Management of Containment Level 3 Laboratories

1 Containment Level 3 Laboratories

The management of containment level 3 (CL 3) laboratories and facilities requires robust controls to be in place to ensure that people are protected from exposure to biological hazards and prevent any release into the environment. The precise containment and control measures required for any activity are a combination of the relevant legal standards, regulatory guidance, the outcomes of risk assessments, notifications and licence requirements and regulatory consents and derogations. This guidance details various aspects of the safe management and operation of CL 3 laboratories and related activities. Please note that this brief guidance is in addition to detailed regulatory guidance that must be followed and implemented and is not a replacement for these resources.

2 Guidance Sources for Containment Level 3 Laboratories

The Health and Safety Executive (HSE) provides guidance on the management of work at containment level 2 and 3 in the document 'HSE ACDP Management and operation of microbiological containment laboratories'. There is also HSE guidance on genetically modified organisms and specific animal pathogens that has important additional information about work at CL 3. In addition, there are regulatory guidance that are available for specialist types of work. However, the general guidance listed below are the main documents that must be used by Schools, Principal Investigators, CL 3 Lab Managers, School Safety Advisers and Biological Safety Advisers and they are full of valuable information about how to manage CL 3 laboratories and related activities. Please see the links below to find the guidance and some of the related website resources.

2.1 Guidance

- HSE ACDP Approved list of biological agents
- HSE ACDP Management and operation of microbiological containment laboratories
- HSE Control of substances hazardous to health
- HSE Genetically modified organisms (contained use)
- HSE Containment and control of specified animal pathogens
- HSE SACGM Compendium of guidance
- HSE Sealability of microbiological containment level 3 and 4 facilities

2.2 Websites

- HSE Biological Safety
- HSE Biological Agents
- HSE Genetically Modified Organisms

- HSE Specified Animal Pathogens

There is extensive guidance and training information in relation to management of biological safety and CL 3 laboratories on the Health and Safety Department (H&S Dept) and Biosafety Unit (BSU) websites. The links to key HSE, ACDP, SACGM guidance are on the BSU website. British, European and international standards are available on the British Standards Online (BSOL) database accessed through the University Library.

3 Full and Derogated Containment Level 3 Laboratories

There are two types of CL 3 laboratories, and these are designated in the University as either full CL 3 or derogated CL 3. The type of containment level and control measures needed for an activity depends on the regulatory requirements, risk assessments, licences, notifications and the related consents including any derogations from the containment and control measures that are normally required as a minimum standard.

- **Full Containment Level 3** (Full CL 3) is used for work involving hazard group 3 biological agents, pathogens, infectious materials or class 3 genetically modified microorganisms (GMM), where all the containment or control measures normally required as a minimum for full CL 3 are needed. In particular, full containment level 3 is required for work with biological agents or GMM that present an inhalation hazard.
- **Derogated Containment Level 3** (Derogated CL 3) is used for work involving hazard group 3 biological agents, pathogens, infectious materials or class 3 genetically modified microorganisms (GMM), subject to risk assessment and regulatory permission, where not all the containment or control measures normally required as a minimum for full CL 3 are needed. In particular, derogated containment level 3 might be used for work with biological agents or GMM that do not present an inhalation hazard.

This guidance provides general information on the basic requirements for the management and operation of full and derogated CL 3 laboratories but it is not exhaustive and you will need to do many other things as well depending on the specific laboratories and facilities and the nature of the work and outcomes of risk assessments. The containment and control measures required for a project will depend on the requirements of the relevant regulations and guidance, risk assessments, notification, licence and consent conditions including approved derogations.

The regulatory guidance contains important information about the containment levels and control measures required for work and include tables that summarise the minimum control measures normally required for each containment level. However, in certain circumstances where it is safe and reasonable it may be acceptable to

derogate to use less than the minimum containment and control conditions normally required. The HSE ACDP Approved list of biological agents (Annex 1) has a list of biological agents that may be used under derogated conditions at containment level 3. Derogation always requires a specific written application to the regulator for consent as part of a notification or licence application. The regulator may approve derogations that may be minor and not affect the type of containment laboratory required in which case the work will still require a full CL 3 laboratory. The regulator may approve derogations that may be major and mean that the work requires only a derogated CL 3 laboratory.

4 Code of Practice and Standard Operating Procedures

There should be robust safety and security arrangements in place for work at CL 3 to ensure compliance with relevant legal standards and protect people and the environment. Principal Investigators and CL 3 Lab Managers are responsible for health and safety management, local rules, risk assessment, containment and control measures, standard operating procedures and emergency procedures.

4.1 Code of Practice and Standard Operating Procedures

A Code of Practice (CoP) that details the safety management arrangements and written standard operating procedures (SOP) must be in place for all CL 3 laboratories and their related facilities. The CoP must include details of the safety management systems and arrangements including for example, a description of how to operate the lab and a plan of the CL 3 laboratory. It should include details of key roles and responsibilities (eg Principal Investigators, CL 3 Lab Managers, staff, students and visitors), training and assessment of competence, standard and emergency procedures, general containment and control measures, transport, waste, maintenance, monitoring, auditing and inspection.

