

## PROCESS FOR REPORTING SERIOUS ADVERSE EVENTS

Investigators must promptly report to the REB all adverse events that are both serious and unexpected and any new information regarding the safety of research subjects. Based on international guidance documents (ICH E2B (R3 - <http://www.ich.org/LOB/media/MEDIA632.pdf> ), the following always constitute SAEs: congenital anomalies, significant disability or incapacity, prolonged hospitalization, and any other life-threatening or medically-important events. Occasionally, changes to the study documentation are required as a result of these events. These revised documents must be submitted to the office for approval.

The reporting form provided on page 61 can be used for this purpose. The Chair and the Pharmacy representative to the board review the SAE reports regularly. These SAEs are also presented to the REB members for their review. A signed copy of the report will be returned to the Research Assistant or Primary CHEO Site Investigator. Please submit two copies of this submission form (with appropriate documentation), or you may submit reports directly from the sponsor.

The investigator must verify the dose and administration of all study medications associated with SAEs having occurred at CHEO (see Policy with respect to considering Medication Error in the Differential Diagnosis of Severe Adverse Events (SAE) Associated with Drugs Administered in a Clinical Trial, please see page 63. Also, listed on CHEONET, at [http://cheonet/data/1/rec\\_docs/3792\\_Medical%20Error%20Policy%20revised%20january%2020061.doc](http://cheonet/data/1/rec_docs/3792_Medical%20Error%20Policy%20revised%20january%2020061.doc)



**REPORTING FORM – SERIOUS ADVERSE EVENTS (SAEs)**

This form can be used if you wish, but it is not required. However, the REB does require the SAE reports/MEDWatch reports for review. Please submit an **original and one copy** of all SAE documentation for review.

REPORT INFORMATION				
REB Protocol Number	Protocol Title:			
SAE Report Number / Tracking Number	Date of this Report		Report Type <input type="checkbox"/> Initial <input type="checkbox"/> Follow Up # _____	
PATIENT INFORMATION				
Patient Initials or Other Unique Identifier	Country	Date of Birth (dd/mm/yyyy)	Age	<b>Check all appropriate to Adverse Reaction</b> <input type="checkbox"/> Patient Died <input type="checkbox"/> Involved or Prolonged Inpatient Hospitalization <input type="checkbox"/> Involved a Persistent or Significant Disability or Incapacity <input type="checkbox"/> Life Threatening <input type="checkbox"/> Congenital anomaly or birth defect <input type="checkbox"/> Other medically important condition
	CHEO Patient: <input type="checkbox"/> Yes <input type="checkbox"/> No		Sex	
INFORMATION REGARDING SAE				
Onset of Symptoms (dd/mm/yyyy):			Time interval between suspect drug administration (last dose) and start of reaction/event:	
<b>Action(s) taken with respect to Suspect drug:</b> <input type="checkbox"/> Drug withdrawn <input type="checkbox"/> Dose reduced <input type="checkbox"/> Dose increase <input type="checkbox"/> Dose unchanged <input type="checkbox"/> Unknown <input type="checkbox"/> Not applicable	<b>Did Reaction Abate After Stopping Drug?</b> <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not applicable	<b>Was drug re-introduced?</b> <input type="checkbox"/> Yes <input type="checkbox"/> No	<b>Did reaction reappear after reintroduction?</b> <input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> Not applicable	
Suspect Drug(s) (Include Active Substances)			<b>For placebo controlled trials, was there blinding as a result of the SAE?</b> <input type="checkbox"/> Yes <input type="checkbox"/> No	
Daily Dose(s)	Route of Administration		<b>Outcome of reaction/event at the time of the last observation:</b> <input type="checkbox"/> Recovered /resolved <input type="checkbox"/> Recovering resolving <input type="checkbox"/> Not recovered/not resolving <input type="checkbox"/> Fatal <input type="checkbox"/> Unknown	
Indication(s) for use (e.g., immunization, anti-cancer):			<b>Physician's Opinion as to causality of the SAE:</b> <input type="checkbox"/> Unrelated to the Study Drug <input type="checkbox"/> Possibly Related to the Study Drug <input type="checkbox"/> Related to the Study Drug	

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## REPORTING FORM – SERIOUS ADVERSE EVENTS (SAEs) – CONT'D

### NARRATIVE CASE SUMMARY AND FURTHER INFORMATION

*Describe the severe adverse event and the management thereof (Please attach any other related documentation). The narrative should normally include the following elements. The Board recognizes that not every data element will be available for every report.*

#### **REACTION INFORMATION**

- Relevant Tests/Laboratory Data *(Please provide a brief description of the results or attach a copy of the lab results)*
- The number of cases of the same toxicity observed among other patients enrolled in trials using this drug & the total number of patients having received this drug on clinical trials (that is, the relevant numerator and denominator relative to this SAE)

#### **CONCOMITANT DRUG(S)**

- Dates of Administration & duration of treatment with suspect drug
- Dates Concomitant therapies administered (including those used to treat event)
- Relevant past medical history (concurrent conditions, previous diagnoses)
- Other Relevant History (if appropriate, the narrative should specify tests of Renal and hepatic functioning)

