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The Technical Aspects of Pathogen Testing in Canada

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Conflict of Interest Disclosures
Nancy Angus

- I have not had, in the past 5 years, a financial interest, arrangement or affiliation with one or more organizations that could be perceived as a direct or indirect conflict of interest in the content of this presentation.

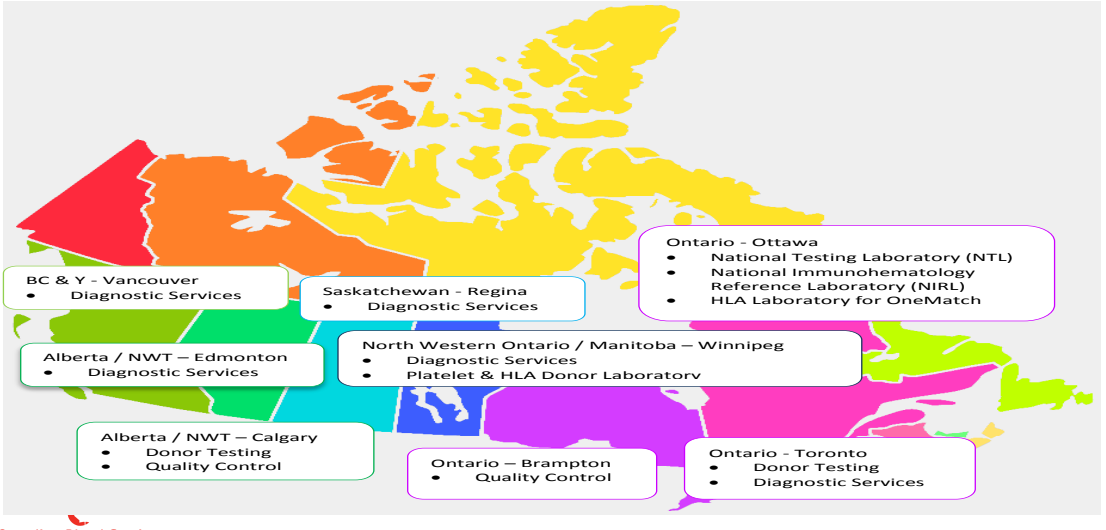
Outline

- Overview of Canadian Blood Services Testing
- Laboratory tests currently in use by blood operators, and in particular by Canadian Blood Services, for the detection of blood-borne pathogens
- Summarize the differences in sensitivity of the currently laboratory tests for blood-borne pathogens
- Long term horizon for Transmissible Diseases testing at Canadian Blood Services
- CBS planning to implement a new test

Over View of Testing at Canadian Blood Services

Overview of Testing at Canadian Blood Services

Testing Sites



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Testing at Canadian Blood Services

- Effective July 2014, all Testing service moved into one management structure reporting into Ian Mumford, Chief Supply Chain Officer and indirect accountability to Dana Devine, Chief Medical and Scientific Officer
- This included the following testing sites:
  - Donor Testing (Calgary and Toronto)
  - Diagnostic Services (BC/Y, Edmonton, Regina, Winnipeg and Toronto)
  - National Testing Laboratory(Ottawa)
  - National Reference Laboratories (Red Cell –Ottawa, Platelet/HLA –Winnipeg)
  - QC Product Laboratories (Toronto and Calgary)
  - HLA laboratory (Stem Cell and Cord – Ottawa)

Testing at Canadian Blood Services

Moving towards one management structure for all the laboratories at Canadian Blood Services would provide many benefits. These benefits include the following:

- Aligning of medical and technical expertise that are in low supply
- Making better use of expensive equipment and information systems
- Greater standardization in laboratory best practise
- Creates a work environment that facilitates recruitment, retention and mentorship of staff
- Opportunity for staff to learn new skills

Regional Donor Testing Sites

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Transformation of Donor Testing

In September 1998, CBS took over the responsibility for the blood supply in 9 provinces and 3 territories outside Quebec

- CBS responsible for 13 Centres
- Each performed all mandatory testing for the collections in their area
- Testing reported to each individual Centre Director and Medical Director

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Transformation of Donor Testing

- Consolidation of testing completed
  - Two site model located in Calgary, Toronto

- Based on ability to transport samples to location reliably during routine and contingency conditions.
- Next phase is two new facilities in Toronto and Calgary

Donor Testing Sites

Testing Site	Collection Site
Toronto 60% workload	Toronto, Ottawa, Hamilton, London, NS/PEI, New Brunswick and Newfoundland/Labrador samples
Calgary 40% workload	Edmonton, Calgary, Saskatoon, BC & Y, Regina and Winnipeg samples

Donor Testing Sites

- Each site is a mirror image for equipment and are back up for each other for business continuity issues
- Equipment at each site:
  - Four PK7300 instruments
  - Four NEO instruments
  - Three PRISM instruments
  - Four Roche s201 clusters per site for NAT and WNV testing

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Laboratory tests currently in use by blood operators, and in particular by Canadian Blood Services, for the detection of blood-borne pathogens

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CBS Testing Menu

Mandatory		Non-Mandatory
Test	Date Introduced	
ABO/ Rh, Antibody Screen	1947	
Syphilis	1949	❑ Antibody identification for donors with positive antibody screen
HBsAg	1972	
Anti-HIV	1985	
HTLV I/II	1990	❑ Phenotyping ▫ Identifies additional antigens present or absent on red cells
Anti-HCV	1990	
HCV NAT	1999	
HIV NAT	2001	❑ CMV ▫ CMV Negative products required by some immunodepressed patients
WNV NAT	2003	
Anti HBc	2005	
Chagas	2010	

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What Transmissible Diseases tests do we perform on Donor Samples?

