

COVID-19 RESOURCES AND FAQs

1. *Do COVID-19 positive samples represent a different sort of biohazard and do they need to be stored separately? How does the Biorepository currently handle potentially HIV-infected samples (e.g., is BSL2 or BSL3 required?). Will this also depend on specimen type?*

The Biorepository is currently receiving, processing, storing, and distributing a variety of COVID-19 sample types in support of government and commercial clients. The materials, in general, are treated like other infectious pathogens, including HIV, that are handled using universal precautions and as BSL-2 items, with some exceptions as detailed below.

Given that there is still much to learn about COVID-19 we have put some enhanced procedures in place for staff as it relates to handling and disinfecting incoming COVID-19 specimens. These procedures have been introduced to ensure the safety of the Biorepository team and to mitigate the potential of airborne exposure to COVID-19 virus particles. These enhanced procedures were developed following guidance from the Biosafety in Microbiological and Biomedical Laboratories (BMBL), Centers for Disease Control and Prevention (CDC)/World Health Organization (WHO) guidance and following best practices.

As described below in the response to questions 2 and 3, the Biorepository staff have been trained to follow SOPs that have been crafted to address the nuances associated with Biobanking and Specimen Handling of COVID-19 Samples. These documents ensure that all laboratory personnel are properly trained with the enhanced safety guidelines for handling COVID-19 samples and that training has been documented.

As mentioned above, the additional precautions have been put in place primarily because of the concerns for the potential for airborne transmission with some types of COVID-19 samples or under a specific set of scenarios that arise during transport or downstream sample processing. The potential for airborne transmission of COVID-19 presents a challenge which is not typical for the vast majority of incoming frozen clinical samples that are handled by the Biorepository, including HIV. Given that we are doing minimal downstream processing, the primary tasks we are addressing surround the receipt of material types that have the possibility of generating aerosols upon unpacking (e.g. frozen material that may have thawed in transit) or where we assume the samples collected from COVID-19 patients may be, or have become, contaminated on the outside of containers (e.g. swab containers, etc.).

The procedures put in place at the Biorepository include requirements to don extra PPE (e.g. N95s, disposable sleeves over lab-coats, double gloving, etc.) as well as prescribed usage of disinfectant/cleaning solutions and wipes. We should note that, at times, there have been reports of limited supplies of disinfectant/cleaning solutions being available. To ensure the safety of the staff, the Biorepository operational team has invested considerable time and effort to bolster their supply chain to ensure that sufficient quantities of these supplies are available on-site.

Beyond the PPE requirements, some sample types are being accessioned in a biosafety cabinet (e.g. frozen material that is suspected to have thawed in transit or specimens that contain patient swabs). For these situations, the secondary packing and primary containers are handled

in a biological safety cabinet. The team is careful to ensure the primary and secondary packing, as well as the outside of the vials, are wiped down with appropriate disinfectants. Any sample processing (e.g. aliquoting or nucleic acid extraction) is also handled in the biosafety cabinet with additional PPE requirements in place. Once frozen sample materials have been decontaminated they are handled essentially like any other infectious pathogen, including HIV.

Known COVID-19 samples are currently being stored in segregated freezers and the samples have been given specific identifiers in our sample management software (BSI) to indicate that they are COVID-19 samples or even more specifically COVID-19 samples of international origin. These designations assist in the identification of suspected and confirmed COVID-19 samples and assist with the maintenance of regulatory compliance as discussed in more detail below.

2. *What are the current, or proposed, protocols for COVID-19 related safety procedures in terms of Biorepository staff and sample handling for future COVID-19-related incoming collections?*

Universal precautions are used when handling all clinical samples, following well-established processes and procedures for working with infectious material including infectious pathogens. Prior to handling any type of clinical samples, the Biorepository technicians have to prove proficiency and show documented training on the relevant Biorepository SOPs. This includes supplementary training for all Biorepository technicians who are handling COVID-19 samples on SOP-Biobanking and Specimen Handling of COVID-19 Samples and SOP-Procedures for Processing Incoming Frozen Specimens. These documents provide the processes for safely receiving, accessioning, and handling of COVID-19 positive and COVID-19 PUI (person under investigation) samples. These SOPs were developed following guidance from the Biosafety in Microbiological and Biomedical Laboratories (BMBL), Centers for Disease Control and Prevention (CDC)/World Health Organization (WHO) guidance and following best practices.

