Clinical Process Instruction Manual

Unexpected Serious Adverse Reaction Process Instruction

Policy:

As source establishment for deceased organ and composite tissue donors, Trillium Gift of Life Network (TGLN) is responsible for determining safety of organs and composite tissues for transplantation. TGLN ensures that the requirements of the *Safety of Human Cells, Tissues & Organs for Transplantation Regulations* are met. If a transplant program or another organ procurement organization to which an organ/composite tissue was supplied, notifies TGLN of an adverse reaction, TGLN will fully investigate the case and ensure the appropriate establishments are notified of the adverse reaction. TGLN will determine if the adverse reaction is serious and/or unexpected.

A Serious Adverse Reaction is defined as: "*An undesirable response in a tissue, organ, composite tissue recipient, including transmission of disease or disease agent".* Malignancy is not considered a reportable disease to Health Canada but will be communicated to Quality for tracking purposes and will be communicated to the transplant programs.

A Serious Adverse reaction can result in any of the following consequences to the recipient of an organ and/or tissue transplant:

a) In-patient hospitalization or its prolongation;

b) Persistent or significant disability or incapacity (including transmission of a disease or failure of the transplant's function or integrity);

c) Medical or surgical intervention to preclude a persistent or significant disability or incapacity;

d) A life-threatening condition; and

e) Death.

Only unexpected serious adverse reactions require Health Canada notification. As such, in cases of known risk (i.e., exceptional distribution), a serious adverse reaction does not need to be reported to Health Canada.

If the reaction is both serious and unexpected, TGLN will ensure it is appropriately reported to Health Canada (Canada Vigilance) and relevant establishments (transplant programs, tissue banks, organ procurement organizations).

Clinical Process Instruction Manual

Unexpected Serious Adverse Reaction Process Instruction

Furthermore, in the event that a tissue bank advises TGLN of an adverse reaction in a tissue recipient, TGLN will notify all transplant programs, organ procurement organizations and affected tissue banks that accepted organs/tissues for the corresponding donor. However, as TGLN is not source establishment for tissues, it is not required to formally report the reaction to Health Canada, unless an unexpected serious adverse reaction is recognized in an organ recipient.

TGLN retains all documentation related to adverse reaction reporting and investigation in the TGLN donor chart for a minimum of 16 years.

Process:

TGLN as Source Establishment

1. When TGLN receives an organ and/or composite tissue donor referral from an Ontario hospital, TGLN is considered to be "the source establishment" and the hospital or transplant program is considered to be an "establishment".

Initial Unexpected Serious Adverse Reaction Reporting

2. When TGLN is advised of an unexpected serious adverse reaction, the Clinical Services Coordinator (CSC) performs the following tasks:

   2.1 Obtains the TGLN identification number of the donor, linked to the recipient.

   2.2 Reviews the corresponding donor chart to determine the accepting program and recipient identification number, if available, for all organs and tissues accepted.

   2.3 Immediately telephones all accepting transplant programs, organ procurement organizations (OPO) and tissue banks and notifies all pertinent establishments that an unexpected serious adverse reaction has been detected in a recipient of the donor. The CSC provides an explanation of how the organ(s)/tissue(s)/composite tissue(s) may have been compromised, if known. The CSC charts these conversations in the donor chart's clinical notes, or uploads as attachments on iTransplant.

   2.4 Ensures that any implicated organs/composite tissues in TGLN's possession are quarantined in the designated surgical recovery storage room.

   2.5 Completes the *Suspected Error/ Accident or Serious Adverse Reaction Report*. The CSC sends the report to all relevant organ and tissue establishments, such as:

- Source establishment(s) for tissues, to which a donor referral was made.
- Any establishment which was distributed implicated organs/composite tissues.

The CSC charts the programs that were sent the report in the clinical notes. Copies of the *Suspected Error/Accident or Serious Adverse Reaction Report*, and fax transmittals (or equivalent) are forwarded to the Quality Department.

2.6 Notifies the Director Provincial Resources Centre (PRC) or designate and the Director Quality or designate during business hours (9:00 am to 5:00 pm).

2.7 Contacts the Director Quality or designate verbally and/or via email, after hours and on weekends.

Canada Vigilance Reporting

3. Director Quality or designate is responsible for initiating an investigation into the adverse reaction situation.

4. If notified during business hours, the Director Quality or designate initiates the investigation immediately. If notified outside of business hours, the Director Quality or designate will initiate the investigation on the next business day.

