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# Guidance on Classification of Observations for Inspection of Cells, Tissues and Organs Establishments



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Canada 

**Guidance on Classification of observations for Inspection of Cells, Tissues and Organs establishments (GUI-0101)**

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**Disclaimer**

This document does not constitute part of the *Food and Drugs Act* (the Act) or its regulations and in the event of any inconsistency or conflict between the Act or regulations and this document, the Act or the regulations take precedence. This document is an administrative document that is intended to facilitate compliance by the regulated party with the Act, the regulations and the applicable administrative policies.

Ce document est aussi disponible en français.

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# About this document

## 1. Purpose

Establishments that process, import, distribute or handle human cells, tissues and organs (CTO) intended for transplantation must comply with the [Food and Drugs Act](#) (the Act) and the [Safety of Human Cells, Tissues and Organs for Transplantation Regulations](#) (CTO Regulations).

Health Canada inspects CTO establishments for compliance with these laws. This guide:

- provides examples of inspection ratings and observations
- helps classify observations made during inspections of CTO establishments
- promotes consistency in individual observations and in overall inspection ratings



You should read this document along with:

- the [Food and Drugs Act](#)
- the [CTO Regulations](#)
- relevant sections of the National Standard, including:
  - CAN/CSA Z900.1: Cells, tissues, and organs for transplantation: General requirements and appropriate subsets
- [Guidance Document for Cell, Tissue and Organ Establishments – Safety of Human Cells, Tissues and Organs for Transplantation](#)
- [Inspection Policy for Cells, Tissues and Organs Establishments \(POL-0057\)](#)

## 2. Scope

This guide applies to all Health Canada inspections of CTO establishments governed by the CTO Regulations.

# Classifying inspection observations and ratings

## 3. Assigning risk to an observation

During an inspection, Health Canada inspectors make observations when they note areas where the establishment is not adequately meeting the regulatory requirements.

An observation is classified as critical, major or minor:

- A **critical (risk 1) observation** either:
  - directly affects CTO safety and is likely to result in a health risk to the recipient
  - constitutes fraud, misrepresentation or falsification of products or data
- A **major (risk 2) observation** potentially affects CTO safety and could result in a health risk to the recipient.
- A **minor (risk 3) observation** has low or negligible impact on CTO safety.

Inspectors consider the following criteria when classifying an observation:

- potential or immediate health risk
- type of non-compliance
- number of times an issue has happened
- context of the situation



Refer to [Appendix C](#) for examples of critical, major and minor observations made during the inspection of establishments that handle, process, distribute or import human cells, tissues or organs.

It is expected that all observations—critical, major and minor—will be corrected within an appropriate timeframe.

## 4. Determining the overall compliance rating

After an inspection, Health Canada sends an “exit notice” to the establishment. This document summarizes all observations made by the inspector.

The exit notice also gives the establishment an overall rating of **compliant (C)** or **non-compliant (NC)**. This rating is based on the number and risk level of the observations.

### Compliant rating

A **compliant** rating means the establishment’s activities complied with the requirements of the Act and CTO Regulations.



A compliant rating does not mean there were no observations or that corrective actions are not required.

When Health Canada assigns a **compliant** rating, the inspector found:

- no observations
- minor observations
- major observations, but the establishment showed that it was in control of its regulated activities

### Non-compliant rating

A **non-compliant** rating means the establishment’s activities did not comply with the requirements of the Act and CTO Regulations.

When Health Canada assigns a **non-compliant** rating, the inspector found:

- one or more critical observations that show a systemic problem within the program
- major observations that show the establishment is not in control of its regulated activities
- no corrective actions had been taken to address critical or major observations made in a previous inspection

When an inspector finds a critical observation, Health Canada informs the establishment that this may result in a non-compliant rating. Health Canada will also request an action plan specifying corrective measures and time needed to implement.



A non-compliant rating will have serious consequences for an establishment that may include cancelling their registration. Health Canada enforces non-compliances according to the [Compliance and Enforcement Policy \(POL-0001\)](#).

# Appendices

## Appendix A – Glossary



These definitions explain how terms are used in this document. If there is a conflict with a definition in the [Food and Drugs Act](#) or [CTO Regulations](#), the definition in the Act or Regulations prevails.

