# Genetic Modification Safety Committee (GMSC) Guidance

## Laboratory work with COVID-19 samples and SARS-CoV-2 virus

## What is it for?

This guidance is written to set out required risk controls for receiving, handling, storing or otherwise working with samples from patients with suspected or laboratory-confirmed COVID-19; or those planning to work with the SARS-CoV-2 virus directly.

## What about my regular samples?

This document should be used to determine controls for all respiratory samples, faecal samples, urine, CSF and amniotic fluid during the present pandemic.

## What about blood and unfixed tissues?

The guidance below does not apply to handling of blood and human tissues from patients of unknown or presumed COVID-19 negative status. In these cases, you should follow the guidance on [safe working with blood, bodily fluids and human tissue](https://www.ucl.ac.uk/safety-services/sites/safety-services/files/safe_working_with_blood_and_human_tissue.docx).

## SARS-CoV-2 Hazard Group

The UK’s Advisory Committee on Dangerous Pathogens (ACDP) has agreed on the provisional classification of SARS-CoV-2 as a hazard group 3 pathogen, which means that by default it must be handled at Containment Level 3. To provide tailored, risk based approached for UCL, The GMSC has agreed approaches which can be summarised in 4 categories as below:

1. Receipt and storage **only** of samples collected or processed outside of UCL, which must be handled at containment level 3, is permitted in containment level 2 laboratories if storage space is constrained.
2. If government agencies (NHS, PHE etc.) request that UCL laboratories support diagnostic work, this may be permitted at Containment Level 2, strictly following the [Public Health England](https://www.gov.uk/government/publications/wuhan-novel-coronavirus-guidance-for-clinical-diagnostic-laboratories/wuhan-novel-coronavirus-handling-and-processing-of-laboratory-specimens) guidelines for safe handling and processing of samples in laboratories.
3. Research with samples confirmed as negative, inactivated samples, all blood samples, all urine and CSF samples and specific lower risk respiratory samples may be handled at Containment Level 2.
4. All COVID-19 research not fitting into the definitions above; SARS-CoV-2 viral culture or work with infected animals must be carried out at Containment Level 3, in one of UCL’s existing approved facilities.

A table summarising the containment level required to work with different sample types is shown below.

## Summary table for COVID-19 sample types

The table below will help you to understand the containment level required to work with different sample types. Click the links to jump to the relevant section, read the guidance notes and ensure a suitable [risk assessment](https://www.ucl.ac.uk/safety-services/policies/2020/apr/risk-assessment) is approved before you begin work.

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| **Sample type** | **Respiratory samples**; nasopharyngeal or oropharyngeal swabs, bronchoalveolar lavage (BAL), aspirate samples, saliva and sputum. | **Faecal samples.** | **Blood samples**;Including serum and PBMC. | **CSF and urine samples.** | **Other tissues and fluids** |
| **Confirmed or presumptive COVID-19 positive samples** | [**Containment Level 3**](#_Research_activity_/) | [**Containment Level 3**](#_Research_activity_/) | [Containment Level 2](https://www.ucl.ac.uk/safety-services/sites/safety-services/files/safe_working_with_blood_and_human_tissue.docx) | [Containment Level 2](https://www.ucl.ac.uk/safety-services/sites/safety-services/files/safe_working_with_blood_and_human_tissue.docx) | [**Containment Level 3**](#_Research_activity_/) |
| **Samples from people of unknown status** | [**Containment Level 3**](#_Research_activity_/) | [**Containment Level 3**](#_Research_activity_/) | [Containment Level 2](https://www.ucl.ac.uk/safety-services/sites/safety-services/files/safe_working_with_blood_and_human_tissue.docx) | [Containment Level 2](https://www.ucl.ac.uk/safety-services/sites/safety-services/files/safe_working_with_blood_and_human_tissue.docx) | Containment Level 3 unless evidence otherwise |
| **Convalescent or recovered COVID-19 patient samples (without negative test results)** | [Containment Level 2](#_Research_with_blood) **[IF](#_Research_with_blood)** [>42 days (6 weeks) after onset of symptoms](#_Research_with_blood) **[AND](#_Research_with_blood)** [if asymptomatic](#_Research_with_blood) | [**Containment Level 3**](#_Research_activity_/) | [Containment Level 2](https://www.ucl.ac.uk/safety-services/sites/safety-services/files/safe_working_with_blood_and_human_tissue.docx) | [Containment Level 2](https://www.ucl.ac.uk/safety-services/sites/safety-services/files/safe_working_with_blood_and_human_tissue.docx) | Containment Level 3 unless evidence otherwise |
| **Confirmed COVID-19 negative samples** | [Containment Level 2](#_Research_with_blood) | [Containment Level 2](#_Research_with_blood) | [Containment Level 2](#_Research_with_blood) | [Containment Level 2](#_Research_with_blood) | [Containment Level 2](#_Research_with_blood) |
| **Inactivated samples\*** | [Containment Level 2](#_Research_with_blood) | [Containment Level 2](#_Research_with_blood) | [Containment Level 2](#_Research_with_blood) | [Containment Level 2](#_Research_with_blood) | [Containment Level 2](#_Research_with_blood) |