5. The Director Quality or designate, in collaboration with the CSC (if required), completes the *Canada Vigilance Report*. See Exhibit 1 for a copy of the report. See Exhibit 2 for instructions on completing the *Canada Vigilance Report*. The Director Quality or designate sends the report to Canada Vigilance within 24 hours of the start of the investigation of the unexpected serious adverse reaction. The Director Quality or designate obtains the fax transmittal confirmation sheet (or equivalent).

6. The Director Quality or designate notifies the Chief Medical Officer or on-call designate of the unexpected serious adverse reaction.

Unexpected Serious Adverse Reaction Follow-up

7. Director Quality or designate provides an update on the unexpected serious adverse reaction investigation to Health Canada after 15 days, and every 15 days thereafter until completion of the investigation. If the 15-day update is due over the weekend or on a holiday, the update report will be submitted earlier (i.e. on the Friday) to ensure it meets the requirements.

8. Director Quality or designate submits a final report to Health Canada upon case closure, including the results, root cause (if known), final disposition of tissue(s)/organ(s)/composite tissue(s) and any corrective actions taken.

9. The final report is provided to all establishments that were notified of the unexpected serious adverse reaction after notification of case closure from Health Canada is received but before the next scheduled Health Canada Inspection.

10. For all reports sent to relevant organ and tissue establishments and Health Canada, copies of these report(s), and the fax transmittal confirmation sheets (or equivalent) will be filed by the Quality Department.

TGLN as Establishment

11. When TGLN accepts an organ(s)/composite tissue(s) from an OPO from another province, TGLN is considered to be “an establishment” with the provincial OPO as the “source establishment”.

12. When TGLN is advised of an unexpected, serious, adverse reaction from the source establishment, the CSC works with the Director Quality or designate to perform the following tasks:

    12.1 Obtains the donor identification codes of the transplanted organ(s).

    12.2 Ensures that any implicated organs/composite tissues in TGLN’s possession are quarantined in the designated surgical recovery storage room.

    12.3 Telephones all accepting Ontario Transplant Programs and advises that a serious adverse reaction has been detected in a recipient of the donor.

    12.4 Forwards a copy of the Serious Adverse Reaction Report from the source establishment to all establishments to which TGLN distributed the implicated organ(s)/composite tissue(s), as well as to the Director Quality or designate.

13. When TGLN is advised of an unexpected, serious, adverse reaction from another establishment, to which organ(s)/composite tissue(s) were distributed, the CSC works with the Director Quality or designate to perform the following tasks:

    13.1 Obtains the donor identification codes of the transplanted organ(s).

    13.2 Ensures that any implicated organs/composite tissues in TGLN’s possession are quarantined, in the designated surgical recovery storage room.

    13.3 Telephones all accepting Ontario Transplant Programs and advises that a serious adverse reaction has been detected in a recipient of the donor.

13.4 Ensures that the source establishment is provided with a copy of a *Suspected Error/Accident or Serious Adverse Reaction Report* if TGLN documented the adverse reaction or a copy of the Serious Adverse Reaction Report if the originating establishment which identified the adverse reaction, provided one.

13.5 TGLN will also provide the source establishment with a listing of all of the establishments to which TGLN distributed the organ(s).

TGLN as Importer

14. When TGLN accepts an organ(s)/composite tissue(s) from an OPO from another country, TGLN is considered to be “an importer” with the international OPO as the “source establishment”.

15. When TGLN is advised of an unexpected serious adverse reaction from the source establishment, the CSC works with the Director Quality or designate to perform the following tasks:

15.1 Obtains the donor identification codes of the transplanted organ(s).

15.2 Ensures that any implicated organs/composite tissues in TGLN’s possession are quarantined in the designated surgical recovery storage room.

15.3 Telephones all accepting Ontario Transplant Programs and advises that a serious adverse reaction has been detected in a recipient of the donor.

15.4 Forwards a copy of the *Serious Adverse Reaction Report* from the source establishment to all establishments to which TGLN distributed the implicated organ(s)/composite tissue(s), as well as to the Director Quality or designate.

16. When TGLN is advised of an unexpected serious adverse reaction from another establishment, to which organ(s)/composite tissue(s) were distributed, the CSC works with the Director Quality or designate to perform the following tasks:

16.1 Obtains the donor identification codes of the transplanted organ(s)/composite tissue(s).

16.2 Ensures that any implicated cells, tissues, organs, and composite tissues in TGLN’s possession are quarantined, in the designated surgical recovery storage room.

