Biological Safety

May 2021

The Safe Use of Human Blood and Tissues

Occupational Health and Safety Service

HSD094B

UNIVERSITY OF CAMBRIDGE

University Guidance

The Safe Use of Human Blood and Tissues

Scope:

This guidance seeks to assist researchers, BSOs/DSOs and others who may not have background knowledge in medicine, human or animal pathogens. It is designed to further understanding of the risks associated with working with human blood and tissues. It will also help to ask the 'right' questions of others who are writing a risk assessment and/or those who may provide researchers with these particular types of biological research material.

1. What to do at the research project planning stage

1 **Contact the departmental BSO.** The earlier the BSO knows about the project, the faster the project will be reviewed and approved by the departmental H&S Committee where required. The BSO will also advise whether the work might need to be 'registered' with certain agencies/government bodies (eg notification) or a licence be obtained.

2 **Write an experimental plan and carry out a risk assessment** by using the correct template. The Safety Office has a variety of GM/Bio/COSHH risk assessment templates and the BSO will advise which of these need completing. See the Safety Office intranet: https://www.safety.admin.cam.ac.uk/subjects/biologicals

3 **Regulatory considerations:** the list below is not exhaustive and might change over time. Some of these are further mentioned in separate sections within this guidance.

- HSE Health & Safety Executive
- HTA (Human Tissue Act and Human Tissue Authority) and consent
- Research Ethics approval
- HFEA (Human Fertilisation and Embryology Authority - for embryos and embryonic stem cells)
- Material Transfer Agreements (MTA)

4 Gather background information about the research material (see other Sections below) and share this with the BSO as early as possible.

5 **Role of PI, researcher, student.** It is the role of the PI to write the RA, with the input from other members of the research group as appropriate. The PI has the overall responsibility that a risk assessment has been written and all personnel are appropriately trained (including keeping of the training records). Bio RAs are signed off by the PI and then submitted to the BSO who may sign off with input from the Departmental Biological Safety Committee. Students are not permitted to sign-off risk assessments, but are permitted to (co-)author risk assessments.

6 **Consider whether involvement of Occupational Health** is required. If the work includes the handling of human whole blood/tissue (or fractions of these), then Occupational Health must be consulted. A job hazard evaluation form (OHF29) should be completed and health monitoring/intervention might be necessary. See OH website for more information: https://www.oh.admin.cam.ac.uk/advice-and-guidance/bloodborne-virus-bbv-infections. The risk assessment will determine whether any vaccination (eg HBV) or other precautions are required or not. If vaccinations are required, be aware it will take several months for the vaccine to give protection.

7 **Intra-departmental blood collection.** All personnel involved in the collection of blood must be adequately trained and must be able to provide evidence of their competency (ie

competence in obtaining donor consent and phlebotomy). Full donor anonymity must be ensured, one way this can be achieved would be by setting up a dedicated phlebotomy 'team' who will be responsible for the blood collection and subsequent anonymization of all samples. In addition, the study should be set up in such a way that ensures potential donors, especially if involved in running the study, are not pressurised into donating blood samples and that there is a clear rule that no-one is permitted to handle/experiment with their own blood.

8 **Ethics and Consent.** If any blood and/or tissue is to be collected from staff, colleagues or any other subjects, with the correct consents in place, for the purposes of research, then independent ethical oversight is required. This will have to be in the form of a positive opinion from an NHS Research Ethics Committee (REC); the University Human Biology Research Ethics Committee (https://www.bio.cam.ac.uk/hbrec) or a Departmental Ethics Committee.
See further information on: https://www.research-integrity.admin.cam.ac.uk/research-ethics/research-ethics-committees. In addition, studies that may involve interaction with living people need to be registered via the University of Cambridge's Insurance guidance website on 'Human Volunteer Studies and Clinical Trials':
https://www.insurance.admin.cam.ac.uk/insurance-guidance/human-volunteer-studies-and-clinical-trials

2. Human Tissue Act (HTA)

1 Human blood and tissue is **'HTA relevant material'** and there are strict rules governing its use. The Safety Office has plenty of information on its intranet, including a FAQ area to assist researchers in taking the right steps. See
https://www.safety.admin.cam.ac.uk/subjects/biologicals/human-tissue-act

2 The University and Addenbrooke's Hospital hold **HTA licences** for research for certain University departments. Check with your BSO, who will be able to advise if your department is part of the licence and which one is relevant should you require further information.