4.2 Safety Folder

The CL 3 Lab Manager should maintain a CL 3 Safety Folder with the CoP and full set of SOP, management arrangements for the CL 3 laboratory and work activities as well as important records. The CL 3 Safety Folder should include all the relevant safety documents and be kept for the records in electronic format in the School's safety folder on the University's protected secure computer systems. The CL 3 Safety Folder might include the following documents although many others may be required, although many relevant documents such as maintenance records may be stored on separate databases or systems.

- CL 3 Code of practice (CoP).
- General, COSHH, Biological Agent (BA) and Genetic Modification (GM) risk assessments.
- Safety data sheets.

- Standard operating procedures (SOP) for all routine, non-routine and emergency procedures.
- Plans for the laboratory, equipment, plant, and controls.
- Suppliers and manufacturer's instructions.
- Maintenance and service records.
- Validation and test reports and certificates.
- Auditing and inspection reports.
- Checklists.
- Inventories.
- Training and assessment of competence records.
- Lists of authorised persons.
- List of workers with HG 3 pathogens they have used.
- Security plans.
- Emergency contact information.

There should be a list of workers exposure records detailing the hazard group 3 (HG 3) pathogens that a person has used or been exposed to during their CL 3 work. This information is part of an individual's health record under COSHH so can also be stored in the COSHH Health Passport System.

Key information from the full CL 3 Safety Folder stored on the computer system should also be available in the CL 3 laboratory. The CoP, SOPs and the emergency procedures and emergency contacts should be available as hardcopies in the CL 3 laboratory so that workers will have immediate access to the written management arrangements and procedures where needed. There should be a list of authorised persons permitted to have access to the laboratory. The Safety Folder should be reviewed regularly and at least annually, and records retained for the relevant timescales.

4.3 Biosecurity Plans

Biosecurity plans are required for work involving designated pathogens, toxins or other relevant materials controlled under laws relating to terrorism and serious crime. Biosecurity plans should follow standard templates or similar and will include site, building, laboratory, personnel, data, handling, storage, waste, transport and emergencies. Transport security plans are required for work involving transport of high consequence dangerous goods (HCDG) and pathogens or toxins controlled under terrorism laws. The security plan and transport security plans may be separate or integrated into a single document.

4.4 CL 3 Roles and Responsibilities, Competence and Training

The effective management and operation of a CL 3 laboratory requires staff and students who are trained and competent to carry out their work safely. The CoP should specify the designated roles, responsibilities, training and assessment

requirements. This will include the roles and responsibilities, training and competence of PI, CL 3 Lab Manager, staff and students, and visitors.

4.4.1 Role and Responsibilities of Principal Investigators

Schools and Principal Investigators (PI) have overall accountability and responsibility for the management of their CL 3 laboratories and facilities. The School and PIs must ensure that the management, operation and maintenance of their CL 3 laboratories meets the required standards for health and safety and environmental protection. The PI may designate a CL 3 Lab Manager to assist them in the management of their CL 3 laboratories. This does not change the overall management responsibility of the PI. If the PI does not appoint a CL 3 Lab Manager to assist them in the operational duties then the PI is the CL 3 Lab Manager with direct responsibility for the day-to-day management, operation and supervision of their labs and staff, students and visitors. PIs need to support and cooperate with the CL 3 Lab Manager to ensure the safe and effective management and operation of the CL 3 laboratories.

4.4.2 Role and Responsibilities of CL 3 Laboratory Managers

Every CL 3 laboratory must have a designated CL 3 Lab Manager and also a deputy. The CL 3 Lab Manager will be the PI(s), or else a person appointed to take on the day-to-day responsibilities of the laboratory management and operational control. The CL 3 CoP should specify the general responsibilities of the CL 3 Lab Manager and deputy, and briefly, they will include overseeing the safety systems and arrangements for the management, operation and maintenance of the laboratory and related activities and dealing with contractors. The CL 3 Lab Manager should monitor and review the effectiveness of the safety arrangements. The CL 3 Lab Manager should ensure that there is adequate supervision of staff, students and visitors to their laboratory. They should ensure that there are systems in place for training and assessment of competence of workers. The appointment of a CL 3 Lab Manager does not remove the responsibility and accountability of line management and Principal Investigators. The CL 3 Lab Manager assists management in planning, implementing, monitoring and reviewing the risk controls.

4.4.3 Role and Responsibilities of Staff and Students

The CoP should specify the general responsibilities of staff and students and this would include cooperation with the School and CL 3 Lab Manager and compliance with the safety systems and arrangements for the management and operation of the CL 3 laboratory and project specific activities. Staff and students should comply with the CoP, SOPs and emergency procedures and report any issues or incidents to the CL 3 Lab Manager as soon as practicable.

4.4.4 Role and Responsibilities of Visitors

The CoP should specify the general responsibilities of visitors and this would include cooperation with the School and CL 3 Lab Manager and compliance with the safety systems and arrangements for the management and operation of the CL 3 laboratory. Visitors should comply with the CoP, SOPs and emergency procedures and report any issues or incidents to the CL 3 Lab Manager as soon as practicable. Contractors need to communicate and cooperate with the CL 3 Lab Manager in relation to maintenance, servicing and others activities.

