Standard Operating Procedure **CBE/HTA-MI-SOP008**

Title: REPORTING ADVERSE EVENTS RELATING TO HTA LICENSABLE MATERIAL

Location: CBE Laboratories

1. PURPOSE

To describe the procedure for identifying, managing and reporting adverse events relating to the acquisition, storage, use and disposal of HTA licensable material for research.

2. SCOPE

As part of the CBE Quality Management System (QMS) for research, this procedure applies to all individuals involved research activities under the University's HTA licence, in accordance with the requirements of the HTA legislation, the HTA Codes of Practice and the University's HTA Licence Compliance Quality Manual. This procedure does not cover adverse events/incidents relating to the safety of individuals or related to non-relevant material, which should be reported according to local procedures or procedures stipulated by the University Safety Office, as applicable.

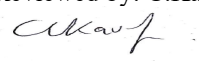
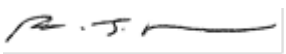
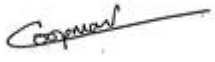
Complaints related to activities involving HTA licensable material and associated adverse events should be directed to the DI as specified in the Loughborough University HTA Quality Manual.

3. RESPONSIBILITES

3.1. The departmental Quality Manager (dQM) shall ensure that this SOP is aligned with the University procedure for reporting adverse events related to HTA licensable material and that it does not conflict with any other part of the CBE Quality Management System.

3.2. All individuals working with HTA licensable material have the responsibility to report any actual, or potential for, theft, damage or loss of the material, as it occurs or once it has occurred, or where it could be predicted to occur.

3.3. All staff and students have the responsibility to report any event they believe may compromise the University's compliance with the licensing obligations under the HTA, or the good governance and output of their research using HTA licensable material.

Written by: P.Hourd/C.Kavanagh Date: 26.01.2016 Reviewed by: C.Kavanagh  Date: 04/12/2023	Reviewed by: R.Thomas  Date: 13/12/2023	Approved by: M.Gleeson Date:28.01.2016 Approved by: K Coopman  Date:13/12/2023

3.4. The departmental Person Designate (dPD) and the dQM are responsible for ensuring that all corrective and preventative actions related to a reported adverse event are completed to an agreed timeframe and the results documented and fed-back to the custodian of the material (Principal Investigator or Person Responsible) and the Designated Individual (DI), as required.

4. REFERENCES

The Human Tissue Act (2004) and HTA guidance and Code of Practice E

The University HTA Licence Compliance Quality Manual

The CBE Quality Manual

5. PROCEDURE

5.1. Identifying an adverse event

For research purposes, adverse events relate to the acquisition, storage, use and disposal of HTA licensable material that lead to or had potential ('near miss' event) to lead to:

- Non-compliance with the HT Act and Codes of Practice and deviations from local policies, processes and procedures
- Harm or had the potential to harm staff, visitors, researchers or research participants.
- Loss or damage to HTA licensable material
- Breach of security to premises and contents
- Contravention or had the potential to contravene subject consent or confidentiality
- Any other event that gave rise to an internal inquiry/investigation

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A number of adverse events are listed below as a guide to what might require a report but this is not an exhaustive list:

Consent
• Relevant material collected, stored or used without appropriate consent • Relevant material collected, stored or used without appropriate ethical approval • Staff member seeking consent without appropriate training
Governance and quality
• Conduct of non-licensed activities • Incorrect version of policy, process or SOP in use - failure of change control mechanisms • Not registering new SOPs or updating existing SOPs to reflect changes in scope or practice • Loss of documentation • Breach of data protection/confidentiality (e.g. sample bearing patient identifiers) • Relevant material transferred without appropriate authorisation eg material transfer agreement
Acquisition of Relevant Material
• Relevant material received without appropriate authorisation • Incorrect material samples received • Unlabelled or unidentifiable material samples received • Material n inappropriate or unusable condition • Material packaging damaged in transit and material compromised
Material Tracking
• Labelling error leading to incorrect use of relevant material • Discrepancy between database record and storage location of relevant material eg no record of stored relevant material, relevant material logged on database but not in the correct location • Incomplete audit trail resulting in failure to trace relevant material • Database failure
Premises, equipment and facilities
• Cold chain storage breakdown with alarm failure and/or alarm failure detected in time – near miss • Cold chain storage breakdown with alarm failure and/or alarm failure not detected in time – material loss • Any other event which compromises relevant material integrity • Unauthorised access to storage facilities/breach of security
Transfer & Transportation
• Relevant material transferred out of CBE without appropriate authorisation • Loss of relevant material during transportation • Compromised relevant material integrity during transportation
Disposal

