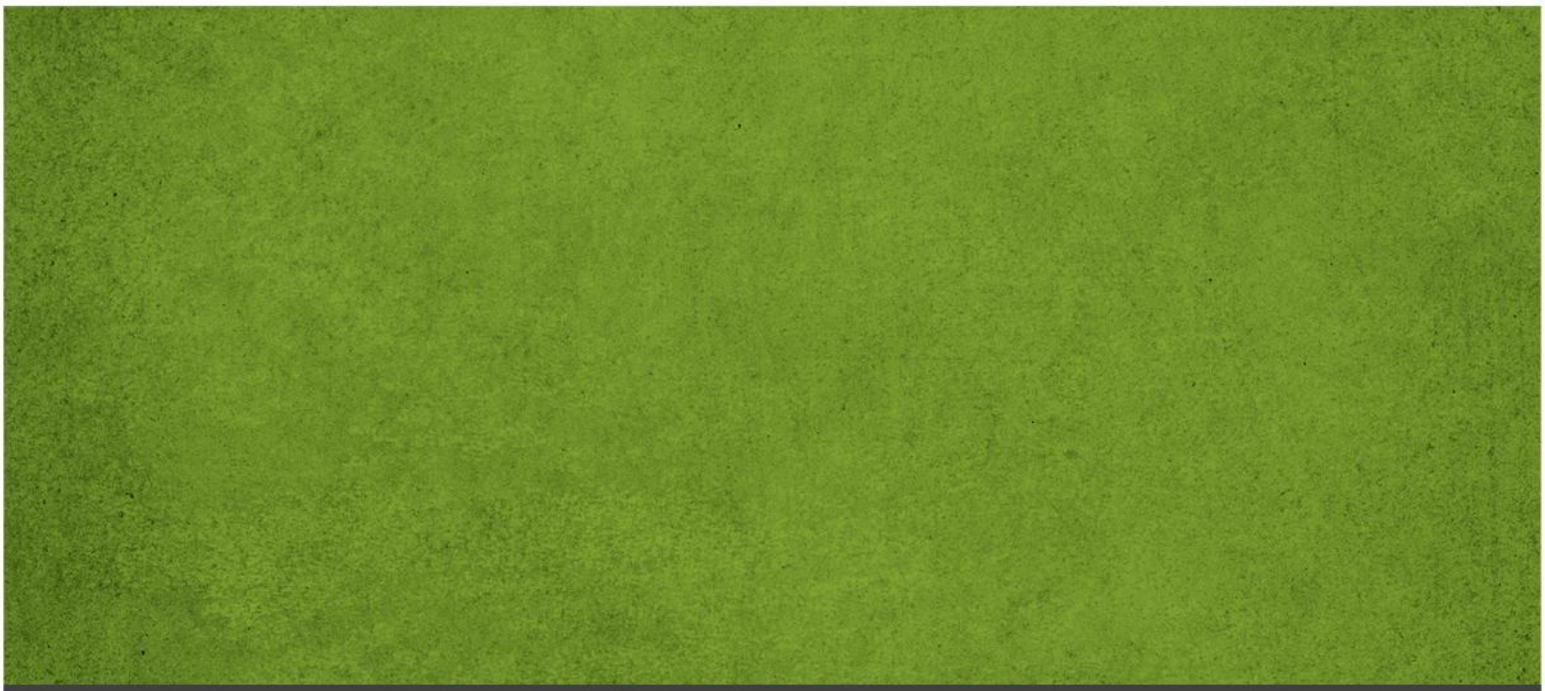
CELLS, TISSUE AND ORGAN SURVEILLANCE SYSTEM

PROJECT PROGRESS REPORT APRIL 2007 – DECEMBER 2013



PROTECTING CANADIANS FROM ILLNESS

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Canada

TO PROMOTE AND PROTECT THE HEALTH OF CANADIANS THROUGH LEADERSHIP, PARTNERSHIP, INNOVATION AND ACTION IN PUBLIC HEALTH.

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I. INTRODUCTION

A significant number of transplant procedures take place each year in Canadian health care facilities, including procedures in clinics, physician and dentist offices. These can include solid organ transplants such as kidney and heart, and tissues such as bone chips and corneas. Transplantation procedures also include processed biological tissues for organ components, replacement orthopaedic and dental procedures such as demineralized bone putty.

The Surveillance and Epidemiology Division (SED) of the Centre for Communicable Disease and Infection Control (CCDIC) at the Public Health Agency of Canada (the Agency) is responsible for leading the development of activities supporting the evolving Cell, Tissue and Organ Surveillance System (CTOSS).

In 2012, 2,225 organ transplant procedures were performed in Canada – an increase of nearly 5% over 2011. In the same year, there were 41,252 Canadians living with end-stage kidney disease receiving some form of dialysis and 3,428 patients were on the waiting list by December of the same year.[1] A significant gap exists between donations and the need for organ transplants. While transplants cannot and do not cure patients, they can improve quality of life dramatically, and are more cost-effective than available alternatives.[2] In Canada, over 90,000 tissue allografts are distributed for transplantation, including musculoskeletal, vascular, skin, cardiac and corneal tissues.[3]

The Agency works to protect the health and safety of Canadians through preventing and controlling chronic diseases and injuries and infectious diseases, preparing for and responding to public health emergencies, serving as a central point for sharing Canada's expertise with the rest of the world, applying international research and development to Canada's public health programs; and strengthening intergovernmental collaboration on public health policy and planning.

The Agency is leading the development of CTOSS as a national system, the objective of which is to improve safety for Canadians receiving transplants by capturing and analyzing adverse event data and disseminating the resulting knowledge. Transplantation adverse event surveillance data is critical to our ability to improve patient safety by limiting and preventing transplant associated adverse events. Adverse event data is needed because the requirements for transplantation are expected to rise, and currently there is no surveillance data available to provide incidence rates for transplantation adverse events in Canada. "The need for organs is predicted to increase by 152 percent over the next two decades. Canada's aging population will require more and donate fewer organs, medical advances will enable more patients to benefit from transplantation and the demand for organs will increase significantly due to rising rates of chronic disease."[4]

The safety of both prospective and post-transplanted patients is the prime focus of CTOSS, as the data will support informed surgical consent and the potential avoidance of transplantation adverse events through the development of appropriate programs and policies.

Historically, Canada has not had a public health surveillance system in place for identifying adverse reactions from cell, tissue and organ (CTO) transplantation and no systematic way of identifying emerging issues and trends in public health threats arising from CTO transplants.

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[1] Canadian Organ Replacement Register, 2013, Canadian Institute for Health Information

[2] Ibid

[3] Canadian Council for Donation and Transplantation, Surveillance of Recipients of Organ and Tissue Transplants, February 2008.

