



BIOSAFETY GUIDANCE: COVID-19 RESEARCH AT UNIVERSITY OF SOUTH CAROLINA

Note: No virus culture or isolation, initial characterization of viral agents recovered in cultures of SARS-CoV-2 specimens, or FACS/High Speed Cell Sorting of samples can be performed in any USC laboratory. Experiments involving isolation, amplification, or use of materials with a high viral load can only be conducted in a Biosafety Level 3 (BSL-3) laboratory using BSL-3 practices.

OVERVIEW & SCOPE

This document provides biosafety guidance for research laboratories that will be handling samples from COVID-19 suspected or positive patients. The guidance outlined below serves to assist labs in implementing proper biosafety procedures to handle and transport COVID-19 samples. All COVID-19 research projects using biohazardous materials must be approved by the Institutional Biosafety Committee (IBC) prior to performing any experiments. Please notify the Biosafety Office ([Sherika Smith](#) or [Mark Robbins](#)) if you plan to conduct any COVID-19 research using biological materials.

RISK ASSESSMENT

The CDC has provided laboratory biosafety and COVID-19 guidance that encourages labs to take precautions in handling specimens that are suspected or confirmed for SARS-CoV-2 until more information becomes available. According to this [CDC guidance](#), “All laboratories should perform a site-specific risk assessment to identify and mitigate risks and determine if enhanced biosafety precautions are warranted based on situational needs...Risk assessments and mitigation measures are dependent on the procedures performed, identification of the hazards involved in the process and/or procedures, the competency level of the personnel who perform the procedures, the laboratory equipment and facility, and the resources available.” The CDC also indicates the risk assessment should identify activities that could produce a negative outcome, and prioritize those negative outcomes or risks based on their likelihood and the consequences of each identified risk. Control measures should be effective and based on this risk assessment. These issues should be carefully evaluated for COVID-19 research projects.

Questions to ask when conducting a lab-specific risk assessment include:

- What are the types of specimens that will be handled (blood, respiratory secretions, fixed or unfixed tissues, etc.)?
- What lab procedures will be performed when handling specimens that could increase the risk of exposure (centrifugation, sharps usage, procedures outside a BSC, etc.)?
- What is the relevant training and experience for lab personnel conducting COVID-19 related experiments?
- What potential situations are there in which exposure or release could occur?
- What is the likelihood of an exposure/release occurring?
 - Unlikely: not very possible to occur in the near future
 - Possible: feasible to occur in the near future
 - Likely: very possible to occur in the near future
- What is the severity of the consequences of an exposure/release (negligible, moderate, severe)?

IBC PROTOCOLS

The following biosafety containment considerations should be addressed (if applicable) for experiments involving COVID-19 patient specimens in the Human-Derived Materials Summary of your IBC protocol:

- The PI will control access to the laboratory.
- All lab personnel will wash hands after working with potentially infectious samples and before leaving the lab.
- The use of sharps will be eliminated whenever possible. If sharps are used, describe the type of contaminated sharps that will be used and precautions to prevent exposure. Also, specifically indicate if no sharps will be used for any experiments involving potentially infectious samples.
- All procedures will be performed to minimize the potential for generating splashes or aerosols.
- Work surfaces will be decontaminated after completion of work and after any spill or splash of potentially infectious material using EPA List N: Disinfectants for Use Against SARS-CoV-2.
- All potentially infectious materials will be decontaminated before disposal. If materials will be decontaminated outside the lab, they will be transported in a durable, leak-proof container.
- If potentially infectious samples are centrifuged in the open lab, a centrifuge with sealed rotor heads or centrifuge safety cups will be used for containment of potential aerosols.
- The PI will ensure lab personnel receive appropriate training and will be provided information regarding immune competence and conditions that may predispose them to infection. Individuals with health conditions or concerns will be encouraged to contact their healthcare provider for counseling and guidance.
- Lab personnel handling human samples will complete Bloodborne Pathogens training annually.
- The PI will ensure that laboratory personnel demonstrate proficiency in standard and special microbiological practices before working with samples used in this project. This includes proper use and doffing of personal protective equipment.
- Lab equipment will be routinely decontaminated. Spills involving infectious materials will be contained, decontaminated, and cleaned up according to the BSL-2 spill procedures.
- Incidents that may result in exposure to infectious materials will be immediately reported using the Laboratory Incident Report Form, evaluated, and treated. Lab personnel will follow the university's procedures for incidents involving a biological hazard.
- All procedures involving the manipulation of potentially infectious materials that may generate an aerosol will be conducted in a biosafety cabinet (BSC).
- Patient specimens will be inactivated prior to flow cytometry.
- Eye and face protection will be used any time potentially infectious samples will be handled outside the BSC or containment device. PPE may include an N95 respirator based on a risk assessment.
- The use of N95 respirators requires medical clearance, annual fit testing, and annual training. Contact Leigh Ann Wood at 803-960-1103 or lw32@mailbox.sc.edu for N95 approval requirements.
- Double gloves will be used when handling samples. Gloves will be changed when contaminated or the integrity has been compromised.
- Protective clothing will be removed before leaving for non-lab areas.

