Canadian Blood Services

BLOOD
PLASMA
STEM CELLS
ORGANS
& TISSUES

DIAGNOSTIC SERVICES

SASKATCHEWAN

YEAR IN REVIEW

JANUARY – DECEMBER 2019

Diagnostic Services “Year in Review” statistics are based on a January to December calendar year. The calendar year provides better correlation with Health Canada birth statistics.

SENIOR STAFF AND CONTACT INFORMATION

Laboratory Medical Director Gwen Clarke, MD, FRCPC	Phone # 1-780-431-8738 gwen.clarke@blood.ca
Diagnostic Services Manager Lhevinne Ciurcovich, MLT	604-707-3449 lhevinne.ciurcovich@blood.ca
Assistant Manager, Testing Heba Abukhadra, MLT	604-707-3573 heba.abukhadra@blood.ca
Supervisor Vivian Stephens, MLT	604-707-3483 vivian.stephens@blood.ca
Diagnostic Services Laboratory	Phone# 604-707-3434 Fax# 604-874-6582

After hours
Phone # 604-876-7219
Toll free #1-888-332-5663 ext. 7219

Diagnostic Services Website https://blood.ca/en/hospital-services/laboratory-services

TABLE OF CONTENTS

FIGURES

TABLES

PERINATAL LABORATORY

The Perinatal Laboratory within Diagnostic Services at Canadian Blood Services provides diagnostic testing of pregnant women for blood type and red blood cell antibodies. Results from this screening assist physicians, midwives and nurse practitioners in ensuring the appropriate management of a pregnancy for both the mother and baby. As of 2017-10-02, Vancouver Diagnostic Services site provides Perinatal Testing Services for Saskatchewan.

A. Testing Performed

Canadian Blood Services Perinatal Laboratory routinely performs the following tests:

- ABO/Rh blood type
- Screen for red blood cell antibodies
- Antibody Identification, if antibodies are detected
- Antibody Identification referrals
- Antibody Titration, if a clinically significant antibody is identified
- Phenotyping
- Direct Antiglobulin Test for detection of HDFN (Hemolytic Disease of the Fetus/Newborn)

B. Testing Frequency

Mothers – Initial Testing: All women should be tested upon their first prenatal visit.

Mothers – 26-28 Weeks Gestation: All Rh negative women should be retested at 26-28 weeks gestation. Rh positive women should also be retested at 26-28 weeks gestation when there is only one blood group result available (usually first pregnancy) or if patient is at increased risk of allo-immunization (e.g. previous transfusion, Maternal trauma or obstetrical procedure).

Mothers – Antibody Present: If the antibody is known to cause HDFN, it is recommended that specimens be submitted every three to four weeks for the duration of the pregnancy dependant on the specificity of the antibody and the strength of the antibody titre. More frequent testing may be indicated if the antibody titre rises rapidly or if clinical monitoring mandates that additional sampling would provide helpful information. Less frequent sampling may also be recommended for antibodies that are unlikely to be clinically significant or in cases where clinical monitoring through fetal Doppler ultrasound has commenced.

Mothers – Postnatal: Following delivery, specimens from the mother and her baby should be tested if the Rh of the mother is unknown, the mother is Rh negative, the mother has a clinically significant antibody or if the baby shows signs of HDFN (i.e. anemia or jaundice).

Newborns (Cords): Cord blood or neonate specimens must be submitted with the mother's specimen as noted above. ABO/Rh testing is performed on cord or neonatal specimens submitted to Canadian Blood Services. The direct antiglobulin test is performed if the mother has a clinically significant antibody or on request if the baby shows signs of HDFN (i.e. anemia or jaundice). This is especially important when the mother is Rh negative or when the mother has a clinically significant antibody. If the baby has unexpected anemia or jaundice assessment of the cord blood sample for blood group and DAT may also be helpful.

Partners: When a woman has an antibody capable of causing HDFN, specimens from the partner will be requested for ABO/Rh and antigen phenotyping. This will assist in assessing the probability of the baby being affected by the antibody. Partners' specimens may also be tested to assess Rh Immune Globulin (RhIG) eligibility of Rh negative mothers.

