Biological Safety Series

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Cell (Tissue) Culture:

ACDP Guidelines

Occupational Health and Safety Service
HSD195B (rev 1)

UNIVERSITY OF CAMBRIDGE

Cell (tissue) culture – ACDP guidelines

Cell culture is defined in COSHH as *'the* in-vitro *growth of cells derived from multicellular organisms'* and is included in the definition of a 'biological agent'; cells may be infected (deliberately or adventitiously) with other biological agents so they could present a risk of infection or could, in exceptional circumstances, proliferate if inoculated *in vivo*.

Generally cells themselves do not appear to present a significant hazard as even direct dermal inoculation may result in only local inflammation; however the long term consequences are uncertain. NB tumour cells, primary and established lines, can evade immune responses and have been rarely documented in being transmitted to humans. The main risk presented by cell cultures is as a result of their ability to sustain the survival and/or replication of a number of adventitious agents. The major agents of concern are viruses, but other agents, eg, mycoplasmas (some of which are HG2 human pathogens) should also be considered.

In addition to these risks, other hazards that should also be assessed include the components of the cell culture media (products of animal origin can act as a source of microbial contamination) and cell products that could be biologically active (allergy or toxicity).

Assessing the risks

Stage 1: Identify the hazards

There are a number of factors that should be addressed in a risk assessment, including:

Origin of cell line and source species from which cell line was derived: the risk from any cell line should be considered in terms of the likelihood of contamination **and** the ability of the cell line to support growth. Agents infectious for humans are most likely to arise from cells of human or primate origin but other mammalian, avian and invertebrate cell lines may also present risks (zoonoses).

Source population and type of tissue: this will give an indication of potential contaminant microbes and potential for expression/reactivation of latent viruses. Cells derived from peripheral blood and lymphoid cells present the greatest likelihood of contamination with serious human pathogens. Foetal neural tissue should present significantly lower risk than blood from a GU clinic.

Type of cell line: primary cell cultures present the greatest risk of carriage followed by continuous cell lines unless known to be persistently infected (e.g. B95-8 with EBV, MT4 with HTLV), and then well authenticated/characterised cell lines such as those used for the manufacture of vaccines or recombinant proteins.

Information should be available from the supplier or the originator of the cell line and/or peer-reviewed literature. Some cell lines may have undergone passage in different laboratories and this may not have been recorded. The risk of infection would be difficult to assess so it is better to obtain material from the originator of the cell line or a culture collection where the cell lines will have been well characterised/authenticated, have a documented provenance and should have been screened for human pathogens.
You should not use your own cells (or cells of anyone else who is working in the laboratory) for experimental purposes. This presents a particular hazard as any cells from a self-inoculation injury would essentially circumvent the normal protection of the immune system.

Stage 2: Consider the nature of the work

Consider in particular:

- Where the work will be carried out
- Whether the work could create aerosols - eg pipetting, pouring or scraping - or splashes

- Whether the work will require the use of sharps
- The level of production of any virus (reassess if influencing culture conditions change)
- Volume of cultures and number of samples.

Stage 3: Evaluate the risks and select control measures

Table 1 should be used as a guide to select appropriate containment measures. A baseline containment level is given for different cell types.

Some commercially available cell lines have been used in research for several decades and are well characterised. Other cell lines, which have only been recently established from primary human/primate tissue might harbour a yet unknown adventitious agent and should therefore be handled with extra care.

Where a cell line is deliberately infected with a biological agent, or where it is likely that the cell line is contaminated with a particular agent, the containment level used must be appropriate for work with that agent.

COSHH requires the use of a microbiological safety cabinet if the procedures carried out are likely to give rise to infectious aerosols. However, many users will automatically use a cabinet (Class II) to protect the cells from contamination. It is important that workers understand this difference and ensure that the work is carried out safely, eg, by regularly checking the performance of the cabinet by measuring airflows.

Table 1 Guidance on containment measures for work with cell cultures

Hazard	Cell Type	Baseline Containment Level
Low	Well characterised or authenticated finite or continuous cell lines of human or primate origin with a low risk of endogenous infection with a biological agent presenting no apparent harm to laboratory workers and which have been tested for the most serious pathogens	CL1
Medium	Finite or continuous cell lines/strains of human or primate origin not fully characterised or authenticated except where there is a high risk of endogenous biological, eg, blood borne viruses.	CL2
High	Cell lines with endogenous biological agents or cells that have been deliberately infected.	CL appropriate to agent
	Primary cells from blood or lymphoid cells of human or simian origin.	CL appropriate to risk

Note: Any work that could give rise to infectious aerosols, such as with medium or high risk cell lines, must be carried out in suitable containment, eg, a microbiological safety cabinet.

A useful resource for cell culture in general is a handbook by ECACC, available via Sigma: https://www.sigmaaldrich.com/life-science/cell-culture/learning-center/ecacc-handbook.html

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References

Geraghty, R J et al, Guidelines for the use of cell lines in biomedical research, Br. J Cancer (2014)

Lazebnik, Y and Parris G E, Comment: Human-to-human cancer transmission as a laboratory concern, Br. J Cancer (2015), 112, 1976-1977

Management and Operation of Microbiological Containment Laboratories (2019) http://www.hse.gov.uk/biosafety/management-containment-labs.pdf

The SACGM Compendium of Guidance, HSE/SACGM, Part 2, 66-69

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