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- Relevant material disposed of without appropriate authorisation
- Failure to dispose of relevant material appropriately
- Incorrect labelling of relevant material waste
- Record of disposal of material not updated on the sample register

5.2. Initial reporting and investigation of an adverse event

5.2.1. At the earliest opportunity, and within 48 hours of the event occurring or found to have occurred, the event must be reported to the dPD and/or dQM who will inform the relevant PI or Person Responsible.

5.2.2. On the advice of the dPD/dQM, a local investigation must be conducted to establish root cause and identify Corrective and Preventative Actions (CAPA) using the local CAPA procedure.

5.2.3. Immediate remedial/corrective actions should be implemented as soon as possible, ideally within the same working day that the adverse event was reported.

5.2.4. On the advice of the dPD/dQM, the impact of the adverse event should be assessed based on severity of harm to HTA licensable material (e.g. loss or damage to material) and/or departure from the local and/or national requirements using the matrix in Table 2.

5.3. Reporting an adverse event

5.3.1. On completion of the investigation, a report must be compiled using the 'Adverse Event Report' template form.

5.3.2. To ensure that reports are controlled and a register is maintained, each report should be given a unique and sequential number.

5.3.3. The report should include a list of the corrective actions that have been or will be conducted. Preventative actions must also be identified.

5.3.4. The report should include a risk rating (RPN number) that considers the severity of the adverse event, the probability of re-occurrence and the likelihood of detecting the event should it occur again. Using the matrix in Table 2 calculate the RPN (S x P x D) for the failure mode before and after implementation of the CAPAs.

5.3.5. Once completed, the dPD, based on the impact assessment, shall decide whether to submit the report to the DI. If required, the report must be submitted to the DI within 7 working days of the event occurring or being known to the dPD.

5.3.6. Where major or critical adverse events relate to the integrity of the HTA licensable material obtained from an external collaborator or customer they should be notified within 14 calendar days of the event occurring or non-conformance being identified – unless alternative arrangements have been made with the customer.

5.4. Corrective and Preventative Action (CAPA)

5.4.1. Corrective and preventative actions (CAPA) based on the investigation should be identified. These measures must be documented and implemented to an agreed timeframe according to local CAPA procedures.

Note: Where agreed actions cannot be completed, this should be discussed with the dQM and a suitable course of action agreed.

5.4.2. If applicable (see section 5.3), a copy of the completed CAPA report should be submitted to the DI by the dQM within 90 days of the adverse event first being reported, unless otherwise negotiated with the DI or external collaborators / customers.

5.4.3. Once all CAPAs have been completed and no further action is required, the adverse event should be marked as closed on the adverse event register. All relevant parties should be informed by e-mail.

5.4.4. The FMEA risk assessment for CBE HTA processes and practices should be reviewed by the dQM to identify further potential failure modes or where the risk rating for previously identified failures modes may have changed. The risk assessment should be updated accordingly.