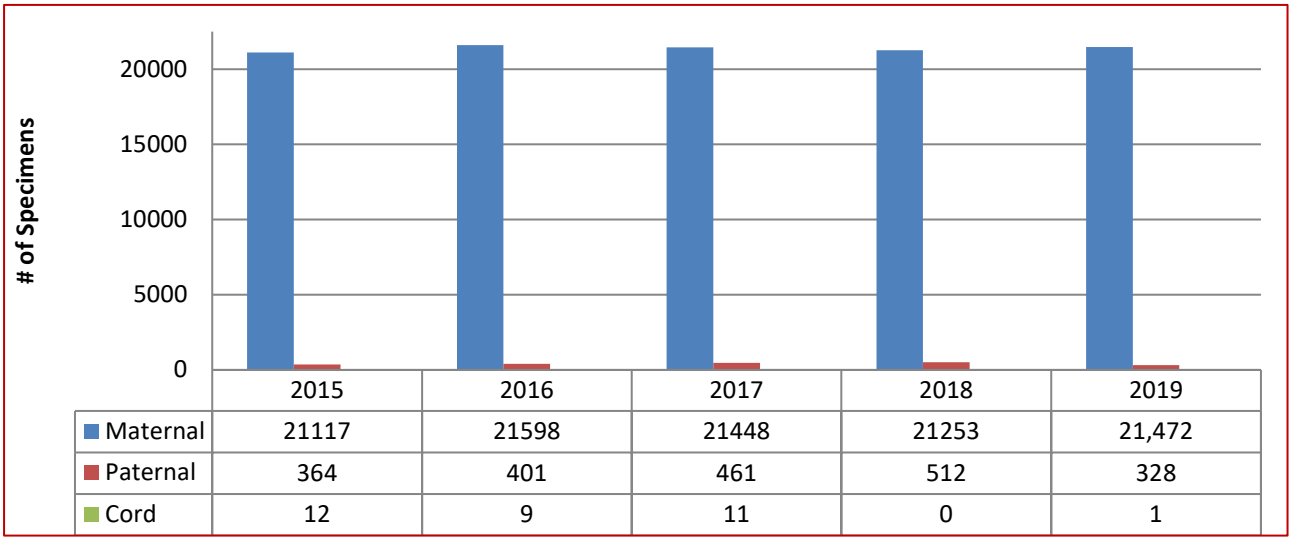
C. Specimens Tested

The data includes all women tested, including referrals.

Table 1: Perinatal Specimens Tested

Specimen Type	Test Type	2015	2016	2017	2018	2019
Maternal	Maternal	21117	21598	21448	21253	21,472
Paternal	Paternal	364	401	461	512	328
Cord	Cord	12	9	11	0	1
Total # of Specimens Tested		**20973**	**21493**	**22008**	**21765**	**21,801**
Total # of Patients Tested		**17450**	**17631**	**18069**	**17601**	**17,308**

Figure 1: Total Perinatal Specimens Tested



D. Antibodies Identified

In 2019, a total of 115 antibodies were reported (see *Table 2*). This is slightly lower than 2018. One hundred and twenty-nine women had antibodies identified during their pregnancies, of these; sixteen had multiple antibodies.

Antibodies identified were considered to be clinically significant if they have been reported to cause HDFN. The most common clinically significant antibodies identified were: anti-D, anti-E, anti-c, and anti-K which together represented 69% of the total antibodies identified.

Titres for 4 of the clinically significant antibodies increased from non-critical to critical levels during the pregnancy with a total of 11 antibody titres at critical levels (see *Table 3*). Recommendations were made for all patients with a critical titre level (current or previous pregnancy) and all Kell system antibodies to be referred to a High Risk Fetal Assessment Clinic for further follow-up and monitoring during pregnancy.

Table 2: Total Number of Perinatal Antibodies Detected

Clinically Significant Antibodies	**2015**	**2016**	**2017**	**2018**	**2019**
Anti-D	10	8	7	5	11
Anti-C	10	8	7	4	5
Anti-E	38	28	33	46	34
Anti-c	12	13	15	17	16
Anti-e	5	6	1	2	6
Anti-Cw	3	1	0	3	2
Anti-K	30	37	21	25	18
Anti-M*	10	6	11	8	6
Anti-S	3	2	2	6	4
Anti-s	1	1	0	0	0
Anti-Fya	6	2	3	0	1
Anti-Fyb	1	1	0	0	0
Anti-Jka	8	10	7	9	6
Anti-Jkb	3	1	2	5	4
Anti-Lua	0	1	0	0	0
Anti-Lub	0	0	0	1	1
Anti-Kpa	0	1	1	0	0
Anti-G	1	1	2	1	1
Anti-Cob	1	0	0	1	0
Anti-Wra	1	1	1	2	0
Anti-V	0	0	1	0	0
Anti-Mit	0	0	1	0	0
Anti-Dantu	0	0	1	0	0
TOTAL: Clinically Significant Antibodies	**143**	**131**	**113**	**135**	**115**

*Anti-M – IgG antibody detected

Clinically Insignificant Antibodies	2015	2016	2017	2018	2019
Anti-Le[a]	14	9	7	12	5
Anti-Le[b]	2	1	1	2	1
Anti-N	0	1	1	1	1
Anti-Sda	0	0	0	1	0
Anti-A_1	0	3	1	6	1
Anti-P1	0	0	0	4	2
Passive Anti-D *(not included in total)*	178	217	158	183	237
TOTAL: Clinically Insignificant Antibodies	**16**	**14**	**10**	**26**	**10**