**Inspection** – Assessment of compliance against any of the applicable requirements of the [Food and Drugs Act](#) and its associated regulations by a designated inspector. Inspections are conducted at predetermined intervals or on a risk basis.

**Observation** – A deviation from or deficiency in compliance with the Act or Regulations found during an inspection. An observation is classified according to the level of risk associated with the deficiency. All observations must be documented in the inspection report (exit notice).



# Appendix B – References

## Laws and regulations

### *Food and Drugs Act*

[laws-lois.justice.gc.ca/eng/acts/f-27/](http://laws-lois.justice.gc.ca/eng/acts/f-27/)

### National Standard of Canada CAN/CSA-Z900 – Cells, Tissues and Organs for Transplantation

[shop.csa.ca/en/canada/transplantation/z900-12-package/invnt/27031572012](http://shop.csa.ca/en/canada/transplantation/z900-12-package/invnt/27031572012)

National Standard of Canada CAN/CSA-Z900.2.2: Tissues for Transplantation

National Standard of Canada CAN/CSA-Z900.2.3: Perfusable Organs for Transplantation

National Standard of Canada CAN/CSA-Z900.2.4: Ocular Tissues for Transplantation

National Standard of Canada CAN/CSA-Z900.2.5: Lymphohematopoietic Cells for Transplantation

### Safety of Human Cells, Tissues and Organs for Transplantation Regulations

[laws-lois.justice.gc.ca/eng/regulations/SOR-2007-118/](http://laws-lois.justice.gc.ca/eng/regulations/SOR-2007-118/)

## Guidance documents and policies

### *Compliance and Enforcement Policy (POL-0001)*

[www.hc-sc.gc.ca/dhp-mps/compli-conform/gmp-bpf/pol/pol\\_1\\_tc-tm-eng.php](http://www.hc-sc.gc.ca/dhp-mps/compli-conform/gmp-bpf/pol/pol_1_tc-tm-eng.php)

### *Guidance Document for Cell, Tissue and Organ Establishments- Safety of Human Cells, Tissues and Organs for Transplantation*

[www.hc-sc.gc.ca/dhp-mps/brgtherap/reg-init/cell/cto\\_gd\\_ld-eng.php](http://www.hc-sc.gc.ca/dhp-mps/brgtherap/reg-init/cell/cto_gd_ld-eng.php)

### *Inspection Policy for Cells, Tissues and Organs Establishments (POL-0057)*

[www.hc-sc.gc.ca/dhp-mps/compli-conform/info-prod/cell/pol-0057\\_doc-eng.php](http://www.hc-sc.gc.ca/dhp-mps/compli-conform/info-prod/cell/pol-0057_doc-eng.php)

# Appendix C – Examples of observations and ratings



During an inspection, each observation is classified by a Health Canada inspector, who uses:

- this document
- other relevant information, including policies and guidance documents
- his or her judgment

Although the following examples of observations have been assigned a risk rating, each observation could be classified as higher or lower in risk. The examples are intended to illustrate the process by which an inspector assigns a rating to his or her observations and are not intended to limit the discretion of an inspector in determining compliance with the Act and CTO Regulations. For example, observations that are repeated from previous inspections might be assigned a higher risk.

## Section of the CTO Regulations

### Section 4: Prohibition

#### Critical

- An establishment transplanted a CTO that was not determined safe for transplantation.
- An establishment transplanted tissue that was not processed by a registered establishment.
- An establishment imported tissues that were not processed by a registered establishment.

### Sections 5 to 14: Registration

#### Major

- The establishment did not register all types of CTOs they were processing.

## Minor

- The establishment did not notify Health Canada in writing within the required timeframe of changes to their registration information.

## Section 15: Source establishment

## Major

- No documentation demonstrated the source establishment reviewed the donor suitability assessment to determine that the CTO were safe for transplantation.

## Sections 16 to 17: Processing – general

## Major

- No documentation demonstrated activities, processes or technical procedures were validated.

## Sections 18 to 23: Processing – donor suitability assessment

## Critical

- No documentation demonstrated a physical exam was performed on the donor.
- There were no test results available for a required infectious disease marker.
- No documentation demonstrated the donors were assessed against exclusion criteria.