All Biorepository team members are regularly reminded of the COVID-19 monitoring and workplace re-entry/self-quarantine procedures. Amongst other activities, the staff continues to take their temperatures daily before leaving home for work and are instructed to not come in if their temperature is at 100.4°F or higher, or if they have a cough or any general malaise (the Biorepository has issued thermometers to support self-monitoring).

3. *Does the Biorepository recommend requiring COVID-19 testing on incoming specimens? What are the recommendations on how to handle these potential biohazardous biospecimens?*

This is an evolving situation, but at this time the Biorepository would not recommend that non-COVID study samples (e.g., sickle cell, asthma, etc.) be tested before being accepted into the Biorepository as we consider all incoming clinical materials potentially hazardous and train our teams to handle them accordingly using appropriate PPE and procedures that were developed for safe handling of HIV and other infectious pathogens.

At the moment, the Biorepository is working under the assumption that samples being supplied to us are collected and packaged according to special guidance that was issued by CDC:

- a) 11/03/2020: Lab Advisory: CDC Updates Specimen Collection Guidelines for COVID-19 - <https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html>;

- b) Collection and Submission of Postmortem Specimens from Deceased Persons with Confirmed or Suspected COVID-19 - <https://www.cdc.gov/coronavirus/2019> and WHO [“Guidance for laboratories shipping specimens to WHO reference laboratories that provide confirmatory testing for COVID-19 virus”](https://www.who.int/publications/i/item/guidance-for-laboratories-shipping-specimens-to-who-reference-laboratories-that-provide-confirmatory-testing-for-covid-19-virus)
<https://www.who.int/publications/i/item/guidance-for-laboratories-shipping-specimens-to-who-reference-laboratories-that-provide-confirmatory-testing-for-covid-19-virus>) to collection centers.

These documents lay out recommendations for the special handling of COVID-19 samples to help reduce contamination of shipping materials. Even so, additional precautions will be utilized at the Biorepository during the receiving process.

The Biorepository is committed to working closely with clients, early and often, to better align shipping and packing processes to ensure the safety of our staff. In particular, the Biorepository communicates to our shipping sites the necessity that all shipments are prepared and packaged following the **Required Shipping Guidelines**:

- CDC recommends that shippers “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 International Air Transport Association (IATA) Dangerous Goods Regulations.” (link: <https://www.cdc.gov/coronavirus/2019-ncov/lab/lab-biosafety-guidelines.html>)
- The Biorepository recommends that collection/shipping sites wipe down secondary and primary vessels (sealable bag, and vial container, respectively) with an appropriate disinfectant (e.g. 70% ethanol solution) before packing and shipping.
- The Biorepository requires non-COVID study specimens to be shipped in a separate package from COVID-related samples. When received at the Biorepository, COVID-related samples will be received, accessioned, and stored separately from non-COVID samples. The primary and secondary vessels for COVID-related samples will be wiped with 70% ethanol as a precautionary measure prior to data accessioning and storage.

The Biorepository is in regular communication with the shipping sites and frequently reminds them that it is imperative that the Biorepository receives advanced notice as to when the shipments might be arriving. This is particularly important when the Biorepository may be receiving both COVID-19 and non-COVID-19 samples from the same originating site. The Biorepository reminds the shipping sites that it requires non-COVID study specimens to be shipped in a separate package from COVID-related samples.

Additionally, the Biorepository is in communication with its stakeholders to understand downstream sample utilization towards ensuring a suitable and safe solution can be delivered for our clients in a timely fashion. A few sample questions that NIH Biorepositories consider are outlined below:

- Will any processing (e.g., aliquots, etc.) be required to be performed by the Biorepository? Or are these primarily receipt, storage, and distribution?

- What are the vial types? This will help us to ascertain if there is anything new or different from current NIH institutes' studies?
- Do you envision these samples coming from existing sites or new sites?
- For sites shipping vials, will the outside of vials and packages be cleaned/disinfected? As mentioned above, new procedures are in place where it is assumed that the samples collected from COVID-19 patients may be/become contaminated on the outside of swab containers, etc. and therefore, they are all opened in BSC and the outside of the vials is wiped down with an appropriate disinfectant solution.
- Upon receipt and storage of these new samples, what is the expected turnaround time for the vials to be shipped out again?
- Are we expecting any international shipments (receiving or shipping)?