Table 3: Perinatal Patient Antibody Titres 2019

Antibody	Critical Level	Non-Critical Level	Non-Critical to Critical
Anti-C		3	
Anti-c	1	12	
Anti-CG		1	
Anti-Cw		2	
Anti-D	3	10	1
Anti-DC	1		
Anti-E	4	30	3
Anti-e		5	
Anti-Ec		3	
Anti-Fya	1		
Anti-Jka		7	
Anti-Jkb		4	
Anti-M	1	3	
Anti-S		4	
Unidentified Antibody		1	

Figure 2: Total Number of Perinatal Antibodies

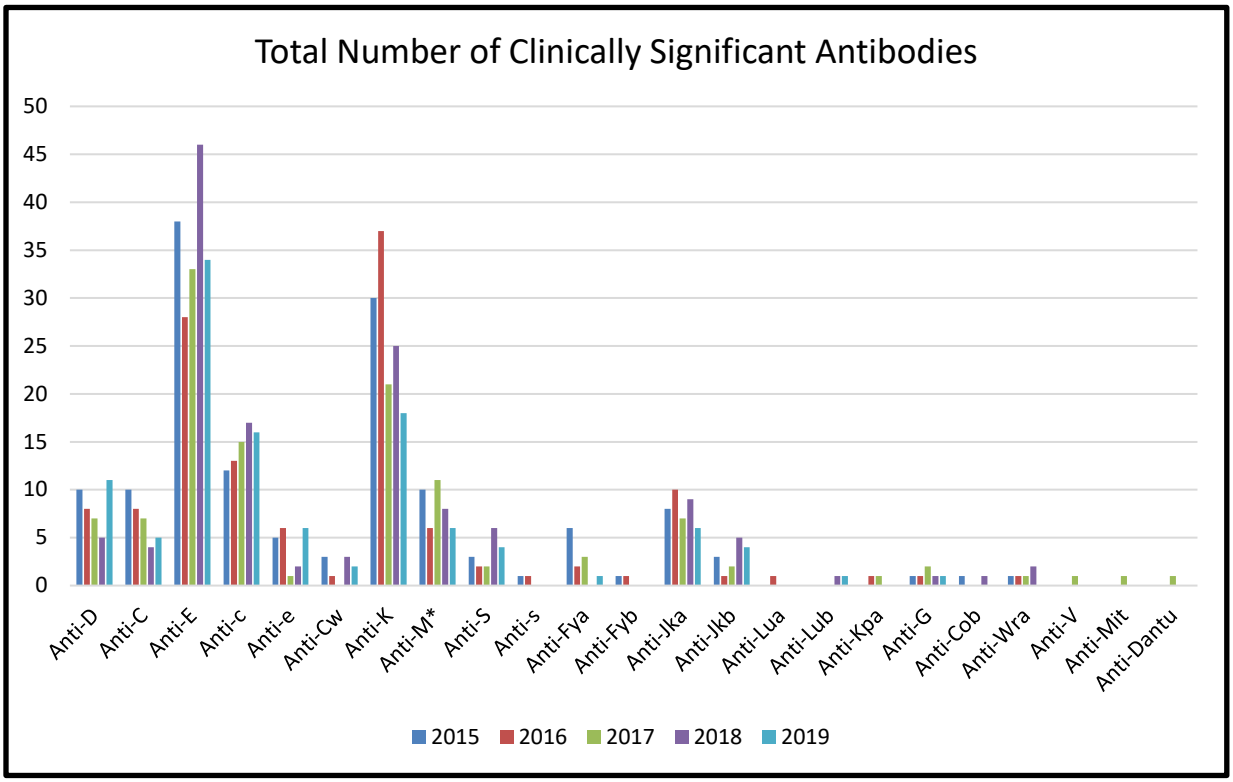


Figure 3: Frequency of Clinically Significant Antibodies

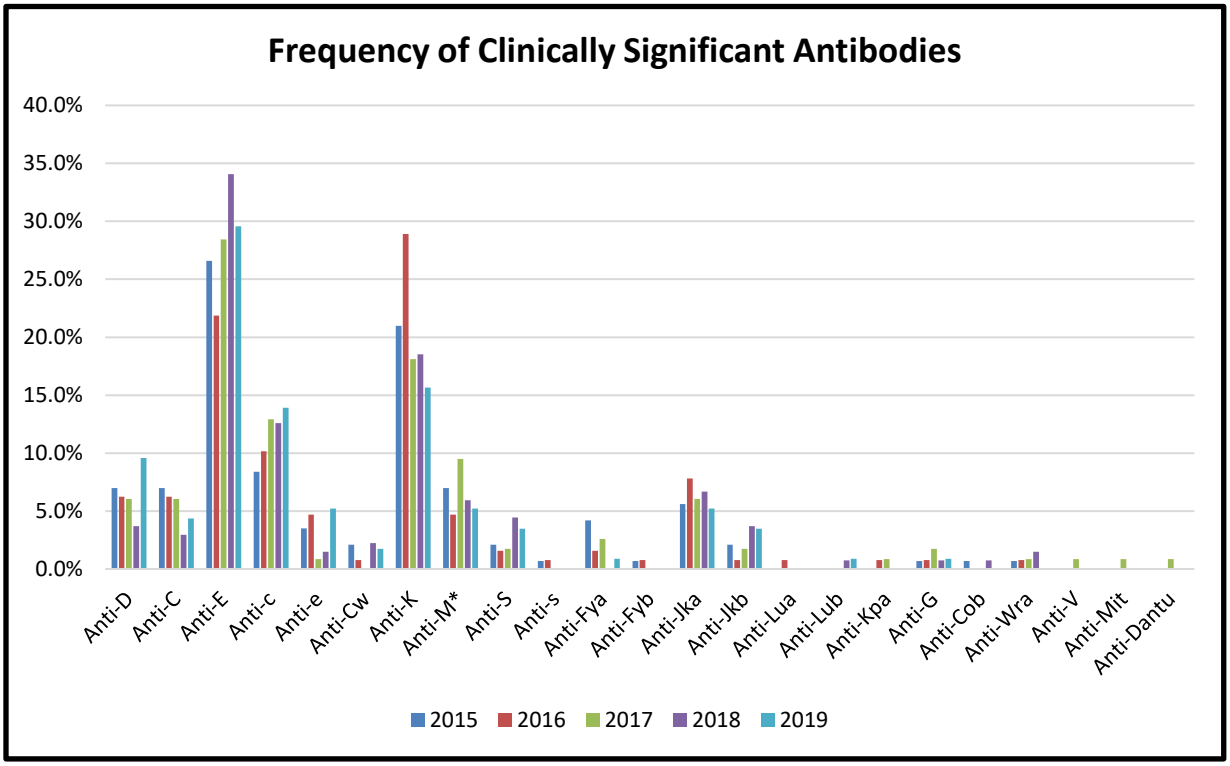


Table 4: Combination Antibodies 2019

Combination Antibodies	Number
Anti-A1 Anti-S Unidentified Antibody	1
Anti-C Antibody to an HLA related antigen Unidentified Antibody	1
Anti-C Anti-G	1
Anti-c Anti-Jka	1
Anti-c Anti-S	1
Anti-D Antibody to an HLA related antigen	1
Anti-D Anti-C Unidentified Antibody	1
Anti-D Unidentified Antibody	1
Anti-E Antibody to an HLA related antigen Unidentified Antibody	1
Anti-E Anti-c	4
Anti-E Anti-Jkb	2
Anti-E Cold Agglutinin Unidentified Antibody	1
Anti-e Unidentified Antibody	2
Anti-E Unidentified Antibody	1
Anti-Fya Unidentified Antibody	1
Anti-Jka Warm Autoantibody	1
Anti-M Anti-P1	1
Anti-N Anti-S Cold Agglutinin	1
Anti-P1 Unidentified Antibody	1
Anti-S Warm Autoantibody	1
Warm Autoantibody Unidentified Antibody	1

FETAL GENOTYPING

Canadian Blood Services in Saskatchewan has been coordinating specimen referrals for fetal genotyping with Edmonton Diagnostic Services. Samples are prepared by Edmonton for referral to the International Blood Group Reference Laboratory (NHS) in Bristol, England, for detection of fetal DNA in maternal plasma.

