Status of Transfusion and Transplantation safety

Canadian experience

Advisory Committee on Blood Safety and Availability (ACBSA)
Washington, DC, May 11 2007

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« What is the current state of safety in transfusion and transplantation ? »

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Blood and blood products

1. Two transfusion agencies:
   - Héma-Québec (Pop: 7.6 millions)
   - Canadian Blood Services (Pop: 25.8 millions)
2. Standards and regulations
3. Licencing requirements (incl. audits)
4. Surveillance through TTISS and Québec hemovigilance system
5. Risk management structure (CBS and HQ)
6. Incidence and prevalence of TTDs in Canada (<= U.S.)
7. Blood is safe

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Cells, Tissues & Organs

Standards & regulations

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The role of Health Canada

- Health Canada: Federal department of health
- Regulatory role (Drugs & Health Products):
    - Biologics, Radiopharmaceuticals and Genetic Therapies
    - Blood and blood products,
    - **Cells, tissues and organs**,
    - Gene therapies,
    - Viral and bacterial vaccines,
    - Etc.

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Canadian Standards for Cells, Tissues and Organs

- In 2000: Health Canada contracted the Canadian Standards Association (CSA)
- Group of experts drafted standards in the following areas:
  - Cells, Tissues, and Organs for Transplantation and Assisted Reproduction: General Requirements
    (CAN/CSA Z900.1-03)
  - Tissues for Transplantation
    (CAN/CSA Z900.2.2-03)
  - …And others for organs, cells, ocular tissues, assisted reproduction
- First publication in June 2003
- CSA standards are voluntary
- CSA standards for tissues are very similar to AATB standards

Health Canada and Human Tissue Regulations

- In January 2003, issuance by HC of:
  - Directive: *Technical Requirements to Address the Safety of Human Cells, Tissues and Organs for Transplantation*
  - Guidance document: *Basic Safety Requirements for Human Cells, Tissues and Organs for Transplantation.*

  What is covered by these documents: Donor screening, donor testing, CTO retrieval/collection, processing, preservation, packaging and labeling, storage, quarantine, record keeping, importation, distribution, transplantation, adverse reaction monitoring and error and accident reporting, investigation and recall

  Replicate of CSA Standards

Health Canada and Human Tissue Regulations

- Interim phase: National review
  - Started March 2003
  - Documentation stage
    - CTO's asked to provide information on their level of compliance with the directive (checklist format)
  - Compliance monitoring stage (audits)
    - Mostly targeted on Donor qualification
    - First « round » is completed (except organ programs)
    - Only within Canada

Health Canada and Human Tissue Regulations

Regulatory framework - Phase I

- Scope: activities falling under HC's authority:
  - Donor screening
  - Donor testing
  - Collection/retrieval
  - Processing
  - Preservation
  - Packaging
  - Labeling
  - Storage
  - Quarantine
  - Record keeping
  - Distribution
  - **Importation**
  - Error, accident and adverse reaction monitoring and reporting
  - Investigation and recall
- Draft regulations: Direct reference to specific sections of the standards (« Standard-based regulations »)
- Some requirements are separately defined in the regulations (e.g. adverse reaction reporting to HC)
- Several sections of the CSA standards are not referenced in the regulations

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Health Canada and Human Tissue Regulations

Regulatory framework - Phase I

- **Registration mechanism** for establishments that handle, process, **import** and **distribute** human CTOs

  Canadian establishments can only use cells and tissues from source establishments registered with Health Canada (including foreign providers).

  Registration form contains a certification of compliance with the CTO Regulations that must be signed by the medical or scientific director.

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Health Canada and Human Tissue Regulations

Regulatory framework - Phase I

- **Excluded** from « Phase I » :
  - Cells and tissues that are currently regulated under the Medical Devices Regulations (e.g. **heart valves**, dura mater, **demineralized bone**, wound covering containing human cells)
- Timeline:
  - December 2005: Publication of the proposed regulations
  - 75 day comment period (ended February 23, 2006)
  - Health Canada has reviewed comments
  - Expected publication date: May 2007
  - Compliance date: 6 months after publication

Health Canada and Human Tissue Regulations

Regulatory framework - Phase II

- More comprehensive compliance monitoring and enforcement provisions
- Surveillance and adverse reactions reporting strategies
- **Heart valves** and **dura mater** will fall under CTO regulations.
- Timeline ?

