Loughborough University **The Centre for Biological Engineering**	**Quality Manual**			
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Purpose and Scope

The Centre for Biological Engineering (CBE), located at Loughborough University, is a multi-disciplinary research centre, bridging the fields of engineering and biology. The primary purpose of the CBE is translational research with particular focus on manufacturing and bio-processing. The central aim of the research activity is to realise the potential of regenerative medicine to improve human health and functioning of the human body.

The CBE acknowledges its responsibility as a research unit within Loughborough University to adhere to all applicable regulatory, licensing standards, codes of practice and national/local ethical guidelines connected with research that involves the acquisition, storage, transport, use and disposal of hazardous or potentially hazardous chemical materials and biological materials, including those of human origin that may or may not fall under the remit of the Human Tissue Act 2004 (HTA) in England, Wales and Northern Ireland as 'Relevant Material' (*see Appendix for definition*).

The CBE acquires human biological material (cellular and acellular) from third party commercial suppliers and/or other academic research institutes located primarily in the UK but also abroad, either through collaborative research or commercial arrangement. It may also acquire human tissue directly from donors or patients in the UK adhering to strict consent procedures. Unless the material is acquired, collected or otherwise transferred as part of a recognised Research Ethics Committee (REC) approved study (*and is not retained after that project for unspecified future use*) or is acquired from a HTA licensed tissue bank with REC approval for generic research use, the CBE shall ensure that all Relevant Material (to be termed 'HTA licensable material' for the purposes of this Quality Manual) is acquired, transferred, stored, used and disposed of in accordance with the Human Tissue Act (2004). For reasons of good practice, this shall also apply to the temporary storage of HTA Relevant Material incidental to transportation or prior to a processing step that will render the material acellular or otherwise non-relevant, even if it is held for less than 7 days prior to being processed or transferred to another establishment.

The requirements under the HTA do not derogate from the basic principles and practices laid down in the CBE Code of Practice. The purpose of this Quality Manual (QM) is therefore to integrate the policies and procedures of the existing Quality Management System (QMS) with the additional and supplementary standards and codes of practice that apply under the Human Tissue Act 2004 for current and future research activities within the CBE.

Quality Management System Requirements

This Quality Manual describes and forms part of the Quality Management System (QMS) of the CBE. The CBE has developed and implemented this QMS to ensure that the CBE delivers high quality translational research outcomes needed to fulfil the Quality Policy and objectives and that meet the needs and requirements of the users, that meets or exceeds our stakeholder requirements and expectations and that provides a governance process that ensures that the CBE fulfils its requirements and responsibilities under the following:

1. The Human Tissue Act 2004 (HTA) and Codes of Practice for Research
2. The Loughborough University HTA Licence Compliance Quality Manual
3. The UK Code of Practice for the Use of Human Stem Cell Lines
4. The Control of Substances Hazardous to Health (COSHH) Regulations 2002
5. The Genetically Modified Organisms (Contained Use) Regulations 2005
6. The Loughborough University Biological Safety Policy

This Quality Manual represents the scope of the QMS and its application throughout the CBE, references the processes established, and identifies the sequence and interaction of these processes to ensure that the operation and control of these processes are effective. This quality manual provides the information necessary to implement the QMS and support the operation and monitoring of these processes to achieve the required level of quality and safety assurance, and continually improve their effectiveness conducted within the framework of management reviews of the QMS.

Figure1 shows the scope of the QMS and its application throughout the CBE. References the policies (shaded blue), the CBE Codes of Practice (shaded orange) and the core procedures (shaded purple) established. Identifies the sequence and the vertical/horizontal interaction of these processes (shaded green) to ensure that the operation and control of these processes are effective.

Figure1. Schematic of CBE Quality Management System (QMS).

