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THE UNIVERSITY OF BRITISH COLUMBIA

SOP 901

TITLE	**901: Quality Assurance Inspections**
SCOPE	All research submitted to the University of British Columbia's Research Ethics Boards
RESPONSIBILITIES	The Vice-President, Research & Innovation, delegated to the Director, Office of Research Ethics, all Research Ethics Board (REB) Chairs and members and all REB Office Personnel
APPROVAL AUTHORITY	The Vice-President, Research & Innovation
EFFECTIVE DATE	May 2018
Supersedes documents dated	August 2013; May 2011; April 2009; July 2003

1.0 PURPOSE

The purpose of this standard operating procedure (SOP) is to:

- Describe the processes for monitoring, evaluating and improving the effectiveness of the human research enterprise;
- Define the policy regarding the compliance auditing of research studies under the oversight of the Research Ethics Boards (REBs) operating under the direct authority of the University of British Columbia (UBC);
- Define and promote Researcher, Institution, and REB compliance with national and international policies, regulations, and guidance, plus UBC Policy and Standard Operating Procedures (SOPs), in the conduct of research;
- Assure that research study participants' rights, safety, and welfare are protected;
- Ensure research study data integrity and control of bias;
- Foster a culture of responsible research conduct and review.

2.0 DEFINITIONS

See the Glossary of Terms.

3.0 PROCEDURE

The University of British Columbia is responsible for conducting ongoing oversight/continuing review of approved protocols of human participants research based on applicable regulations and policy[1]. The designated REB Office Personnel, within the Office of Research Ethics at UBC, conducts the resultant compliance oversight activities including routine and directed/for-cause inspections of REB approved protocols.

The process of Quality Assurance Inspections is meant to accomplish several important purposes. First, it is intended to assure that human participants are properly protected, and that the procedures used to accomplish this goal are carefully documented. Second, the process is intended to assist Researchers in complying with the current regulatory standards for protecting human participants and in avoiding any external sanctions that may result from non-compliance with the standard of practice. Finally, this process is intended to assure that the University of British Columbia and its affiliated institutions remain in good standing with federal agencies having oversight of human participant's research activities.

Quality Management programs, Quality Assurance (QA), and Quality Control (QC) activities, such as inspections of the REB and of Researchers, allow for a continuous evaluation and subsequent assurance of the human research protection enterprise. Findings are measured against established policies and procedures and all of the applicable ethical, legal, and regulatory requirements[2]. When areas for improvement are identified, corrective action is taken including training, education, and the revision of SOPs.

3.1 REB Quality Assurance Inspections (Internal)

3.1.1 The designated Office of Research Ethics (ORE) Office Personnel will initiate ad hoc inspections in response to complaints or other concerns;

3.1.2 QA inspections may include the REB and the REB office;

3.1.3 When the designated ORE Office Personnel conducts a QA inspection of the REB and the REB office the inspection may include the following:

- An assessment of the SOPs and compliance with applicable regulations and guidance,
- A review of research files, REB membership rosters, REB attendance records, and REB agendas and minutes,
- A review of workload, performance metrics and annual reports,
- A review of stakeholder satisfaction surveys,
- An assessment of quality control procedures for compliance with the SOPs,
- A review of checklists, forms, and templates,

- Interviews with REB members, REB Office Personnel, Researchers, sponsors, and regulators,
- A review of training/education records,
- A review of all continuous improvement activities,
- An assessment of whether any new requirements (ethical, legal, or regulatory) were incorporated into the policies and procedures,
- A review of the status of any corrective action items from previous reviews,
- A review of any deviations from ethical, legal, or regulatory requirements, or deviations from the organization's policies, and whether the deviations require remediation,
- An assessment of compliance with all applicable requirements;

3.1.4 The designated ORE Office Personnel compares the findings against established policies, SOPs and applicable ethical, legal, and regulatory requirements[3];

3.1.5 The designated ORE Office Personnel prepares a written summary of the inspection, including areas requiring improvement;

3.1.6 The designated ORE Office Personnel reports the findings to the REB Chair or designee, and to the REB and/or to the appropriate Organizational Official as required;

3.1.7 The designated ORE Office Personnel works with the REB Chair or designee to implement improvements (e.g. new or revised SOPs or forms, training, education, additional resources or modifications to existing resources).

3.2 Researcher Quality Assurance Inspections

3.2.1 The designated ORE Office Personnel and/or the designated Health Authority Personnel will develop a schedule for routine QA inspections and implement inspections in response to Researcher requests.

