UNIVERSITY OF BIRMINGHAM

Health & Safety Guidance

Interim guidance on handling clinical samples in light of SARS-CoV-2

GUIDANCE: HCS_COVID/1/20

INTERIM GUIDANCE ON HANDLING HUMAN SAMPLES KNOWN TO CONTAIN, OR POTENTIALLY CONTAINING, SARS-CoV-2 IN RESEARCH ACTIVITIES

Classification of agent

SARS-CoV-2 is a Hazard Group 3 (HG3) virus and is the causative agent of the disease COVID-19. HG3 agents must be handled at Containment Level 3 (CL3), unless they are subject to a specific derogation.

COVID-19 and Respiratory Samples

Detection of SARS-CoV-2 RNA in human respiratory tract samples is highest around the time of symptom onset and gradually declines over time. Virus transmission is linked to aerosol and droplet exposure, or via fomites (contaminated surfaces), and therefore respiratory tract related samples are likely to present a high risk from exposure during processing. **All** respiratory samples, regardless of source, must be handled at a minimum of CL2 and any sample processing must take place in a microbiological safety cabinet (MSC). Samples must be sufficiently contained if handled outside the MSC, unless a risk assessment justifies a reduced infection risk. Risk assessments should consider the likely presence of SARS-CoV-2 and other pathogens based on the source of the material and adjust the containment level accordingly. Any procedures that are likely to generate large amounts of aerosol or splashing must be identified and may require additional control measures such as a specific class of MSC, or use of specialist equipment.

COVID-19 and other samples

Other tissues and body fluids will require a careful assessment of the likelihood that SARS-CoV-2 is present. This will be a changing situation as more research is undertaken and will necessitate a periodic review of existing risk assessments. Currently there is limited information available on the presence of viral RNA and infectious virus in body fluids including blood, urine, faeces and CSF. A minimum of CL2 must be used and adjusted to take into account the likely presence of HG3 pathogens. Any aerosol or droplet generating procedures must be undertaken in a microbiological safety cabinet and any procedures that are likely to generate large amounts of aerosol or splashing must be identified and may require additional control measures such as a specific class of MSC.

Work at CL3

Any deliberate work with the virus, or where there is a risk of inadvertent culture of the virus from contaminated tissues, **must** be undertaken at full CL3. **This will include all research activities where they cannot be mapped to the Public Health England guidance (see below)**, including incubation of cells. Activities that may generate aerosols, such as the use of FACS sorters, will need to be individually risk assessed.

Scope of Public Health England Guidance

Public Health England have produced guidance for the safe handling of SARS-CoV-2 in clinical diagnostic laboratories - COVID-19: safe handling and processing for samples in laboratories. This guidance was recently extended by the Health and Safety Executive to those laboratories handling specimens from patients with suspected or laboratory-confirmed COVID-19 in non-clinical diagnostic laboratories, for example in laboratories undertaking research, or developing diagnostic assays with such samples.

The guidance allows **specified** activities to be carried out at Containment Level 2 in a Microbiological Safety Cabinet. Therefore, work with human samples (e.g. blood, sputum, saliva, bronchoalveolar lavage fluid, tissue samples) that are **known/suspected** to contain SARS-2 **may** be handled at CL2 in a Microbiological Safety Cabinet (MSC), **but only under specified circumstances, subject to risk assessment. Samples must be inactivated in an MSC before being removed from the cabinet for handling elsewhere. Any exceptions to this must be fully justified in a risk assessment and approved by the University's Advisory Group for the Control of Biological Hazards before work begins.**

Samples that **could potentially contain** the virus (i.e. have not tested negative but are "unknowns") must be handled at CL2 in an MSC unless it can be shown that they do not contain virus. The risk assessment should define the source population, assess the likelihood that SARS-2 may be present and assign control measures accordingly.

