of cross-contamination in the repository.[4] While all samples may be contaminated with SARS-CoV-2, this virus, such as other coronaviruses, is considered to be inactive in formalin-fixed, paraffin-embedded samples heated to 56°C (133°F).[4] Coronaviruses are generally very stable in a frozen state based on studies of other coronaviruses that showed survival at −20°C for up to 2 years.[11]

In conclusion, cross-contamination should always be considered a significant and serious issue for biobanks. Standard operating procedures (SOPs) should be defined to mitigate the possibility of viral contamination in biospecimens, especially during this pandemic. Moreover, it is recommended to update these SOPs relevant to the handling and storage of COVID-19 samples at regular short intervals. Furthermore, careful processes should be be undertaken to keep the biobank staff and researchers safe from any potentially infectious biospecimens within the facilities. Labeling and electronic systems should identify such specimens for further safety precautions.

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[1]Endocrinology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran.
[2]Personalized Medicine Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran.

Table 1. A Brief Overview of Safety Guidelines for Collecting, Processing, and Storage of COVID-19 Samples from the WHO, CDC, GOV.UK, and PAHO

Title	*Comments*
Handling of samples	• Pack and ship patients' specimens and viral cultures ○ ''All materials transported within and between laboratories should be placed in a secondary packaging, to minimize the potential for breakage or a spill.''[8] ○ Suspected or confirmed SARS-CoV-2 samples must be packaged and transported according to the regulation of the IATA as UN3373, ''Biological Substance,'' ''Category B.''[2,7,8,13–16] ○ ''Pack and ship suspected and confirmed SARS-CoV-2 patient specimens, cultures, or isolates as UN 3373 Biological Substance, Category B, in accordance with the current edition of the IATA Dangerous Goods Regulations external.''[5] ○ ''The transport of samples that may contain 2019-nCoV must use triple packaging and comply with international standards related to air transport of infectious substances: ''Biological Substance, Category B.'''''[16] ○ ''Wrap the primary container with cushioning material. If packaging more than one sample, warp each primary container individually.''[16] ○ ''Place the secondary leak-proof container into a styrofoam container and surround with ice packs.''[16] ○ ''Place styrofoam container into the rigid shipping box (tertiary container).''[16] ○ Viral cultures or isolates samples must be packaged and transported as Category A,[2,8] ''UN2814, infectious substance, affecting humans.''[8] • Information on the packaging container ○ ''Write (clearly) the precise name and address''[16] ○ Name and phone number of the contact person in laboratory[5,16] ○ ''Person should be available 24 hours a day until shipment arrives.''[16] ○ ''Name and telephone number of responsible person''[16] ○ ''Write the proper shipping name and UN number ''Biological Substance, Category B, UN 3373.''''[16] ○ Patient's ID number[14] ○ Specimen type[14] ○ Date and time of sampling[6,14] ○ ''For each sample, the date and time of sampling and the exact location should be noted, as well as the conditions for transportation and the time of arrival at the laboratory.''[6] • ''Put laboratory form/letter and epidemiological questionnaire into the rigid shipping box.''[16] • ''Accompanying paperwork is not placed inside the packaging with or within the primary container.''[2]
PPE	• Disposable gloves[2,5,8,14,16,17] • Cover ○ Laboratory coat[2,5,8] ○ Gown[2,5,12,14,16,17] ○ ''Solid front or wrap-around gowns, scrub suits, or coveralls with sleeves that fully cover the forearms''[8] ○ Head covering[8] ○ ''Shoes cover or dedicated shoes''[8] ○ Closed work shoes[12] ○ ''Ensure that cuts or broken skin are covered before entering the laboratory.''[8] • Eye protection equipment[2,5,8,14,16,17] ○ Safety goggles[8,17] ○ Face shield (visors)[5,8,12,17] • Respiratory protection equipment[2,5,8,14] ○ ''Fit-tested particulate respirator, e.g., EU FFP2, US 6 NIOSH-certified N95 or equivalent, or higher protection''[8] ○ Particulate respirator (N95, FFP2 or equivalent)[17] ○ N95 or higher-level respirator[14] ○ Surgical mask[5,6,16,17] ○ ''Masks or respirators are not an appropriate substitute for processing samples in an MSC when there is a risk of aerosols being generated.''[2] • ''PPE must be removed on leaving the laboratory.''[2] • Personal hand cleanliness ○ Hand hygiene[2,5,6,17] ○ Washing hands[2,8] ○ ''Wash hands thoroughly, preferably with warm running water and soap, after handling biological material and/or animals, before leaving the laboratory or when hands are known or believed to be contaminated.''[8] • ''Protect written documents from contamination using barriers (such as plastic coverings), particularly those that may need to be removed from the laboratory.''[8] • ''Keep portable electronic devices in areas where they cannot easily become contaminated or act as fomites that transmit infection. Where close proximity of such devices to biological agents is unavoidable, ensure the devices are either protected by a physical barrier or decontaminated before leaving the laboratory.''[8]