Specimens are accepted if they meet the following criteria:

- The mother has an antibody capable of causing hemolytic disease of the fetus/newborn (HDFN), AND
- The father is heterozygous for the corresponding antigen (or unknown), AND
- The antibody titre has reached a critical level, OR
- There has been a previous fetus/newborn affected by HDFN, OR
- The antibody is Rh and/or anti-K

Discussion with a Canadian Blood Services physician is required prior to submitting specimens for testing outside of these criteria.

The number of specimens referred for fetal genotyping has ranged between two and eight specimens in recent years.

Table 5: Referred out Specimens

	2019
Total samples sent	3
# of patients tested	3
# of patients not requiring MFM follow-up. (Fetus tested negative for the corresponding antigen)	0

Table 6: Fetal Genotyping Results Summary 2019

Patient	**Maternal Antibody**	**Predicted Fetal Phenotype negative for the corresponding antigen**	**Follow-up required?**
1	Anti-D	RhD Pos	Yes
2	Anti-E	RhE Pos	Yes
3	Anti-E	E Inconclusive	Yes

RHD RED CELL GENOTYPING

Based on the following testing algorithm patients with a serologically variable Rh D typing results may have a genetic testing for the RHD gene. For 2018, the following results were obtained in patients using one of the two Red Cell antigen genotyping platforms available at CBS.

