WOMEN'S COLLEGE RESEARCH INSTITUTE
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Research Ethics Board Standard Operating Procedures

Internal Unanticipated Events Including Adverse Events Reporting

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CATEGORY	Research Ethics Board	**Reviewed/Effective Date:**	February 13, 2017
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ISSUED BY:	Research Ethics Office		
APPROVED BY	Vice President, Research		

The WCH REO webpage version of this document is considered the most current.

Please ensure that you have reviewed all linked documents and other reference material within this SOP

1.0 POLICY STATEMENT:

The Women's College Hospital (WCH) Research Ethics Board (REB) has adopted the Canadian Association of Research Ethics Boards' *Guidance on Reporting of Unanticipated Problems including Adverse Events to Research Ethics Boards in Canada* guidance document issued in July 2010.

Together with the new Unanticipated Problem Reporting Form, the purpose of this Standard Operating Procedure (SOP) is to describe the procedures for reporting unanticipated events including adverse events to the WCH REB.

Unanticipated/Adverse Event reporting is the responsibility of the WCH Principal Investigator (PI), who must complete the **WCH REB Unanticipated/Adverse Event Reporting Form**, including information on the seriousness of the Event, assessing whether or not it is a direct consequence of the research intervention, and recommendations for any further action. The PI is also responsible for reporting this information to other appropriate regulatory or advisory bodies including, but not limited to, the Data and Safety Monitoring Board (DSMB), safety monitoring committees, and external advisory boards.

The WCH REB is always available for consultation regarding non-reportable events.

2.0 DEFINITION(S):

See Glossary of Terms

3.0 RESPONSIBILITY:

This SOP applies to the Investigator, the REB Chair, Vice-Chair, REB members and Research Ethics Office (REO) staff.

4.0 PROCEDURES:

4.1. Criteria for Reporting

4.1.1. Local (Internal) Adverse Events

The PI is required to report to the WCH REB local events that are deemed to be unanticipated problems (unexpected, related, and involving greater risk). Upon becoming aware of a local AE, the PI should assess whether the AE represents an unanticipated problem. If the PI determines that the AE represents an unanticipated problem, the investigator must report it to the WCH

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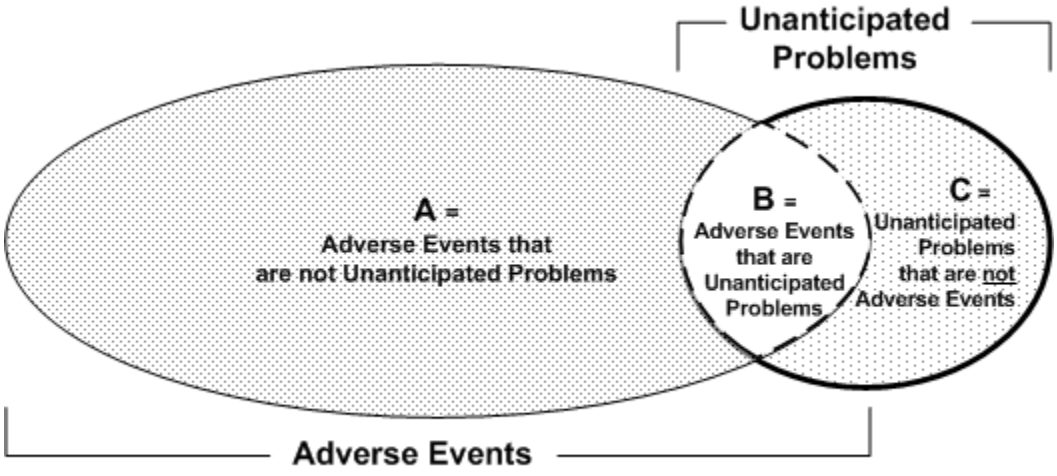
REB. If the PI determines that an AE is not an unanticipated problem, but the Sponsor subsequently determines that it is, the Sponsor should report this determination to the PI, and such reports must then be submitted to the WCH REB. The PI must clearly explain how the AE represents an "unanticipated problem". A description of any proposed protocol changes or other corrective actions to be taken by the PI or Sponsor in response to the AE must also be described in the report.