Requirements for work with COVID+ samples to be undertaken at CL2 in an MSC

The following requirements must be met for work to be carried out on clinical samples containing SARS-CoV-2 at CL2:

1) All work must have a risk assessment (a legal requirement), and
2) The activities covered by the assessment **must** clearly be aligned to those activities listed in sections 5.1 and 5.2 of the PHE Guidance document (see Appendix 1). **If the activities cannot be mapped to those listed, they must be carried out at CL3. Samples may only be removed from the cabinet for handling elsewhere once they have been inactivated via a validated method.**

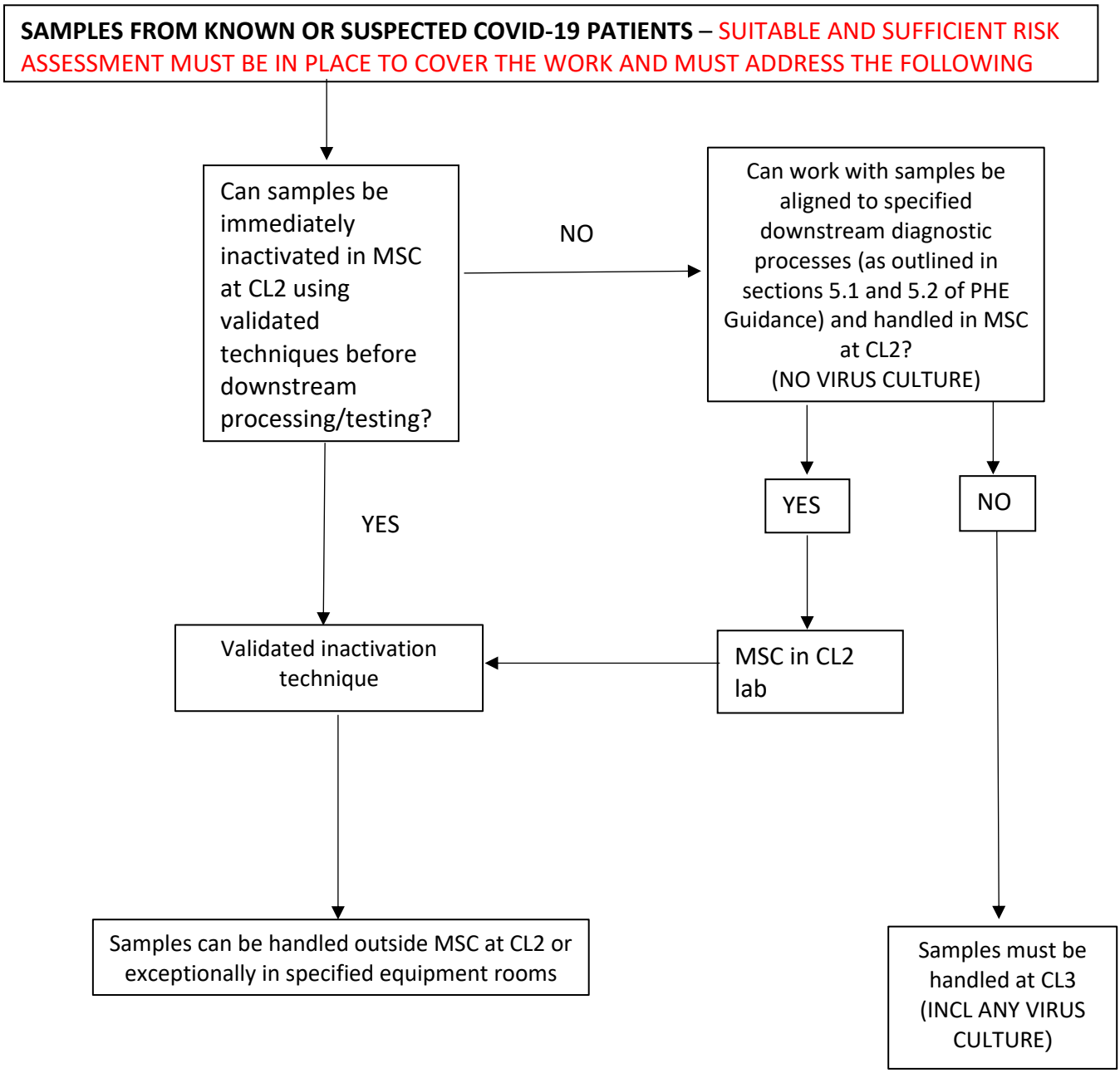
The risk assessment must justify the decision to operate at CL2 and the controls must be clearly outlined. Validation data must be supplied for inactivation protocols. Other aspects of CL3 must still be applied even if all procedures will take place in a designated CL2 laboratory. These include restricted access to named staff, provision of a code of practice and SOPs, competency checks and provision of training records, establishment of clear emergency procedures and validated waste inactivation processes. **As indicated above, work involving culturing/propagation of the virus must be carried out at CL3.**