The driver for the last question revolves around the CDC permit requirements regarding the import of COVID-19-related items. In short, at the current time, anyone who desires to import Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), or receive a transfer of previously imported material containing SARS-CoV-2 within the United States, is required to obtain a CDC Import Permit.

At the current time, the CDC has indicated that Permits are required for the following activities:

- Import of isolates or cultures of SARS-CoV-2.
- Import of infectious substances (e.g., blood, bodily fluids, tissues) that are reasonably expected to contain SARS-CoV-2.
- Import of nucleic acids capable of producing SARS-CoV-2 (i.e., full-length genomic RNA extracted from SARS-CoV-2).

At the current time, A permit is NOT required for the following activities:

- Specimens or isolates/cultures of SARS-CoV-2 within the United States or its territories that were not generated from imported material.
- Nucleic acids encoding partial sections or fragments of SARS-CoV-2 incapable of producing infectious virus (i.e., partial or degraded SARS-CoV-2 genomic RNA).
- Diagnostic samples not known or suspected of containing SARS-CoV-2. See FAQ "Do I need an import permit" <https://www.cdc.gov/cpr/ipp/faq.htm>

The Biorepository is currently importing material from multiple sites worldwide in support of NIAID-funded studies and has an active import permit. This permit has been amended several times, to add additional labs, as the study has grown.

As noted above, the CDC has implemented restrictions on the domestic transfer of imported material. Subsequent transfers of previously imported material containing SARS-CoV-2 within the United States also requires a CDC import permit. Several domestic labs have requested transfer of previously imported material containing SARS-CoV-2. The Biorepository has leveraged its regulatory experience to support these domestic labs procuring their own CDC import permit and has completed the requested transfer of previously imported material containing SARS-CoV-2.

NOTE: The regulatory landscape is rapidly evolving and it is important that the end-user regularly check with the CDC Import Permit site to ensure they comply with CDC regulations.

4. *Do investigators need to factor in COVID testing as an additional cost to sample preparation?*

At this time, the Biorepository does not require that non-COVID-19 study samples (e.g., sickle cell, asthma, etc.) be tested before being accepted into the Biorepository. This is in alignment with ongoing protocols dictating the handling of HIV and other infectious pathogens. Were the NIH Biorepositories to require testing of incoming samples independently, samples would need to be tested at the time of collection, and this would then most likely be the responsibility of the collection sites. Individual programs and sites should amend this policy to reflect local and institutional regulation and best practices.

Additional Resources Relevant to Biorepositories and COVID-19

Vaught J. Biobanking during COVID-19 pandemic. *Biopreservation and Biobanking* 2020, vol 18(3). DOI:10.1089/bio.2020.29069.jiv <https://pubmed.ncbi.nlm.nih.gov/32297797/>

Abdalhamid B, Bilder CR, McCutchen EL, Hinrichs SH, Koepsell SA, Iwen PC. Assessment of Specimen Pooling to Conserve SARS CoV-2 Testing Resources. *Am J Clin Pathol.* 2020;153(6):715-718. doi:10.1093/ajcp/aqaa064 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7188150/>

Radbel J, Jagpal S, Roy J, et al. Detection of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Is Comparable in Clinical Samples Preserved in Saline or Viral Transport Medium. *J Mol Diagn.* 2020;22(7):871-875. doi:10.1016/j.jmoldx.2020.04.209 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7219422/>

ISBER - Comments on “Responsible Data Sharing to Respond to the COVID-19 Pandemic: Ethical and Legal Considerations (v 2.0): The Perspective of the Regulatory and Ethics Work Stream of the Global Alliance for Genomics and Health.” https://cdn.ymaws.com/www.isber.org/resource/resmgr/docs/Comments_on_GA4GH_Responsibl.pdf

ASCP - Laboratories on the Front Lines: Battling COVID-19. [https://www.ascp.org/content/get-involved/institute-of-science-technology-policy/coronavirus-2019-\(covid-19\)-resources/battling-covid-19](https://www.ascp.org/content/get-involved/institute-of-science-technology-policy/coronavirus-2019-(covid-19)-resources/battling-covid-19)