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| **Section 400:** | **REVIEW OF RESEARCH** | | |
| **Standard Operating Procedure (SOP):** | **410 REPORTING** | | |
| **This SOP pertains to:** | All Research submitted to the REBs | | |
| **Responsibility for executing this SOP:** | Director, Research Ethics, Research Ethics Staff, the Chairs of the U of S Research Ethics Boards and the Vice President Research | | |
| **Approval Authority** | The Vice-President Research | | |
| **Effective Date:** | July 1,2012 | **Superseded documents dated:** | |

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| 1. PURPOSE:<br>This SOP builds upon the policies described in SOPs 405, 408, and 409 and details the procedures for supplementary reporting of unanticipated problems, serious and continuing non-compliance, and suspension and termination of REB approval. | **REFERENCES**<br><br>SOPs 405,408, and 409 |
| 2. POLICY:<br>It is U of S policy to require that investigators report as soon as reasonably possible (within seven (7) calendar days) any unanticipated problems involving risk to participants or other to the relevant U of S REB. Once reported, the REB will make determinations about the reported problems and direct appropriate follow-up with the investigative team.<br><br>The REB then has the responsibility to promptly report the unanticipated problems or instances of serious or continuing non-compliance, with the resulting determinations (including suspension or termination of REB approval) to all appropriate study contacts (including the study sponsor/CRO and institutional officials, when appropriate), and the appropriate government agencies (OHRP, FDA) when applicable.<br><br>Unanticipated problems include anything that could significantly impact the conduct of the study or alter the REBs approval or favourable opinion to continue the study. | SOP 405<br><br>45 CFR 46.103(b)(5)<br>21 CFR 56.108(b) |
| 3. SPECIFIC PROCEDURES:<br>3.1 Definitions<br>Unanticipated Problems: Unanticipated problems are any incident, experience or outcome that meet all of the following criteria:<br>1) Unexpected (in terms of nature, severity or frequency) given the research procedures that are described in the protocol-related documents, and b) the characteristics of the population being studied;<br>2) Related or possibly related to participation in the research (possibly related means there is a reasonable possibility that the incident, experience or outcome may have been caused by the drugs, devices or procedures involved in the research); and<br>3) Suggests that the research places participants or others at a greater risk of harm (including physical, psychological, economic or social harm) | |

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| than was previously known or recognized, or that were not described in the original application.<br><br>Unanticipated problems include anything that could significantly impact the conduct of the study or alter the REBs approval or favourable opinion to continue the study. | |
| Unanticipated problems include, but are not limited to:<br>• Serious unexpected adverse events / drug reactions (including medical device serious adverse events) [See 3.5. below]<br>• A breach of confidentiality or privacy<br>• Problems with the investigator or study personnel<br>• Fire flood or other natural disaster<br>• Incidents of continuing and serious noncompliance with the ICH-GCPs, REBs requirements or applicable laws and regulations<br>• Termination or suspension of the study by a regulatory authority<br>• Any complaint by a participant that includes a report of an unanticipated risk or which cannot be resolved by the research staff<br>• Protocol deviations that in the opinion of the Investigator places one or more participants at increased risk, or affects the rights, safety or welfare of research participants.<br>• For an "expected" serious adverse drug reaction, an increase in the rate of occurrence which is judged to be clinically important<br>• A significant hazard to the research participant populations such as lack of efficacy with an investigational product used in treating life-threatening disease<br>• A major safety finding from a newly completed animal study that suggests a significant risk for human participants (such as carinogencity)<br>• Recommendations of the Data and Safety Monitoring Committee , where relevant for the safety of the research participants<br>• Protocol deviations / violations that impact data integrity or the safety of research participants.<br><br>Non-compliance:<br>• Failure on the part of the PI, any member of the study team, or any individual involved in research review or oversight to follow the terms of the REB approval, or<br>• Failure of the PI, any member of the study team, or any individual involved in research review or oversight to abide by applicable laws, regulations or policies, including failure to submit research for REB review and approval prior to commencing research Serious non-compliance:<br>• Serious non-compliance is non-compliance that adversely affects the rights and welfare of participants or places participants at increased risk of harm.<br><br>Continuing non-compliance: | OHRP Guidance on Reviewing and Reporting Unanticipated Problems January 2007<br>FDA Guidance for Clinical Investigators, Sponsors and IRBs Adverse Event Reporting January 2009<br>. |

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| • Continuing non-compliance is a pattern of non-compliance that indicates an unwillingness to comply or a lack of knowledge that may lead to an adverse effect on the rights and welfare of participants or may place participants at an increased risk of harm.<br><br>"As soon as reasonably possible" & "promptly":<br>• The term "as soon as reasonably possible" means that the timing of reporting will vary in accordance with the severity/seriousness of the information being reported, including the nature of the research associated with the problem. Unless, however, the event is a routine safety letter, DSMB report, summary report or changes to the Investigator's brochure that are minor and/or routine in nature, all new information and unanticipated problems must be reported by the investigator to the REB within seven (7) calendar days of the incident, occurrence, outcome event, or the Investigator's receipt of the notice of the event or the new information.<br>• The regulations at 45 CFR 46.103(a) and (b)(5) do not specify a time frame for reporting incidents, except "promptly." For a more serious incident, this may mean reporting to OHRP within days. For a less serious incident, a few weeks may be sufficient. It may be appropriate to send an initial report, and indicate that a follow-up or final report will follow by the earlier of:<br>o A specific date; or<br>o When an investigation has been completed or a corrective action plan has been implemented. | OHRP Guidance on Reporting Incidents to OHRP June 2011 |
| **3.2. Reporting Procedures**<br>The REB has the responsibility to report, as soon as reasonably possible, to the Director, Research Ethics concerns with regard to research studies in which any of the following have been identified:<br>• Unanticipated problems involving risk to participants or others<br>• Serious or continuing non-compliance<br>• Suspension or termination of approved research by the REB.<br><br>The Director, Research Ethics will be responsible for promptly notifying external agencies through the completion of incident reports, based on jurisdiction as follows:<br>• The Office of Human Research Protections (OHRP) if the research is conducted, funded, or overseen by the Department of Health and Human Services (DHHS)<br>• The US Food and Drug Administration (FDA) is the research is regulated by the FDA<br>• Health Canada<br>Other agencies that are signatories to the Common Rule, if the research is conducted, funded, or overseen by DHHS. | |

