**Serious Adverse Events (SAEs)/****Serious Unexpected Adverse Drug Reaction (SUADR)
Guidance and Report Form**

In accordance with N2 *SOP012\_09: Serious Adverse Drug Reaction Reporting in Clinical Trials* investigators must report study-related serious and unexpected adverse drug reactions to the REB. Requirements for reporting external and local SAEs to the MGH REB are identified below. Investigators should also familiarize themselves with reporting requirements identified in the study protocol, sponsor Standard Operating Procedures, and by applicable regulatory authorities.

**DEFINITIONS**

**Adverse Drug Reaction (ADR):** In the pre-approval clinical experience with a new medicinal/natural health product or its new usages, particularly as the therapeutic doses may not be established: all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug/natural health product reactions. The phrase “responses to a medicinal product” means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility; i.e., the relationship cannot be ruled out.

Marketed medicinal/natural health products: a response to the drug/natural health product which is noxious and unintended, and which occurs at doses normally used in humans for prophylaxis, diagnosis, or therapy of diseases or for modification of physiological function.

**Adverse Event (AE):** Any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An adverse event (AE) can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

**Serious Adverse Event (SAE)** also referred to as **Serious Adverse Drug Reaction (SADR):** An adverse drug/natural health product reaction that at any dose:

* requires in-patient hospitalization or prolongation of existing hospitalization; or
* causes congenital malformation; or
* results in persistent or significant disability or incapacity; or
* is life threatening or results in death.

**Serious Unexpected Adverse Drug Reaction (SUADR)** also referred to as **Suspected Unexpected Serious Adverse Reaction (SUSAR):** A serious adverse drug/natural health product reaction that is not identified in nature, severity or frequency in the risk information set out in the investigator's brochure or on the label of the drug/natural health product.

**Unexpected Adverse Drug Reaction:** An adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g., Investigator Brochure for an unapproved investigational product or package insert/summary of product characteristics; Product Monograph for an approved product).

**EXTERNAL SAE/SUADR REPORTING**

MGH Qualified Investigators must inform the REB of all serious and unexpected adverse drug reactions (i.e., SUADRs) experienced by research participants enrolled by investigator(s) at other centres outside the jurisdiction of the MGH REB. I.e., the research participant experiencing the SUADR is enrolled at an external site in a multi-centre trial in which MGH is also a participating site. Sponsors/Sponsor-Investigators are required to distribute multi-centre expedited reports to investigators within 15 days of notification. MGH Investigators should submit blinded external SAE/SUDAR reports, periodic safety updates or safety summary reports in a timely manner to the MGH REB. External reports should be consolidated submitted to the MGH REB on a monthly basis according to REB meeting deadlines. External reports should include the following information:

* The description of the serious and unexpected event(s),
* All previous safety reports concerning similar adverse events,
* An analysis of the significance of the current adverse event(s) in light of the previous reports, and
* The proposed research changes, informed consent form changes or other corrective actions to be taken by the sponsor in response to the event(s)

External SAE/SUADR notifications are submitted to the REB for review which includes:

* The report from the sponsor
* A cover letter from the MGH investigator

These will be reviewed and acknowledged by the REB.

If the external SAEs result in a modification to the study protocol, Informed Consent Forms, and/or a notification to study participants these must be reported to the REB in the same fashion, along with the revised documents (see Appendix A).

**LOCAL MGH SAE/SUADR REPORTING**

The MGH REB must be informed of all local SAE/SUADRs as soon as possible, but no longer than 7 days if the SUADR is fatal or life threatening and 15 days if the SUADR is neither fatal nor life-threatening. Follow up reports and final reports related to the SAE/SUADR are submitted to regulatory authorities (i.e., Health Canada) and must also be submitted to the MGH REB in a timely fashion as a SAE/SUADR update. All reports submitted to the REB must have all participant identifiers removed (i.e., only participant research unique identification codes may remain).

In the case of SAEs occurring in clinical studies without an investigational product, the MGH Qualified Investigator should follow the MGH REB reporting timelines identified above.