Figure 4: Rh D Testing Algorithm

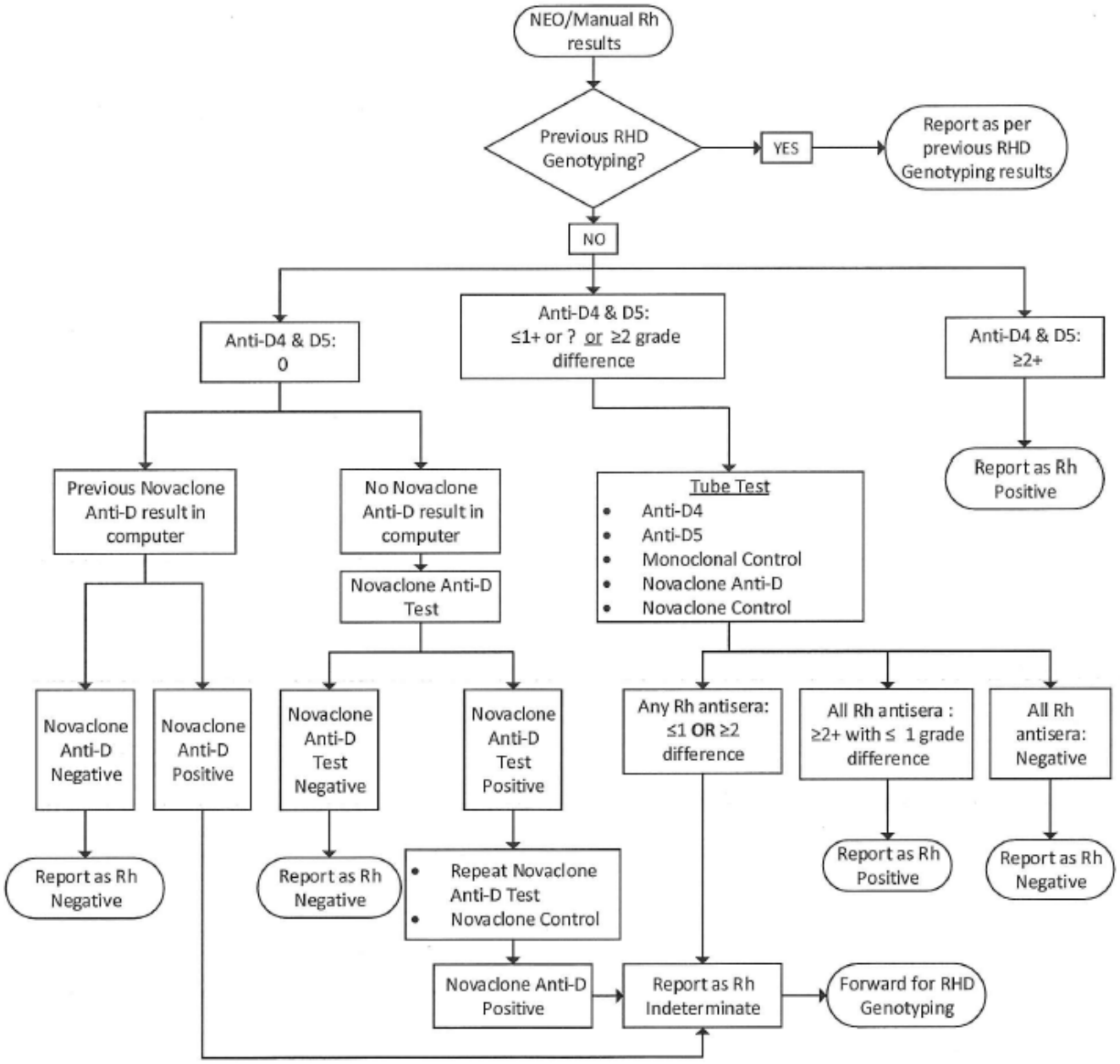


Table 7: Patient # - RHD Type/Result 2019

# of Patients	RHD Genotype	Predicted Phenotype	RHD Sequencing	Rh(D) Group
1	DAR	D variant	NO	NEG
1	DAR/Weak D 4.0 or 4.03	weak D	NO	NEG
1	DAU2	D variant	NO	NEG
1	DIII-CE-(4-7)-D and Possible D	D positive	NO	POS
20	Possible D	D positive	NO	POS
1	RHD Deletion	RHD Deletion	NO	NEG
2	RHD psi / Weak D type 4.0 or 4.3	D variant	NO	NEG
10	weak D type 1	weak D	NO	POS
1	weak D type 1/ weak D type 4.0 or 4.3	weak D	NO	NEG
4	Weak D type 2	weak D	NO	POS
7	weak D type 3	weak D	NO	POS
4	weak D type 4.0 or 4.3	weak D	NO	NEG
Total number tested	**53**			

The array used for RHD genotyping (Immucor's BioArray BeadChip™ Molecular Assay) is extensive and can detect the most common mutations of the *RHD* gene. The most common variants detected are weak D type 1, weak D type 2 and weak D type 3. Individuals with these phenotypes can be safely treated as Rh positive as it has been established that they will not form alloanti-D. Patients with any other weak or partial D phenotypes are capable of forming alloanti-D, and should be treated as Rh negative. When none of the variants present on the array are detected, the software will produce a result of "Possible D". Prior to 2018, it was decided to err on the side of caution, and Canadian Blood Services recommended that patients with a result of "Possible D" be treated as Rh negative. However, based on clinical experience and sequencing studies, it has been confirmed that the vast majority of these patients do not have a mutation of the *RHD* gene. In 2018 the reporting was changed to reflect this and patients with results of "Possible D" were reported as Rh positive individuals.