4.5 Information, Instructions, Training and Supervision

All workers and visitors must have suitable information, instructions, training and supervision on health, safety and security aspects of the work. The CL 3 Lab Manager should ensure that there is adequate information and instructions provided to workers on the hazards, risks and control measures such as safe handling, storage, transport, disinfection, waste inactivation and disposal and emergency procedures. Staff and students all need to understand the CoP, SOP and emergency procedures and be able to implement the safe working practices. There should be clear written information given to workers about any significant relevant diseases and infections relevant to their work or which might pose a potential danger to other people or the environment. Visitors and contractors should receive suitable information and instructions about health and safety and be adequately supervised. Contractors will need to have risk assessments and method statements (RAMS) where required for their work. There should be suitable permit to work systems in place where needed for maintenance and testing by engineers and contractors working on the CL 3 laboratory and related facilities that involves the CL 3 Lab Manager.

4.5.1 Safety Critical Information

Important safety critical information and instructions from the CL 3 Safety Folder or other sources should be on display in the laboratory including for the safe operation of equipment, emergency procedures and emergency contacts so that they are immediately available to staff and students. The CL 3 Lab Manager should provide suitable training and supervision of staff, students and visitors to their CL 3 laboratory to ensure they can carry out their work safely and comply with the local rules. It is important that there is good communication and cooperation between CL 3 Lab Managers and PIs and user groups of CL 3 laboratories in relation to the safety arrangements and working practices.

4.5.2 Training and Assessment of Competence of Staff and Students

There should be suitable systems in place for the training and assessment of competence of workers based on a training needs analysis and training matrix. There should be a training programme for the CL 3 laboratory and the competence of each worker should be assessed using a checklist and training records kept. Training and

the assessment of competence should be carried out at induction and for general or project specific duties and then reviewed and updated where required and at least annually. Typically, the CL 3 Lab Manager should provide general training for the CL 3 laboratory and the PI and their research group provide their project specific training.

Prior microbiology training and experience is obviously valuable for work at CL 3. It is preferable that workers have prior experience working at CL 2 before working in a CL 3 laboratory. New CL 3 Lab Managers, staff or students may already have significant and valuable previous experience working in CL 3 laboratories. However, irrespective of previous experience, all new and existing CL 3 Lab Managers, staff and students should follow the CL 3 training programme and have their competence assessed and recorded.

There are formal training courses that are valuable for CL 3 Lab Managers, staff and students in relation to working in CL 3 laboratories and facilities including University, College, School, H&S Dept and BSU as well as external training courses. CL 3 Lab Managers, staff and students should complete the main assessed BSU training courses: 'Introduction to biological safety', 'Biological and genetic modification safety', and 'Transport of biological materials'. The SafTPak certified training course 'Transport of biological materials and infectious substances' should also be completed by relevant persons in the School or CL 3 laboratory management team. The H&S Dept Biosafety Training Institute (BTI) provides a Biosafety Practitioner training course that is a very useful advanced course that includes a lot of material relevant to work at CL 3 and is particularly useful to CL 3 Lab Managers and their deputies but for any CL 3 workers. All of these formal training courses require trainees to complete and pass an assessment.

Practical training in the general safety arrangements and safety critical controls and emergency procedures is required in addition to formal training courses for working in CL 3 laboratories and facilities. Practical training should be assessed using checklists and the results kept as part of the training records.

4.5.3 Training and Assessment of Competence of CL 3 Lab Managers

The training and competence of CL 3 Lab Managers and their deputies is obviously a key priority for Schools, PIs and the effective management of CL 3 laboratories. New CL 3 Lab Managers should receive induction training and need adequate support and supervision by their manager / PI. CL 3 Lab Managers may need further training provided by the PI or others in the School, College or University. The training of new or inexperienced CL 3 Lab Managers should include 'shadowing' experienced CL 3 Lab Managers in the School or in other Schools with CL 3 laboratories.

There is valuable specialist training available for CL 3 Lab Managers and their deputies on the management and operation of CL 3 laboratories that is available from external providers including for example HSE or UK Health Security Agency

(UKHSA). The BTI offers general training that is useful for CL 3 Lab Managers and their deputies as well as staff and students.

- Biosafety Training Institute, Health & Safety Department, University of Edinburgh. This training course is e-learning: Biosafety Practitioner Level 1.

CL 3 Lab Managers can do advanced formal training in CL 3 laboratory management such as those delivered by HSE or UKHSA. This type of formal training should be very useful to CL 3 Lab Managers and their deputies but it is particularly valuable and strongly recommended for those who are involved in the management of 'full CL 3 laboratories'.

- HSE Training, Buxton, Derbyshire. This training course is in person: Biosafety - Working Practices and Managing Safety at Containment Level 3.
- UKHSA Biosafety and Applied Microbiology Training, Porton Down, Wiltshire. This training course is in person: An Introduction to the Principles and Practices of Working Safely at ACDP Containment Level 3.