Testing for:	Serological/NAT	Implementation
HIV 1/2	Antibody and NAT	1985 and 2001
HBV	HBsAg, Anti-HBc and NAT	1972, 2005 and 2011
HCV	Antibody and NAT	1990 and 1999
HTLV I/II	Antibody	HTLV I 1990, both 1998
WNV	NAT	2003, Seasonal 2015
Syphilis	Antibody	1949
CMV	Antibody (selected units)	1984
Chagas	Antibody (selective testing based on risk)	2010

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Screening versus Confirmatory

Donor Testing performs mandatory screening tests

- If donation reactive (initial reactive (IR)), then sample tested x 2
- If donation reactive on ≥ 2 tests, donor repeat reactive (RR)
- Supplemental/confirmatory testing performed to determine if donor is a "true" positive
- Donor notification and counselling based on final test results

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Transmissible Diseases Serological Testing

- **Abbott PRISM® Platform:**

The ABBOTT PRISM® screens donated blood in over 30 countries, processing more than 40 percent of the global blood supply.

Health Canada approved Chemiluminescent assays used to detect:

- HBsAg
- Anti-HBc
- Anti-HIV1/2
- Anti-HTLV I/II
- Chagas Antibody

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Transmissible Diseases Serological Testing

- **Beckman Coulter PK®7300 Platform:**

Health Canada approved assays used to detect:

- Syphilis Antibody (Microhemagglutination Assay)
- CMV Antibody (Passive Particle Agglutination Assay)

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NAT Platform

- **Roche cobas ®s201 System:**

Health Canada approved RT-PCR assays used to detect:

- HIV-1 RNA (Groups M and O)
- HIV-2 RNA
- HCV RNA
- HBV DNA
- WNV RNA

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Current Assays and Sensitivity used to perform Transmissible Diseases Testing at Canadian Blood Services

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Transmissible Diseases Serological Assays Performed on the PRISM Platform

Marker	Assay	Sensitivity Claim in Current Package Insert Version
HBsAg	Abbott **PRISM® HBsAg**, Antibody to Hepatitis B Surface Antigen (Mouse Monoclonal IgM), Abbott Laboratories, Diagnostics Division	Subtype *ad* = 0.10 ng/mL Subtype *ay* = 0.08 ng/mL
Anti-HBc (IgM and IgG)	Abbott **PRISM® HBcore**, Hepatitis B Virus Core Antigen (E.Coli, Recombinant), Abbott Laboratories, Diagnostics Division	Assay: 99.49% (95% CI 98.82% to 99.83%) Analytical: <0.8 PEI Units/mL(Paul Ehrlich Institute)
Anti-HCV	Abbott **PRISM® HCV**, Hepatitis C Virus encoded Antigens (Recombinant c100-3, HCr43, NS5), Abbott Laboratories, Diagnostics Division	Assay: 100% (95% CI 99.49% to 100%)
Anti-HIV 1&2	Abbott **PRISM® HIV O Plus**, Human Immunodeficiency Virus Types 1 and 2 (E.coli, B. megaterium, Recombinant) Antigen and Synthetic Peptide, Abbott Laboratories, Diagnostics Division	Assay: 100% (95% CI 99.56% to 100%)
Anti-HTLV I/II	Abbott **PRISM® HTLV-I/HTLV-II**, Human T-Lymphotropic Virus Types I and II Antigen (Inactivated), Abbott Laboratories, Diagnostics Division	Assay: 100% (95% CI 99.48% to 100%)
Chagas Antibody	Abbott **PRISM® Chagas**, *Trypanosoma cruzi* (E coli, Recombinant) Antigen, Abbott Laboratories, Diagnostics Division	Assay: 98.47% (95% CI 94.59% to 99.81%)

All assays are Health Canada and FDA approved.

Transmissible Diseases Serological Assays on the PK7300 Platform

Marker	Assay	Sensitivity Claim in Package Insert
Syphilis Antibody	Beckman Coulter® **PK® TP System**, Microhemagglutination Test for Detection of *Treponema pallidum* Antibodies using the Beckman Coulter PK® Instrument, Beckman Coulter, Inc.	EDTA Plasma: EDTA Plasma: 100% (CI 0.555-0.97)
CMV Antibody	Beckman Coulter® **PK® CMV-PA System**, Passive Particle Agglutination Test for Detection of **Total** Cytomegalovirus Antibodies using the Beckman Coulter PK® Instrument, Beckman Coulter, Inc.	Serum: 99.40% (95% Lower Conf. Bound) EDTA Plasma: 99.93% (95% Lower Conf. Bound)

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Both Assays are Health Canada and FDA approved.