If an investigator is unsure whether or not an AE constitutes an unanticipated problem, they should consult with the REB.

The following local AEs ordinarily should not be reported to the WCH REB:

- SAEs that are considered to be expected;
- SAEs that are considered not related (i.e. the causal relationship can be ruled out) to the investigational product or research procedures, whether the event is expected or not;
- non-serious AEs, whether expected or not.

In summary, only AEs that are unanticipated problems should be reported to the WCH REB, as illustrated in the OHRP diagram below[1], and with the required accompanying documentation:



Under 45 CFR part 46: Do not report A, Do report (B+C)

[1] Office for Human Research Protections (OHRP) and Department of Health and Human Services (HHS) – *Guidance on Reviewing and Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events.*

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4.2 Other Unanticipated Problems

There may be other incidents, experiences, or outcomes not considered AEs, but that meet the definition of unanticipated problems; such events, in the opinion of the PI or Sponsor, place research participants or others at a greater risk of physical or psychological harm than was previously anticipated, or have implications for the conduct of the study or the integrity of research data.

Upon becoming aware of any other incident, experience, or outcome that may represent an unanticipated problem, the PI should assess whether it constitutes an unanticipated problem. If the PI determines that it is an unanticipated problem, the PI must report the problem to the WCH REB. In general, only those incidents, experiences, or outcomes that require a change to the study procedures, study documents, and/or require notifying the research participants of a change in the risk/benefit ratio should be reported to the WCH REB. This may include, but are not limited to:

- for an “expected” serious adverse reaction, an increase in the rate of occurrence which is judged to be clinically important;
- a significant hazard to the research participant population, such as lack of efficacy with an investigational product used in treating life threatening disease;
- a major safety finding from a newly completed animal study that suggests a significant risk for human participants (such as carcinogenicity);
- breaches of privacy and/or confidentiality;
- acts of nature that impact the study conduct or data integrity (e.g. floods, hurricanes, earthquakes, pandemics, etc.);
- unanticipated events and problems;
- published reports in the medical literature or news media;
- a complaint received from a participant;
- complaints received from any source concerning any aspect of the conduct of the trial;
- a report from the Sponsor which has not been covered in the above categories (e.g. an amendment to the Investigator’s brochure);
- mandated HC or FDA changes in drug labeling or marketing restrictions.

4.3 Reporting Unanticipated Problems to the REB

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4.3.1 Reportable internal AEs (i.e. those that represent unanticipated problems) should be reported to the WCH REB using the Unanticipated/Adverse Event Reporting Form in the following timeframe:

- where it is neither fatal nor life-threatening, within 15 calendar days from the date of the first person on the research team becoming aware of the information;
- where it is fatal or life-threatening, immediately where possible and, in any event, within 7 calendar days from the date of the first person on the research team becoming aware of the information;
- if any new information becomes available after submitting the WCH REB report, it is the responsibility of the PI to ensure subsequent reports are submitted to the WCH REB as they occur, referencing the initial report.

4.3.2 The Unanticipated/Adverse Event Reporting Form must include an original signature of the PI.

4.3.3 If the study action recommended (as indicated on the form) requires any changes to the study, the PI must submit relevant documents including new version dates, a clean version, and a tracked change version of the document(s).

4.3.4 The WCH REB procedure for reporting internal SAEs supersedes any other time frame specified in a research protocol.

4.3.5 The WCH REB has no regulatory obligation to acknowledge receipt of internal SAEs, however, the WCH REB will make every effort to ensure that SAEs are acknowledged. It is the responsibility of the sender to retain proof of submission.

4.3.6 PIs shall continue to report unanticipated problems to the WCH REB for the duration of the study (i.e. until the study is closed at the PI's institution).

4.3.7 Periodic safety update reports, individual reportable external AEs (i.e. those that represent unanticipated problems), and other unanticipated problems should be reported to the WCH REB within 15 calendar days of the Sponsor (i.e. the Health Canada Clinical Trial Application holder) becoming aware of or receiving the event/report.