(*continued*)

TABLE 1. (CONTINUED)

Title	*Comments*
Disinfectant materials	• Disinfect with appropriate disinfectants ○ All work surfaces[2,5,8,12,16] ○ Equipment[2,5,16] • Disinfectant agents ○ ''Sodium hypochlorite (bleach) (e.g., 1000 ppm [0.1%] for general surface disinfection and 10,000 ppm [1%] for disinfection of blood spills)''[8] ○ ''Sodium hypochlorite (bleach) may be used at a recommended concentration of 0.1% (1000 ppm).''[12] ○ Ethanol 62%–71%[8]/Ethanol 70%–90%[12]/Ethanol 60%–80%[6]/Ethanol 80%[17] ○ Hydrogen peroxide 0.5%[8]/Hydrogen peroxide ≥0.5%[12] ○ Quaternary ammonium compounds[8,12] ○ Phenolic compounds[8] ○ 0.05%–0.2% benzalkonium chloride[8] ○ 0.02% chlorhexidine digluconate[8] • Prepare and use disinfectant solutions according to manufacturer's recommendations ○ Contact time[5,8,12,16] ○ Volume[12] ○ Dilution[5,8,16] ○ Safe and care handling[5,16] ○ Expiry date expiry[8] ○ ''Concentrations with inadequate dilution during preparation (too high or too low) may reduce their effectiveness.''[12] ○ ''High concentrations increase chemical exposure to users and may also damage surfaces.''[12] ○ ''Enough disinfectant solution should be applied to allow surfaces to remain wet and untouched long enough for the disinfectant to inactivate pathogens, as recommended by the manufacturer.''[12] • No-touch methods[12] ○ ''Some countries have approved no-touch technologies for applying chemical disinfectants (e.g., vaporized hydrogen peroxide) in health-care settings such as fogging-type applications.''[12] ○ ''Devices using UV irradiation have been designed for health-care settings. Notably, these technologies developed for use in health-care settings are used during terminal cleaning (cleaning a room after a patient has been discharged or transferred).''[12] ○ ''If using a no-touch disinfection technology, environmental surfaces must be cleaned manually first by brushing or scrubbing to remove organic matter.''[12]
Laboratory equipment	• Handle routine diagnostic and molecular testing of all specimens from suspected or confirmed cases, such as the following activities in BSL-2 laboratories[5,7,8] ○ ''Samples for confirmation of known or presumptive positives must be processed at full CL3.''[2] ○ ''Using automated instruments and analyzers''[5] ○ ''Routine laboratory blood tests can be carried out in auto-analysers using standard practices and procedures at CL2.''[2] ○ ''Processing initial samples''[5] ○ Staining and microscopic investigation of fixed smears[2,5,16] ○ Assay of bacterial, fungal and mycotic cultures[2,5,16] ○ ''Pathologic examination and processing of formalin-fixed or otherwise inactivated tissues''[5,16] ○ Analysis of molecular extraction of viral nucleic acids[5,16] ○ ''Final packaging of specimens for transport to diagnostic laboratories for additional testing (specimens should already be in a sealed, decontaminated primary container)''[5,16] ○ ''Using inactivated specimens, such as specimens in nucleic acid extraction buffer''[5] ○ Conduct electron microscopic investigations with glutaraldehyde-fixed grids[5,16] ○ ''Nonpropagative diagnostic laboratory work (e.g., sequencing, NAAT) should be conducted at facilities and procedures equivalent to BSL-2.''[8] ○ Analysis using virus-inactivated specimens, including nucleic acid extraction buffer[2,16] ○ ''Preparation of specimens for molecular testing (e.g., respiratory virus PCR) prior to sample inactivation''[2] • The below activities should only be performed in a BSL-3 laboratory ○ Live SARS-CoV-2 virus culture[5,7,8] ○ Virus isolation[5,8,14] ○ ''Initial characterization of viral agents recovered in cultures of novel SARS-CoV-2''[5] ○ Neutralization assays[8] ○ ''Any propagation, culturing or deliberate work on SARS-CoV-2 for diagnostic or research purposes''[2] • Controlled ventilation system ○ ''A controlled ventilation system maintains inward directional airflow into the laboratory room.''[8] ○ ''Exhaust air from the laboratory room is not recirculated to other areas within the building. Air must be HEPA filtered, if reconditioned and recirculated within the laboratory. When exhaust air from the laboratory is discharged to the outdoors, it must be dispersed away from occupied buildings and air intakes. This air should be discharged through HEPA filters.''[8]

(*continued*)

Table 1. (Continued)