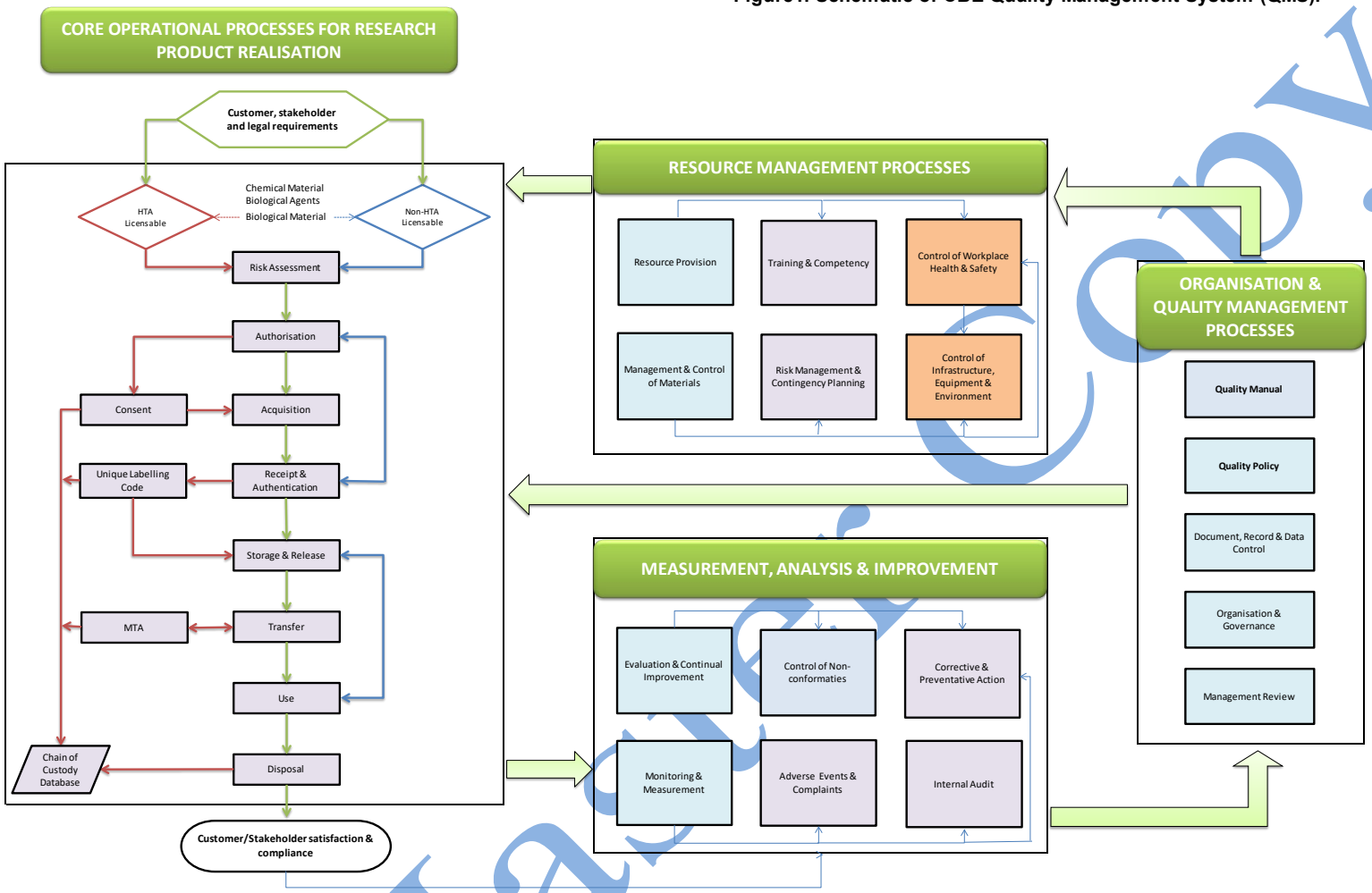

Table 1. Alignment of CBE Quality Management System processes with the requirements of research guidelines* and the HTA standards for research (Code of Practice 9). ***R J Geraghty et al. Guidelines for the use of cell lines in biomedical research. British Journal of Cancer, p1-26, 2014.***

QMS Process/System	Current systems under CBE Code of Practice	Biomedical Research Guidelines for use of cell lines*	HTA Standards for Research
Quality Management Processes			