Note: BSL-2 labs should avoid culturing primary cells from COVID-19 patients due to the potential for growing infectious virus. Flow cytometry of unfixed patient specimens is also not permitted at BSL-2. Since SARS-CoV-2 is a novel virus, there is regularly new information available that can better inform a

risk assessment for this research. A PI may request an exception to conduct experiments that do not conform to the general guidance contained in this policy IF the PI provides adequate justification required by the IBC to consider approval of the proposed experiments. This justification must include any relevant references or documentation to support claims that the experiments present an acceptable risk and can be conducted safely in a BSL-2 lab with the work practice or safety equipment enhancements described by the PI in their protocol.

TRANSPORT OF PATIENT SPECIMENS

Patient specimens transported by personal or university vehicle are considered materials of trade according to the Hazardous Materials Regulations (HMR). Materials of Trade are hazardous materials other than a hazardous waste, that are carried on a motor vehicle for purposes that include being carried by a private motor carrier to directly support a principal business that is not transportation. (e.g., academic and laboratory research, pest control, plumbing, painting) (49 CFR 171.1). Because patient specimens are being transported for research purposes, transport directly from hospitals or clinics to university laboratories is a function not subject to the requirements of the HMR. Specimens from patients positive for or suspected of COVID-19 are considered a Category B infectious substance according to the Hazardous Materials Regulations.

- **Infectious substance Material of Trade definition** (49 CFR 173.6): Division 6.2 material, other than a Category A infectious substance, contained in human or animal samples (including, but not limited to, secreta, excreta, blood and its components, tissue and tissue fluids, and body parts) being transported for research, diagnosis, investigational activities, or disease treatment or prevention, or is a biological product or regulated medical waste.

When transported by motor vehicle in conformance with section 173.6 (Materials of Trade Exceptions), a material of trade is only subject to the requirements referenced in the following section:

- The material must be contained in a combination packaging (refer to the CDC [schematic](#) for packaging UN3373 Category B). For liquids, the inner packaging must be leakproof, and the outer packaging must contain sufficient absorbent material to absorb the entire contents of the inner packaging. For sharps, the inner packaging (sharps container) must be constructed of a rigid material resistant to punctures and securely closed to prevent leaks or punctures, and the outer packaging must be securely closed to prevent leaks or punctures. For solids, liquids, and sharps, the outer packaging must be a strong, tight packaging securely closed and secured against shifting, including relative motion between packages, within the vehicle in which it is being transported.
- Other than a regulated medical waste, the amount of Division 6.2 material in a combination packaging must conform to the following limitations: (A) One or more inner packagings, each of which may not contain more than 0.5 kg (1.1 lbs) or 0.5 L (17 ounces), and an outer packaging containing not more than 4 kg (8.8 lbs) or 4 L (1 gallon); or (B) A single inner packaging containing not more than 16 kg (35.2 lbs) or 16 L (4.2 gallons) in a single outer packaging.
- The operator of a motor vehicle that contains a material of trade must be informed of the presence of the hazardous material (including whether the package contains a reportable quantity) and must be informed of the requirements of this section.