5 Risk Assessments, Notifications and Licences

The risk assessments, containment and control measures will need to cover general safety as well as biological safety. General risk assessments, COSHH, BA and GM risk assessments should be in place for the CL 3 laboratory and related facilities and activities prior to the commencement of any work or possession or import of any biological materials. Regulatory notifications, licences and consents need to obtained where required and in place and kept up to date. The risk assessments and control measures need to be closely monitored, reviewed and amended where there are changes to the activity or risks or after incidents with the relevant GMBSC and regulatory permissions obtained where needed. There is detailed guidance on risk assessment, containment and control measures on the H&S Dept and BSU websites.

6 Containment and Control Measures for Full and Derogated Containment Level 3 Laboratories

The containment and control measures required for work in CL 3 laboratories depends on the specific work, local policies, risk assessments, regulatory notifications, licences, derogations and consents. There is detailed guidance on specific containment and control measures for each containment level including CL 3 already on the HSE and BSU guidance and websites. The Estates Department has a design specification for containment laboratories that provides an outline of the common standards required for CL 3 laboratories (University of Edinburgh specification for containment laboratories). The containment measures required for full and derogated CL 3 laboratories are similar, but there may be differences where there is a regulatory consent (derogation) to use less than the minimum containment conditions normally required.

6.1 General Requirements for Full and Derogated CL 3 Laboratories

The design, construction, operation and maintenance of CL 3 laboratories and related facilities must meet the statutory requirements in the relevant legislation such as the COSHH, SAPO and GMOCU Regulations. The design requirements for CL 3 laboratories are set out in HSE guidance and the following is only a brief overview of the general requirements. There are many possible variations for the design of full or derogated CL 3 laboratories based on construction methods and on the requirements of the relevant regulations, risk assessments, notifications, licences and consents and any approved derogations. Briefly, a full CL 3 laboratory usually consists of at least a lobby and laboratory although there may be multiple rooms. A CL 3 laboratory suite consists of several CL 3 laboratories. A derogated CL 3 laboratory may consist of a lobby and laboratory or may just be single laboratory room.

CL 3 laboratories must be safe and secure and separated from other work activities in dedicated rooms in the building. Access to CL 3 laboratories must be restricted to authorised persons only. There must be safe and reliable access and egress systems. Doors must have appropriate access controls using suitable means, so they are closed and secure at all times (eg lock and key, swipe card, digital lock or a combination). Safe means of escape is an absolute priority and must not be obstructed by systems or controls. Safety signs must be displayed on the access doors of CL 3 laboratories. Below is a typical example of this type of signage that includes (a) access to authorised personnel only, (b) biological hazards and (c) containment level 3.

There may be a requirement for other safety signs to be displayed on the laboratory and or equipment such as chemical hazards, radiation hazards, flammables and gas cylinders.

CL 3 laboratories have to be maintained at an air pressure negative to atmosphere with the extract air filtered using high efficiency particulate absorption (HEPA) or equivalent. CL 3 laboratories may require complex engineering, plant and ventilation

control systems and there is usually a cascade of air pressures from inlet to output depending on the type of ventilation system in the design and number of rooms in the laboratory. There is no specific required pressure differentials since these will depend on the design and complexity of the laboratory and ventilation systems although HSE provides guidance. Input and output air supplies need to be interlocked to prevent positive pressurisation of the laboratory if the something goes wrong with the ventilation systems. There must of course always be adequate ventilation to maintain fresh breathable air and suitable temperature control.

An observation window and if needed mirrors, or suitable alternative (eg CCTV) has to be present so that occupants can be seen. A laboratory has to contain its own equipment. Typical equipment required in CL 3 laboratories will include microbiological safety cabinets (MSC), isolators, incubators, centrifuges, autoclaves, fixed gas installations, portable gas equipment, hotplates, PCR machines and many more depending on the work activities. Floor, wall and furniture surfaces have to be impervious to water and easy to clean. Surfaces have to be resistant to acids, alkalis, solvents, disinfectants. Infected material, including any animal, has to be handled in an MSC, isolator or other suitable containment where there is the risk of infectious or hazardous aerosols. There has to be safe storage of biological agents.

There has to be suitable disinfection methods. The CL 3 laboratory suite has to contain an autoclave. Autoclaves should be located in the laboratory suite unless there is an approved derogation in the regulatory consent for an alternative location. There has to be validated methods of inactivation of waste in contaminated materials and if required in effluents from sinks and showers. There has to be efficient vector controls (eg rodents and insects) where needed. Access to an incinerator may be required for disposal of infected animal carcases. The laboratory has to be sealable to permit fumigation with specified routine and emergency fumigation procedures required. Sealability and fumigation of the facility may not be required for a derogated CL 3 laboratory where there is a consent for derogations.

There should be phones provided for ordinary communications as well as for calling for internal assistance or the emergency services if needed. Phones may be connected by traditional cables or through the internet. It may be useful to have another second line communications in addition to phones on the fixed installations. A practical option may be to use mobile phones such as for situations when the main phones do not work because the internet connection is down or just as a back up in case of emergencies. This could be a mobile phone owned by the School for the CL 3 laboratory (preferable to personal mobiles) or other mobile phones. It is always a local management decision whether or not to allow mobile phone use in CL 3 laboratories and how they are to be safely used, but either way the local arrangements should be detailed in the CL 3 CoP and SOPs, induction and training etc.

There should be computers installed linked to the internet to minimise the use of paperwork and pens and reduce the need to take them in and out of the laboratory.