QMS Process/System	Current systems under CBE Code of Practice	Biomedical Research Guidelines for use of cell lines*	HTA Standards for Research
Quality Manual [QS-MAN-001]			GQ1 – Policies & procedures in place covering all licensable activities as part of the governance process
Document & Record Controls [QS-POL-002]		3.5 – Recommendations for QC, record keeping, document control and research integrity	GQ2 – Documented system of quality management and audit GQ4 – Systematic and planned approach to the management of records
Quality policy [QS-POL-001]			GQ1 – Policies & procedures in place covering all licensable activities as part of the governance process
Organisation & Governance [QS-POL-003]	Section 1: Organogram for facility, laboratory management and safety responsibilities Section 4.6: Management responsibility, supervision and other duties - GMOs Section 1: Laboratory meeting, Laboratory Leader meetings, Safety Committee meetings		GQ1 – Policies & procedures in place covering all licensable activities as part of the governance process GQ7 – systems to ensure that all advers events are investigated promptly
Management Review [QS=POL-004]			GQ1 – Policies & procedures in place covering all licensable activities as part of the governance process
Resource Provision & Management Processes			
Provision of training and awareness [RM-POL-005]	Section 2.2. Provision of information, instruction and training Section 3: Information, Training and Supervision	3.2 – Recommendations for training and competency	C3 – Staff receive training in essential requirements of taking consent GQ3 – Staff appropriately trained in techniques relevant to their work and are continuously updating their skills GQ8 – Risk assessments of practices and procedures completed regularly, recorded and monitored appropriately PFE5 – Equipment is appropriate for use, maintained, quality assured, validated and monitored
Provision and control of infrastructure & work environment	Section 2 – Part 2. Precautions and measures for controlling exposure to biological agents – Engineering controls Section 2 – Part 3: Additional measures – Working Practices Section 5: Disinfection, cleaning and waste disposal procedures Annex 9: Information on specific types of disinfectant	1.5 - Precautions to minimise cell line misidentification 3.4 – Standards for equipment - BSCs, incubators, microscopes, autoclaves 4.2 – Prevention and eradication of mycoplasma contamination 4.3 – Prevention and eradication of other microorganism contamination	PFE2 – Environmental controls in place to avoid to avoid potential contamination PFE3 – Appropriate facilities for storage of licensable material, consumables & records PFE5 – Equipment is appropriate for use, maintained, quality assured, validated and monitored

QMS Process/System	Current systems under CBE Code of Practice	Biomedical Research Guidelines for use of cell lines*	HTA Standards for Research
	Annex 4: Use and maintenance of BSCs CoP on Use and maintenance of BSCs Annex 5: Use and maintenance of autoclaves		
Provision and control of safe working practices	Section 2 – Part 2. Precautions and measures for controlling exposure to biological agents – Engineering controls Section 2 – Part 3: Additional measures – Working Practices Section 2 – Part 4: Additional precautions for cell/tissue culture work Section 4: Safe working with GMOs Annex 1 - Work with blood, blood products, and human tissues Annex3: Guidance on use of chemicals in biologicals laboratories CoP on use of carcinogens Annex 6: Guidance for contractors working in CBE laboratories Annex 7: Lone working guidance	3.1 – Guidelines on operator safety - liquid nitrogen - biohazards - clinical specimens, primary cultures, stem cell lines, GMOs - containment - disposal	PFE1 – Premises are fit for purpose D1 – Disposal policy for disposing of human organs and tissue
Research Product Realisation Processes			
Risk Management [RM-POL-006]	Section 2.1: Procedures to be adopted before starting work – administration and exposure controls		GQ1 – Policies & procedures in place covering all licensable activities as part of the governance process GQ1 – Risk management systems GQ2 – Documented system of quality management and audit GQ8 – Risk assessments of practices and procedures completed regularly, recorded and monitored appropriately PFE1 – Premises are fit for purpose PFE4 – Systems to protect the quality and integrity of licensable material during transport and delivery to a destination
Materials Management & Control [RM-POL-006] Research Product Realisation [PR-POL-010]			
Acquisition & authentication of human tissues, cells and reagents	Section 2.6: Notifications Section 4.5: Acquisition of GMOs Annex 2: Controls on animal and plant	1.1- Recommendations for developing new cell lines 1.2 - Recommendations acquisition &	C1 - Consent obtained in accordance with requirements of HTA and Code of Practice C2 – Information about the consent process is