All risk assessments must be approved by the University's Advisory Group for the Control of Biological Hazards before work begins.

Notification under Control of Substances Hazardous to Health Regulations and/or GM Contained Use regulations

As SARS-CoV-2 is a HG3 agent work involving the agent is subject to notification by Safety Services to the Health and Safety Executive under COSHH, or if modified, under the GMO (Contained Use) Regulations. Therefore, assessments for work with the agent will be sent to HSE as part of the notification process.

HANDLING COVID+ SAMPLES FOR RESEARCH ACTIVITIES



Appendix 1

Extract from COVID-19: Safe handling and processing for samples in laboratories (Public Health England

Section 5.1: Work that may be conducted at CL2 (PHE Guidance)

Routine laboratory blood tests can be carried out in auto-analysers using standard practices and procedures at CL2, but only after a suitable and sufficient risk assessment has been conducted which considers the potential for the generation of infectious aerosols. Auto-analysers should be disinfected following local procedures after sample processing and before scheduled maintenance in accordance with manufacturers' recommendations.

Some auto-analyser protocols for routine laboratory tests may require specimen tubes to be opened first, or initial processing of the sample to be performed. Evidence suggests that capping and uncapping of samples is not a high-risk aerosol generating procedure which is dependent on the cap and tube design. These factors must be considered in a suitable and sufficient risk assessment which also considers if the sample needs to be centrifuged, vortexed or pipetted manually. The risk assessment must include consideration of whether a MSC needs to be used.

The following work may also be conducted at CL2 following standard laboratory precautions, where this is consistent with the terms of the local risk assessment for those activities:

- diagnostic assays using whole blood, serum and plasma, including routine biochemistry and haematology, unless there is a risk of generating aerosols
- assays using virus-inactivated specimens, including molecular testing of inactivated specimens
- examination of bacterial or fungal cultures
- staining and microscopy of heat-fixed or chemically-fixed smears
- centrifugation of routine blood samples. However, where there is infectious potential, samples must be centrifuged using sealed centrifuge rotors or sample cups which are loaded and unloaded in a MSC.

University Guidance: It is likely that this section has limited applications in a University setting. The diagnostic assays in this section are likely to relate primarily to NHS laboratories running automated systems (blood counts, biochemical markers) on large, track-based systems with enclosed automated analysers. Other work involves handling specimens that have been inactivated or enclosed in some way (e.g. sealed buckets in centrifuges).

Section 5.2: Work that may be conducted at CL2 in an MSC (PHE Guidance)

Following completion of a suitable and sufficient risk assessment, the following work with samples potentially containing SARS-CoV-2 may be conducted in a MSC at CL2:

- preparation of specimens for molecular testing (for example respiratory virus PCR) prior to sample inactivation
- division, aliquoting, or diluting of respiratory tract specimens, faecal specimens, urine specimens, and tissue specimens in which virus has not been inactivated
- inoculation of bacterial or fungal culture media from high risk patients
- urine antigen testing (such as for detection of Legionella pneumophila or Streptococcus pneumoniae)

Note: if the above is not possible (for example, testing instrument does not fit inside the CL2 cabinet), undertake a local risk assessment.