[4] Canadian Blood Services, Call to Action – A Strategic plan to improve organ and tissue donation and transplantation performance for Canadians, April 2011

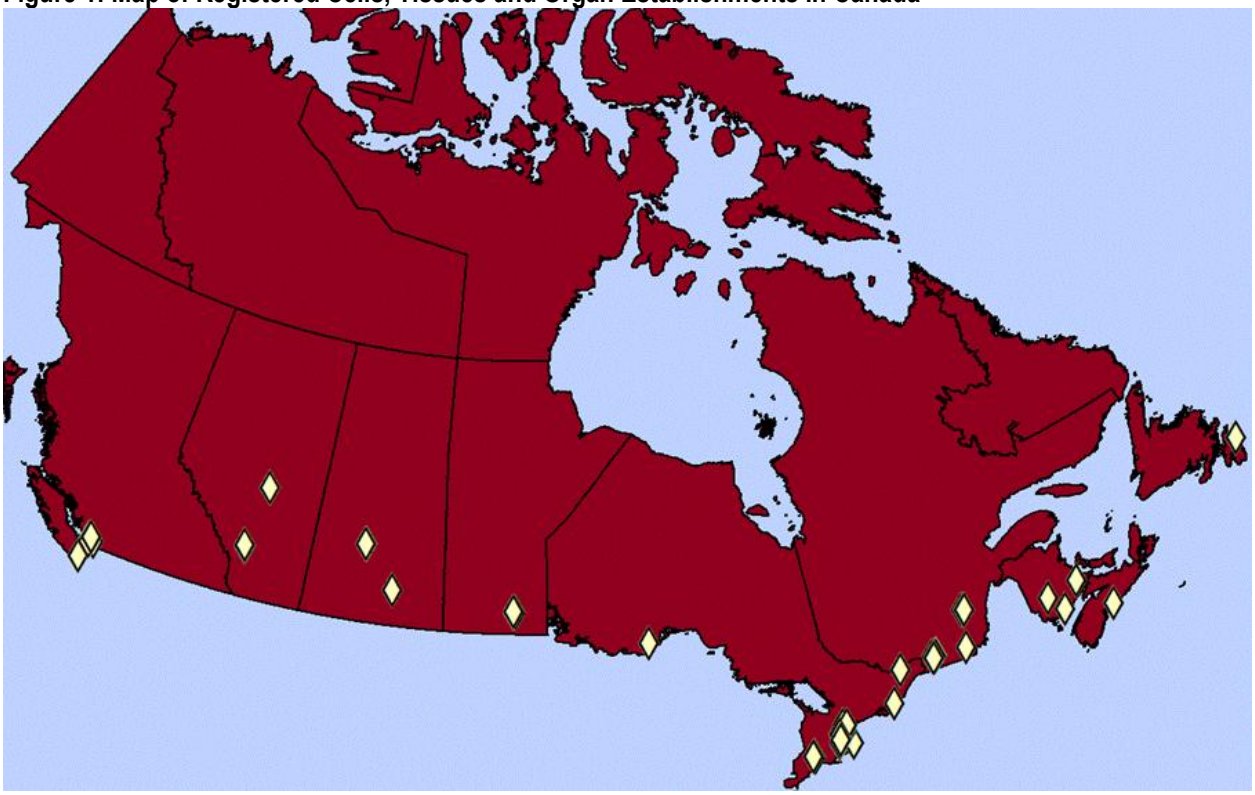
At the inception of this project, there were very few national statistics available with regard to CTO supply or demand. While almost all of the organ supply is retrieved from donors within Canada, tissue products are routinely purchased from international sources, primarily from the United States (U.S).

Over the years, Canadian patients have been affected by a number of high profile tissue recalls in relation to imported tissue products.[5] Tissues are processed and distributed for transplantation at over 160 registered cells, tissues and organs establishments in Canada (see Figure 1 – Map of Registered Cells, Tissues and Organ Establishments in Canada). The trajectory for an anticipated increase in transplantation has highlighted the necessity of establishing a public health surveillance system for CTOs to ensure patient safety.

Data collection on adverse events related to human allograft tissue transplants began in April 2011 at five pilot sites: Alberta Health Services, Edmonton; Sunnybrook Hospital, Ontario; the province of Quebec; Horizon Health Network, New Brunswick; and the province of Nova Scotia. Prior to the commencement of data collection, minimum data elements and definitions were established for tissues. To date, these components have not yet been established for the cell and organ components of CTOSS. The CTOSS initiative continues to support the Agency strategic objective of "protecting Canadians and empowering them to improve their health" by strengthening public health capacity in order to support public health decisions and actions relating to transplantation.

[5] Integrated RMAF/RBAF for the Blood Safety Contribution Program, January 11, 2008, p.5

Figure 1: Map of Registered Cells, Tissues and Organ Establishments in Canada



◊ =geographic locations of Registered Cells, Tissues and Organ Establishments in Canada

II. BACKGROUND AND HISTORY

The Krever Commission was established in October 1993 to review all aspects of the blood system in Canada. The mandate was to assess the objective, organization, management, operation, financing and regulation of all Canadian blood system activities. Five of the 17 recommendations of the final report were aimed at strengthening public health programs through enhanced blood-borne surveillance activities, while the balance were specifically aimed at strengthening Health Canada's blood regulatory system. Recommendation number forty (40) specifically called for an active program of post-market surveillance for blood components and blood products.[6]

In March 1998, Health Canada's Laboratory Centre for Disease Control created the Surveillance and Epidemiology in Transfusion (SET) Working Group (WG) to develop a plan and design a program for a comprehensive blood surveillance system in Canada. In their final report, the WG established a class of contributions to support Provincial and Territorial transfusion and transplantation adverse event surveillance activities.[7]

In October 1998, the Government of Canada approved the Blood Safety Program (BSP) to be managed by Health Canada. This initiative represented an investment of $125 million over five years and $25 million per year ongoing beginning in 2003-2004. The objective of this investment was "to establish strong regulatory and surveillance programs for the blood system." Included in the approval of the BSP was a contribution program that received Treasury Board (TB) authorities of $7.1M over five years and 1.9M per year ongoing beginning in 2003-04 to support transfusion and transplantation adverse event surveillance activities in the provinces and territories. In June 2005, the

[6] Integrated RMAF/RBAF for the Blood Safety Contribution Program, January 11, 2008, p.5
[7] Ibid, pg.5.

Agency received authority to establish a Cell, Tissue and Organ (CTO) public health pilot surveillance network for pathogens that pose a risk to human health via CTO transplantation.

In 2003, an expert working group was established to support the development of a Canadian cell, tissue, organ and assisted reproduction national surveillance registry and network. The working group supported the notion of developing a web-based surveillance system and included the identification of pilot sites. Development included the establishment of a database framework, standard processes and standard definitions including guidelines for adverse event identification and reporting. The expert working group last met in 2005. Continued development of the database, the funding proposal and pilot projects were put on hold while the national strategy was pursued.

In June 2006, the Agency approached the Canadian Council for Donation and Transplantation (CCDT) to assist in developing a Tissues and Organs Surveillance System in Canada. The collaborative work between the Agency and CCDT began in July 2007, with an executive strategy session. Following this event, a Core Planning Group met on eleven occasions between 2007 and 2008 to advance the foundational work components of the surveillance system. This effort resulted in the formation of the CTOSS National Steering Committee.

In September 2007, the Conference of Deputy Ministers announced the merger of CCDT with Canadian Blood Services (CBS). This merger resulted in a pause in activity by CCDT prior to moving forward and engaging stakeholders in further planning. The remaining available time was utilized to work with the Agency to further develop the background research and foundational documents such as the evaluation plan, consultation plan, environmental scan and surveillance framework.

2.1 The Early Developmental Phase: 2007-2008

The consultative phase began with CCDT's Enhancing Tissue Banking in Canada Task Force meeting on April 27-28, 2007. The meeting was attended by participants from across Canada, the United States, and Europe. The purpose of the meeting was to consult with stakeholders in the tissue transplant community regarding possible future options for surveillance and traceability and to provide input to the CCDT and stakeholders. Recommendations arising from this meeting included the proposed development of a centralized national surveillance system built on the existing blood system and linking both surveillance and traceability systems.