There should of course be suitable means of detection and warning of hazards and emergencies (eg fire detection/alarms, gas monitors/alarms etc). Personal protective equipment (PPE) and gloves are required. Lone working should be avoided but if there is no alternative then adequate controls must be used including buddy systems in the building, supervision, active monitoring and the use of lone worker monitor/alarms. There have to be written records of safety systems and arrangements, procedures, maintenance, validations and training. There should be specific checklists used to carry out and record the various checks on the laboratory, equipment and activities.

6.2 Fumigation of CL 3 Laboratories and Microbiological Safety Cabinets

CL 3 laboratories, safety cabinets and isolators may require fumigation to sterilise them so they can be safely maintained and tested, and they be decontaminated if there is a spillage of biological materials. The fumigation requirements vary depending on whether it is a full or derogated CL 3 laboratory. Facility fumigation is required for full CL 3 laboratories but is not usually required for derogated CL 3 laboratories. The fumigation of safety cabinets and isolators is required for all types of CL 3 laboratories. Fumigations need to be performed safely so they do not expose workers or other persons to danger or hazardous substances. There should be suitable risk assessments and a safe system of work for carrying out fumigations of CL 3 laboratories and safety cabinets. The methods used for routine and emergency fumigation need to be developed and fully validated to prove they work effectively. There must be suitable emergency procedures in place in case anything goes wrong with the fumigation.

There are many fumigant chemicals used for various purposes in laboratories and other work activities. All fumigant chemicals are of course biocides and hazardous since their purpose in fumigations is to kill microorganisms, but their use is reasonable where it is required as long as it is adequately controlled. The choice of fumigant has to be determined based on the requirements for the activity and related safety aspects taking into account the hierarchy of risk control under COSHH. Generally, hydrogen peroxide based methods and systems are used for fumigation of CL 3 laboratories and safety cabinets. Schools should not use formaldehyde for laboratory or safety cabinet fumigations unless there is a specific requirement. Formaldehyde is a category I human carcinogen and powerful sensitizer so should not be used for fumigation unless there is no reasonable alternative and it is required for a specific purpose with clear justification.

If formaldehyde or other chemical method is required for any specialist fumigations, then properly controlled physical methods and equipment should be used to generate the vapours or gases. CL 3 laboratories and safety cabinets must not be fumigated using chemical methods of generating formaldehyde vapours or gases for fumigations, such as by adding oxidizers like potassium permanganate to formalin solution to generate fumigants gases for rooms or safety cabinets/MSC etc since these are not easily controlled and too hazardous.

6.3 Fumigation of CL 3 Laboratories

A CL 3 laboratory needs to be validated or proven as sealable to permit fumigation before any fumigation can be carried out on a facility. The detailed validation report provided by the contractor should demonstrate that fumigant vapours or gases will be safely contained inside the laboratory envelope during a fumigation and not released or leak out of the structure until safely exhausted through the ventilation system and or absorbed by specialised fumigation equipment. The fumigation of a facility may be done by the CL 3 Lab Manager and their local team or by a competent external contractor. If carried out by a contractor then they need to supply the CL 3 Lab Manager in advance with the RAMS and the written protocols developed for routine and emergency fumigation procedures including their emergency plans and procedures in case anything goes wrong. The CL 3 Lab Manager and contractors as always need to exchange relevant safety information and discuss and agree the local safety arrangements.

There should be standard operating procedures for routine as well as emergency fumigations of the laboratory. These fumigation protocols need to be validated to prove they work under the actual conditions involved. There may need to be a number of different methods developed for different situations used for fumigation of a CL 3 laboratory to ensure that fumigation can be safely performed under various circumstances. Complex CL 3 laboratories with multiple rooms in particular may require a sequence of separate fumigations to be performed before the laboratory is safe and fully fumigated. For example, several associated fumigations may be needed depending on where contamination or a spillage occurs in different parts of a laboratory. The validation of protocols for fumigations should always include the use of safe biological indicators to prove that (surrogate) microorganisms are actually killed by the fumigation method to the required standard of inactivation. The levels of fumigant in the CL 3 laboratory need to be measured using gas monitoring methods and verified in each of the validation protocols. Suitable validation reports need to be completed for every variant of both the routine fumigation and emergency fumigation procedures irrespective of whether done in-house by the CL 3 Lab Manager and their team or by an external contractor.

The CL 3 Lab Manager should check validation reports promptly after their completion to ensure they demonstrate safe and effective fumigation protocols to use for the CL 3 laboratory. The CL 3 Lab Manager should take up any concerns or repairs identified with contractors, facilities or Estates etc where needed. The validation of fumigation should be done at commissioning and before first use and periodically thereafter at least once every five years, or immediately if any relevant changes or significant failures have occurred for example to the CL 3 laboratory, ventilation or engineering plant, controls or changes of fumigation system, equipment or fumigants.

The validated fumigation methods can then be used for routine and emergency fumigations in practice either by the CL 3 Lab Manager and their team or by a

contractor on a service contract. Routine fumigation of the CL 3 laboratory should be done typically every six months before the periodic shutdown of the CL 3 laboratory for the maintenance and servicing of the CL 3 laboratory and equipment such as maintenance and six monthly validations of MSC and autoclaves. Emergency fumigation of the CL 3 laboratory will be needed and should be done where required such as after relevant incidents, failures, contamination or spillage events. The CL 3 laboratory should be isolated, and access locked with the ventilation on until the emergency fumigation is carried out and then it is proven safe for entry.