QUALITY INDICATORS

The laboratories monitor many quality indicators and the two which are most relevant to this document are turnaround times and rejected specimens which are presented below.

A. Turnaround Times

To ensure timely reporting of patient test results, Canadian Blood Services monitors turnaround time (TAT) from when the specimen is received at Canadian Blood Services in Vancouver to the time when the results are available. Since monitoring of this quality indicator began in 2008, the percentage of specimens has consistently exceeded the predefined TAT threshold. Samples whose testing exceeds the expected TAT are usually those where clinically significant antibodies are detected or where difficulty in finding compatible blood is encountered.

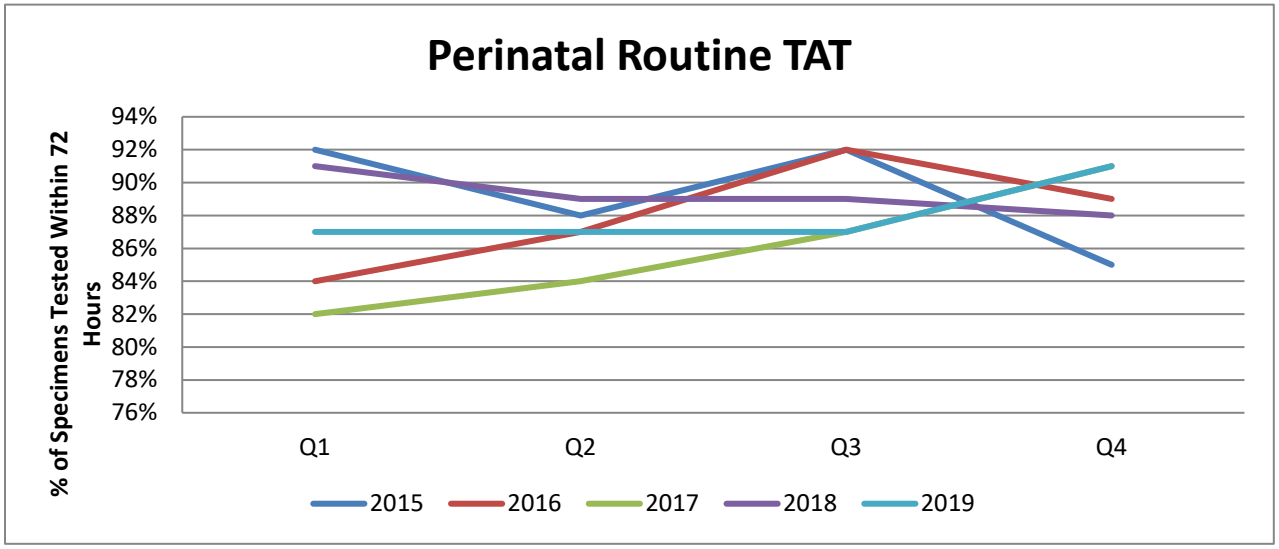
Table 8: Turnaround Time – Routine Criteria by Specimen Type

Specimen Type	Expected Turnaround Time	Expected % of Specimens Which Meet or Exceed Expected TAT
Routine Perinatal Specimens	< 72 hours	85%

Table 9: Turnaround Time – Routine Perinatal Specimens

Turnaround Time (TAT)	2015	2016	2017	2018	2019
% of Specimens Tested within 72 hours	89%	88%	86%	89%	88%
% of Specimens Tested > 72 hours	11%	12%	14%	11%	12%

Figure 5: Perinatal Routine TAT



B. Rejected Specimens

Each time a specimen is rejected, a reason for rejection is captured in the laboratory information system (LIS). This data is retrieved and analyzed on a quarterly basis.