\*Includes inactivation on collection (e.g. blood samples in Tempus tubes), inactivation post-collection, fixation with para-formaldehyde and treatment with lysis buffers. Note that inactivation post-collection must take place at Containment Level 3. Samples can be moved out to containment level 2 after inactivation.

An explanation for the risk levels above, including literature review, is available on request by emailing to safety@ucl.ac.uk

## Contents for quick reference

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## Receipt and storage of samples which must be handled at containment level 3

**Activity which is limited only to receipt and storage of samples (processed or unprocessed) from third parties (NHS Trusts, HSL, Francis Crick Institute etc.) is permitted, but the criteria below must be met:**

* A suitable and sufficient risk assessment must be approved, before samples are received and stored. As an interim measure, you are asked to add the UCL Biological Safety Adviser (Andy Minnis) as an approver on your risk assessment.
* The location of stored samples, quantity of samples, reason for storage at UCL and planned duration of storage should be documented in your risk assessment.
* Receipt and storage must take place in a Containment Level 2 laboratory. If opened, packages must be opened in a microbiological safety cabinet prior to transfer to storage. If available, use a Class I cabinet. Some samples received at University laboratories have been found to be packaged inappropriately and some have leaked inside packaging. This risk must be acknowledged and documented in your risk assessment.
* You must consider spill response, in case samples leak or are dropped and have an appropriate procedure in place.
* Samples must be clearly identified on the outside of containers and in the storage location, especially if storage is shared with other research groups or in a shared laboratory. Use the [COVID-19 equipment sign](https://www.ucl.ac.uk/safety-services/sites/safety-services/files/covid-19_laboratory_signage.docx) template available online.
* You must restrict access to your laboratory only to those receiving and storing samples whilst samples are being handled. The ‘[safe to clean](https://www.ucl.ac.uk/estates/our-services/ucl-cleaning-service)’ system must be used to protect cleaning staff and contractors who may need to enter the laboratory during this period. Also affix a warning sign at the entrance door to the laboratory, using the [COVID-19 template](https://www.ucl.ac.uk/safety-services/sites/safety-services/files/covid-19_laboratory_signage.docx) available online.
* Refer back to this guidance and seek additional approval, if planning further manipulation, processing, analysis or research using the samples.

## Diagnostic work, requested to support the national response

**If government agencies (NHS Trusts, PHE etc.) request that UCL laboratories support diagnostic work, this can take place in Containment Level 2 laboratories, provided the criteria below are met:**

* Planned work must be diagnostic work requested by the government as part of UCL’s efforts to support the national response to the COVID-19 pandemic. You must be able to demonstrate that a request has been made for your group / laboratory to carry out this work, for example by sharing a letter or email from a recognised organisation.
* If the request for diagnostic work is recognised and you can proceed, you must strictly follow the [Public Health England](https://www.gov.uk/government/publications/wuhan-novel-coronavirus-guidance-for-clinical-diagnostic-laboratories/wuhan-novel-coronavirus-handling-and-processing-of-laboratory-specimens) guidelines for safe handling and processing of samples in laboratories. In particular, your planned diagnostic work should be non-propagative activity that does not result in the concentration or extraction of SARS-CoV-2.
* As above, a suitable and sufficient risk assessment must be approved, before samples are received and work begins. As an interim measure, you are asked to add the UCL Biological Safety Adviser (Andy Minnis) as an approver on your risk assessment.
* In addition to the PHE guidance, you must also restrict access to your laboratory only to those carrying out the diagnostic work. The ‘[safe to clean](https://www.ucl.ac.uk/estates/our-services/ucl-cleaning-service)’ system must be used to protect cleaning staff and it is recommended that no cleaners, contractors or visitors enter the laboratory at all during this period of work, unless for essential activities. Also affix a warning sign at the entrance door to the laboratory, using the [COVID-19 template](https://www.ucl.ac.uk/safety-services/sites/safety-services/files/covid-19_laboratory_signage.docx) available online.
* If your building is otherwise shut down, you must ensure you can inactivate and remove waste from the building in a safe and compliant manner. Waste must be not allowed to accumulate. You must also follow [lone working](https://www.ucl.ac.uk/safety-services/a-z/lone-working) guidance.
* Work with samples received for the purposes of research or education, including activity aimed at identifying potential treatments must not take place at Containment Level 2. Refer back to this guidance and seek additional approval.