A final report of the Tissues and Organs Surveillance System Consultation, September 2007-March 2008 was issued by CCDT on March 27, 2008. The report consolidated the approaches taken in order to provide guidance and relevant expertise to the development of the surveillance system.

2.1.1 CTOSS National Steering Committee

During the CCDT's consultation phase, a CTOSS National Steering Committee was established. Broad representation was sought during the early phase to ensure diverse views were brought forward during formative development. The role of the National Steering Committee was to provide leadership through a review of project deliverables as well as to provide advice and recommendations by collaborating with system designer/builders. The CTOSS National Steering Committee met on three occasions, with the initial meeting held on January 7, 2008 and the final meeting held on February 3, 2009.

Project Deliverables:

2.1.2 CTOSS Program Charter

The program charter was finalized in 2007 and outlined three key phases in the development of a surveillance system for transplantation adverse events:

- Phase 1: Plan (2007-08)

- Phase 2: Design/Build (2009-10) and
- Phase 3: Deploy (2011-2012)

It is important to note the CTOSS began with the Plan, Design/Build and Deploy elements of the tissue component of the CTOSS surveillance system. Data elements and definitions were completed for the tissue component, and data collection began in April 2011. The organ component will subsequently be developed, followed lastly by cells. Each component will have been developed separately largely due to the unique differences in the nature of transplantation requirements and complexities of the individual components.

The Program Charter was updated in September 2012 to reflect progress in the development of the tissue component. Representatives from the CTOSS National Data Working Group (representing the five pilot sites) as well as representatives from Health Canada and Héma-Québec were invited to provide input into the Charter update at a teleconference meeting held in June 2012 and a face-to-face meeting held on October 18, 2012, in Ottawa. The Program Charter continues to function as a high-level planning document to continuously ground and guide program development and implementation. An iterative approach is used to support the ongoing development of the overall surveillance framework and associated infrastructure elements.

2.1.3 CTOSS Environmental Scan including literature review and Canadian survey

In January 2008, CCDT issued an environmental scan which focused on a review of the literature and national and international programs in order to provide a foundation of information from which to develop a comprehensive pan-Canadian cell, tissue and organ transplant surveillance system. Considerations included the development of an educational and marketing campaign to promote adverse event reporting by end-users, legal opinion regarding health privacy legislation, the identification of minimum data elements including severity and causality and processes to support the identification of trends and concerns.

2.1.3.1 Canadian Programs Surveillance Practices Survey

A web based survey was used to solicit information about current practices in tissue and organ surveillance and perceptions about barriers and/or challenges in the establishment of a national surveillance system including possible solutions. The survey also served the purpose of informing the Canadian Organ and Tissue Donation and Transplantation (OTDT) community of the commencement of development of the surveillance system.

Summary of Key Survey Findings:

Respondents described a successful system as being a secure web-based surveillance system defined by standardized data elements and definitions, and readily available to end users.

2.1.4 Surveillance Framework

Creation of a surveillance framework document commenced in 2009, and was completed in November 2012. Elements relating to data reporting, management, analysis, dissemination, security, privacy, storage and archival considerations were included in the document and encompassed under the following sections:

- Purpose of the Surveillance System
- Planned uses of data from the Surveillance System
- Purpose of the Framework
- Definitions of adverse transplantation (events- should use either reaction or event throughout the entire document)

- Legal authorities for data collection
- Level of integration with other systems
- CTOSS Data Flow Chart
- Components of the System:
    - Population under surveillance
    - Data collection time period
    - Data to be collected
    - Reporting sources of data
    - Management of system data
    - Methods of data analysis and dissemination
    - Data security and privacy
    - Data storage and archival

2.1.5 Minimum Data Elements, Definitions and Agreements

A Canadian Transplantation Adverse Event Reporting Form for Tissues (see Appendix 1) was developed following agreement on the specific data elements for inclusion by the Agency, Health Canada, and members of the National DWG. The data elements selected followed from broad international and domestic consultation. Data definitions were also developed as a companion document, in addition to a Minimum Data Elements Agreement, co-signed by pilot site participants and the Agency.

Since tissue data reporting began in April 2011, most sites submit tissue transplantation adverse events to the Agency via an Excel spreadsheet, developed by pilot site partners in Nova Scotia, and reviewed and approved by all participants. Quarterly reports including declaration of zero cases for tissue adverse events and denominator data are also forwarded electronically to the Agency.

2.1.6 Performance Measurement and Evaluation Framework

A Performance Measurement and Evaluation Framework was Included within the central planning components of CTOSS. It consisted primarily of a formative evaluative approach of the processes involved in the developmental phase as well as an evaluation of the piloting of the surveillance system.

A Logic Model was developed to illustrate the causal or logical relationships between activities, inputs, outputs and outcomes. The logic model formed the foundation for performance measurement and evaluation. Suggested methodologies for data collection relating to performance measures included general document review, file review and pilot site surveys.

A report for Phase 1 of the CTOSS Program Charter was completed in December 2010. The report concluded that most key process activities including the program charter, environmental scan, pilot site engagement, stakeholder consultations, surveillance framework in addition to a performance measurement and evaluation framework had been completed. Tissue-related data elements had also been defined.

2.1.7 Pilot Sites

Armed with advice from international experts as well as the Canadian Organ and Tissue Donation and Transplantation community including opinion leaders, pilot sites were selected based on their regional expertise, readiness to participate, existence of an active tissue recovery and distribution program, existence of an Organ Procurement Organization (OPO) and an organ transplant program that included at least one organ in addition to kidney. Based on the aforementioned criteria, as well as discussion with the respective governments, the provinces of Quebec and Nova Scotia were confirmed as the initial pilot sites in

2008, as well as Alberta Health Services Edmonton. In fiscal year 2010-2011, two additional pilot sites joined the project – Sunnybrook Health Sciences Centre in Ontario and the province of New Brunswick.

In December 2007, individual meetings were held with the three original pilot sites to introduce the TOSS project and provide an opportunity for those sites to ask questions. Pilot site team members identified several areas of focus during the developmental phase of the surveillance system:

- Limit duplication of data entry;
- Respect diversity of jurisdictions
- Need for a different approach for tissue and organ surveillance
- Different provincial management of Cell, Tissue and Organ donation and transplantation
- Identify benefits to users as a means to engage groups.

On February 12 and 13, 2008, members from the three original pilot sites attended a consultation session focused on information and resources requirements. The input received during the consultation process was non-binding and contributed to the development of a preliminary system requirements document. Open discussion focused on the following topics:

- The types of adverse events to be included
- Initial major categories of information for capture
- Options for denominator data
- Process and resource requirements and the appropriate level of responsibility
- Timelines for data submission and analysis

It was further reiterated that the surveillance system under development would not constitute an "alert system" nor reflect "real-time" adverse event reporting, as the processes that require more timely processing and sharing of information such as risk management involving potential adverse events remain the responsibility of local and provincial stakeholders. Additionally, the surveillance system is not intended to replace reporting requirements for Health Canada, but rather to augment them.

Brief Overview of Pilot Sites

Alberta

At the inception of the pilot, transplant services were located within the University of Alberta Hospital Complex and provided organ and tissue transplant services to residents of Alberta, British Columbia, Manitoba, Saskatchewan, Yukon, Northwest Territories and Nunavut. The Comprehensive Tissue Centre continues to recover, process, store and distribute tissue for transplantation across Canada. At the inception of CTOSS, it was one of a few American Association of Tissue Banks (AATB) accredited tissue banks in Canada, distributing tissues across the country.