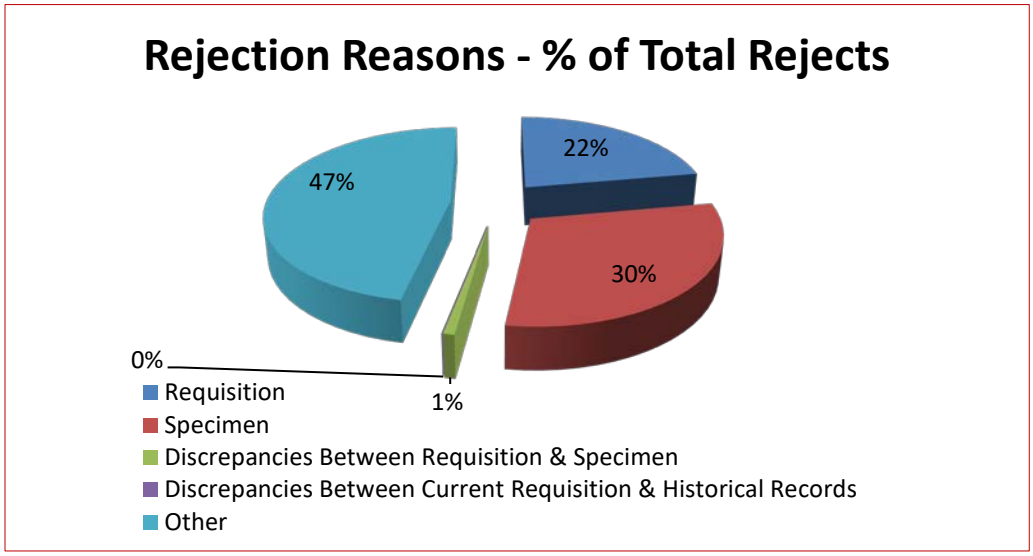
As described in *Table 9*, the reasons for rejecting specimens in the Perinatal Laboratory are distributed similarly between problems with requisitions and discrepancies between the requisition and the specimens. Also, a number of samples fell outside of the testing criteria, having been tested within the current pregnancy (Other category). Rejection rates have consistently stayed 2 – 3% for each quarter. *Table 13* describes the reasons for rejecting specimens in the Crossmatch Laboratory.

Note: As of 2017-10-02, the Vancouver Diagnostic Services site provides Perinatal Testing Services for Saskatchewan.

Table 10: Quarterly Rejection Rates – Perinatal Specimens 2019

Rejection Category	Q1	Q2	Q3	Q4
Requisition	0	4	48	2
Specimen	5	4	21	43
Discrepancies Between Requisition & Specimen	2	0	0	0
Discrepancies Between Current Requisition & Historical Records	0	0	0	0
Other (Duplicates, etc.)	65	21	21	7
Total # specimens rejected	72	29	90	52
Total # specimens received	5217	5329	5069	2537
Rejections as a % of total	1.4%	0.5%	1.8%	2.0%

Figure 6: Perinatal Rejection Reasons 2019



DIAGNOSTIC SERVICES UPDATE 2019

Updates pertain to all Diagnostic Services sites within Canadian Blood Services: Vancouver, Edmonton, Winnipeg and Brampton

ALL CBS Diagnostic Services Sites	**Implementation of eTraceline Nov 2019**: eTraceline was implemented at all CBS reference laboratory sites in November 2019.
	Implementation of Antigen Plus April 2019 Antigen Plus, a program to allow development of panels from reagent cell collections was implemented along with a review and re organization of the reference lab inventory of rare reagent red cells and antisera.
	Perinatal Advisory Committee The PNAC continues to collaborate throughout the year and at an annual November meeting. The group reviewed and discussed an ongoing project related to the titration of multiple antibodies using cells with both antigens represented versus the standard method involving separate titrations of each antibody. An update of the plans for repatriation of Saskatchewan patient samples to a provincial hospital-based program was provided and a collaborative study to compare titer levels using the Saline IAT method at CBS vs the automated gel titration method in the Saskatchewan perinatal program was discussed. A review of the form used for notification of Intra uterine transfusion by the BC maternal fetal medicine group was provided Results of the recent Canada wide survey distributed to perinatal testing labs by the Canadian Obstetrical Perinatal network were reviewed and discussed. A project in the Manitoba Red Cell Serology lab involving development of a new process for preparing aliquots of red cell units for neonatal transfusion was described. New interpretive reporting comments for specimens with features suggesting Fetal /neonatal Alloimmune thrombocytopenia were discussed.