3 For those departments on the University licence: the University has a **HTA Quality Manual** to ensure it complies with the HTA Codes of Practice and Standards and can be found on the Safety Office intranet: https://www.safety.admin.cam.ac.uk/subjects/biologicals/human-tissue-act

4 If the department does not have a licence, contact the Head of Biological Compliance within the Safety Office: hta@admin.cam.ac.uk, who will be able to advise before work commences.

5 **HTA Training.** All personnel working with human blood and tissues in HTA-licenced departments must undertake HTA training (the link for HTA training is on the Safety Office website: https://www.safety.admin.cam.ac.uk/subjects/biologicals/human-tissue-act) and provide the BSO and HTA PD (Person Designate) with a copy of the training certificate. The training covers the rules around HTA such as clinical/research ethics approved studies, Material Transfer Agreements (MTA), the 7-day rule, storage licences, consent, confidentiality of patient information, appropriate storage and disposal of human tissue, training and record keeping.

3. Importance of Origin of Human Blood Samples and Tissues

1 **What are the risks?** Certain countries have a higher incidence rate for serious diseases caused by bacteria and viruses, often well above countries in the EU or the UK. Global travel to and from countries with higher incident rates have the potential to increase the risk. Problems can arise if researchers, who don't have a biological science background, want to work with certain type of human tissue in a laboratory that is not well equipped to do so. The sharing of equipment, lack of knowledge about diseases and 'infection control' can increase the risks further by unknowingly contaminating equipment with pathogens through handling and touch points, thereby putting themselves and others at risk.

- **Polio.** It is worth noting that there are still countries where the polio virus is still endemic (Afghanistan, Pakistan) and faecal/stool samples, blood and lymphatic tissue could be a concern. For more information, see: https://www.who.int/health-topics/poliomyelitis and https://www.safety.admin.cam.ac.uk/subjects/biologicals/polio-eradication
- **Tuberculosis.** The same applies to tuberculosis, in particular the multi-drug resistant strains are becoming increasingly a problem due to global travel and migration. The WHO produces an annual report on Tuberculosis (https://www.who.int/teams/global-tuberculosis-programme/data). Sputum samples and bronchial lavages could be a concern.
- **HIV.** There are some countries where the incidence rate of HIV is often up to 40-50 % of the population in certain age categories. The WHO has an up-to-date list of HIV prevalence on their website: https://www.who.int/health-topics/hiv-aids#tab=tab_1 . HIV can be present in various body fluids, hence the assessor should take into consideration the type of material being worked on.
- **Hepatitis B and C (HBV and HCV).** The same principles apply as for HIV. To assess the risk, check the prevalence for the disease, the study population (if applicable) and the human 'tissue' being used.

2 **NHSBT (NHS Blood and Transplant) and 'Screened' blood – what does that mean?** Even if a test certificate is available, this will not be unequivocal. Bloods are not tested for all pathogens, but mainly for the most common, riskiest blood-borne viruses and pathogens: HIV, HBV, HCV, HTLV-1, HTLV-2, Syphilis and sometimes CMV (Cytomegalovirus). This leaves the possibility that other known pathogens as well as new, emerging and hitherto unknown pathogens in human blood/tissues are present in the samples. Historically 'screened' blood was considered safe to use, but there is a new way of thinking that takes these unknown pathogens into account.

3 In addition, it is often assumed that blood from the NHSBT is 'pre-screened' and therefore 'safe' to use, however the Safety Office has been informed that often bloods are released before the test results become available. Therefore, all human blood samples should be treated as potentially infectious and be handled under CL2 conditions, as is written in the NHSBT supply documentation. The same applies to other human specimens: all primary human tissues should be risk assessed and handled at Containment Level 2 unless there is evidence to the contrary.

4 **Use of blood from donors within the department: is it 'safe'?** No, not without testing by an accredited laboratory. However, it is illegal to conduct testing of blood/tissues for diseases without the donor's consent. It would also break donor confidentiality if these test results were traced back to the donor, opening up the possibility of subsequent 'donor profiling'. Without ethical approval and the oversight of an independent, medically qualified person,

combined with a guarantee of complete donor confidentiality and the required provision of counselling to discuss any adverse finding, such testing is unethical.