Sunnybrook

Sunnybrook Health Sciences Centre became a pilot site in 2010. This pilot site is a unique entity among blood banks within Canada, as they are not only a blood bank, but are also a source establishment for femoral heads and allograft skin. They also receive, track, store, and dispense minimally manipulated tissue products as well as altered tissue and xenografts. The practices engendered by blood bankers are applied to tissue products, resulting in timely recall and quarantine if applicable.

Quebec

The province of Quebec, more specifically, Le Ministère de la Santé et des Services sociaux undertook a two part pilot project, aimed at adverse reactions in both ocular and musculo-skeletal tissue. The project involved a five year retrospective chart audit, following initial work which defined adverse reactions associated with each, and associated methods for data collection.

Within Quebec, most of the tissues transplanted are provided by Héma-Québec. Héma-Québec is the authority responsible for efficiently providing adequate quantities of safe and optimal blood components, substitutes, human tissues, stem cells and human milk. The organization provides and develops expertise along with specialized and innovative services and products relating to transfusion medicine and human tissue transplantation. Over the last 15 years, a comprehensive hemovigilance system has been developed in Quebec, including robust procedures for reporting adverse events related to blood transfusions. This system and the reporting procedures were subsequently deemed as a model to consider for the development of the new transplantation adverse event surveillance system.

New Brunswick

New Brunswick also became a pilot site in 2010. New Brunswick has an eye and tissue bank as well as a tissue and organ procurement program. Although the site joined the project following the establishment of draft data elements and definitions, it helped to test and consolidate the foundational components of the tissue stream. This was determined useful in order to establish the applicability to a diversity of transplant communities in Canada.

Nova Scotia

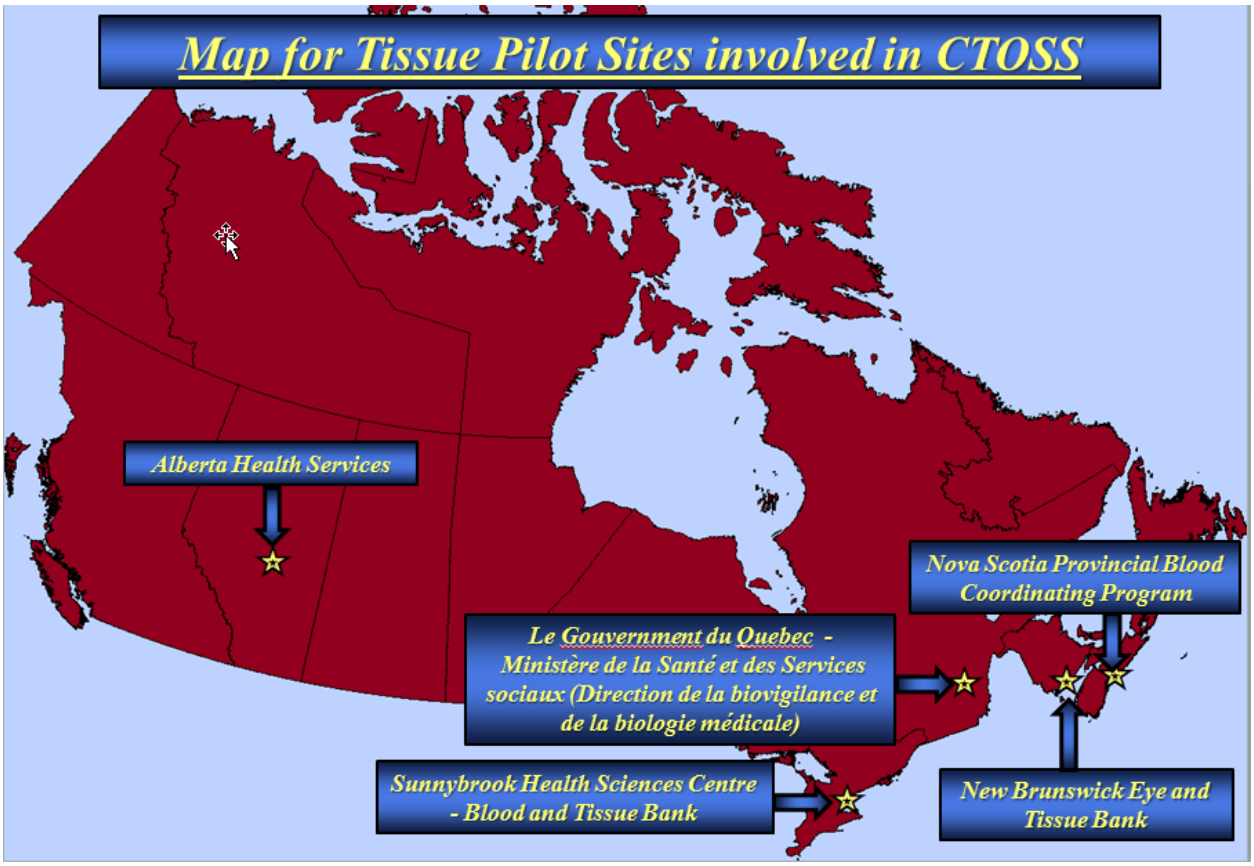
As a provincial program of the Department of Health and Wellness (DHW), the Nova Scotia Provincial Blood Coordinating Program (NSPBCP) was identified as the appropriate program to lead tissue and organ surveillance. This decision was made based on several factors, including the NSPBCP's previous success with Agency surveillance initiatives and the decision by the DHW that the ultimate responsibility for adverse event surveillance should be the responsibility of the provincial government and not lie within one of the District Health Authorities (DHAs). Nova Scotia's participation in CTOSS enabled the following: an environmental scan to determine all of the stakeholders in the OTDT community and the current reporting mechanisms for transplantation adverse events; a survey of physicians, dentists, and hospital administrators around their knowledge of Health Canada's *Safety of Human Cells, Tissues, and Organs for Transplantation Regulations;* the establishment of a Cells, Tissues, and Organs Advisory Group, consisting of experts in the OTDT field in Nova Scotia; identification of tissues imported for surgical use; development of a mechanism for the Regional Tissue Bank (RTB) to report adverse events to the NSPBCP; a survey of the dental community to determine allograft usage in the dental setting; and the development of a provincial policy for adverse event reporting.

The RTB is a source establishment for human allograft tissues located in Nova Scotia. This organization distributes tissues to multiple transplant centres across Canada. At the inception of the pilot, transplantation adverse event reporting elements such as a surgical surveillance reporting form and reporting procedures had been developed by the RTB as part of its legislative and accreditation requirements. In addition to tissues from the RTB, some of the DHAs are known to import surgical allografts from other source establishments both within and external to Canada.

III. DATA COLLECTION AND METHODS

3.1 Data Sources

Currently, there are 5 CTOSS (tissue component) pilot sites across Canada shown in Map 1.



Map 1: Geographical Distribution of CTOSS Pilot Sites (Tissue Component) in Canada

Methodology

3.1 The mechanisms used to gather transplantation adverse event reporting are varied amongst the participating CTOSS pilot sites, and are described as follows:

3.1.1 Alberta

Within Alberta Health Services, the Comprehensive Tissue Centre (CTC) coordinates tissue transplantation for the northern part of the province. A paper-based Postoperative Surveillance form is sent to the transplanting physician 90 days post-transplantation. Between July and December 2012, a total of 1,611 surveillance forms (representing over 2,000 tissues transplanted) were sent to treating surgeons for completion. Of the 1,611 forms sent, 1,299 were returned to the CTC, with an average compliance rate of approximately 81%. The average turnaround time was 24 days. The next steps are to include the surveillance of imported tissue other than those originating from the CTC as well as to expand to a new focus on organ surveillance.