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NAT Assays Performed on the s201 Platform – MPX 2.0

Marker	Assay	Pool Size	Sensitivity Claim in Package Insert
HIV-1 Group M RNA, HIV-1 Group O RNA, HIV-2 RNA, HCV RNA, HBV DNA	cobas® TaqScreen MPX Test, version 2.0, for use on the cobas s201 system, Roche Molecular Systems	Donor Samples are screened in Pools of 6.	Single Unit Limit of Detection (LOD): HIV-1M: 50.3 IU/mL HIV-1 O: 18.3 copies/mL HIV-2: 57.4 copies/mL HCV: 6.8 IU/mL HBV: 2.3 IU/mL Theoretical sensitivity for a Pool of 6 by multiplying each Single Unit LOD by 6, this represents concentration of the sample , not true sensitivity

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MPX 2.0 Assay is Health Canada and CE approved

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NAT Assays used on the s201 Platform - WNV

Marker	Assay	Pool Size	Sensitivity Claim in Package Insert
WNV RNA	cobas® TaqScreen West Nile Virus Test for use on the cobas s 201 system, Roche Molecular Systems	Donor Samples are screened in Pools of 6. Single Unit Testing is evoked when a positive donation is identified	Single Unit: 40.3 copies/mL (95% LOD) Pool of 6: represents concentration of the sample of 241.8 copies/mL, this is a calculated "theoretical" sensitivity

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WNV Assay is Health Canada and FDA approved

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Platforms currently used to perform Transmissible Diseases Testing in other blood agencies

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Immucor NEO Platform

Health Canada approved assay to detect:

- Syphilis Antibody
  - Capture®-S, *Solid Phase System for the Serological Detection of Syphilis in Blood Donors*
- CMV Antibody
  - Capture-CMV®, *Solid Phase System for the Detection of IgG & IgM Antibodies to Cytomegalovirus (CMV)*

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Grifols Tigris Platform

Health Canada approved RT-PCR assays to detect:

- HIV RNA, HCV RNA, HBV DNA
  - *Procleix Ultrio assay*
- WNV RNA
  - *Procleix West Nile Virus (WNV) Assay*

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Transmissible Diseases Confirmatory Testing

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Transmissible Diseases Confirmatory Testing Menu

- Performed at Canadian Blood Services:
  - Performed at the Donor Testing sites
    - *HBsAg Neutralization Assay on the PRISM Platform*
  - Performed at the National Testing Laboratory in Ottawa
    - *HCV Immunoblot*
    - *HIV-1 Western Blot (WB)*
    - *HIV-2 WB*
    - *HIV-2 EIA*
    - *HTLV I WB*
    - *HTLV II WB*
    - *Anti-HBs (Supplemental)*

Transmissible Diseases Confirmatory Testing Menu

- Performed outside of Canadian Blood Services:
  - Syphilis Confirmatory Testing performed at Provincial Public Health Laboratories:
    - *Alberta PH (Western Canada samples) – RPR, EIA, Immunoblot*
    - *Ontario PH (Eastern Canada samples) – RPR,TP.PA, FTA-Antibody*
  - Chagas Confirmatory Testing performed at National Reference Centre for Parasitology (NRCP) in Montreal:
    - *ELISA*
    - *Immunoblot*

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On the horizon for Transmissible Diseases (TD) Testing.....

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On the Horizon…

- Seasonal WNV Testing at Canadian Blood Services
  - Implementation at the end of November 2015
- Hepatitis E NAT
- CMV NAT
- Testing for Babesiosis
- Next Generation NAT Platform

Implementation of a New Assay

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Implementation of a New Assay

- Health Canada licensed assay and equipment
- Must be licensed for Donor Screening – end labeling of donor products
- Pre work of decision document and policy TD algorithms documents
- After decisions have been made by EMT , it usually take approximately 18 months to implement the new assay or system

Implementation of a New Assay

- Testing is supported by two Testing Process Development groups
  - Blood Group Serology
  - Transmissible Disease
- Each group is lead by an Associate Director
- These groups provide technically and project management to the Testing sites

Implementation of a New Assay

- First steps are always the purchase of test bed instrument
- Validation plan
- IT impacts- usually changes to ePROGESA
- This allows for validation scripts , procedures and training material to be developed
- An IOQ is performed on one instrument
- There is an submission to Health Canada (HC) which will includes; executive summary, training and validation summary

Implementation of a New Assay

- After permission to proceed from HC an IPQ script is tested on each test system
- Depending on the scope of the project they may be an logistic continuity plan developed for shipping sample to other site
- Training will take place two months before implementation
- Go- Live meeting
- Implementation and CELEBRATION!!!!!!!!!!!!

SPECIAL ACKNOWLEDGEMENTS

- Donor Testing Staff
- Donor Testing Management team
- National Testing Process Staff
- Medical Staff
- Validation and Quality Staff

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