## Research with samples confirmed as negative, inactivated samples, all blood samples, all urine and CSF samples and specific lower risk respiratory samples may be handled at Containment Level 2.

**Work with COVID-19 samples confirmed as negative, inactivated samples, all blood, urine and CSF samples can take place in Containment Level 2 laboratories, provided the criteria below are met. In addition, respiratory samples from convalescent or recovered patients who are >42 days (6 weeks) after the onset of symptoms and asymptomatic can also be handled at containment level 2.**

* Planned work in this category **must** fit the definition in the box above. Particularly, higher risk respiratory and faecal samples must continue to be handled at containment level 3, as in section 4 below.
* A suitable and sufficient risk assessment must be approved locally, before samples are received and work begins.
* **For handling samples in this category,** also follow the guidance on [safe working with blood, bodily fluids and human tissue](https://www.ucl.ac.uk/safety-services/sites/safety-services/files/safe_working_with_blood_and_human_tissue.docx). Urine samples particularly should be handled in safety cabinets, where manipulation will generate aerosols.
* If your building is otherwise shut down, you must ensure you can inactivate and remove waste from the building in a safe and compliant manner. Waste must be not allowed to accumulate. You must also follow [lone working](https://www.ucl.ac.uk/safety-services/a-z/lone-working) guidance.
* If you change the scope of your work, beyond the sample types defined above, you must refer back to this guidance and seek additional approval.

## Research activity / deliberate work; including handling of high risk respiratory and faecal samples

**All COVID-19 research not fitting into the categories above; work with SARS-CoV-2 viral culture or infected animals must be carried out at Containment Level 3, in one of UCL’s existing approved facilities. This ranges from sample manipulation; non-propagative activity that may concentrate or isolate SARS-CoV-2; to propagative work and all *in vivo* work.**

Based on current standards and what is known so far about the virus, below is guidance to follow when planning your research work at Containment Level 3:

* **Document a risk assessment**; use the Hazard Group 3 or GM Class 3 specialist templates in [riskNET](https://www.ucl.ac.uk/safety-services/risknet).
* **A safety cabinet must be used;** this can be Class I or Class II. If both types are available and samples / culture do not require sterile air, Class I cabinets are preferred as Class II cabinets are more affected by external factors and internal flow rates than Class I. If using a Class II, careful operation is crucial to prevent disruption to airflow and contaminated air escaping from the aperture. Use this [WHO video](https://www.youtube.com/watch?v=18QEJUA9XBs) for reference and share with your colleagues.
* **Procedures to minimise/prevent aerosols** must be clearly outlined in your risk assessments. Examples:
	+ Prior to opening any samples or cultures, wait at least 1 minute for aerosols to settle.
	+ Centrifugation must be performed using 'biosafe' (sealed) rotors, which are loaded and unloaded in a safety cabinet.
	+ All pipetting work must be carried out inside a safety cabinet.
	+ When pipetting, tips should be submerged in liquid prior to release; tips drained against the inner wall of the receiving vessel; do not forcibly expel liquid; eject pipette tips carefully into waste containers.
* **Vortexing, sonication or other high energy mixing** which is uncontained must not be carried out. In addition, carefully consider use and containment of samples in rockers, if these are required.
* **If planning to culture the virus -** volumes should be limited to no more than 10ml per individual flask / container.
* **Waste handling** - consider use of [Vernagel](https://www.vernacare.com/our-products/products/vernagel-100-sachets/) in ‘dispo jars’ so that waste containers can be removed without liquid, avoiding splashes and aerosols. This applies to solid and liquid waste and means liquid does not need to be poured down sinks. If Vernagel is used, all waste is solidified and can then be autoclaved.
* **Emergency response** - compare your approach to other labs and discuss any differences.
* **If fixing / treating samples** for removal to lower containment (CL2), you should cite references to support the efficacy of the method to fix or inactivate. For example fixing with formaldehyde (4% PFA) you can reference [this paper](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4353909/); using lysis buffers such as TriZol, you can reference [this paper](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4555185).

## Sample collection

Where UCL staff plan to collect samples in primary and community care settings or in private homes, the following guidance from PHE must be considered:

* [Recommended PPE](https://www.gov.uk/government/publications/wuhan-novel-coronavirus-infection-prevention-and-control/covid-19-infection-prevention-and-control-guidance-low-risk-pathway#personal-protective-equipment) for low risk pathways, observing standard infection control precautions
* Guide to what is considered as [aerosol generating procedures](https://www.gov.uk/government/publications/wuhan-novel-coronavirus-infection-prevention-and-control/covid-19-personal-protective-equipment-ppe#ppe-guidance-by-healthcare-context) in **healthcare settings.**
* [Best practice guidance](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/877531/Best_Practice_management_of_blood_body_fluid_spillages.pdf) on blood and bodily fluid spillages.