4.4 Reporting Unanticipated Problems Beyond the REB

4.4.1 Reporting Unanticipated Problems to Institutional Officials

It is the responsibility of the PI to promptly report any local AEs or unanticipated problems to the appropriate individuals within the Institution using the critical incident management procedures outlined in the WCH Critical Incidents Management and Disclosure of Unanticipated Outcomes or Critical Incidents Policies.

4.4.2 Reporting Unanticipated Problems to Health Canada

Only adverse drug reactions that are both **serious** and **unexpected** are subject to expedited reporting to Health Canada. **Expedited reporting of reactions which are serious but expected is not required**. Expedited reporting is also inappropriate for serious events from clinical investigations that are considered unrelated to the study product, whether or not the event is expected.

4.4.3 During a clinical trial the Sponsor is required to inform Health Canada of any serious, unexpected adverse drug reaction that has occurred inside or outside Canada:

1. where it is neither fatal nor life-threatening, within 15 days after becoming aware of the information;
2. where it is fatal or life-threatening, immediately where possible and, in any event, within 7 days after becoming aware of the information; and
3. within 8 days after having notified Health Canada of the ADR, submit as complete a report as possible, and include an assessment of the importance and implications of any findings.

4.4.4 Each ADR which is subject to expedited reporting should be reported individually in accordance with the data element(s) specified in the Health Canada/ICH Guidance Document E2A: Clinical Safety Data Management; Definitions and Standards for Expedited Reporting.

4.5 REB Review of Unanticipated Event Reports

4.5.1 Once the REO staff, Manager, or other WCH REB member receives an initial Unanticipated/Adverse report, it is their responsibility to record it immediately (if informed verbally) and pass along this preliminary information to the WCH REB Chair or delegate for review.

4.5.2 The WCH REB Chair or delegate has the authority to request, where appropriate or necessary, more information or take immediate action (e.g. suspend enrolment).

4.5.3 All updates to all Unanticipated Event Reports will be reviewed promptly by the WCH REB Chair or delegate, who will advise the WCH REB and or Investigator/Research Staff on any necessary follow-up actions.

4.5.4 The WCH REB Chair or delegate may seek, where appropriate or necessary, further information from the PI and/or expert advice from any appropriate source.

4.5.5 All internal unanticipated problems should be reported back to the WCH REB at the next full board meeting.

4.5.6 The WCH REB Chair or delegate has the authority to suspend WCH REB approval as a result of an Unanticipated Event report, however, termination of WCH REB approval can only be determined by the full board.

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4.5.7 When reviewing a report of an unanticipated problem, the WCH REB should assess the appropriateness of any proposed corrective or preventative measures by the sponsor and/or PI, consider any additional appropriate measures that may or may not have been identified or proposed by the sponsor and/or PI, and consider whether the affected research still satisfies the requirements for WCH REB approval.

4.5.8 The WCH REB should consider whether risks to the research participants are still minimized and reasonable in relation to the anticipated benefits, if any, to the research participants and the importance of the knowledge that may reasonably be expected to result.

4.5.9 The WCH REB should consider whether some or all of the research participants should be notified of the unanticipated problem (i.e. if it may affect the participant's willingness to continue participation in the research).

4.5.10 The WCH REB should also consider whether suspension or termination of the research site is warranted.

4.5.11 Upon the receipt of satisfactory responses to all of the WCH REB's questions/concerns (if any), the WCH REB Chair or delegate shall sign and date the Unanticipated Event Report Form.

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5.0 REFERENCES:

1. Health Canada, Guidance for Industry, Good Clinical Practice: Consolidated Guideline, ICH Topic E6, 1997
2. Health Canada, Guidance for Industry, Clinical Safety Data Management: Definitions and Standards for Expedited Reporting, ICH Topic E2A, 1995
3. Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans 2014 (TCPS2)
4. Canadian Association of Research Ethics Boards Guidance on Reporting of Unanticipated Problems Including Adverse Events to Research Ethics Boards in Canada, FINAL July 2012 (http://www.careb-accer.org/sites/default/files/uploads/en/Recently%20Filed%20Comments/CAREB%20Guidance%20-%20AE%20Reporting%20-%20July%202010.pdf)
5. WCH Critical Incident Management Policy (Policy Number 1.40.005)
6. WCH Disclosure of Critical Incidents and Unanticipated Outcomes Policy (1.40.006)