A study may be randomly selected for inspection from amongst those that have been reviewed and approved by one of the UBC-affiliated REBs. The Researcher voluntarily allows for the audit of the documents, data, systems, and procedures associated with the study to assure compliance with relevant policies, regulations, and guidelines;

3.2.2 The designated ORE Office Personnel will work with the REB and the organization at which the research is being conducted to determine if and when a for-cause inspection of a Researcher is warranted[4];

3.2.3 The REB Chair or designate and/or the Director, Office of Research Ethics may direct the designated ORE Office Personnel to conduct for-cause inspections. These audits are often initiated when there are concerns about whether or not the rights and welfare of

study participants enrolled, or to be enrolled, in a particular research protocol are being adequately protected. Other triggers include:

- A response to an externally initiated complaint of potential protocol violations or regulatory non-compliance, or
- A response to an internally initiated complaint or concern, or
- A Researcher with a history or poor adherence to UBC policies and procedures.

Any of the UBC-affiliated REBs may request a directed inspection in order to:

- Respond to any unanticipated problems and/or complaints involving increased risks to participants or others,
- Investigate whether or not serious or continuing non-compliance with national and/or international policies, regulations, and guidelines is occurring,
- Determine if suspension or termination of a protocol is needed, and
- To identify what essential remedial actions are required by the Principal Investigator (PI) to remedy any identified problems;

3.2.4 The designated ORE Office Personnel or designee may request copies of the sponsor's monitoring reports for a designated research project or that a questionnaire from the REB is completed[5];

3.2.5 The criteria for selecting Researchers or research projects for inspection may include[6]:

- Random selection,
- Sufficient cause as determined by the REB,
- The results of a previous external audit or inspection,
- The results of a sponsor audit,
- Researcher-initiated studies (i.e., where the Researcher is also the sponsor),
- Studies that involve a potentially high risk to participants,
- Studies that involve vulnerable populations,
- Studies in which Researchers are enrolling large numbers of participants,
- Suspected non-compliance,
- Unanticipated problems involving risks to participants or others,
- Suspected or reported protocol deviations,
- Research terminated by the REB due to failure by the investigator to submit the study for continuing review or failure to respond to a request for information from the REB;
- Verification of continuing review reports/applications for renewal;
- Studies reporting a large number of serious adverse events/unanticipated problems and/or protocol deviations,
- Participant complaints,
- Research Staff complaints,
- Any other situation that the REB deems appropriate;

3.2.6 The designated ORE Office Personnel or designee will notify the Researcher of the inspection via email and a mutually acceptable time will be scheduled. It may be necessary to schedule an inspection without first obtaining the formal consent of a Researcher (e.g., participant safety or suspected non-compliance);

3.2.7 The designated ORE Office Personnel or designee will conduct the inspection using designated/ appropriate evaluation tools;

3.2.8 When the designated ORE Office Personnel conducts an inspection of the Researcher, the inspection may include some or all of the following (as applicable):

- An assessment of the SOPs and compliance with applicable regulations and guidance,
- A review of all regulatory binders including the REB approval documentation, REB approved consent documents, signed consent documents, correspondence between the Researcher and sponsor, etc.,
- Interviews with the research staff and/or the Researcher,
- A review of test article accountability,
- A review of specimens and associated collection processes,
- A review of computer hardware and/or software associated with the research,
- A review of the consent form(s) and associated processes including eligibility requirements,
- A review of the completed case report forms (CRFs) or other data collection mechanisms,
- A review of appropriate source material (participant medical records), and
- A review of other documentation, as relevant and available;

The Researcher will be requested to provide a list of all study participants to the designated ORE Office Personnel:

- The number participant records to be reviewed will be determined at the discretion of the designated ORE Office Personnel;
- In the case of a directed audit, the REB Chair, the Director, Office of Research Ethics, and/or designated ORE Office Personnel may request a 100% audit of study participants' records;

3.2.9 A pre-audit interview is conducted with the investigator and/or other key study personnel. At the outset of the interview the investigator will be asked to describe the study and discuss such things as the recruitment and consent process. The interview also serves to document the delegation of responsibility for the following activities:

- Regulatory files/essential documents,
- REB submissions,
- Obtaining Informed Consent,
- Recruiting Study Participants,
- Reporting adverse events/protocol deviations,

- Maintaining study documents/CRFs,
- Test article accountability, and
- Analyzing study data;

3.2.10 The document review includes a thorough review of the research participant record, the source documents, all regulatory binders, and consent forms. This portion of the audit is conducted to get the most information in the most efficient way. The order of contents may vary from audit to audit and other documents may be examined as needed. The PI or designee does not need to be present during this part of the audit; however, he/she should be available to answer questions;

3.2.11 The REB Chair, the Director, Office of Research Ethics, or the designated ORE Office Personnel may choose to have a qualified impartial observer to monitor the consent process or to interview research participants;

3.2.12 At the conclusion of the evaluation, the designated ORE Office Personnel or designee will discuss the findings with the Researcher;

3.2.13 The designated ORE Office Personnel or designee will draft a report or provide a summary of the inspection including: positive findings, areas for improvement and recommendations for corrective action, and submit the report to the REB Chair or designee for review;

3.2.14 The Researcher will be given an opportunity to respond to the report with responses and/or corrective action plans within a time specified by the REB;

3.2.15 The designated ORE Office Personnel or designee will send a copy of the final report to the Researcher and the REB Chair. When applicable, the REB Chair or designee will provide the findings to the Director, Office of Research Ethics[7].