Table 2. Matrix for grading Adverse Events and other HTA related incidents

Severity Level (S)	**1**	**4**	**9**	**16**	**25**
Failure effect/impact	**Low**	**Minor**	**Moderate**	**Major**	**Critical**
Breach of ethical standards	Minor infringement of normal practice or near miss	Single failure to adhere to internal standards, policy & procedures	Single failure to adhere to HTA Codes of Practice and Regulations	Multiple failures to comply with internal standards, policy & procedures	Multiple failures to comply with HTA Codes of Practice and Regulations
Loss or damage to Licensable Material and/or data. Breach of data protection/confidentiality	Temporary loss of data - recoverable No loss or damage to material	Minimal/minor loss of data Minimal/minor loss or damage to material	Single failure to ensure material/ data security & integrity Significant loss or damage to material	Multiple failures to ensure material / data security & integrity Multiple data losses. Material destroyed but replaceable	Total loss of material / data. Confidentiality jeopardised Material destroyed and irreplaceable

Probability of Re-occurrence	**1**	**3**	**5**	**7**	**9**

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(P)	Unlikely	Remote	Occasional	Moderate	High
Probability of the adverse event occurring again without CAPA to address the failure mode	Failure never been seen but theoretically possible	Failure potential noted on one occasion	Failure potential recorded as near miss on one occasion	Failure potential/ near miss has been noted on more than one occasion	Failure has been potential has been noted on one or more occasions

Likelihood of Detection	1	3	5	7	9
(D)	High degree	Good	Likely	Fair	Low or none
Likelihood that if the adverse event were to occur again that it would be detected	Excursion is obvious & always detected prior to impact	Excursion usually detected & corrected prior to having any impact	Excursion can be detected but not until after it has had an impact	Difficult to detect an excursion and not until after it has had an impact	Little or no ability to detect excursion. Not tracked or alarmed

Risk Priority Number (RPN)	1-400	401-720	>720
Risk	Low risk	Medium risk	High risk
Action	No further action required	Additional control measures may be required to improve risk control	Additional and/or alternative risk control measures required

6. DOCUMENTATION

The following records are outputs of this SOP:

6.1. HTA-MI-FORM/008 Adverse Event Report Form

6.2. Entry in the Adverse Event Register

These records shall be stored on the CBE network and/or stored in the CBE Office or otherwise archived for future review or retrieval. The signed original Adverse Event Report will be retained for up to 3 years.

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SOP 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	No Amendments required Minor Editorials only including revision details	1.0 New version not required
1.0	2nd December 2019 by C.Kavanagh	N/A No changes	No Amendments required Minor Editorials only including revision details	1.0 New version not required
1.0	6th December 2021 by C.Kavanagh	N/A No changes	No Amendments required Minor Editorials only including revision details	1.0 New version not required
1.0	4th December 2023 by C.Kavanagh	N/A No changes	No Amendments required . New revision date only.	1.0 New version not required

SOP Withdrawal Date:	

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Document Control

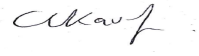
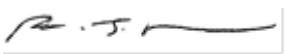
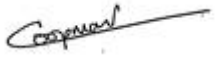
The Master Copy of all SOPs is filed by the dQM. The latest version is maintained on the CBE network. This document is not a controlled copy once printed from the network. If this SOP appears inadequate or outdated it is the responsibility of all staff to bring this to the attention of the dQM or their Supervisor immediately.

Security Statement

This SOP is the intellectual property of the CBE within Loughborough University, and as such, must not be circulated outside of the University without the written approval from the dQM and the author.

Acknowledgements

This SOP has been produced with advice and input from colleagues and with reference to Loughborough University School of Sport, Exercise and Health Sciences (SSEHS) SOPs and publically available SOPs used at a number of other UK universities. We also acknowledge the contributions of Andreea Iftimia-Mander to the original draft versions of this SOP.

Written by: P.Hourd/C.Kavanagh Date: 26.01.2016 Reviewed by: C.Kavanagh  Date: 04/12/2023	Reviewed by: R.Thomas  Date: 13/12/2023	Approved by: M.Gleeson Date:28.01.2016 Approved by: K Coopman  Date:13/12/2023