Although there have only been a few transplantation adverse events reported, the reporting pathway is described as follows: At 90 days post-transplant, the CTOSS Coordinator sends out a "post-operative tissue surgical surveillance form" to the treating surgeon. The surgeon completes the form and sends it back to the Comprehensive Tissue Centre. If the nature of the transplantation adverse reaction was particularly unusual or if it was deemed reportable to Health Canada, the surgeon notifies the CTC directly and the CTC then investigates and determines if the event is reportable to Health Canada. The CTOSS Coordinator (also a Quality Assurance Coordinator) and the Medical Director at the CTC would undertake an investigation and gather the required details for report completion.

3.1.2 Sunnybrook Hospital

The Blood and Tissue Bank at Sunnybrook Health Sciences Centre is unique in that it was not only a blood bank to receive, test and dispense various blood products supplied by Canadian Blood Services, but was also a source establishment for femoral heads and allograft skin. Their tissue activities include electronically receiving, tracking, storing and dispensing minimally manipulated tissue products as well as altered tissue and xenografts. If an adverse event were to be reported from the treating physicians or surgeons, the Blood and Tissue Bank could determine in minutes if they were in possession of any other products from the same donors and those kinds of products would be immediately quarantined.

A retrospective chart audit of 445 transplanted skin allografts from December 2002 to December 2011 has been completed. The audit did not identify any "missed reporting" of an adverse tissue event. Further retrospective audits are planned and tissue recipients continue to be provided monthly to the hospital's Infection Prevention and Control departmental database where infection can be linked to tissue transplant. This further enhances the ability to ensure missed reporting does not go undetected.

3.1.3 Quebec

The Ministry of Health and Social Services in Quebec was responsible for leading the CTOSS pilot project. The initial activities focused on corneal graft and other eye tissues and were carried out by the National Eye Bank Quebec Branch and the Eye Bank of Quebec at Montreal. A five year retrospective chart review was conducted among 730 ocular tissue recipients in 2008-2009. This pilot study was to identify the most common adverse events related to ocular tissue transplants as well as to evaluate the potential causal link with the grafts. Héma-Québec was in charge of the surveillance of adverse events related to tissue transplants in Quebec. There are several factors which influence adverse event reporting in Quebec. The main factors are the following: 1) the type of tissue; 2) the astuteness of the physician in recognizing the clinical signs of a transplantation adverse event; and 3) once a potential tissue-related adverse event is recognized, physicians may not know where and how to report the event.

3.1.4 New Brunswick

The New Brunswick Department of Health offered their expertise and resources to help in standardizing the surveillance system for the reporting of tissue transplantation adverse events.

Prior to New Brunswick joining as a participating CTOSS pilot site, the National CTOSS Data Working Group had already established definitions of tissue transplantation adverse events, data elements and associated tissue adverse event reporting form. The New Brunswick site committed to test and consolidate the tissue component of the CTOSS surveillance system.

From 2010 to March 31 of 2013, the Office of the Chief Medical Officer of Health (OCMOH) led the New Brunswick CTOSS pilot project along with a designed project manager and coordinator. The main partners were The New Brunswick Eye and Tissue Bank and Hospital Services of the Department of Health.

New Brunswick contributed its comments and feedback regarding the CTOSS adverse event reporting form and the CTOSS user guide. They also delivered quarterly denominator data reports to the Agency. Educational materials for health care professionals in both English and French were designed and distributed.

After April 2013, Horizon Health Network was designated to lead the CTOSS pilot project in New Brunswick and to ensure regular reporting of adverse events and denominator data.

3.1.5 Nova Scotia

In Nova Scotia, the NSPBCP works directly with the Regional Tissue Bank (RTB) to obtain denominator and adverse event data. This collaboration results in an approximate capture rate of 70% of all tissues transplanted in Nova Scotia's hospitals. This capture does not include any allografts imported by the individual hospital sites, or any allografts transplanted at any private medical or dental clinics. The RTB has a comprehensive recipient tracking system in place which includes a surgical surveillance form with every allograft distributed and a second surgical surveillance form mailed to the transplanting surgeons at approximately 60 days post-transplant. The RTB has achieved a compliance rate of 95% with this program. This program allows the surgeons to quickly report any suspected events associated with the transplanted allograft and allows the RTB to conduct investigations in a timely manner.

For in-patients, if the treating physician or surgeon suspects a transplantation adverse event, the event is reported to the source establishment*. After receiving the suspected transplantation adverse event report, the Regional Tissue Bank will initiate a case investigation with the assistance of the transplanting surgeon. If the severity of the transplantation adverse event is deemed to be significant and reportable, the tissue establishment then fulfills the obligation to report to Health Canada. For out-patients, the patient can call either his/her family doctor's office or transplanting surgeon's office and report the symptoms. The patient may be subsequently directed to present to the appropriate medical office or to the Emergency Room for assessment.

The NSPBCP has to date, under the advisement of Nova Scotia's Cells, Tissues, and Organs Advisory Group (CTOSSAG), focused on the development of a provincial policy for reporting adverse events associated with cell, tissue, and organ transplants. Once implemented, this policy will require all hospitals in the province to report to the DHW annually regarding their compliance with adverse event reporting requirements, both provincially and federally.

Note: For grading of severity related to the adverse event, the spectrum of nil, non-serious, serious, life-threatening and death were defined and applied to the case report. The grading system for imputability was applied to assess the probability that an adverse reaction or event in a recipient may be attributed to the process of donation or clinical application of the tissues applied.

Data definitions for the tissue component of CTOSS were developed in conjunction with definitions from Eustite (European Union Standards and Training in the Inspection of Tissue Establishments) and the Transplantation Transmission Sentinel Network (TTSN) under development by the U.S. Centre for Disease Control.

IV. ANALYSIS, RESULTS AND DISCUSSION

Analysis

Data received from the sites were compiled into a MS Excel data base which were maintained in the SED Division and exported to SAS Enterprise (Version 5.1) for further analysis. Descriptive analyses of the data were conducted, including numbers of tissue transplanted, number of tissue adverse events and incidence rate (%) of specific tissue. For the purpose of this analysis, only adverse events occurring during April 1, 2011 to December 31, 2013 were included.

Results

The detection of tissue-related adverse events depended upon both the level of knowledge of surgeons and physicians in identifying possible tissue-related adverse events, and knowledge of appropriate reporting mechanisms. During the 3 years of data collection, a total of 8 tissue-related adverse events were reported to the Agency and their provincial distribution is noted in Table 1.

Table 1 Overview of tissue transplantation adverse events reported by CTOSS sites from April 2011 to December 2013

Year	Site 1	Site 2	Site 3	Site 4	Site 5
2011	0	0	0	0	1
2012	4	0	1	0	0
2013	1	0	1	0	0
Total	5	0	2	0	1

* Source establishment – (in the case of tissues) - an establishment regulated by Health Canada that is responsible for the processing of safe tissues for transplantation.