3.3 Corrective Action

3.3.1 The designated ORE Office Personnel may recommend corrective action based on the findings;

3.3.2 Corrective action may include a recommendation for the provision of additional resources, training, or education, the development of, or revisions to the SOPs, and changes to forms, checklists or templates;

3.3.3 The designated ORE Office Personnel will evaluate the effectiveness of the implemented improvements and adjust processes accordingly;

3.3.4 The designated ORE Office Personnel will follow-up with the Researcher in a timely manner to determine if the corrective actions have been implemented by the Researcher following a Researcher audit or inspection;

3.3.5 Upon completion of the inspection, the collected data will be analyzed and a written report generated. The report will specifically address all findings, itemizing and describing all of the observations of non-compliance (if any) made during the conduct of the inspection, along with the corresponding regulatory references and required remedial actions, if necessary. For directed audits, the report will include an assessment of whether the preponderance of evidence shows that any of the allegations of non-compliance are findings of non-compliance. If the audit results in findings of non-compliance, the designated ORE Office Personnel will recommend an appropriate course of action to the applicable REB Chair and, if appropriate, the Director, Office of Research Ethics;

3.3.6 If the non-compliance is determined to be serious and/or continuing, and it is in relation to a study that is funded or supported by the U.S. Federal government or regulated by the U.S. Food and Drug Administration, the REB Chair or the Director, Office of Research Ethics, will notify the applicable regulatory authorities[8].

3.4 Documentation

3.4.1 The designated REB Office Personnel or designee files all reports and correspondence concerning QA inspections in the appropriate QA Files.

4.0 REFERENCES

1. *UBC Policy 89*:
http://universitycounsel.ubc.ca/files/2012/06/policy89.pdf
Health Canada Guidance for Industry, Good Clinical Practice: Consolidated Guideline, ICH Topic E6, 1997:
https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/efficacy/guidance-document-good-clinical-practice-integrated-addendum-e6-r1-topic-e6-r2.html
The Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS2 2014):
http://www.pre.ethics.gc.ca/eng/policy-politique/initiatives/tcps2-eptc2/Default/
Government of Canada, Canadian General Standards Board. CAN/CGSB -191.1-2013 Research ethics oversight of biomedical clinical trials (2013):
http://publications.gc.ca/collections/collection_2017/ongc-cgsb/P29-191-001-2013-eng.pdf
U.S. Department of Health and Human Services – Title 45 Code of Federal Regulations Part 46 (45 CFR 46):
http://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html
U.S. Department of Health and Human Services – Title 21 Code of Federal Regulations Part 56 (21 CFR 56):
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=56

2. *U.S. Department of Health and Human Services – Title 45 Code of Federal Regulations Part 46 (45 CFR 46.103):*
https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html#46.103

3. *The Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS2 2014),* Article 6.17*:*
http://www.pre.ethics.gc.ca/eng/policy-politique/initiatives/tcps2-eptc2/chapter6-chapitre6/#ch6_en_a6.16
U.S. Department of Health and Human Services – Title 45 Code of Federal Regulations Part 46 (45 CFR 46.115):
https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html#46.115
U.S. Department of Health and Human Services – Title 21 Code of Federal Regulations Part 56 (21 CFR 56.115):
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=56.115

4. *U.S. Department of Health and Human Services – Title 45 Code of Federal Regulations Part 46 (45 CFR 46.112):*
https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html#46.112

5. *Health Canada Guidance for Industry, Good Clinical Practice: Consolidated Guideline*, ICH Topic E6, 1997, Section 5.19:
https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/applications-submissions/guidance-documents/efficacy/guidance-document-good-clinical-practice-integrated-addendum-e6-r1-topic-e6-r2.html#a5.19

6. *U.S. Department of Health and Human Services – Title 45 Code of Federal Regulations Part 46 (45 CFR 46.108):*
https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html#46.108

7. *Government of Canada, Canadian General Standards Board.* CAN/CGSB -191.1-2013 Research ethics oversight of biomedical clinical trials (2013), Section 4.2.3.4:
http://publications.gc.ca/collections/collection_2017/ongc-cgsb/P29-191-001-2013-eng.pdf

8. *U.S. Department of Health and Human Services – Title 45 Code of Federal Regulations Part 46 (45 CFR 46.103(b)(5)):*
https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html#46.103
U.S. Department of Health and Human Services – Title 21 Code of Federal Regulations Part 56 (21 CFR 56.108):
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=56.108