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	pathogens	authentication of cell lines form another laboratory 2.1 – UK ethical/legal requirements for obtaining tissue for cell lines, including patient consent & MTAs 3.3 – Recommendations for purchase and testing of culture reagents	provided in a variety of formats
Storage & banking	Section 7: Storage and transport of biological materials Annex 8: Storage samples in liquid nitrogen	1.4 - Recommendations for storage & banking of cell lines	GQ1 – Policies & procedures in place covering all licensable activities as part of the governance process GQ1 – Risk management systems PFE3 – Appropriate facilities for storage of licensable material, consumables & records
Identification & traceability		4.4 – Minimising genetic instability and phenotypic drift in cell lines	GQ6 – A coding and records system facilitates traceability of licensable material ensuring a robust audit trail D2 – Disposal is documented
Transfer and transport	Section 7: Storage and transport of biological materials Annex 10: Transport of biological material outside the CBE	1.6 - Recommendations for transferring cell lines between laboratories 1.7 – Compliance with regulations for transport of cells	GQ5 – Documented procedures for distribution of licensable material PFE4 – Systems to protect the quality and integrity of licensable material during transport and delivery to a destination
Use of tissues and cells	Section 2 – Part 2. Precautions and measures for controlling exposure to biological agents – Engineering controls Section 2 – Part 3: Additional measures – Working Practices Section 2 – Part 4: Additional precautions for cell/tissue culture work Section 4: Safe working with GMOs Annex 1 - Work with blood, blood products, and human tissues		
Disposal	Section 5: Disinfection, cleaning and waste disposal procedures Section 4.4: Disposal of GMOs		D1 – Disposal policy for disposing of human organs and tissue D2 – Disposal is documented
Measurement, Analysis and Improvement Processes			
Control of non-conformities [MI-POL-007]	Section 6: Emergency Response Procedures	5 – Troubleshooting cell culture problems	GQ1 – Policies & procedures in place covering all licensable activities as part of the governance process GQ7 – systems to ensure that all adverse events

QMS Process/System	Current systems under CBE Code of Practice	Biomedical Research Guidelines for use of cell lines*	HTA Standards for Research
			are investigated promptly
Monitoring & Measurement [MI-POL-008]			GQ2 – Documented system of quality management and audit
Evaluation & Continuous Improvement [MI-POL-009]			GQ7 – systems to ensure that all adverse events are investigated promptly

Appendix: Definition of Relevant Material under Human Tissue Act 2004

Under the HT Act, relevant material is defined as that which consists of, or contains, human cells. The fundamental principle is that if a sample is known to contain even a single cell that has come from a human body then the sample should be classified as relevant material.

Relevant material under the HTA licence excludes:

- Gametes and embryos outside the human body (these are covered by legislation under the Human Embryology and Fertilisation Act, 2008);
- Hair and nail from a living person;
- Cell lines which have divided outside the human body (see note below);
- Extracted DNA and RNA.

Note: If primary cells remain, then the cell line or cell culture could be considered relevant material. There is a judgement to be made in such instances depending on knowledge of the rate of cell division and culture conditions.

Examples of relevant material

1. Specifically identified relevant material
This includes material such as bodies, organs and tissues, consisting largely or entirely of cells, and clearly identifiable.

2. Processed material
Where a processed material is generally agreed – as a result of the process – to leave it always either cellular or acellular, then the presumption should be that all examples should be regarded as such. The HTA would rely on an assurance that the process in question had been carried out and that it can be relied on to render samples acellular (i.e. using data from either in-house or published research). Under this category, plastinated tissue and plastinated body parts (where the cellular structure is retained by the plastination process) are considered relevant material; while plasma or serum, for example, will not be regarded as such.

3. Bodily waste products (including excretions and secretions)
The HTA considers that bodily waste should normally be regarded as relevant material. The Act's wording is clear and reflects the possibility that even a single cell can be subject to an activity such as research. There will be cases where a person believes that material, intended for a scheduled purpose, is actually acellular. In such cases, the HTA can be approached for advice.

4. Cell deposits and tissue sections on microscope slides
In general, cell deposits or tissue sections on microscope slides are considered to constitute relevant material. This is because such deposits or sections are likely to contain whole cells or are intended to be representative of whole cells.

The HTA has produced a list that provides stakeholders with further guidance on whether specific materials fall within the definition of relevant material under the HT Act – refer to the HTA website.

Version History

Version Reviewed	Date Revised/ Reviewed	DCN No	Revision Summary	New Version Number
1.0	4th December 2017 by C.Kavanagh	**N/A** No changes required.	No changes. Minor Editorials only and additon of review date.	**1.0** No new version number required.

1.0	2nd December 2019 by C.Kavanagh	**N/A** No changes required	No changes. Minor Editorials only and additon of review date.	**1.0** No new version number
1.0	20/04/2021 by C.Kavanagh	DCN009	Added note to say ‘ It may also acquire human tissue directly from donors or patients in the UK adhering to strict consent procedures.’	2.0
2.0	6th December 2021 by C.Kavanagh	N/A No changes required	No changes. Minor Editorials only and additon of review date.	2.0 No new version number required
2.0	4th December 2023	N/A No changes required	No changes . Only addition of review date.	2.0 No new version number required.
2.0	8th December 2025 by C.Kavanagh	N/A No changes required	No changes . Only addition of review date.	2.0 No new version required

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