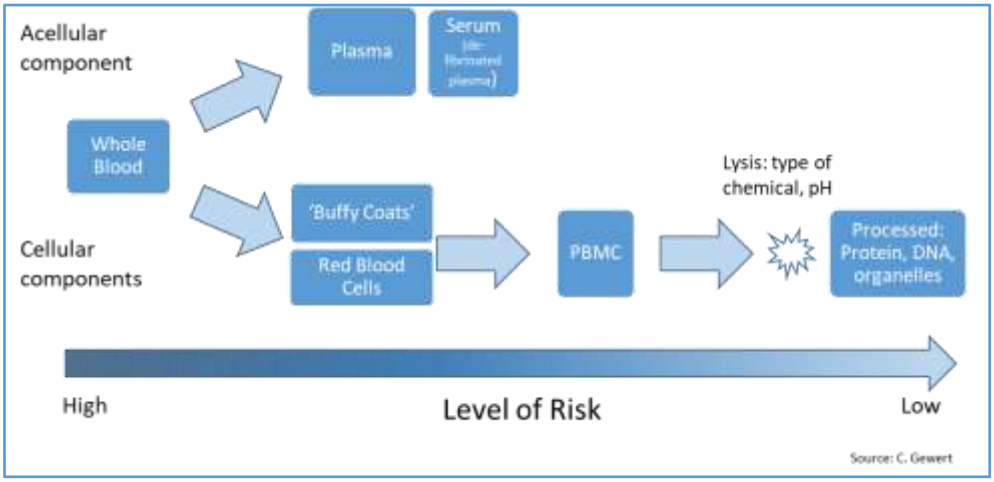
5 **Stem cells/cord blood** could be considered of lower risk – most likely to be Containment Level 1. However, depending on the research study, the researcher might be able to enquire with the clinic what the health status of the donor was or whether any testing was done.

6 **Commercially available human material** will often be 'pre-screened', but most companies will still advise to handle the material as infectious. The material data safety sheet should provide this information, often the phrase BSL 2 is in such documentation. In the UK, the regulations refer to Containment Level 2 (CL2), not BSL 2. If the material safety data sheet is not provided in the shipment of the human material, then researchers must ask the supplier for this information.

7 Depending on the research, blood and tissue could be 'contaminated' with **other hazardous agents** (eg cancer drugs), or adventitious biological agents that may have been unintentionally introduced during handling, such as mycoplasma, rickettsia, protozoa, fungi etc. Hence additional care should be taken when handling blood/tissue.

4. Working with Human Blood

1 **Blood in research.** The level of risk when working with human blood is determined not only by the health/disease status of the donor and its origin (see Section 2), but also by how much blood (volume) is processed at a time and how much the blood will be processed following collection. Whole blood carries the largest risk, followed by plasma (all white/red blood cells are removed; clotting factors intact) and serum (defibrinated plasma). 'Buffy coats' are highly concentrated white blood cell preparations, which could harbour latent blood borne viruses. PBMC (peripheral blood mononuclear cells) are the product of white blood cell separation and will undergo several washes with salt solutions so that any biological agent (virus/bacteria/parasite) present in the plasma will have been mostly washed out with only (in theory) the PBMC cells themselves potentially harbouring virus. Once white (or red) blood cells have been lysed, the lysis reagent and its associated pH will determine whether a biohazard risk has been eliminated.



2 **Workers should never ever work on their own blood** – if (viral) transformation were to occur, the body's immune response may not provide protection in the event of re-exposure through a needle-stick or other accident.

3 **The 100-hour-rule.** This really only applies when working with certain types of white blood cells from known or suspected HIV+ patients. It is thought that if the cells are incubated for

longer than 3-4 days, then the virus could start to accumulate in significant numbers to pose a risk. Whilst the level of risk of viral propagation is likely to be low, the risk assessment should take this possibility into account and control the risk by working at CL2 using a microbiological safety cabinet and avoiding the use of sharps/glass items. The worker must be seen by Occupational Health prior to starting this work.

4 **Immortalisation/transformation/transduction of human blood cells (and other primary tissue derived cells) using viruses.** Various human pathogenic viruses are used for this work such as Epstein-Barr-virus, Cytomegalovirus and Lentivirus. Although some of these viruses are common in humans, they can pose a serious risk to vulnerable persons such as pregnant women or immunocompromised individuals. The use of viruses for immortalisation purposes is one of the reasons for why workers should never work on their own blood (see above).