Patient specimens must be transported in such a way as to minimize exposure to infectious agents (packages must always remain upright and secured in the vehicle). The inner or outer container must be labeled with the contents and contact information for the lab. The secondary container is required by the Bloodborne Pathogens Standard to be labeled with the biohazard symbol. All outer labeling must be included on the package per DOT/IATA requirements for "Biological Substance, Category B". Biohazardous materials must never be left unattended during transport and must always be under the supervision of lab personnel trained in proper spill and emergency procedures.

If dry ice will be used, the packaging must be constructed in a way to allow for the release of carbon dioxide gas and the outside must be labeled "Dry ice". The package should be located as far away from the passengers as possible, and windows must be opened to allow for adequate ventilation of the cabin.

It is strongly recommended that only university vehicles be used in the transport of patient specimens. Consult with your Department Chair for guidance on the availability of a university vehicle and request approval from your Chair before using a personal vehicle for transporting specimens. If a personal vehicle will be used, it must be exclusively used to transport patient specimens during the transport operation (no stops in between). If an employee is approved by their Chair or supervisor to use their own vehicle, they are encouraged to speak with their auto insurance carrier for liability and coverage questions.

All spills or exposures during transport must be reported immediately to the supervisor and Environmental Health & Safety using the Laboratory Incident Report Form. A spill kit must be present in the vehicle. The person transporting patient specimens must have knowledge of the emergency procedures in case of an accident or spill.

DISINFECTION/INACTIVATION

Work surfaces and equipment should be routinely decontaminated. Appropriate disinfectants with proven activity against enveloped viruses should be used for disinfection. These include sodium hypochlorite, alcohol, hydrogen peroxide, quaternary ammonium compounds, and phenolic compounds. Refer to the EPA's [List N for registered disinfectants](#) for use against SARS-CoV-2.

SARS-CoV-2 is suspected of being inactivated by heat (70°C for 5 min or 60°C for 30 min) and UV radiation (30 min)

Commonly used disinfectants in laboratories that can be used against SARS-CoV-2:

- 10% bleach, 20% bleach (0.5% and 1% sodium hypochlorite, respectively; contact times vary with concentration and organic matter present)
- 70% ethanol (10 min contact time)
- Cavicide, Caviwipes, Caviwipes Bleach, Cavicide Bleach (3 min contact time)
- Lysol® Disinfecting Wipes, Lysol® Disinfectant Spray (10 min contact time)
- Lysol® Brand All Purpose Cleaner (2 min contact time)
- HaloSpray (10 min contact time)

TRAINING

Laboratory personnel that will be conducting COVID-19 research using patient specimens or other biohazardous materials must be up to date on BSL-2 and Bloodborne Pathogen training.

BSL-2 Training for Labs: Training is currently being conducted through Microsoft Teams. Personnel need to register by sending an email to smiths69@mailbox.sc.edu. Future dates will be added to the training schedule on the [Training webpage](#).

Bloodborne Pathogens Training for Labs: A training PowerPoint is posted [online](#). Lab personnel should review the slides and complete the quiz with a score of 80% or higher to receive a certificate. Certificates will be emailed to you upon successful completion of the quiz.

COVID-19 Training: All personnel working in laboratories conducting COVID-19 research must complete SARS-CoV-2 specific training. The [Research Safety website](#) includes a Laboratory-Specific Training Verification for COVID-19 Research form that can be used to document lab staff completion of training.

SARS-COV-2 AGENT SAFETY INFORMATION

CHARACTERISTICS

SARS-CoV-2 is a novel coronavirus that is responsible for the COVID-19 pandemic. It is a positive sense single stranded RNA β Coronavirus that is genetically similar to SARS-CoV.