## Sample transport

All COVID-19 patient samples must be transported as UN3373 Category B infectious substance. [PHE guidance](https://www.gov.uk/government/publications/wuhan-novel-coronavirus-guidance-for-clinical-diagnostic-laboratories/wuhan-novel-coronavirus-handling-and-processing-of-laboratory-specimens#packaging-and-transport-of-samples) includes a table showing different types of samples and the correct transport category to use. A [step-by-step poster](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/875914/PHE_Packaging_requirements_for_COVID-19_samples_A3_poster.pdf) explaining the packaging requirements is also available. Cultured samples for research or calibration must be transported as UN2814 Category A infectious substance. As with any transport of dangerous goods, you should use a courier or walk with samples. Do not use taxis or public transport.

## Training, competency, supervision and support

In addition to containment measures, it is important to consider training needs, competency assessment, adequate supervision and support from other teams including professional services for the duration of your activity.

* Only fully trained and competent staff should undertake work in containment laboratories. The level of training provided should be appropriate to the level of risk and the complexity of the procedures being undertaken. A competent person with prior experience must carry out training, with line managers responsible for ensuring training and competency assessments are completed. Records of training should be kept.
* Previous experience or seniority does not mean a person is necessarily competent to perform a particular activity. Competence should be viewed as the combination of training, skills, experience and knowledge that a person has, along with their ability to apply them to perform a task safely. Competence gained in one situation, or with one technique does not mean that an individual can carry out all work or any technique.
* Supervision helps to prevent people deviating from established procedures that may result in ill health or injury. The level of supervision required will depend on the risk associated with the task and the competence of the worker.
* As many UCL buildings may remain partly shutdown at this time; support teams and colleagues including laboratory managers may not be available. Anyone planning work must consider the impact of reduced support. This includes supply of consumables and chemicals, removal of waste, support for alarms and response in emergencies. As in normal circumstances, you must consider lone working and make appropriate arrangements following [UCL guidance](https://www.ucl.ac.uk/safety-services/a-z/lone-working).

## Vulnerable groups

Consideration must be given in your risk assessment to vulnerable groups who are at increased risk of severe illness from coronavirus (COVID-19). Further information on this, including a list of underlying health conditions can be found in the UK Government [guide on protecting vulnerable persons.](https://www.gov.uk/government/publications/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19).

## Third party use of UCL laboratories and equipment

Partner organisations, such as NHS Trusts or HSL may request use of UCL laboratories or equipment during the pandemic. This situation should be approached in the same manner as for contractors carrying out work in UCL areas. Ask for risk assessments and if appropriate, associated protocols/procedures. Provide a local induction where needed. Ensure that UCL users of the area are informed and that access control is restricted wherever possible, so that COVID-19 work and other activities do not take place simultaneously in the same space. If appropriate, also restrict access to other contractors and visitors, including cleaning staff.

## Contacts

For more advice and guidance, please contact the UCL Biological Safety Adviser.

This guidance was agreed by the UCL Genetic Modification Safety Committee. The committee advises principally on Genetic Modification work at UCL, however it also advises Council, through the UCL Health & Safety Committee, on work involving wild-type hazard group 3 organisms.

## Document control

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| Version 1 | First issued by Safety Services 18th March. |
| Version 2 | Updated on 27th March – revised to provide more structure and reflecting a consensus position approved by GMSC. |
| Version 3 | Updated 22nd April - new sections on sample collection; training, competency, supervision and support; vulnerable groups; third party use of UCL laboratories and related research activity where there is no risk of infection. |
| Version 4 | Updated 6th of May – new appendix added; a summary table for COVID-19 sample types. Requirement to affix signs on laboratory doors and equipment added into sections 1 and 2. Section ‘note on blood samples’ removed, replaced by appendix 1. |
| Version 5 | Updated 22nd of June - clarification to scope of the guidance added (first page) and summary table moved. Changes in containment level for handling certain blood samples, reflecting changes in understanding of the risk level. New section 3 added (see page 4). Section on ‘Other research activity’ removed. Appendix updated. |
| Version 6 | Updated 6th August – Updated to reflect changes in recommended containment level (3 to 2) for handling blood and CSF samples of all types and for certain convalescent respiratory samples, based on the latest available evidence. Appendix 1 (explanation of recommended containment levels) has been removed to reduce document length. |
| Version 7 | Updated 5th November – Updated to reflect changes in recommended containment level (from CL3 to CL2) for handling urine samples of all types, based on the latest available evidence. Updated sample collection section to remove broken links. |