5 **Blood can also be used as a reagent**, eg for the feeding of biting insects, parasites, bacteria and tissue culture and use in immuno-assays. The risk of whole blood for this purpose is the same as the one 'for research use' and additional risks arise through use of tools (blades, sharps, etc) and extended incubation times at elevated temperatures, which could allow biological agents to be inadvertently propagated. The risk assessment should take this into consideration alongside the control measures.

6 The **use of equipment** can expose workers to biological agents. The use of centrifuges, vortexes and shakers carry the risk of spills and associated aerosolisation. Cryostats, needles and other sharps pose the risk of biological agents entering the worker's blood system through cuts to the skin. It is important that the use of these be avoided as much as possible through the early stages of primary tissue processing and to wear appropriate PPE, including the protection of face and eyes. The use of Microbiological Safety Cabinets (MSCs) are essential where the risk exists.

5. Working with Human Tissue (For HTA related information, see Section 2)

The risks arising from working with human primary tissue is determined by the same principles as described for working with human blood (See Section 4). The risk to the worker will be larger in the initial processing steps and will decrease the more the tissue is processed and the isolation of individual cells are achieved. There are also specific risks associated with certain tissues and some of these are listed below (the list is not exhaustive).

1 **Aerosol generation:** there are a range of procedures that create aerosols such as vortexing, pipetting or centrifuging (this list is not exhaustive). The use of flow cytometers for FACS analysis also bears the risk of aerosolisation. Control measures must be put into place to contain aerosols and the risk assessment should list these.

2 **Fixed versus unfixed tissue.** Wherever possible, cells/tissues should be fixed prior to analysis to reduce the risk of infection. Slicing fresh frozen tissue using a cryostat is a higher risk activity than cutting paraffin wax blocks with embedded fixed tissue. Please note: working with formaldehyde/glutaraldehyde-fixed neural tissues does not make it 100% safe: prions are only immobilised with these chemicals, but they are not inactivated with these. Well written SOPs and training are good control measures.

3 **Disposal of human tissue.** See Section 9 for more information.

4 **Disposal of GM tissue.** See Section 9 for more information.

5 **Disposal of human tissue samples with risk of containing Polio virus** (see Section 3, Paragraph 1 for more information). To comply with the worldwide polio eradication programme, researchers working with these tissues should generate evidence that such material has been successfully destroyed following completion of the research work. It is recommended that all waste is autoclaved in a dedicated autoclave run and the autoclave record (cycle number, date of run, pass/fail information) is kept for auditing purposes.

6 **Storage**. It is illegal to store human blood and/or tissue samples without either a HTA licence or an NHS REC Approval. In addition, such samples must be stored in such a way that other personnel are not put at risk and that it also complies with HTA regulations (see Section 2). Whole blood and human tissue should be stored in access-restricted locations with appropriate biohazard signage and contact details for responsible persons in case of emergencies. Accurate inventories will contribute to the safe handling and storage of such samples. The inventory should document the life-cycle of such samples from 'source to disposal' to comply with HTA standards and any associated MTAs (Material Transfer Agreements) from eg research tissue banks. The storage method should prevent spills and contamination of adjacent areas, eg by using double containment and by preventing of storage boxes becoming 'soggy'. Storage areas should be inspected at regular intervals either during sample audits or safety inspections.

7 **Collaboration with other departments.** Where research using (human) blood and tissue samples are carried out between several departments, the BSOs of both departments need to be made aware of the work and risk assessments need to be signed off by the BSO of each department. Researchers should check that they are permitted to transfer HTA relevant material between departments.

8 **Specific pathogen risks arising from working with certain human tissues:**

- Brain/spinal cord/ lymphatic tissue: prions leading to Transmissible Spongiform Encephalopathies (TSE) such as classic and new variant CJD. Please note that working with prions falls under the TSE regulations (Transmissible Spongiform Encephalopathies). The Approved List of Biological Agents by the Advisory Committee on Dangerous Pathogens (ACDP) lists the relevant containment level. Please contact the Safety Officer of the School of Biological Sciences during the planning stage of any new work.
- Gut/faeces: polio virus, Sars-CoV-2, bacterial pathogens, norovirus, parasites (eg helminths)
- Lung, sputum: Tuberculosis (Mycobacterium tuberculosis), Sars-CoV-2, other bacterial pathogens
- Bone: Tuberculosis (Mycobacterium tuberculosis)
- Breast milk, semen: HIV (see Section 3)
- Since the beginning of the Covid-19 pandemic at the beginning of 2020, there is now an additional risk of Sars-CoV-2 being present in certain types (see above). Currently Sars-CoV-2 is not on the 'Schedule 5' list, but it is possible that this might change once the disease is under control. Hence we recommend that human samples should be categorised as 'before/after Covid-19' to allow departments to segregate those samples from their other holdings to meet legal requirements. This cut-off period for the 'Covid-19-safe' sample threshold might be eg the autumn of 2019.