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CTO’s in Canada

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CTO's in Canada

- Organs: Provincial programs
- Tissues:
  - Only a few comprehensive tissue banks
  - Many small surgical bone banks
  - Several eye banks with limited resources
  - All hospital-based (except Héma-Québec)
  - All not-for-profit
  - Only the major banks are accredited by AATB

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Comprehensive Tissue Center (Edmonton)

Statistics (2002):

- 81 cadaveric donors
- 347 living donors

Trillium Gift of Life (Ontario)

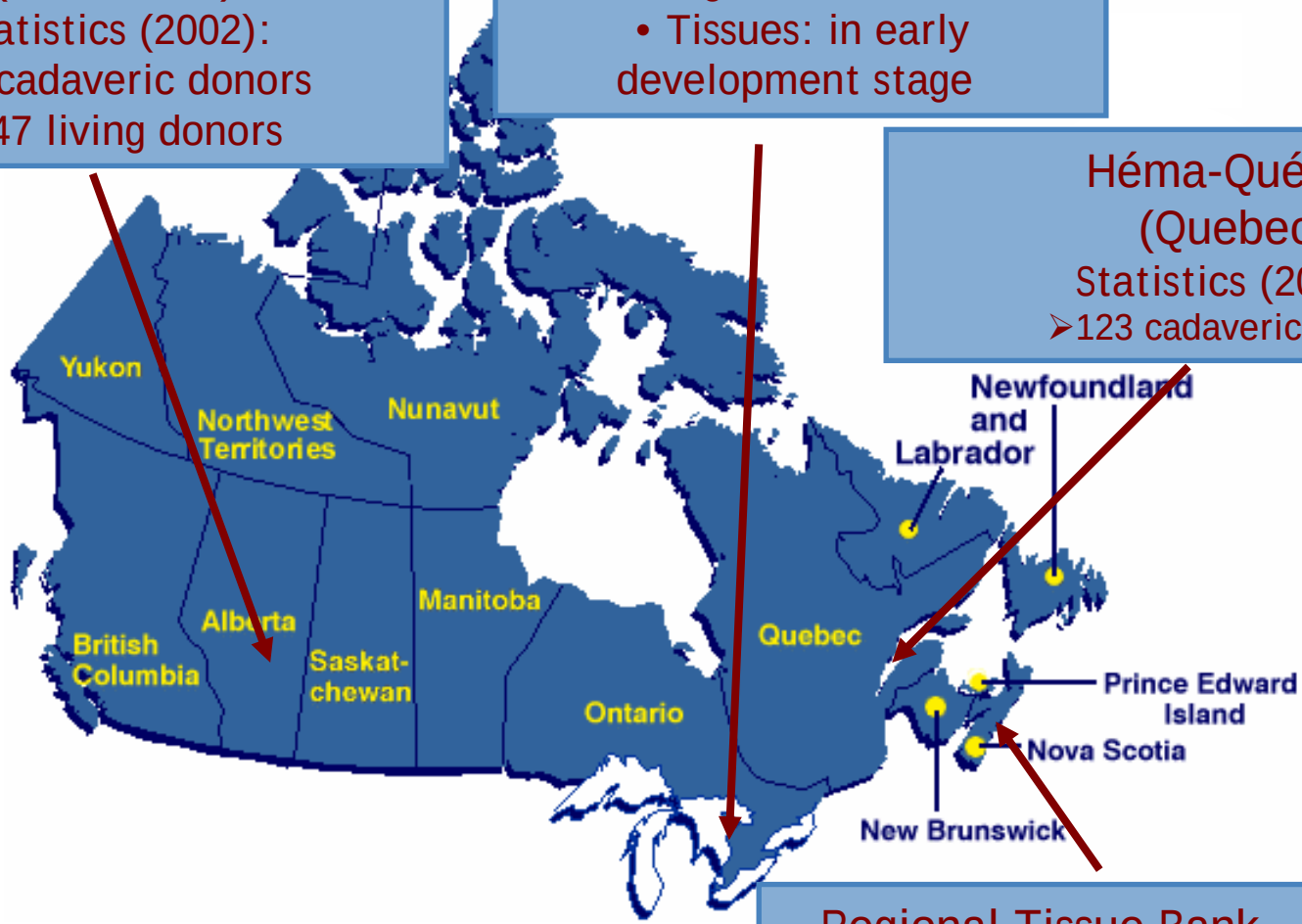
Organ & Tissues

- Tissues: in early development stage

Héma-Québec (Quebec)