At the Alberta pilot project, there were a total of 5 corneal tissue transplantation adverse events (TAEs) reported to Public Health Agency of Canada since April 1, 2011. A description is included to provide additional context to the cases reported. The first Alberta case involved a fungal and bacterial infection believed to have resulted from contamination after harvesting. The source of contamination could not be determined. It was classified as severe with a major consequence as the outcome. The second Alberta case involved primary graft failure resulting from right eye endophthalmitis associated with poor follow up procedures. The outcome was enucleation and ball implant. The third Alberta case is characterized by diffuse endothelial rejection “pump failure” due to unknown etiology. The severity was classified as non-severe with minor/no consequence. The fourth Alberta case involved endothelial rejection due to unknown etiology. This case is referenced to the previous one by virtue of the fact that both the left and right corneas were transplanted from the same donor, and both failed to function. The severity was classified as non-severe with minor/no consequences. The fifth Alberta case also involved graft failure from poor function of endothelial graft cells due to unknown etiology. The severity was classified as non-severe with minor/no consequence.

At the Quebec pilot project, one cardiovascular tissue-related serious adverse event was reported in 2012. The incident involved the transplantation of a sub-optimal cardiac valve which was transplanted on the basis of the condition of the patient. The event resulted in significant aortic valve insufficiency (persistent incapacity) and its severity was graded as “serious”. In this case, the patient survived but suffered significant blood-supply inefficiency. In 2013, a corneal adverse event involving contamination (*E. faecalis)* was reported. The donor was positive and the same bacteria was found in the preservative solution.

At the Nova Scotia pilot project, only one corneal TAE was reported. This incident was observed in a patient who had received a cornea transplant in 2011. Following the transplant, the patient developed corneal failure. The underlining cause was unknown and the patient subsequently received a second cornea.

Overall, most surveillance sites delivered complete TAE reports and annual reports. It generally took 3-6 months for the site and tissue establishment to conduct a complete investigation of a suspected transplantation adverse event. There were several factors which affected the reporting of TAEs including: the expertise and experience of the treating physician in the detection of TAEs in recipients, the effectiveness of coordination between procurement organizations and the hospitals as well as the workload of the coordinators.

Discussion

Most of the foundational pieces for the CTOSS (tissue component) such as the surveillance framework, the program charter, tissue transplantation adverse event reporting form, instruction manual and the minimum data elements have been built. Due to the complexity of the transplantation environment and the diversity of stakeholders involved, it is not uncommon for a system of this type to take time to be developed. However, now that the building blocks are in place and the tissue component is functioning and collecting data, it is now time to turn attention to the cell and organ component. The Agency will be looking to partner with existing and other potential sites to develop both the cell and organ components.

The results of the first 3 years of data collection are similar to when the Transfusion Transmitted Injuries Surveillance System (TTISS) first began and reports increased over time as health professionals became more familiar with reporting and awareness of transfusion adverse events.

Data collected to date demonstrate the tissue pilot sites' commitment to this project and the ongoing awareness being raised in CTOSS at the hospital levels for health professionals to report Transplantation Adverse Events.

V. IDENTIFIED CHALLENGES IN THE ONGOING ADVANCEMENT OF CTOSS

From the outset, it has been identified that the CTOSS has significant complexity brought about by the range of stakeholders and their independence from each other, the inherent differences between the cell, tissue and organ communities, the variance in maturity of existing cell, tissue and organ transplantation surveillance systems in Canada, and the variety of information systems in place in stakeholder locations which are not well-integrated.

Delayed transplantation adverse events can take place long after a patient has been discharged from a transplant hospital, often in a community or province at a distance from the surgical centre providing the transplant procedure. Follow-up of patients may be undertaken by a family physician or health care team without specific expertise in the identification of adverse events, and the means by which to report same to the appropriate sources. For this reason, under-reporting of transplantation adverse events is generally suspected. Subsequently, pilot site projects have included educational efforts targeted to health care professionals in order to create clarity around reporting requirements.

VI. FUTURE CONSIDERATIONS

An examination of the possibility of expansion of tissue pilot sites is required to ascertain the feasibility of increasing the quantity of transplantation adverse event data potentially available for aggregation and analysis in order to advance the notion of a more representative national picture.

When the initial tissue adverse event surveillance products have been made available, it will be important to undertake an evaluation of the accessibility and utility of the information products. Novel approaches such as the development of a mobile application to easily access data on transplantation adverse events, may be useful for surgeons and patients in terms of accessing important data to support informed consent when considering transplantation surgery.

Respecting the organ component, a National Data Working Group for Organs will be established in order to provide direction to the project. Key detailed decisions are required in terms of the specific organ(s) for inclusion, the identification of associated data elements and definitions, as well as agreements with organ pilot sites for transmission of data.

The next priority for the CTOSS program is the establishment of the organ component and the cell component development will follow. For the final component (cell), it may not be as difficult to develop as the cells are sequestered within the blood banks prior to transplantation and follow the same rigorous regimes as the blood bank does for transfusion.

APPENDIX A – REPORTING FORM

Case ID: _____

CANADIAN TRANSPLANTATION ADVERSE EVENT (TAE)
REPORTING FORM FOR TISSUES

PAGE 1 OF 4

1. RECIPIENT IDENTIFICATION

LAST NAME / FIRST NAME	Date of Birth: Day / Month / Year
HEALTH CARD NUMBER / HOSPITAL CARD NUMBER	Sex: ☐ MALE ☐ FEMALE ☐ UNKNOWN
PROVINCE/TERRITORY OF RESIDENCE	

2. GENERAL INFORMATION

Transplanting/Implanting Facility	Source Establishment
NAME	NAME
ADDRESS	ADDRESS
CITY / PROVINCE	CITY / PROVINCE
NAME OF TRANSPLANTING/IMPLANTING PHYSICIAN	CONTACT PERSON
TELEPHONE / FAX	HC REGISTRATION #
EMAIL	NOTIFIED: ☐ YES ☐ NO DATE: Day / Month / Year
REPORTER	ADDITIONAL SOURCE ESTABLISHMENT (IF APPLICABLE)
☐ SAME AS ABOVE IF DIFFERENT, PLEASE SPECIFY BELOW:	NAME
NAME OF REPORTER	ADDRESS
ADDRESS	CITY / PROVINCE
CITY / PROVINCE	CONTACT PERSON
TELEPHONE / FAX	HC REGISTRATION #
EMAIL	NOTIFIED: ☐ YES ☐ NO DATE: Day / Month / Year

3. DATE AND LOCATION OF THE TAE

DATE OCCURRED:	Day	Month	Year	DATE REPORTED:	Day	Month	Year

LOCATION WHERE THE TAE WAS RECOGNIZED:

- ☐ HOSPITAL WHERE GRAFT TRANSPLATED/IMPLANTED;
- ☐ OTHER FACILITY, E.G. WALK-IN CLINIC, HOME _____
- ☐ OTHER HOSPITAL;
- ☐ MEDICAL OFFICE OF PHYSICIAN/SURGEON WHO PERFORMED TRANSPLANTATION/IMPLANTATION
- ☐ MEDICAL OFFICE OF OTHER PHYSICIAN WHO RECOGNIZED THE TAE.