16.3 Telephones all accepting Ontario Transplant Programs and advises that a serious adverse reaction has been detected in a recipient of the donor.

16.4 Ensures that the source establishment is provided with a copy of a *Suspected Errors/Accidents or Serious Adverse Reaction Report* if TGLN documented it or a copy of the *Serious Adverse Reaction Report* if the establishment which identified the adverse reaction, provided one.

Clinical Process Instruction Manual

Unexpected Serious Adverse Reaction Process Instruction

Records:

Record Name	Form No. (if applicable)	Record Holder	Record Location	Record Retention Time (as a minimum)
Suspected Error/Accident or Serious Adverse Reaction Report	CSF-9-90	Quality Assurance Department	Quality Assurance Department	16 years
Canada Vigilance Report	____	Quality Assurance Department	Quality Assurance Department	16 years

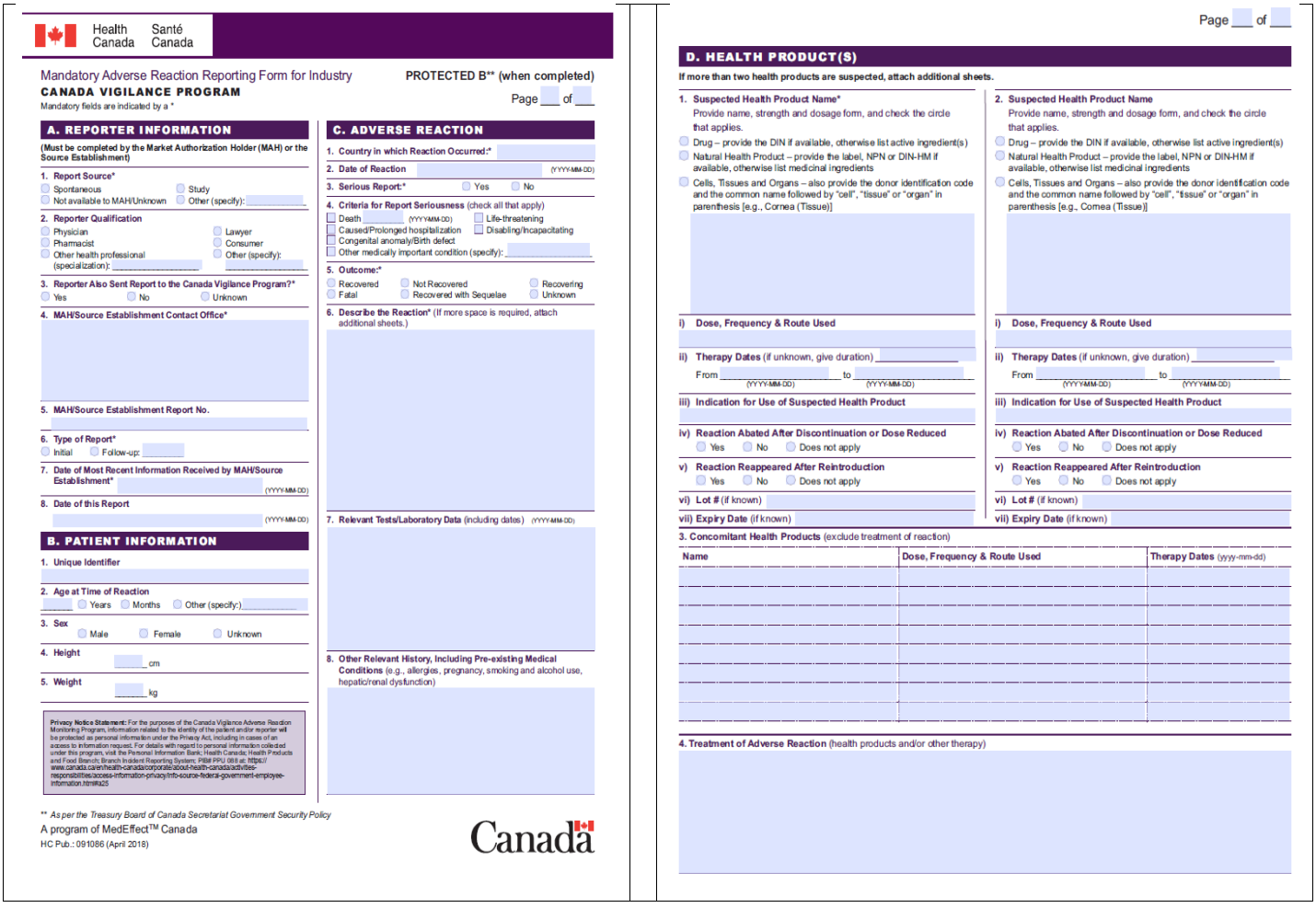
References:

- *Safety of Human Cells, Tissues and Organs for Transplantation Regulations*
- *Canada Vigilance HC/SC 4016 Form (Health Canada Adverse Reaction Report)*

Clinical Process Instruction Manual

Unexpected Serious Adverse Reaction Process Instruction

Exhibit 1: Canada Vigilance Report



Health Canada / Santé Canada

Mandatory Adverse Reaction Reporting Form for Industry
CANADA VIGILANCE PROGRAM
Mandatory fields are indicated by a *

PROTECTED B (when completed)**
Page ___ of ___

A. REPORTER INFORMATION
(Must be completed by the Market Authorization Holder (MAH) or the Source Establishment)

1. Report Source*
○ Spontaneous ○ Study
○ Not available to MAH/Unknown ○ Other (specify):

2. Reporter Qualification
○ Physician ○ Lawyer
○ Pharmacist ○ Consumer
○ Other health professional ○ Other (specify):
(specialization):

3. Reporter Also Sent Report to the Canada Vigilance Program?*
○ Yes ○ No ○ Unknown

4. MAH/Source Establishment Contact Office*

5. MAH/Source Establishment Report No.

6. Type of Report*
○ Initial ○ Follow-up:

7. Date of Most Recent Information Received by MAH/Source Establishment* (YYYY-MM-DD)

8. Date of this Report (YYYY-MM-DD)

B. PATIENT INFORMATION

1. Unique Identifier

2. Age at Time of Reaction
___ ○ Years ○ Months ○ Other (specify:)

3. Sex
○ Male ○ Female ○ Unknown

4. Height ___ cm

5. Weight ___ kg

Privacy Notice Statement: For the purposes of the Canada Vigilance Adverse Reaction Monitoring Program, information related to the identity of the patient and/or reporter will be protected as personal information under the Privacy Act, including in cases of an access to information request. For details with regard to personal information collected under this program, visit the Personal Information Bank: Health Canada; Health Products and Food Branch; Branch Incident Reporting System; PIB# PPU 088 at: https://www.canada.ca/en/health-canada/corporate/about-health-canada/activities-responsibilities/access-information-privacy/info-source-federal-government-employee-information.html#a25

C. ADVERSE REACTION

1. Country in which Reaction Occurred:*

2. Date of Reaction (YYYY-MM-DD)

3. Serious Report:* ○ Yes ○ No

4. Criteria for Report Seriousness (check all that apply)
☐ Death (YYYY-MM-DD) ☐ Life-threatening
☐ Caused/Prolonged hospitalization ☐ Disabling/Incapacitating
☐ Congenital anomaly/Birth defect
☐ Other medically important condition (specify):

5. Outcome:*
○ Recovered ○ Not Recovered ○ Recovering
○ Fatal ○ Recovered with Sequelae ○ Unknown

6. Describe the Reaction* (If more space is required, attach additional sheets.)

7. Relevant Tests/Laboratory Data (including dates) (YYYY-MM-DD)

8. Other Relevant History, Including Pre-existing Medical Conditions (e.g., allergies, pregnancy, smoking and alcohol use, hepatic/renal dysfunction)

** As per the Treasury Board of Canada Secretariat Government Security Policy
A program of MedEffect™ Canada
HC Pub.: 091086 (April 2018)