## Major

- The physical exam for deceased donors did not address all high-risk behaviours.
- The donor medical social history questionnaire included all questions required by the exclusion criteria, but a response was not recorded for some of the questions.

## Section 24: Processing – retrieval

## Major

- The retrieval time was more than the established maximum interval between the cardiac asystole of the donor and the retrieval of the tissue.

## Sections 25 to 27: Processing – testing

### Critical

- The serological test kit used for donor testing was not licensed.

### Major

- The serological test kit used for testing tissue donors was licensed as a diagnostic test kit rather than for donor screening.

## Sections 28 to 33: Processing – packaging and labelling

### Critical

- The donor identification code did not appear on the interior label or package insert and the CTO could not be linked to the donor.

### Major

- The donor identification code was on the interior label but was not included on the package insert.

### Minor

- Contact information for the transplant establishment was not identified on the exterior label.
- There was no process in place to verify the packaging is not damaged.

## Section 34: Processing – quarantine

### Critical

- Tissues were available for distribution even though donor suitability assessment was not completed.

### Major

- Although the donor suitability assessment was done, no documentation demonstrated processing records were reviewed for completeness before releasing tissues from quarantine.

- Tissues from a living donor were not quarantined for at least 180 days and retested before release, in a situation where initial testing did not include nucleic acid testing (NAT).
- The stored cord blood unit was not quarantined even though it had not been determined safe for transplantation.

## Sections 35 to 39: Storage

### Critical

- The establishment did not take action following a significant temperature deviation in the freezer where released tissue was stored and the safety of tissue would have been impacted.

### Major

- Autologous tissues were stored with released allogeneic tissues, without the autologous tissues being clearly labelled "For autologous use only."
- CTO were stored in a room that was not monitored to ensure the right environmental conditions were maintained.
- No records demonstrated the time period used to store adjunct vessels (which were not used immediately in organ transplantation) was decided based on scientific evidence.
- The tissue storage area was not secured to prevent unauthorized persons from entering.

## Sections 40 to 42: Exceptional distribution

### Critical

- The establishment did not always apply exceptional distribution when it was needed.

### Major

- The Notice of Exceptional Distribution did not list all requirements for which the organ was not in compliance.

## Minor

- The Notice of Exceptional Distribution did not include the name of the transplant establishment.

## Sections 43 to 54: Error, accident and adverse reaction investigation

### Critical

- The source establishment did not start an error and accident investigation related to an unexpected adverse reaction involving the transmission of an infectious disease.
- Implicated tissues were released from quarantine when an error and accident investigation was ongoing.

### Major

- Although errors and accidents related to transmissible disease testing were investigated, the source establishment did not report to Health Canada.

## Sections 55 to 63: Records

### Critical

- No records demonstrated to which establishment the adjunct vessels were distributed.

### Major

- Although the donor identification code was assigned, this code was not a part of the establishment's records system.

### Minor

- Records were not always complete and/or accurate. For example:
  - An incorrect digit was recorded for the equipment serial number.
  - An incorrect year was recorded for the date that refrigerator temperature was checked.

## Sections 64 to 69: Personnel, facilities, equipment and supplies

### Major

- No documentation demonstrated an installation qualification of a new automated system used to process cord blood was done.
- Microbiological monitoring was not conducted in the room where aseptic processing activities took place.
- The expiry date of critical supplies was not strictly observed.
- No documentation demonstrated regular maintenance was completed on the refrigerator used to store tissue.

## Sections 70 to 76: Quality assurance system

### Major

- There was no procedure to describe when testing of both the infant donor and the mother is required.
- There was no procedure in place for conducting donor suitability assessment.
- The deceased donor screening procedure did not explain how to assess responses to questions in the medical, social and behavioural history questionnaire that were marked “Unknown.”
- No procedure to investigate, quarantine, and report, suspected errors and accidents to other establishments.
- No audit was completed to verify compliance with the CTO Regulations and the establishment’s standard operating procedures.
- No documentation demonstrated the establishment reviewed the standard operating procedures every two years.

### Minor

- A copy of the current labelling procedure was not available at the location where the labelling was done.
- The record retention time section of the standard operating procedure did not state records must be kept for 10 years.