HOST RANGE

Reservoir (intermediate host) likely bats, possibly pangolins

TRANSMISSION

Human to human; animal (unknown species) to human

INCUBATION PERIOD

7-14 days (average 5-6 days in 90% of cases)

SYMPTOMS OF EXPOSURE

Symptoms range from mild symptoms (cough, fatigue, fever) to severe disease (difficulty breathing, persistent pain or pressure in the chest, and confusion or inability to arouse). The main symptoms are fever, cough, and shortness of breath. Symptoms usually appear 2-14 days after exposure.

LAB-ACQUIRED INFECTIONS (LAIs)

There has been at least one reported LAI for SARS-CoV-2. Since this is a novel virus, data on reported LAIs is limited.

PRIMARY HAZARDS

Respiratory transmission (inhalation): droplets (primarily) and aerosols
Fomite transmission: contaminated surfaces and inanimate objects

SURVIVAL OUTSIDE HOST

Detectable in aerosols for 3hrs, on copper for 4hrs, cardboard for 24hrs, and 2-3 days on plastic and stainless steel⁹

INFECTIOUS DOSE

Unknown

PERSONAL PROTECTIVE EQUIPMENT

Lab coats, gloves, face/eye protection (when risk of splashes, sprays, droplets), surgical mask (blood) or N-95 (respiratory secretions; requires enrollment in Respiratory Protection Program)

LAB CONTAINMENT

BSL-2 containment for molecular analysis of already extracted nucleic acid preparations, pathologic examination and processing of formalin-fixed or otherwise inactivated tissues, analysis of inactivated specimens such as specimens in nucleic acid extraction buffer, certain patient specimens (stool, whole blood, serum, and urine), and flow cytometry for fixed samples.

BSL-2+ containment (BSL-2 with BSL-3 practices) for analysis of respiratory samples and secretions from COVID-19 positive or suspected patients, work with COVID-19 samples or patient specimens done outside a biosafety cabinet that may produce an aerosol, and work with inactivated virus lysate.

- BSL-3 work practices include: all procedures with potential to generate aerosols or droplets done in BSC, enhanced PPE (disposable lab coats, double gloves, face shield, respiratory protection-determined by risk assessment), use of sealed centrifuge rotors or sample cups when centrifuging specimens, SARS-CoV-2 specific training

Biosafety Cabinet (BSC) for any procedure that has the potential to generate droplets or aerosols (e.g. centrifuging, vortexing, opening containers, pipetting) must be performed in a certified Class II BSC. Centrifuging specimens should be in safety cups or sealed rotors that are loaded and unloaded in a BSC.

MEDICAL PRECAUTIONS/TREATMENT

Prophylaxis: Immunization is the most effective way to prevent SARS-CoV-2 infection. Anti-SARS-CoV-2 monoclonal antibodies (mAbs) may also be effective as post-exposure prophylaxis (PEP) for certain groups of people. The risk of transmission can be reduced by maintaining a distance of at least 6 feet from others, wearing a face covering, and frequent handwashing.

Vaccines: Approved and authorized COVID-19 vaccines are: Pfizer-BioNTech (BNT162b2), Moderna (mRNA-1273), and Johnson & Johnson/Janssen (JNJ-78436735). For more information on COVID-19 vaccines, visit the CDC [website](#).

Diagnosis: Currently there are two diagnostic COVID-19 tests. A viral test (i.e., molecular or antigen test) is used to diagnose a current infection. An antibody test (also known as a serology test) is used to detect a recent or prior COVID-19 infection. Antibody tests should not be used to diagnose a current infection.

Treatment: Intravenous remdesivir is approved by the Food and Drug Administration (FDA) for hospitalized COVID-19 patients. The FDA has authorized two oral antivirals, Paxlovid and molnupiravir, for the treatment of COVID-19 in certain patients.