4. SUSPECTED TRANSPLANTED/IMPLANTED TISSUE(S)

(NOTE: PRE AND POST TRANSPLANT/IMPLANT CULTURE DATE AND RESULT IS TO BE COMPLETED BY SOURCE ESTABLISHMENTS ONLY)

TISSUE TYPE	PRODUCT CODE	SUPPLIER NAME	DONOR ID CODE	EXPIRY DATE	QUANTITY TRANSPLANTED	DATE OF TRANSPLANT/ IMPLANT	PRE-TRANSPLANT/ IMPLANT CULTURE DATE AND RESULT	POST-TRANSPLANT/ IMPLANT CULTURE DATE AND RESULT
				Day / Month / Year		Day / Month / Year	Day / Month / Year	Day / Month / Year
				Day / Month / Year		Day / Month / Year	Day / Month / Year	Day / Month / Year
				Day / Month / Year		Day / Month / Year	Day / Month / Year	Day / Month / Year
				Day / Month / Year		Day / Month / Year	Day / Month / Year	Day / Month / Year

COMMENTS (INCLUDING TYPE OF PATHOGEN AND COLONY COUNT):

Public Health Agency of Canada / Agence de santé publique du Canada

Canada

Case ID: _____

CANADIAN TRANSPLANTATION ADVERSE EVENT (TAE)
REPORTING FORM FOR TISSUES

5. CLINICAL HISTORY

TYPE OF GRAFT: ☐ MUSCULOSKELETAL ☐ OCULAR ☐ CARDIAC ☐ VASCULAR ☐ SKIN ☐ OTHER: _____

ANTIBIOTIC PROPHYLAXIS: ☐ YES ☐ NO
DESCRIBE:

UNDERLYING DIAGNOSIS/INDICATION FOR TRANSPLANT/IMPLANT:
DESCRIBE:

CONCOMITANT MEDICATION:

DESCRIBE THE PROCEDURE PERFORMED:

IMMUNE COMPROMISED: ☐ YES ☐ NO
IF YES, DESCRIBE:

ADDITIONAL COMMENTS:

OTHER CLINICAL HISTORY: ☐ YES ☐ NO

6. CLINICAL SIGNS

CLINCAL SIGNS AND SYMPTOMS:

☐ FEVER (Describe): _____
☐ CHILLS/RIGORS
☐ URTICARIA
☐ OTHER SKIN RASH
☐ SHOCK
☐ WOUND REDNESS/SWELLING
☐ PUS
☐ PAIN (Location): _____
☐ DEHISCENCE
☐ DEATH
☐ OTHER (Describe): _____

6A. RELEVANT TESTS/LABRATORY RESULTS

LABORATORY TEST	DATE SPECIMEN TAKEN DAY	MONTH	YEAR	RESULTS NORMAL	ABNORMAL	DETAILS
				☐	☐	
				☐	☐	
				☐	☐	
				☐	☐	
				☐	☐	
				NEGATIVE	POSITIVE	
BLOOD CLUTURE				☐	☐	
WOUND CULTURE (POST-TRANSPLANT)				☐	☐	

X-RAY RESULTS:

COMMENTS:

6B. DESCRIPTION OF TAE AND ACTION TAKEN

DESCRIBE:

Case ID: _____

CANADIAN TRANSPLANTATION ADVERSE EVENT (TAE)
REPORTING FORM FOR TISSUES

7. DIAGNOSIS OF TAE

INFECTION

☐ NOT APPLICABLE

BACTERIAL: _____

VIRAL: _____

FUNGAL: _____

OTHER: _____

TISSUE SPECIFIC EVENTS

☐ NOT APPLICABLE

OCULAR	CARDIAC	MUSCULOSKELETAL
☐ PRIMARY GRAFT FAILURE	☐ VALVE THROMBOSIS	☐ OSTEOLYSIS
☐ ENDOTHELIAL REJECTION	☐ VALVE FAILURE	☐ FRACTURE
☐ DISLODGING OF GRAFT	☐ ENDOCARDITIS	☐ NON-UNION
☐ OTHER:	☐ OTHER:	☐ OTHER:

OTHER TAE

☐ NOT APPLICABLE

☐ ALLERGIC REACTION

☐ MALIGNANCY: _____

☐ AT SITE OF TRANSPLANT

☐ AT REMOTE SITE: _____

☐ OTHER:

COMMENTS:

7A. SEVERITY OF TAE

☐ GRADE 1 (NON-SEVERE) ☐ GRADE 2 (SEVERE) ☐ GRADE 3 (LIFE THREATENING) ☐ DEATH ☐ NOT DETERMINED

DID THE TAE RESULT IN HOSPITALIZATION OR THE PROLONGATION OF HOSPITALIZATION? ☐ YES ☐ NO

NUMBER OF EXTRA DAYS: _____

DID THE TAE REQUIRE REMOVAL OF IMPLANT? ☐ YES ☐ NO

7B. IMPUTABILITY

☐ DEFINITE ☐ PROBABLE ☐ POSSIBLE ☐ DOUBTFUL ☐ RULED OUT ☐ NOT DETERMINED

ARE THERE ANY TAE IN OTHER RECIPIENTS RESULTING FROM IMPLICATED DONOR(S)?

☐ YES ... Please specify: _____

☐ NO

☐ UNKNOWN

7C. OUTCOME

☐ MINOR/NO CONSEQUENCE ☐ MAJOR CONSEQUENCE ☐ DEATH ☐ NOT DETERMINED

IF DEATH OCCURRED, DESCRIBE THE CIRCUMSTANCES RELATED TO THE DEATH:

IMPUTABILITY OF DEATH:

☐ DEFINITE ☐ PROBABLE ☐ POSSIBLE ☐ DOUBTFUL ☐ RULED OUT ☐ NOT DETERMINED

7D. STATUS OF INVESTIGATION

INVESTIGATION BY:

☐ SOURCE ESTABLISHMENT ☐ TRANSPLANTATION/IMPLANTATION FACILITY ☐ OTHER

☐ IN PROGRESS ☐ CONCLUDED (please specify): _____

☐ CANNOT BE CONDUCTED, REASON _____

DATE: ____ ____ ____ (Day Month Year)

SIGNATURE: _____

Case ID: _____

CANADIAN TRANSPLANTATION ADVERSE EVENT (TAE)
REPORTING FORM FOR TISSUES

DATE REPORT RECEIVED: Day Month Year

DATE INVESTIGATION INITIATED: Day Month Year

HOSPITAL REPORTING PERSON:

SIGNATURE:

TELEPHONE NUMBER:

DATE AND TIME: Day Month Year Time (hh:mm)

9. CONCLUSION (TO BE COMPLETED BY SOURCE ESTABLISHMENT, OR IN THE CASE OF IMPORT TISSUES, SUPPLIER)

DATE REPORT RECEIVED: Day Month Year

DATE INVESTIGATION INITIATED: Day Month Year

MEDICAL DIRECTOR OR DESIGNATE:

SIGNATURE:

TELEPHONE NUMBER:

DATE AND TIME: Day Month Year Time (hh:mm)

APPENDIX B – MINIMUM DATA ELEMENTS

Public Health Agency of Canada / Agence de la santé publique du Canada

MINIMUM DATA ELEMENTS
FOR REPORTING OF TRANSPLANTATION ADVERSE EVENTS (TAE) TO THE SURVEILLANCE AND EPIDEMIOLOGY DIVISION,
CENTRE FOR COMMUNICABLE DISEASES AND INFECTION CONTROL (CCDIC),
Public Health Agency of Canada (Agency)

Version 9, June 2014

The data elements listed below will be transferred to the Surveillance and Epidemiology Division, Public Health Agency of Canada for concluded investigations only on the following dates each year:

Date of Transfer	For Concluded Investigations
April 1	October 1 – December 31
July 1 *	January 1 – March 31
October 1	April 1 – June 30
January 1	July 1 – September 30

* Note: Data transferred to the Surveillance and Epidemiology Division, Public Health Agency of Canada on July 1 will include the denominator data for the previous calendar year (January 1 to December 31).