It is essential that the air quality is measured to determine the levels of fumigant gas or vapour in the laboratory before any attempt is made to enter the laboratory and to verify that the air is safe at end of the fumigation procedure. Air quality may be measured using various methods such as electronic gas monitors on fumigation equipment, portable electronic gas monitors, or monitor pump with chemical detection tubes etc. It is preferable to use more than one method to verify the air quality if that is feasible. The CL 3 laboratory should not be entered until the levels of fumigant are well below the workplace exposure limits (WEL). Entry into a room containing fumigant should never be done unless absolutely essential and there is no reasonable alternative to deal with a problem that cannot be dealt with safely from outside. If entry is really required then this should only be done by fully trained and competent persons as part of a suitable emergency plan and procedures with all the necessary risk controls, safety equipment (eg RPE, PPE, Tyvek suits or chemical protection suit, safe decontamination procedure) and support team etc in place needed for the situation. This type of procedure requires specialist expertise and should never be done if there is a safer alternative such as exhausting the fumigant from the laboratory with the ventilation system even if this takes more time or other approach that can be conducted from a safe place outside the laboratory.

The routine and emergency fumigations should be recorded with the issue of a contractor's service certificate or local certificate to verify safe and adequate completion of the process. The CL 3 Lab Manager and their team should check fumigations service certificates and deal with any issues or repairs and follow them up until completion in the usual way. If necessary, a fumigation procedure may need to be done again after a problem or relevant repair until it is satisfactorily completed.

6.4 Fumigation of MSC and Isolators

Fumigations of MSC, isolators and other relevant equipment may be carried out by the CL 3 Lab Manager or by competent contractors. There should be standard operating procedures in place for routine and emergency fumigations of the MSC. The manufacturer's instructions may need to be taken into account where relevant when developing or using any fumigation procedures. Hydrogen peroxide is the most common fumigant used for MSC fumigation and as explained earlier formaldehyde or other fumigant should only be used if really justified and required. Only trained

competent persons who have adequate knowledge of the safety controls should carry out fumigations procedures.

Microbiological safety cabinets should be fumigated before any maintenance or testing work on the cabinet, as well as after a major spillage inside the cabinet. MSC in CL 3 laboratories should have a routine fumigation every six months before they have a thorough examination and KI test. MSC should also be fumigated before any relevant service or repair.

6.5 General Incident and Emergency Procedures

Emergency procedures are required for dealing with safety, environmental and security incidents and incidents. The emergency procedures should be prepared in advance for dealing with personal injury or exposure, minor and major spillages and accidental releases. General emergency procedures will be in place for the building, but additional specific emergency procedures needed for CL 3 laboratories are determined through the risk assessments and set out in the CoP and standard operating procedures. CL 3 laboratories should have the necessary emergency equipment including first aid, eye wash bottles, spillage kits and emergency clothing Tyvek suits, PPE and RPE etc.

The emergency plans and procedures need to provide the information, instructions and training for dealing with incidents, injured or contaminated persons and spillages. Workers should be fully trained and able to implement the emergency procedures and refresher training of workers provided. There should be practice drills of the emergency procedures including in initial training of workers as well as periodically for all workers to help maintain their proficiency. All workers need to know how to obtain assistance from colleagues or the emergency services where needed (eg Ambulance, Fire, Police and Security). All incidents and emergencies should be reported, immediately practicable to the CL 3 Lab Manager, supervisors and PIs and using the University AIR incident reporting system. CL 3 Lab Managers need to investigate incidents and ensure that control measures are reviewed and revised and workers provided with additional training and supervision where needed.

Important safety critical information and procedures should be immediately available and on display in the laboratory including for the safe operation of equipment, emergency procedures and emergency contacts. This will include the key SOP for microbiological safety cabinets (MSC), isolators, autoclaves, incubators, centrifuges, specialist equipment as well as emergency procedures for personal exposure or injury, spillage and release to the environment. The local emergency procedures and contact list should be on display where needed in the laboratory and using a simple format (eg A3 or at least A4 paper, bullets/numbers, large font, laminated). This emergency contact list should include for example the names and contact details of the CL 3 Lab Manager and deputy, Principal Investigators, responsible persons and local safety advisers. Any contractors involved in emergency

procedures will need to have risk assessments, method statements, plans and procedures for their work, agreed in advance in consultation with the CL 3 Lab Manager and local teams.

7 Maintenance and Testing of CL 3 Laboratories and Equipment

Various types of maintenance and testing of the safety critical systems of CL 3 laboratories and their specialist equipment as well as regular local checks are required to ensure they are working to the required standards. The maintenance and tests required depends on the type of CL 3 laboratory and on the relevant regulations such as thorough examination and tests, services and various validation tests to prove integrity or efficacy. There is detailed guidance available in the HSE ACDP Management and operation of microbiological containment laboratories document and relevant British Standards.