SPILL PROCEDURES

Follow USC's Spill Clean-up [Procedures](#)

OCCUPATIONAL HEALTH

Lab personnel health status may impact an individual's susceptibility to infection, ability to receive immunizations or prophylactic interventions as they may become available. Therefore, lab personnel are encouraged to consult with their healthcare provider for information regarding immune competence and conditions that may predispose them to infection, or for counseling and guidance. Lab personnel can also contact [USC's Workers' Compensation](#) for guidance on the management of work-related accidents or exposures and for guidance on how to properly seek prompt treatment for incidents.

EXPOSURE PROCEDURES

An exposure incident means a specific eye, mouth, other mucous membranes, non-intact skin, parenteral contact (e.g., needle stick), or inhalation of aerosols involving a potentially infectious material that results from the performance of an employee's duties. A potentially infectious material or biological hazard may include an incident involving a microorganism (e.g., bacterial agent, viral agent, fungal agent), human-derived material, biological toxin, or an incident involving recombinant DNA research.

Procedures for exposures to a potentially infectious material:

1. Stop work and immediately wash or flush the exposed area with soap and water for 10 minutes. If an eye exposure, flush the eyes (holding open) using the eyewash for 10 minutes.
2. Follow steps outlined in the [USC Workers' Compensation Guidance for Work Related Accidents or Injuries](#).
3. Complete and submit the [USC Laboratory Incident Report Form \[docx\]](#) to the Biological Safety Officer (BSO) at smiths69@mailbox.sc.edu as soon as possible.

Note: The exposed employee and/or their supervisor should provide the healthcare professional evaluating the exposure incident with a description of the job duties relevant to the exposure incident, route(s) of exposure, circumstances of exposure, biological agent or hazard involved in the incident (e.g., SARS-CoV-2, *Vibrio parahaemolyticus*, lentiviral vector), and relevant medical records.

WASTE MANAGEMENT

Currently, there is no evidence to suggest that COVID-19 laboratory waste needs any additional packaging or disinfection procedures. Biohazardous waste collected as normal for BSL-2 laboratories.

SPECIAL CONSIDERATIONS

Lab personnel who need to take extra precautions should consult with their healthcare provider:

- Older adults (65 years and older)
- People of any age with underlying health conditions (e.g., asthma, chronic lung disease, serious heart conditions, immunocompromised, diabetes, obesity, liver disease, chronic kidney disease)

BIOSAFETY GUIDANCE FOR SARS-COV-2 RESEARCH UNDER THE *NIH GUIDELINES*

Risk Group (RG) Classification for SARS-CoV-2:

In Appendix B-II-D of the *NIH Guidelines* (April 2019), coronaviruses other than SARS-associated coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) are classified as RG2 agents. SARS-CoV and MERS-CoV are listed as RG3 agents. This classification reflected the state of knowledge prior to the emergence of the novel coronavirus SARS-CoV-2. The Appendix is intended to serve as a resource and is not to be all-inclusive.

Table 1 in Appendix B of the *NIH Guidelines* provides the basis for the classification of biohazardous agents by RG. RG3 agents are those that are associated with serious or lethal human diseases for which preventive or therapeutic interventions *may be* available.

At the present time, SARS-CoV-2 best meets the definition of an RG3 agent and Institutional Biosafety Committees (IBCs) should consider the agent to be RG3 as a starting point in their risk assessments when reviewing research subject to the *NIH Guidelines*.

The RG classification may change over time as additional information about the virus, such as potential treatments or the development of an effective vaccine, becomes available.

Biosafety Level for handling SARS-CoV-2:

The Centers for Disease Control and Prevention (CDC) has issued [Interim Laboratory Biosafety Guidelines for Handling and Processing Specimens Associated with Coronavirus Disease 2019 \(COVID-19\)](#). Laboratories working with SARS-CoV-2 should adhere to this guidance. IBCs may stipulate additional biosafety precautions based on their risk assessment of specific modifications to and manipulations of the agent. At this time, IBCs should consider the agent to be RG3 as a starting point in their risk assessments when reviewing research subject to the *NIH Guidelines*.