Title	*Comments*
	• Using certified Class II BSC for the following activities ○ All experiments that generate aerosols, droplets or splashes (loading and unloading of sealed centrifuge cups, blending, grinding, vigorous shaking or mixing, etc.) must be carried out in the certified Class II BSC[2,5,8,16] or even CL3.[2] ○ Centrifugation of samples with infectious potential should be loaded and unloaded in the certified Class II BSC using splash shield; centrifuge safety cups; and sealed centrifuge rotors.[2,5,8,16] ○ ''Aliquoting and/or diluting samples''[16] ○ ''Inoculating bacterial or mycological culture media''[16] ○ ''Performing diagnostic tests that do not involve propagation of viral agents *in vitro* or *in vivo* (e.g., preparing slides for immunofluorescence)''[16] ○ ''Nucleic acid extraction procedures involving potentially infected specimens''[16] ○ ''Preparation and chemical- or heat-fixing of smears for microscopic analysis''[16] • ''Any procedure within the laboratory which generates aerosols and is performed outside a BSC (or the cleaning up highly suspicious samples spilling, for example) must be performed using N95 mask.''[16] • ''A dedicated hand-wash sink should be available in the laboratory.''[8]
Storage of COVID-19 samples	• ''Specimens must be stored in containers with adequate strength, integrity and volume to contain the specimen; leak-proof when the cap or stopper is correctly applied; made of plastic whenever possible; free of any biological material on the outside of the packaging; correctly labelled, marked and recorded to facilitate identification; and made of an appropriate material for the type of storage required.''[8] • Set the temperature for shipment in line with expected shipment time ○ 2–8°C if ≤24–72 hours[7,13–15] and 5–12 days for some samples[7,13] o − 20°C[7] or ideally −70°C or below (dry ice) if >72 hours[6,7,13–15] and more than 1–2 days for some samples[7,13] • Avoid repeated freezing and thawing[6,7,13] • ''At least two aliquots of VTM should be made before the specimens are stored or shipped. One of two aliquots should be stored at −70°C or −80°C as soon as possible.''[6]
Waste management	• ''Where decontamination cannot be performed in the laboratory area or onsite, the contaminated waste must be packaged in an approved (that is leak-proof) manner for transfer to another facility with decontamination capacity.''[8] • ''All disposable material must be autoclaved before final disposal.''[16] • Sharp container boxes ○ ''Dispose of any sharps materials (e.g., needles, needles combined with syringes, blades, broken glass) in puncture-proof or puncture-resistant containers fitted with sealed covers.''[8] ○ ''Puncture resistant container for collection and disposing of used, disposable and auto-disable syringes, needles. 5 L capacity accommodating ∼100 syringes. Boxes prominently marked.''[17] • ''Discard specimens and cultures for disposal in leak-proof containers with tops appropriately secured before disposal in dedicated waste containers.''[8] • ''Consider opening tubes with disinfectant soaked pad/gauze.''[8] • ''External surfaces of specimen containers and vials must be decontaminated using a disinfectant with proven activity against enveloped viruses, prior to their removal from the MSC in CL3.''[2] • ''Handle laboratory waste from testing suspected or confirmed COVID-19 patient specimens as all other biohazardous waste in the laboratory.''[5] • ''Bags for medical waste: Disposal bag for bio-hazardous waste, 30 × 50 cm, with ''Biohazard'' print, autoclavable polypropylene. 50 or 70 micro thickness.''[17] • ''Currently, there is no evidence to suggest that this laboratory waste needs any additional packaging or disinfection procedures.''[5]

Sources: WHO,[6–8,12,13,a] CDC,[5,14,a,b] GOV.UK,[2,c] and PAHO[15–17,a,d]

To access more details and whole text of the free resources and to update information visit the relevant websites.

[a]Adapted with permission from the WHO, CDC, and PAHO.

[b]Materials developed by CDC.

[c]According to the terms and conditions for GOV.UK under the Open Government Licence v1.0.

[d]According to the terms and conditions for PAHO under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs 3.0 IGO License.

BSC, Biological Safety Cabinet; BSL-2, Biosafety Level 2; BSL-3, Biosafety Level 3; CDC, US Centers for Disease Control and Prevention; CL2, Containment Level 2; CL3, Containment Level 3; IATA, International Air Transport Association; PPE, personal protective equipment; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; VTM, viral transport medium; WHO, World Health Organization.

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Address correspondence to:
Vahid Haghpanah, MD, MPH, PhD
Endocrinology and Metabolism Research Center
Endocrinology and Metabolism Clinical Sciences Institute
Tehran University of Medical Sciences
Dr. Shariati Hospital, North Kargar Avenue
Tehran 14114
Iran

E-mail: v.haghpanah@gmail.com;
vhaghpanah@tums.ac.ir