Canada

Page ___ of ___

D. HEALTH PRODUCT(S)
If more than two health products are suspected, attach additional sheets.

1. Suspected Health Product Name*	2. Suspected Health Product Name
Provide name, strength and dosage form, and check the circle that applies.	Provide name, strength and dosage form, and check the circle that applies.
○ Drug – provide the DIN if available, otherwise list active ingredient(s)	○ Drug – provide the DIN if available, otherwise list active ingredient(s)
○ Natural Health Product – provide the label, NPN or DIN-HM if available, otherwise list medicinal ingredients	○ Natural Health Product – provide the label, NPN or DIN-HM if available, otherwise list medicinal ingredients
○ Cells, Tissues and Organs – also provide the donor identification code and the common name followed by "cell", "tissue" or "organ" in parenthesis [e.g., Cornea (Tissue)]	○ Cells, Tissues and Organs – also provide the donor identification code and the common name followed by "cell", "tissue" or "organ" in parenthesis [e.g., Cornea (Tissue)]
i) Dose, Frequency & Route Used	i) Dose, Frequency & Route Used
ii) Therapy Dates (if unknown, give duration) From (YYYY-MM-DD) to (YYYY-MM-DD)	ii) Therapy Dates (if unknown, give duration) From (YYYY-MM-DD) to (YYYY-MM-DD)
iii) Indication for Use of Suspected Health Product	iii) Indication for Use of Suspected Health Product
iv) Reaction Abated After Discontinuation or Dose Reduced ○ Yes ○ No ○ Does not apply	iv) Reaction Abated After Discontinuation or Dose Reduced ○ Yes ○ No ○ Does not apply
v) Reaction Reappeared After Reintroduction ○ Yes ○ No ○ Does not apply	v) Reaction Reappeared After Reintroduction ○ Yes ○ No ○ Does not apply
vi) Lot # (if known)	vi) Lot # (if known)
vii) Expiry Date (if known)	vii) Expiry Date (if known)

3. Concomitant Health Products (exclude treatment of reaction)

Name	Dose, Frequency & Route Used	Therapy Dates (yyyy-mm-dd)

4. Treatment of Adverse Reaction (health products and/or other therapy)

Clinical Process Instruction Manual

Unexpected Serious Adverse Reaction Process Instruction

Exhibit 2: How To Fill Out The Health Canada Adverse Reaction (AR) Report

http://www.hc-sc.gc.ca/dhp-mps/medeff/report-declaration/ar-ei_indus_form-eng.php

Mark CTO at top of form

Section A: Reporter Information

- A1: Indicate source of report (from where information originated). For literature sources, provide full literature citation in box C6. Check "Not Available to MAH/Unknown" if initial reporter did not specify report source. Select "Other" to indicate that report source is known, but does not fit into categories provided.
- A2: Indicate type of reporter who initially reported AR.
- A3: Indicate whether initial reporter also reported AR to Canada Vigilance Program.
- A4: Enter full name, civic address, telephone/facsimile number, contact name, and establishment registration number (CTO # 100062).
- A5: Enter TGLN donor ID number.
- A6: Indicate type of report.
- A7: Indicate date when information was received for report.
- A8: Indicate date that form was completed.

Section B: Patient Information

- B1: Enter TGLN recipient ID number.
- B2: Provide patient's age at time of AR.
- B3: Enter patient's gender.
- B4: Enter patient's height, in centimetres (cm).
- B5: Enter patient's weight, in kilograms (kg).

Section C: Adverse Reaction

- C1: Indicate country where AR took place.
- C2: Provide date of onset of AR.
- C3: Indicate if report is serious.
- C4: Check all boxes that apply to definition of serious AR.
- C5: Indicate outcome of AR.
- C6: Provide full description of nature of AR (e.g. body site and severity), all relevant clinical information (medical status prior to event, reported signs and/or symptoms, differential

diagnosis for event in question, clinical course, etc.), and temporal relationship with transplantation.

- C7: Provide all appropriate information, including relevant negative tests and laboratory findings.
- C8: Provide information on patient's history (i.e., race, allergies, pregnancy history, smoking and alcohol use, drug abuse) and other conditions known in patient.

Section D: Health Product(s)

- D1/D2: For each suspected product, provide product name, check box that applies to type of health product. For Cells, Tissues and Organs (CTO), also provide donor identification code and common name, followed by "cell", "tissue" or "organ" in parenthesis [e.g., Kidney (Organ)].
- D.i): Describe how product was used by patient. For CTO, this box is only applicable to cells.
- D.ii): Provide date of transplant.
- D.iii): Provide diagnostic reason or indication for implantation, transplantation or infusion.
- D.iv): Check "Does not apply".
- D.v): Check "Does not apply".
- D.vi): Enter "N/A".
- D.vii): Provide date of expiration on label, if any.
- D3: List and provide therapy dates for any other health products (drugs, biologics, including cells, tissues and organs, natural health products, etc.) that patient was using at time of event. Do not include health products used to treat event.
- D4: Describe treatment of AR, including other health products and/or therapies.

Send form to:
Canada Vigilance Program
Marketed Health Products Directorate
Health Canada
Postal Locator 0701E
Ottawa, Ontario K1A 0K9

Fax: 613-957-0335

Email: CanadaVigilance_CTOs@hc-sc.gc.ca