RESOURCES

1. WHO Lab Biosafety Guidance Related to COVID-19 [https://www.who.int/publications-detail/laboratory-biosafety-guidance-related-to-coronavirus-disease-2019-\(covid-19\)](https://www.who.int/publications-detail/laboratory-biosafety-guidance-related-to-coronavirus-disease-2019-(covid-19))
2. Canada Biosafety Advisory- SARS-CoV-2 <https://www.canada.ca/en/public-health/services/laboratory-biosafety-biosecurity/biosafety-directives-advisories-notifications/novel-coronavirus-january-27.htm>

3. Labconco Biosafety Recommendations for SARS-CoV-2 and COVID-19
<https://www.labconco.com/articles/laboratory-biosafety-recommendations-for-sars-co>
4. ABSA Considerations for Handling Potential SARS-CoV-2 Samples https://absa.org/wp-content/uploads/2020/03/ABSA2020_Covid-19-dr3.pdf
5. CDC Interim Laboratory Biosafety Guidelines for Handling and Processing Specimens Associated with COVID-19 <https://www.cdc.gov/coronavirus/2019-nCoV/lab/lab-biosafety-guidelines.html>
6. CDC Information for Laboratories <https://www.cdc.gov/coronavirus/2019-nCoV/lab/index.html>
7. Safety Considerations for Handling Specimens Suspected or Known to Contain SARS-CoV-2
<https://academic.oup.com/ajcp/article/153/5/567/5810006>
8. Interim Laboratory Biosafety Guidance for Research with SARS-CoV-2 and IBC Requirements under the NIH Guidelines <https://osp.od.nih.gov/biotechnology/interim-lab-biosafety-guidance-for-research-with-sars-cov-2/>
9. Persistence of Coronaviruses on Inanimate Surfaces https://absa.org/wp-content/uploads/2020/04/Kampf_2020.pdf
10. NEJM Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1
https://www.nejm.org/doi/full/10.1056/NEJMc2004973?query=featured_home
11. COVID-19 and Blood Safety <https://www.sciencedirect.com/science/article/pii/S0887796320300146>
12. SARS-CoV-2 Flow Cytometry Sorting Protocol Procedures <https://isac-net.org/news/497501/NEW-SARS-CoV-2-SORTING-PROTOCOLS-RELEASED.htm>
13. NIH COVID-19 Treatment guidelines: Prevention or SARS-CoV-2 Infection
<https://www.covid19treatmentguidelines.nih.gov/overview/prevention-of-sars-cov-2/>
14. CDC Different COVID-19 vaccines <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines.html>
15. U.S. Department of Health and Human Services. COVID-19 Treatments and Therapeutics.
<https://www.hhs.gov/coronavirus/covid-19-treatments-therapeutics/index.html>

Packaging and Transport Information

16. Saf-T-Pak Packaging Checklist <https://www.cdc.gov/coronavirus/mers/downloads/lab/Saf-T-Pak-packaging-checklist.pdf>
17. IATA Packing Instructions 650 for UN 3373 <https://www.iata.org/en/programs/cargo/dgr/download>
<https://www.iata.org/contentassets/b08040a138dc4442a4f066e6fb99fe2a/dgr-62-en-pi650.pdf>
18. Labels for UN3373
 - a. Cold pack <https://www.cdc.gov/coronavirus/mers/downloads/lab/UN3373-label-cold-pack.pdf>
 - b. Dry ice <https://www.cdc.gov/coronavirus/mers/downloads/lab/UN3373-label-dry-ice.pdf>
19. CDC schematic for packaging UN3373 Category B
<https://www.cdc.gov/coronavirus/mers/downloads/lab/UN3373-packaging-schema.pdf>
20. Pipeline and Hazardous Materials Safety Admin., DOT Materials of Trade Exceptions
<https://www.govinfo.gov/content/pkg/CFR-2011-title49-vol2/pdf/CFR-2011-title49-vol2-sec173-6.pdf>
21. 171.1 Applicability of Hazardous Materials Regulations (HMR) to persons and functions :
<https://www.govinfo.gov/content/pkg/CFR-2011-title49-vol2/pdf/CFR-2011-title49-vol2-part171.pdf>