The CL 3 Lab Manager is responsible for ensuring that there is a robust management system in place for planning, organising, monitoring and reviewing of maintenance and repairs so that maintenance, services, tests and checks, are scheduled and carried out and then the reports provided and checked. CL 3 Lab Managers should obtain and review the maintenance and testing, service and validation reports as soon as practicable to ensure they meet the relevant standards and contracts and question any issues. The CL 3 Lab Manager should take up any concerns or repairs identified in maintenance or services with contractors, facilities or Estates etc where needed and retesting may then be needed. The CL 3 Lab Manager should follow up any actions until satisfactory resolution and completion. Detailed records and reports should be kept.

CL 3 Lab Managers should work closely with contractors and engineers that carry out work on their CL 3 laboratory and related facilities to exchange relevant safety information, agree plans, provide inductions and supervision and ensure they comply with local safety and security arrangements. Please note that this is just an overview of what is required and not a replacement for the detailed HSE regulatory guidance, British or industry standards or other general requirements that needs to be followed for the building, laboratory or services. The following guidance is not exhaustive and other things may be required depending on CL 3 laboratory, equipment and activities.

7.1 Maintenance and Testing of CL 3 Laboratories

CL 3 laboratory and its control systems need suitable maintenance to ensure they work, are safe and reliable. The LEV room ventilation systems require a thorough examination and tests to be carried out at least annually. The CL 3 Lab Manager should carefully review the thorough examination and test report to check it meets the statutory requirements and relevant standards and any agreed actions. The CL 3

Lab Manager should not accept any inadequate report and immediately take up any issues with the contractors.

7.2 Validation of Sealability of CL 3 Laboratories

The sealability of the CL 3 laboratory needs to be validated to prove the integrity of the structure and show that there are no leaks so that it can be safely fumigated without any release of fumigant gases or vapours. The validation should be done prior to first use and commissioning and thereafter at least annually and more frequently where needed such as after changes to design, systems or methods, or any significant damage, failure, or repairs. The validation of CL 3 laboratory sealability will not be required if there is relevant derogation from the requirement for sealability in a regulatory consent.

The methods used for validation of laboratory sealability can vary but will typically involve visual inspection of the structure, checks for leak paths with a smoke pencil, room 'smoke' and leak detection tests, and pressure tests. A full pressure test of the CL 3 laboratory structural envelope should be done at first use and periodically thereafter, which could be annual if desired, but at least once every five years or more frequently where required. The sealability will need to be revalidated wherever required such as if there is any significant failure or damage of the lab structure or significant repairs carried out.

The CL 3 Lab Manager should carefully review the validation of sealability report to check it meets the statutory requirements and relevant standards and any agreed actions. The CL 3 Lab Manager should obviously not accept any inadequate report and immediately take up any issues with the contractors.

7.3 Validation of Fumigation of CL 3 Laboratories

The fumigation of the CL 3 laboratory need to be validated to prove the efficacy of the methods and fumigants. There should be validation of routine fumigation and emergency fumigation methods. There may be multiple methods used for routine or emergency fumigation of complex CL 3 laboratories. The validation of these fumigation methods should be done prior to first use and commissioning and thereafter periodically, to ensure it is still effective, and where needed such as where there are any relevant changes to systems, controls, fumigation system or equipment or methods. The validation of fumigation will obviously not be required if there is relevant derogation from the requirement for sealability in a regulatory consent. The validation should include proof of killing of biological indicators that typically involves a six log decimal reduction.

There should be an SOP for each validated routine or emergency fumigation method. The CL 3 Lab Manager should carefully review the validation of routine and emergency fumigation reports to check they meet the statutory requirements and relevant standards and any agreed actions. The CL 3 Lab Manager should obviously

not accept any inadequate report and immediately take up any issues with the contractors.

7.4 Maintenance and Testing of Microbiological Safety Cabinets and Isolators

Microbiological safety cabinets, isolators or other similar equipment are types of local exhaust ventilation (LEV) systems used for controlling exposure to hazardous substances so there is a statutory requirement for regular maintenance examination and testing to ensure they continue to perform their function properly. There are many types of Class I, II or III MSC, isolators or other similar equipment used to contain infectious or hazardous aerosols that are required in CL 3 laboratories. MSC provide containment and protection to the user and the environment including other people in the laboratory from the aerosol hazards. The air discharged from the exhaust of the cabinet is HEPA filtered to remove microbial contamination and then ducted to outside or recirculated into the laboratory. At CL 3 (full or derogated) each MSC or other LEV must be fumigated before any maintenance, testing or service. This must comply with the Code of Practice for LEV (CS CoP004 Local Exhaust Ventilation).

MSC, isolators and similar LEV equipment in CL 3 laboratories (full or derogated) must be have a thorough examination and test done at least every six months (twice in each year) or more frequently where required. The thorough examination and test is carried out according to the relevant British Standard BS EN 12469 Performance criteria for microbiological safety cabinets. The HSE ACDP guidance and BS EN 12469 are very detailed and provide extensive guidance on how to implement the standard including validation methods and user checks. This maintenance must include the full operator protection factor 'KI test' to be done at least every six months on each MSC. Some specialist safety cabinets like Class III MSC or certain types of isolators require a pressure and leak detection test instead of a KI test to prove containment of aerosols.