**References:**

* N2 Investigator SOP012\_09 - Serious Adverse Drug Reaction Reporting in Clinical Trials (*available on iCare*)
* Canadian Association of Research Ethics Boards (CAREB). Reporting of Unanticipated Problems including Adverse Events to Research Ethics Boards in Canada. July, 2010.
* 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. January 15, 2007. <http://www.hhs.gov/ohrp/policy/advevntguid.html>
* U.S. Department of Health and Human Services. Guidance for Clinical Investigators, Sponsors, and IRBs Adverse Event Reporting. January, 2009.
* <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm079753.pdf>
* ICH Harmonised Tripartite Guideline. Clinical Safety Data management: Definitions and Standards for Expedited Reporting (E2A). 27 October 1994
* Personal Health Information Protection Act, 2004, S.O. 2004, c. 3, Sched. A
* Network REB Guidelines for Reporting SAEs/Unanticipated Problems, Unity Health Toronto (Network), Version Date: 12 March 2019
* Network REB SAE/UP Reporting Timelines, Unity Health Toronto (Network), Version Date: 07 Jun 2018
* N2 REB SOP404.003 - Ongoing REB Review Activities

**Submit Form below only – do not print the Guidance pages**

**Form Below**

**Serious Adverse Event (SAE)/Local Serious Unexpected Adverse Drug Reaction (SUADR) Report Form**

Please use this form to report **SAEs/SUADRs** experienced by research participants enrolled by MGH Investigators. A single form is to be used for each study participant.

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| --- |
| **SECTION 1 – Study Identification** |
| MGH REB Reference Number:  |
| Protocol Study Title:  |
|  |
| **SECTION 2 – Contact Information**  |
| **Local MGH** Principal Investigator:  |
| Department/Division/ Program:  |
| Telephone:  |
| Email Address:  |
|  |
| **SECTION 3 – Assessment of Local SAE/SUADRs** |
| Is this adverse event serious?  | [ ]  YES [ ]  NO |
| Is this adverse event unexpected? | [ ]  YES [ ]  NO |
| Is there a reasonable possibility that this adverse event may be related to the research intervention? (*A reasonable possibility means that a causal relationship cannot be ruled out.*) | [ ]  YES [ ]  NO |
| **If you answered “No” to any of the questions above, submission to the REB is not required.** |
|  |
| **SECTION 4 – Report Information** |
| Type of Report: | [ ]  Initial [ ]  Follow up [ ]  Final |
| **Copies of all SAE/SUADR reports to the Sponsor signed by the local investigator and/or CIOMS forms to Health Canada must accompany this form.** |
| Participant ID Number:  |
| SAE ID Number | Date of Adverse Event | Adverse Event |
|  |  |  |
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|  |
| 1. Does this SAE/SUADR require a change to the study protocol and/or consent form and/or require immediate notification to research participants for safety reasons?
 | [ ]  YES [ ]  NO If “YES” please see [Appendix A](#Appendix) |
| 1. Please provide relevant details of the SAE/SUADR.

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|  |
| **SECTION 5 – MGH Local Principal Investigator Attestation** |
| This signature attests that I as the **MGH Local Principal Investigator** or **Co-Investigator** have assessed the safety implications of the SAE/SUDAR, assessed the relationship of the SAE/SUDAR to the study intervention, and the impact on study procedures. Further, I will not implement any changes to, or deviations from the protocol without Research Ethics Board approval except to eliminate an immediate hazard to study participants or when changes involve only logistical or administrative aspects of the study. I attest to the accuracy of this report.I warrant that this study will continue to be conducted in accordance with the Tri-Council Policy Statement Ethical Conduct for Research Involving Humans (TCPS), the Ontario Personal Health Information Protection Act (PHIPA) 2004, and other relevant laws, regulations or guidelines, (e.g., Health Canada Part C, Division 5 of the Food and Drug Regulations, Part 4 of the Natural Health Products Regulations, Medical Devices Regulations, and ICH/GCP Consolidated Guideline E6). |
|  |  |  |  |  |
| Type Name |  | Signature |  | Date  |

**SUBMISSION INSTRUCTIONS**

**One (1)** electronic copy of all SAE reports and correspondence to the sponsor signed by the local investigator must accompany this form, including this signed and dated form. Submit by email to: ResearchEthicsBoard@tehn.ca.

**Appendix A:**

For study amendment changes please use the *Research Amendment Form* (available at <https://www.tehn.ca/education-research/research/research-ethics-board-reb/research-ethics-board-reb-forms>).