Statistics (2006):

- 123 cadaveric donors



Regional Tissue Bank (Halifax)

Statistics (2005):

- 119 cadaveric donors

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Tissue Banking in Canada
- Current challenges -

- Regulatory compliance of smaller tissue banks
- Donor testing / availability of screening tests adapted to CTO donors
- Reliance on U.S. imports
  - Estimated to contribute between **80-90%** of total demand in Canada
- Capacity to manufacture specialized products
  - e.g. freeze-dried bone, demineralized bone, veins
- Capacity to meet full donation potential
- Standardized manufacturing methods
- Traceability
- Surveillance

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Organization of CTO services in Québec

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Québec (Blood, Cells, Tissues, Organs)

- Héma-Québec (Inc. 1998)
  - Blood & Blood products
  - Tissues (since 2001, by decree of the Health Minister)
  - Stem cells:
    - BM donor registry
    - Public cord blood bank
    - Preservation of autologous BM
- Québec-Transplant (O.D.O.):
  - Organs (approx. 140 donors annually)
- Eye banks (2): Hospital-based

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The situation with HumanTissues

- Héma-Québec is the only “multi-tissue” bank in Quebec
- The few remaining hospital-based tissue banks (surgical bone) will likely cease activities
- Still in development phase
- Eye banks will soon join Héma-Québec
- Majority (80%) of MS tissues currently imported from the U.S.

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Cells & Tissues at Héma-Québec: An evolving plan

- **July 2004** : New « GMP » procurement/processing facility for tissues (Quebec City).
- **February 2005:** AATB accreditation (MS tissues).
- **December 2005**: ISO 13485 certification.
- **August 2006**: Medical Device Licence for Allograft Heart valves.
- **May 2007:** Role as exclusive Importer/Distributor (pilot project)

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« What are areas of commonality with blood products, stem cells human tissues and organs ? »

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Why tissues in a Blood Centre?

- Because, Blood, Cells and Tissues have a lot in common:
  - **Quality**
    - Standards, regulations, GMPs
  - **Safety**
    - Donor qualification, testing, lookbacks, tracebacks
  - **Quantity**
  - **Traceability**
    - Record retention, ISBT 128

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Why in a Blood Centre: added advantages

- Human resources available
- Infrastructure present
- Distribution network existant
- Supplier/client relationship established
- Demonstrated ability to qualify external suppliers

Tissues in a Blood Centre: challenges

- Development of new recruitment skills
- Human Resources: development of new technical skills and professionnal expertise
- Safety: bacterial contamination
- Validation
- Infrastructure: Clean rooms
- Customer: development of new relationships

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« Is there scientific/clinical evidence to support a need for a master strategy for transfusion and transplantation safety? »

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Summary: Safety of Blood, Cells, Tissues and Organs in Canada

	Blood	Tissues	Cells	Organs
Standards & regulations				
Donor screening			?	?
Donor testing				
Control of bacterial contamination			?	n/a
Self-sufficiency				
Control of importations			?	?
Traceability			?	?
Surveillance				

Optimal **Needs improvement** **Deficient**

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Public hemovigilance forum
Montreal, April 27, 2007

Safety of Human Tissues in Quebec

- Main talking points:
  - No surveillance system in place (for tissues)
  - Hemovigilance network could include tissues
  - Need to standardize data elements and case definitions for adverse events
  - Traceability within hospitals is unsure
  - Blood banks could serve as central hubs for in-hospital traceability of tissues

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Human Cell & Tissue Banking: Conclusion

- Around the world human cells & tissues have become regulatory products with specifications quite similar to that of blood products;
- Expertise and culture already exist or need minor improvement in Blood Centres to tackle this new challenge;
- Blood components are mature regulatory products and CTOs are in early regulatory mode;
- This opportunity has to be taken in the best interest of the patient.

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QUESTIONS ?

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