**3.2.1. Unanticipated problems involving risk to participants or others**

REB determinations of unanticipated problems involving risk to participants or others in accordance with SOP 405 will be reported to the following entities within 15 days of the REB's determination:

1. Principal Investigator;
2. Department Chair (or equivalent);
3. Dean or unit Director, if appropriate;
4. Vice President Research;
5. OHRP (incident report);
6. FDA, if applicable;

(When research is FDA regulated: The REB requires that the PI reports Unanticipated problems involving risk to participants or others to the sponsor (as applicable), who must report to the FDA. If the PI is also the sponsor, then REB requires that the sponsor-investigator report to the FDA. Regardless of whether such reporting has occurred as indicated by the PI for initial determination or resolution the REB will report to the FDA.)

7. Sponsor, if appropriate;
8. Other administrative personnel as appropriate

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The following information should be Included within the incident report:

- Name of the institution (e.g., university, hospital, health region, school, etc) conducting the research;
- Title of the research project and/or grant proposal in which the problem occurred;
- Name of the principal investigator on the protocol;
- Number of the research project assigned by the REB and the number of any applicable federal award(s) (grant, contract, or cooperative agreement);
- A detailed description of the problem; and
- Actions the institution is taking or plans to take to address the problem (e.g., revise the protocol, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled participants, increase monitoring of participants, etc.).

The Director, Research Ethics, in consultation with the REB Chair, approves the incident report which the Director, Research Ethics sends through the Office of the Vice-President Research to the appropriate federal agency(ies) and copied to the PI and the Chair of the applicable REB.

**3.2.2 Serious or continuing non-compliance**

REB determinations of serious or continuing non-compliance in accordance with SOP 408 will be reported to the following entities within 15 days of the REB's determination:

45CFR46.108(a)
45CFR46.103(b)(5)
21CFR56.108(b)

1. Principal Investigator;
2. Person(s) involved in the non-compliance;
3. Department Chair (or equivalent);
4. Dean or unit Director, if appropriate;

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| 5. Vice President Research;<br>6. OHRP (incident report);<br>7. FDA, if applicable;<br>8. Sponsor, if appropriate;<br>9. Other administrative personnel as appropriate<br>10. Person raising the allegation (if the identity of the person is known and the feedback deemed appropriate)<br><br>The following information should be Included within the incident report:<br>• Name of the institution (e.g., university, hospital, health region, school, etc) conducting the research;<br>• Title of the research project and/or grant proposal in which the noncompliance occurred;<br>• Name of the principal investigator on the protocol;<br>• Number of the research project assigned by the REB and the number of any applicable federal award(s) (grant, contract, or cooperative agreement);<br>• A detailed description of the noncompliance; and<br>• Actions the institution is taking or plans to take to address the noncompliance (e.g., educate the investigator, educate all research staff, suspend the protocol, suspend the investigator, conduct random audits of the investigator or all investigators, etc.).<br><br>The Director Research Ethics, in consultation with the REB Chair, approves the incident report which the Director Research Ethics sends through the office of the Vice-President Research to the appropriate federal agency(ies), and copied to the PI and the Chair of the applicable REB.<br><br>**3.2.3. Suspension or termination of approved research by the REB**<br>REB decisions to suspend or terminate research in accordance with SOP 409 will be reported to the following entities within 15 days of the REB's determination:<br>1. Principal Investigator;<br>2. Department Chair (or equivalent);<br>3. Dean or unit Director, if appropriate;<br>4. Vice President Research;<br>5. OHRP (incident report);<br>6. FDA, if applicable;<br>7. Sponsor, if appropriate;<br>8. Other administrative personnel as appropriate<br><br>The following information should be Included within the incident report:<br>• Name of the institution (e.g., university, hospital, health region, school, etc) conducting the research;<br>• Title of the research project and/or grant proposal that was suspended or terminated;<br>• Name of the principal investigator on the protocol;<br>• Number of the research project assigned by the REB that was | OHRP Guidance on Reporting Incidents to OHRP June 2011 |

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| suspended or terminated and the number of any applicable federal award(s) (grant, contract, or cooperative agreement);<br>• A detailed description of the reason for the suspension or termination; and<br>• The actions the institution is taking or plans to take to address the suspension or termination (e.g. investigate alleged noncompliance, educate the investigator, educate all research staff, require monitoring of the investigator or the research project, etc.)<br><br>The Director Research Ethics, in consultation with the REB Chair, approves the incident report which the Director Research Ethics sends through the office of the Vice-President Research to the appropriate federal agency(ies), and copied to the PI and the Chair of the applicable REB. | |