6. GM of Human Blood and Tissues

1 **GM Risk Assessment.** All work involving GM technology requires the completion of a specific GM risk assessment (see Safety Office intranet: https://www.safety.admin.cam.ac.uk/subjects/biologicals/gm-gmo-gmm-gm-plants)

2 The risk will depend on the type of genetic mutation being carried out: certain gene sequences harbour significant risks to workers such as oncogenes.

7. Transport of Human Blood and Tissue

1 There are explicit transport requirements for transporting biological materials by road and air. Packing, marking and labelling of dangerous goods by road and air must be in accordance with transport regulations (ADR and ICAO/IATA). Typically, this will mean all biohazardous/suspect biohazardous materials must be triple contained, and includes sufficient absorbent material to mitigate any breakage/spill. Please speak to your Department's Dangerous Goods trained person, who will be able to advise you.

2 Movement of biological materials between labs within the same building, or between buildings on the same university site, requires that the material is still safely double contained.

3 It is not permitted to transport hazardous biological materials by public transport. The transport of biohazards using a private car or on a bike must be risk assessed and might in certain circumstances not be permitted at all. The Safety Office has additional information on transport on its intranet: https://www.safety.admin.cam.ac.uk/subjects/biologicals/transportation

4 It is of note that blood collected from the NHS Blood and Transplant Service is specifically exempt from the Department of Transport requirement assign it to UN3373 for transport purposes, unless deemed as potentially infectious.

5 The risk of transporting blood and tissue between departments must be part of the risk assessment and the BSOs of all departments involved must be informed of any transfer activity well in advance (see Section 1)

6 Parcels and packages containing fresh tissues should only be opened in the lab and never in the reception area. They should only be opened by trained staff using good laboratory practice.

7 **Import/Export General.** All imports and exports must be notified to the BSO and DSO and documentation kept for auditing purposes. Please note that following the UK leaving the EU, there are new rules to follow, which are explained in the new post-Brexit document issued by the UK government: https://www.gov.uk/government/publications/the-border-operating-model

8. Control measures and containment level

The final containment classification will be determined following the completion of the COSHH/Biological risk assessment. There are Bio RA templates available on the Safety Office intranet (from May 2021): https://www.safety.admin.cam.ac.uk/subjects/biologicals.

1 **Appropriate PPE** must be worn to control the risk of infection through skin, mucosal surfaces, eyes or inhalation. Double gloving could provide extra security when handling human whole blood. Safety glasses will minimise the risk of splashes to eyes and should always be worn when unpacking deliveries.

2 **Containment Level.** The type of material/hazardous agent used and the activity/methods involved will determine at which containment level the work will need to be carried out. It will also determine whether certain activities can be done on an open bench or not. See the 'Numbers Game' leaflet for more information: https://www.safety.admin.cam.ac.uk/publications/biological/hsd106b-biological-safety-numbers-game

3 **Human blood should be handled at Containment Level 2 by default, even if 'pre-screened', unless a risk assessment has determined it is safe to handle at a lower containment level.**

9. Disposal of human blood and tissue waste

1 **Disposal of human tissue.** The disposal method for human tissue is determined by the HTA regulations and by the risk such waste poses to humans and the environment. Please consult with the University's HTA Quality Manual for further information: https://www.safety.admin.cam.ac.uk/subjects/biologicals/human-tissue-act/quality-manual

2 **Disposal of GM tissue.**
It is University policy that all GM waste must be inactivated prior to disposal.

3 Autoclaving or chemical disinfection methods must be validated to ensure that any hazardous agents (GM/Bio) are successfully inactivated/destroyed prior to the waste removal from site (see: https://www.safety.admin.cam.ac.uk/publications/biological/hsd164b-autoclaves-validation-and-monitoring). Hospital embedded departments should agree with their NHS Estates that the department's waste policy is compliant with both the hospital and the University's waste policy. The same applied to departments using their own waste contractors.