DATA ELEMENTS TRANSFERRED:

Case ID

Section 1: RECIPIENT IDENTIFICATION
Date of birth (month and year)
Sex
Province/Territory of residence

Section 2: GENERAL INFORMATION
Transplanting/implanting facility
Name
City
Province
Source establishment name
Source establishment address, City, Province
Source establishment contact person
HC registration #
Notified; yes; no
Date (day, month and year)
Additional Source establishment (if applicable) name
Additional Source establishment address, City, Province
Additional Source establishment contact person
HC registration #
Notified; yes; no
Date (day, month and year)

Section 3: DATE AND LOCATION OF IDENTIFICATION OF THE TAE
Date occurred (dd/mm/yyyy)
Date reported (dd/mm/yyyy)
Location where TAE was recognized

Section 4: SUSPECTED TRANSPLANTED/IMPLANTED TISSUE (S)
Tissue type
Product code
Supplier name
Donor ID code
Expiry date
Quantity transplanted
Date of transplant/implant (dd/mm/yyyy)
Pre-transplant/implant culture date (dd/mm/yyyy)
Indicate whether result negative or positive
Post-transplant/implant culture date (dd/mm/yyyy)
Indicate whether result negative or positive
Comments (including type of pathogen and colony count)
Additional suspected products

Section 5: Clinical history
Type of graft e.g. musculoskeletal, ocular, skeletal etc.
Underlying diagnosis/indications for transplant/implant
Describe procedure performed
Other clinical history-describe
Status of any antibiotic prophylaxis; yes/no and provide description
Concomitant medication
Immune compromised status; yes/no; If yes, describe
Additional Comments

Section 6: Clinical signs and symptoms
An indication of clinical signs and symptoms post-transplant:

Fever (if indicated, please provide the temperature value post-transplant)
Chills/rigors
Urticaria
Other skin rash
Shock
Wound redness/swelling
Pus
Pain (describe location)
Dehiscence
Death
Other (describe)

Section 6 A. RELEVANT TESTS/LABORATORY RESULTS

Name of Laboratory Tests
Date of laboratory test or date when specimen taken (dd/mm/yyyy)
Results (normal or abnormal) - provide details
Blood Culture Results:
For culture performed on **recipient** post transplantation:
- Date/Specimen Taken
- Results (negative or positive) - provide details such as organism (s) identified (genus/species), # negative

Wound Culture Results (post-transplant):
For culture performed on **recipient** post transplantation:
- Date/Specimen Taken
- Results (negative or positive) - provide details such as organism (s) identified (genus/species), # Negative – please provide colony count if available

X-ray results
Comments
Additional laboratory results

Section 6B. DESCRIPTION OF TAE AND ACTIONS TAKEN

A full description of the TAE and all actions taken related to the TAE
Indication of whether Health Canada was notified as a 'yes' or 'no' response
If 'yes', an indication of date of notification (dd/mm/yyyy)

SECTION 7. DIAGNOSIS OF TAE

An indication of whether TAE was an infection-If not, indicate not applicable
Type of TAE infection e.g. bacterial, viral etc. –If not, indicate not applicable; provide description
An indication of the TAE tissue specific event (s) e.g. ocular, cardiac, musculoskeletal.
Indication of the type of TAE from the list provided under Ocular, cardiac, or musculoskeletal.
If not, indicate not applicable.
An indication of 'other' TAEs e.g. allergic reactions, malignancies etc.
If not, indicate not applicable.
Specify type of allergic reaction ('minor', 'severe/anaphylactic/anaphylactoid', or 'anaphylactic shock') as applicable.
An indication of whether the malignancy occurred at the site of the transplantation/implantation or at a remote site. If at remote site, specify location.
Comments

SECTION 7A. SEVERITY OF TAE

THE EXTENT OF THE ADVERSE EVENT DUE TO THE TRANSPLANT/IMPLANT:
- Grade 1 (Non-Severe)
- Grade 2 (Severe)
- Grade 3 (Life-Threatening)
- Grade 4 (Death) - Describe the circumstances of death
- Not Determined

Indication of whether the TAE caused hospitalization and the number of extra days of hospitalization due to the TAE
Indication of whether the TAE resulted in removal of the transplant/implant; yes or no

SECTION 7B. IMPUTABILITY

Relationship of the adverse event to the transplant/implant:
- Definite
- Probable

Possible
Doubtful
Ruled Out
Not Determined

Are there other TAEs in other recipients due to the implicated donor (s)?
yes, no, or unknown; please specify

SECTION 7C. OUTCOME

OUTCOME OF THE TAE:
MINOR (NO) CONSEQUENCE
MAJOR CONSEQUENCE
DEATH
NOT DETERMINED
IF DEATH OCCURRED, A DESCRIPTION OF THE CIRCUMSTANCES RELATED TO THE DEATH
IMPUTABILITY OF DEATH (RELATIONSHIP OF DEATH TO TRANSPLANTATION/IMPLANTATION):
Definite
Probable
Possible
Doubtful
Ruled Out
Not Determined

SECTION 7D. STATUS OF THE INVESTIGATION

INDICATION ON WHO CONDUCTED THE INVESTIGATION E.G. SOURCE ESTABLISHMENT, TRANSPLANTATION/IMPLANTATION FACILITY ETC.
INDICATION OF IF THE INVESTIGATION IS IN PROGRESS OR CONCLUDED PLEASE SPECIFY
INDICATION OF IF THE INVESTIGATION CANNOT BE CONDUCTED AND A DETAILED REASON
DATE (DD/MM/YYYY)
SIGNATURE (YES/NO)

SECTION 8. CONCLUSION (TO BE COMPLETED BY THE HOSPITAL WHERE THE TRANSPLANTATION/IMPLANTATION OCCURRED OR WHERE THE TAE WAS TREATED)

Date when TAE report received
Date when TAE investigation initiated
Free text space for further details with any patient, donor, health care worker or hospital identifiers removed

SECTION 9. CONCLUSION (TO BE COMPLETED BY SOURCE ESTABLISHMENT, OR IN THE CASE OF IMPORT TISSUES, SUPPLIER)

Date when TAE report received
Date when TAE investigation initiated
Free text space for further details with any patient, donor, health care worker or hospital identifiers removed

TRANSPLANTATION ADVERSE EVENT (TAE) NUMERATOR DATA AND DENOMINATOR DATA:

Numerator: Total number of each of amniotic membrane, cardiac, fascia, ocular, skin, structural bone, surgical bone (chips/ground) and tendon transplantation adverse events reported within reporting site/ jurisdiction by quarter, regardless of severity.

Denominator: Total number of each of amniotic membrane, cardiac, fascia, ocular, skin, structural bone, surgical bone (chips/ground) and tendon allografts transplanted/implanted within reporting site/ jurisdiction by quarter.

This agreement is between the Provinces/Territories/Hospital sites participating in the Tissues and Organs Surveillance System (CTOSS), and the Surveillance and Epidemiology Division, Public Health Agency of Canada. The intent of this agreement is to transfer data as detailed in the document.
I agree to the Minimum Data Elements for Reporting of Transplantation Adverse Events to the Surveillance and Epidemiology Division, Public Health Agency of Canada,

_____ _____
Signature **Date**
Provincial/Territorial Authoritative Representative with address

_____ _____
Signature **Date**
Cindy Hyson, RN, BScN, CON, MN
A/Associate Director, Surveillance and Epidemiology/Directrice de la surveillance et de l'épidémiologie déléguée intérimaire,
Public Health Agency of Canada
100 Eglantine Driveway, Tunney's Pasture AL0603B
Ottawa, ON K1A 0K9