#### **IN THE EVENT OF DEATH**

- Reported cause of death
- Was autopsy done
- Autopsy-determined cause of death

<b>Signature of Principal Investigator:</b>	<b>Date:</b>	<b>Signature of Research Assistant/Coordinator:</b>	<b>Date:</b>

For further information on reporting Serious Adverse Events please see the ICH Guidelines at <http://www.ich.org/LOB/media/MEDIA632.pdf>

**Please forward to:**  
**Ms. Natalie Morocz, Administrative Assistant**  
**Research Ethics Board**  
**Children's Hospital of Eastern Ontario**  
**Room 249, 401 Smyth Road, Ottawa, Ontario, K1H 8L1**  
**Telephone: (613) 737-7600, ext. 3350**

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# POLICY WITH RESPECT TO CONSIDERING MEDICATION ERROR IN THE DIFFERENTIAL DIAGNOSIS OF SEVERE ADVERSE EVENTS (SAE) ASSOCIATED WITH DRUGS ADMINISTERED IN A CLINICAL TRIAL

**Manual/Section:** Clinical Manual/Other

**Policy No.** OTH-2

**Key Words:** Severe Adverse Events, Clinical Trials, Medication Error, Research

- 1. PURPOSE:** 1.01 To ensure that medication error is considered in the differential diagnosis of local SAEs associated with the drugs administered in a clinical trial.
- 2. POLICY:** 2.01 In the event of a local SAE, the QI (Qualified Investigator; or his/her representative) must re-compute the drug dosing and administration using the research protocol as a source document. The study pharmacist must similarly retrace the steps involved in the drug preparation.
- 2.02 The local SAE report submitted to the CHEO REB must be signed and dated by the QI (or his/her delegate) and clearly indicate that the dosing and administration of drugs associated with a local SAE were verified.
- 2.03 The QI (or his/her delegate) must also notify other research staff (including the study pharmacist) of the occurrence of a local SAE.
- 2.04 Given the importance of timely SAE reporting, all health care providers must notify the QI (or his/her representative) of patient symptoms that, to the best of their knowledge, may be related to the drugs administered in the context of a clinical trial.
- 3. SCOPE:** 3.01 This policy applies to all clinical drug trials that are conducted by staff of CHEO or the CHEO Research Institute.
- 4. DEFINITIONS:** 4.01 **Serious Adverse Event:** A serious adverse event is an untoward medical occurrence that may include, but is not limited to:
- any medical occurrence that results in death
  - any life-threatening ailment
  - any congenital birth defects or congenital anomaly
  - any ailment that results in persistent or significant disability or incapacity
  - any hospitalization or prolongation of existing hospitalization
  - any symptom that is unexpected and has a severity grading of 4 or more based on the Common Toxicity Criteria.

In the context of a clinical drug trial, the research protocol specifies both the nature and severity of symptoms that constitute the basis for a 'serious adverse event'.

**Local SAE:** is an SAE occurring within CHEO.

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**POLICY WITH RESPECT TO CONSIDERING MEDICATION ERROR IN THE DIFFERENTIAL DIAGNOSIS OF SEVERE ADVERSE EVENTS (SAE) ASSOCIATED WITH DRUGS ADMINISTERED IN A CLINICAL TRIAL - CONT'D**

**5. RESPONSIBILITY:** As described above.

**6. PROCEDURE:** As described above.

**7. CROSS-REFERENCES:** None.

**8. REFERENCES:** **Canadian Law & guidance document**  
Division 5, Food and Drug Act  
<http://gazette.gc.ca/archives/p2/2001/2001-06-20/html/sor-dors203-eng.html>  
&  
[http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/clini/ctdcta\\_ctddec\\_e.html](http://www.hc-sc.gc.ca/dhp-mps/prodpharma/applic-demande/guide-ld/clini/ctdcta_ctddec_e.html)

**International guidance document**  
International Conference on Harmonization –  
E6 - Guideline for Good Clinical Practice (GCP)  
<http://www.ich.org/cache/compo/276-254-1.html>

**United States (and NIH – funded studies occurring within Canada)**  
Code of Federation regulations (CFR Title 21 Food & Drugs; revised April 1, 2003),  
Department of Health and Human Services  
<http://www.hhs.gov/>

**Food and Drug Administration.** Information sheets: Guidance for Institutional Review Boards (IRB) and clinical investigators.  
<http://www.fda.gov/oc/ohrt/irbs/default.htm>

**Common Toxicity Criteria (CTC):** The CTC is a taxonomy that can be used to categorize adverse events. A grading (severity) scale is provided for each adverse event term  
([http://ctep.cancer.gov/protocolDevelopment/electronic\\_applications/ctc.htm#ctc\\_v30](http://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm#ctc_v30) )

**9. ATTACHMENTS** None.

**10. DEVELOPED BY:**

- Chair, Research Ethics Board
- Chief, Division of Hematology/Oncology and Medical Director, Oncology/Medical Day Unit
- Pediatric Oncology Pharmacist
- Clinical Leader for Inpatient Oncology
- CCRP, Clinical Research Professional, MDU/Oncology

**Approved By:** AEC  
**Revision Number:** 8

**Approval Date:** September 26, 2006