4 **Autoclaving or chemical disinfection** methods must be validated to ensure that any hazardous agents (GM/Bio) are successfully inactivated/destroyed prior to the waste removal from site (see: https://www.safety.admin.cam.ac.uk/publications/biological/hsd164b-autoclaves-validation-and-monitoring). Hospital embedded departments should agree with NHS Estates that the department's waste policy is compliant with both the hospital and the University's waste policy. The same applies to departments using their own waste contractors.

5 **Inactivation Method.** Human whole blood, plasma and serum waste are high in organic matter and can therefore interfere with the antimicrobial activity of disinfectants, especially those which are chlorine based. These materials can be safely decontaminated by one of 2 means: chemical inactivation by using approved biocides such as Virkon and quaternary ammonium compounds (eg Distel, Chemgene) or by using a gelling agents (eg Vernagel) to solidify the liquid waste and subsequent autoclaving. If the use of a chlorine based biocide is desired only approved products should be used such as Presept, which is resistant to inactivation by organic soilage. Household bleach purchased from supermarkets have in general no information on chloride activity levels (expressed as parts per million) and the activity might decay depending on storage conditions and duration.

6 **Disposal of sharps.** Contaminated sharps/needles/scalpels/glass slides should be safely collected in sharps bins with the optional autoclaving prior to commercial waste collection for incineration.
7 Waste bins should not be overflowing with waste and sink areas should be well managed.

10. Considerations regarding vulnerable workers/others

1 The protection of vulnerable persons and other staff must be considered when writing the RA.
2 Some individuals are not able to undergo vaccination against Hepatitis B or pregnant women and their unborn baby are at risk when the mother becomes infected through handling (unknowingly) virus containing samples (eg CMV in blood, saliva and urine).
3 Housekeeping staff and other co-workers using the same lab facility must be made aware of the risk.

11. Accidents/Incidents/Emergencies

1 All workers should be trained about what to do when sustaining a needle-stick or other sharps injury involving human blood/tissue.
2 The following steps should be taken (according to the Occupational Health website: https://www.oh.admin.cam.ac.uk/advice-and-guidance/bloodborne-virus-bbv-infections) in case of a potential exposure incident to human blood/tissue:
   - Encourage the wound to bleed, but do not scrub the wound: this may increase tissue damage
   - Wash any wound or contaminated skin with soap and clean water. Cover with a sterile dressing (eg waterproof plaster)
   - If blood is splashed into the eye or mouth, stop and wash out immediately with tap water or saline
   - Report the incident to the person in charge – supervisor, BSO, DSO, First Aider. Don't delay, or fail to report the accident even if you were not following correct procedures.
   - Contact Occupational Health preferably straight away and at least within 48 hours for advice or treatment with details, including the risk assessment and procedure in an emergency, eg to take a prophylactic medicine.
3 If Occupational Health Staff are not available, go to the Accident & Emergency (A&E) Department, who will advise whether eg anti-retroviral treatment is required. Take with you the details, including the risk assessment and procedure in an emergency.
4 If needles/sharps have been used (during processing of human blood/tissue), retain a sample of your own blood/tissue to test for Hep B/ HIV if necessary (for 'negative' reference sample).
5 If you have not already done so: report all accidents/incidents to the First Aider, DSO, BSO and your line manager and log it on the University incident reporting portal: https://www.safety.admin.cam.ac.uk/subjects/accidents-incidents
6 Any spills should be cleared up immediately to avoid contamination of other work areas, thus avoiding putting others at risk. Large spills within safety cabinets should be mopped up with paper tissues and bagged up for autoclaving. The area is then disinfected with an approved biocidal, eg Virkon, Chemgene, Distel – but not 70% Ethanol. The latter is only suitable for disinfecting clean areas and it would simply 'fix' the blood onto the surface. Spills on open benches or floors should be sprinkled with Virkon powder and left to act for

the recommended time period before being swept up with disposable scrapers and disposed of via the appropriate waste route.

HSD094B

The Safety Office
Greenwich House
Madingley Road
Cambridge CB3 0TX

Tel: 01223 333301
Fax: 01223 330256

Email: safety@admin.cam.ac.uk
www.safety.admin.cam.ac.uk