The CL 3 Lab Manager and users should carry out suitable regular checks on MSC and other LEV, with reporting systems for faults. The CL 3 Lab Manager should do regular, at least monthly, checks on MSC airflows using a calibrated anemometer and keep records of the readings. The anemometer readings can be compared to those in the MSC thorough examination and test report. User checks of MSC and accessories may be needed. The relevant SOPs should detail the various types of checks needed, who should carry them out and any relevant training provided to workers. Checklists should be used that list standard checks.

7.5 Maintenance and Testing of Autoclaves

CL 3 laboratory autoclaves require a thorough examination and test to be done at least annually based on the requirements in the regulations, relevant standards and written scheme of examination (WSE). Autoclaves in CL 3 laboratories and those

outside of the CL 3 laboratory suite where used for CL 3 work, need to have their validation tests for waste inactivation to prove their effectiveness carried out at least every six months (twice each year) or more frequently where required (such as after a major repair). The autoclave validation is done using typical waste loads and multiprobe thermocouple testing to map the profile of temperature, time and pressure for each waste inactivation run set of conditions, following the relevant standards. The maintenance engineer should produce a detailed validation report with the relevant profiles. The CL 3 Lab Manager should check the reports and keep them as a record.

The effectiveness of the autoclave inactivation has to be monitored for every waste run using either electronic probes and data recorders or printers, and or using indicator strips. This monitoring is to check that the waste run complies with the validated waste inactivation conditions as detailed in the validation reports. These monitoring records of waste inactivation need to be kept, typically for at least six months. They may need to be kept for longer if required, such as if there have been problems with the operation or maintenance and repairs of the autoclaves.

The CL 3 Lab Manager should carry out regular local checks of the autoclave, associated equipment, controls, warning indicators and seals etc. User checks of autoclaves and accessories may be needed. The relevant SOPs should detail the various types of checks needed, who should carry them out and any relevant training provided to workers. Checklists should be used and records kept.

7.6 Maintenance and Testing of Centrifuges

Laboratory centrifuges need to be maintained and tested according to the relevant regulations and standards and this has to done by competent engineers. The CL 3 Lab Manager should carry out regular local checks of the equipment, controls, warning indicators, buckets and lids, and seals etc. User checks of centrifuges and accessories may be needed. The relevant SOPs should detail the various types of checks needed, who should carry them out and any relevant training provided to workers.

7.7 Maintenance and Testing of Other Equipment

All safety critical systems and laboratory equipment need to be properly maintained and tested on a suitable frequency and immediately if any issues arise by competent engineers or other relevant trained persons. For example, CL 3 laboratories may have various incubators, cryogenic or gas fixed installations or portable equipment (eg gas cylinders, regulators, manifolds, dewars) etc. The CL 3 Lab Manager should ensure that there are relevant maintenance and service contracts in place and that suitable local safety checks are carried out according to the relevant regulations and standards. Phones and other communication equipment needs to be maintained and checked regularly to ensure they are working. Emergency contacts need to be checked regularly to ensure they are up to date. User checks of equipment and

accessories may be needed. The relevant SOPs should detail the various types of checks needed, who should carry them out and any relevant training provided to workers. Checklists should be used and records kept.

8 Monitoring and Auditing of CL 3 laboratories

CL 3 laboratories are high hazard facilities and require a proportionately high level of oversight in relation to health and safety and environmental protection so there should be regular monitoring and checks by the School and University. PIs, SSA and School BSA should work closely with CL 3 Lab Managers to monitor the safety arrangements for their CL 3 laboratories, related facilities and activities. The University Biological Safety Adviser provides support and advice to the School in relation to the management of CL 3 laboratories.

There should be two full audits of each CL 3 laboratory, related facilities and activities carried out every year as the minimum standard. There should include a joint BSU / School annual audit and another separate School audit of each CL 3 laboratory carried out each year at approximately six months intervals. Specific CL 3 laboratory audit and inspection checklists should be developed and used for these audits. Audit reports should be produced with their findings and recommended actions and then once finalised they should be issued to both the School and BSU. The SSA / School BSA should forward the audit reports to the PIs, CL 3 Lab Manager and other relevant persons in their School and provide any relevant advice in relation to the findings and actions.

The audit reports and any required actions should be carefully reviewed, and a local action plan developed and implemented. Actions should be completed within a suitable and reasonable timescale proportionate to the level of risk of the findings. Inevitably, many actions will be straightforward but some others may be more complex to resolve and require the involvement of multiple parties and higher management decisions and resources.

The SSA / School BSA should check progress on audit actions at reasonable intervals and report any significant issues to local management and to the UBSA, and obtain any advice where needed. The SSA / School BSA should also send the audit reports to the School Genetic Modification and Biological Safety Committee (GMBSC) to review and monitor.

9 Further Information and Guidance

The School Safety Adviser or School Biological Safety Adviser should be contacted if you need advice on the management and operation of containment level 3 laboratories and facilities. Further information and guidance on biological safety and containment and control measures is on the Biosafety Unit (BSU) website.

Document version

Version number	Summary of change	Date and by whom
V1.0	New document	18/08/2023 P. Walsh

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