- rapid antigen tests of respiratory tract specimens
- processing of any non-inactivated specimen that might result in the generation of aerosols
- preparation and fixing (chemical or heat) of smears for microscopy
- haematological or immunological work
- rapid diagnostic tests for malaria parasites

Where risk assessment has identified that work should be conducted within an MSC at CL2 the following still applies to work activities:

- only fully trained and competent staff must undertake the work; in addition to this the level of training provided should be appropriate to the level of risk and the complexity of the procedures being undertaken
- inactivation methods must be in place before removal of sample from MSC; these methods must be validated to ensure effectiveness of the method (for example through use of a surrogate marker)
- effective emergency procedures, including methods for dealing with spillage, are in place
- waste routes for samples are appropriate for HG3 samples

Appendix 2 – Other considerations when working at CL2

For work at CL2, including CL3 work that is permitted in a CL2 laboratory, all material must be contained to minimise the risk from spillage during transport in the laboratory or between laboratories. This should normally consist of at least 2 layers of containment (e.g. a sealed sample tube within a sealed carry box) and where liquids are carried there should be sufficient absorbent material between the first and second layer.

External surfaces of specimen containers and vials should be routinely decontaminated before removal from the MSC. A disinfectant with proven activity against enveloped viruses, must be used prior to their removal from the MSC when working with potential COVID-19 material (while also taking into account any other specific pathogen risk). Care must be taken to avoid accidental contamination of the exterior surfaces of all vessels and containers, regardless of containment level.

Emergencies

Emergency procedures must be reviewed according to the results of risk assessments.
For CL3 work that is permitted in a CL2 laboratory, fumigation of laboratory spaces will not be possible where samples are spilt, therefore consideration must be given to what to do in the event of a spillage, and how effective decontamination of the area will be achieved. Staff must be trained on updated emergency procedures for the CL2 laboratory and records of this training must be kept.

Generally, emergency procedures should consider the following in addition to other issues such as first aid provision:

- Contamination of individuals and their post-exposure treatment;
- An infectious aerosol release outside a MSC;
- Leaking and broken containers and spilled (potentially) infectious substances;
- Breakage of tubes containing potentially infectious material in centrifuges.

Any accident or loss of containment must be reported promptly so that medical advice can be sought if necessary. Personal exposure or a loss of containment will require notification to the enforcing authority.

Decontamination

Work surfaces and equipment must be decontaminated after work has finished in addition to treating any spillages immediately. This should include any surfaces that have been in contact with sample delivery containers.

A broad-spectrum disinfectant can be used during work with routine samples at CL2. In the case of HG3 SARS-2 work at CL2 the disinfectant must have proven activity against the agent.

At CL2, validation data may come from in-house experiments with suitable surrogates or the target pathogen, manufacturers' data or publications. Disinfectant use should follow the validated concentrations and contact times. Inactivated liquid wastes may be discarded to drains. Surface disinfected containers may be autoclaved/incinerated. Other inactivated CL2 waste should be autoclaved before disposal.

Other inactivation/decontamination methods may require clearance from HSE when handling SARS-2 contaminated human material at CL2.

Training and competence

All workers should be fully trained in the risks associated with the work, safety critical procedures and the use of equipment. They must have understood the risk assessment, codes of practice and operating procedures covering the activity.

Workers must only undertake work for which they have been trained, or else be supervised by a competent person until the trainer is satisfied that the worker is competent to work unsupervised. Training should be documented and training records should be signed by trainer and trainee.

Only competent staff must undertake work with HG3 material, and all training completed or experience already gained must be documented and signed-off by the trainer and trainee.