ALL CBS Diagnostic Services Sites	**DBL Novaclone Testing (NCT) on all Rh Negative Perinatal Patients Implemented 2019-01-29** CBS DS sites incorporated NCT testing into their prenatal RhD algorithm for all patients who test RhD negative on the NEO analyzer. NCT testing identifies a group of Rh prenatal patients not eligible for RhIG, who might have been typed as Rh negative based on initial NEO testing and results in a decrease in unnecessary RhIG prophylaxis.
	Critical Anti-M titre – Implemented 2019-11-04 Dithiothreitol (DTT) plasma treatment for critical anti-M titres was implemented at all Diagnostic Services Sites to determine if critical titre is due to IgG or IgM:2019-11-04 DTT is used to inhibit IgM antibody activity which allows for detection of underlying IgG antibodies. Procedure is performed on prenatal patients with a critical anti-M titre ($\geq$ 16) to determine the immunoglobulin class and the risk of HDFN. If the antibody is predominately IgG there is greater risk of HDFN and the mother is referred to the Maternal Fetal Medicine Clinic if the titre remains at $\geq$ 16 after the DTT plasma treatment.
Brampton	**Patient Genotype Testing Implemented 2019:** Reference lab testing of patients' samples for genotyping using the Grifols Progenika Core XT platform was implemented in the CBS Brampton reference laboratory in 2019.
	Transition of National Immunohematology Reference laboratory from Ottawa to Brampton site: The NIRL moved location from Ottawa to CBS Brampton
Vancouver /Edmonton	**Ortho MTS Gel Workstation and Pipettes Implemented 2019** Ortho MTS Gel workstations were implemented in the Vancouver and Edmonton Diagnostic Services Laboratories as a supplementary method to help complete antibody cases referred in from hospitals.
	Passive Anti-D Testing by NEO Cap-R Ready ID Implemented 2019-01-29 Vancouver and Edmonton Diagnostic Services Laboratories modified their Passive Anti-D testing platform from manual PEGIAT method to automated Capture R testing using the NEO analyzer. Automated testing provides a reduction in cost and decreased time to complete passive anti-D identification (which represents > 40% of perinatal antibody investigations), positive sample ID and reduces the risk of transcription errors.
Winnipeg	Collaboration with Shared Health Diagnostics to ensure the Diagnostic Services Business Continuity plan meshes seamlessly with other plans was a focus in 2019.

Winnipeg	**College of American Pathologists (CAP) Laboratory Accreditation** An on-site inspection of the Platelet Immunology Laboratory occurred with the lab successfully being granted accreditation. in the beginning of 2019.
	LEAN Continuous Improvement of Red Cell Serology Laboratories – Staff Cross Training Cross-training of staff to perform both pre-transfusion and perinatal testing continued in 2019. The goal is to more efficiently use people's talents.
	Preparation of Red Cell Aliquots for Neonatal and Pediatric Transfusion The project team for aliquoting smaller, patient appropriate doses of red cells for neonate and pediatric transfusion worked in 2019. The process was implemented on January 27, 2020.
	Process Change for the Distribution of Components in eTraceline In collaboration with Shared Health Diagnostics, the process for distribution of blood components to eTraceline facilities changed from using the Reserve/Transfer function to the Reserve/Issue function. This change was implemented on September 16, 2020. This change is a quality improvement initiative to reduce distribution errors by utilizing the broader functionality of the Issue program

Presentations / Abstracts / Publications Listing
D Lane, R Fallis, B Herdman, A Kabani, C Musuka, L Grabner. **Implementation of Electronic Solution to Reduce the Risk of Mistransfusion in a Regional Transfusion Service,** Poster/Abstract presented at AABB Meeting, San Diego, October 2017.
Tammy Ison, Balkar Gill, Gwen Clarke, Carmela Pote, Melba Sarmiento. **Rare Donors Identified through Selective Genotype Testing using Voluntary Ethnic Donor Information,** CSTM abstract.
L. Ciurcovich, H. Abukhadra, T. Dolnik, B. Gill, I. Resz, M. Yan, G. Clarke. **Maintaining an Inventory of Rare Reagent Red Cells and Antisera Across Multiple Reference Laboratories at Canadian Blood Services,** Poster Presentation at CSTM (Canadian Society for Transfusion Medicine), Calgary, Alberta, May 30 – June 2, 2019.
Heba Abukhadra – Supervisor, BCY Diagnostic Services. **Transfusion Medicine Case Studies,** PBCO/CBS Education Session on Blood Transfusion Issues, October 3, 2019.
Kirsten Hannaford, Supervisor EDM Diagnostic Services. **Monocyte Monolayer Assay Implementation**, Presentation for Immunohematology Working Group, May 07, 2019.
Hannon JL, Berardi P, Hannaford K. **Significance of "Possible D" Variant on BioArray BeadChip™ RHD Genotyping of Prenatal Patients, Abstract for** AABB, San Antonio, TX, October 19 – 22, 2019.

Presentations / Abstracts / Publications Listing
K Hannaford, M Yan, L Ciurcovich, J Hannon, G Clarke. **RHD Genotyping of patients with serological weak D: 2444 Patient samples with no anti D on follow up of 428 with a variant RHD,** Abstract for AABB, San Antonio, TX, October 19 – 22, 2019.
Matthew Yan, Medical Officer, CBS BC & Yukon Centre. **Anti-M: A Case of Hemolytic Disease of the Fetus and an Approach to Prenatal Management**, Abstract, Presentation at CSTM, Calgary, Alberta May 30 – June 2, 2019.
Vivian Stephens, Supervisor BCY Diagnostic Services. **Is it You?,** Lunch N Learn Presentation, June 11, 2019.
Brenda Caruk (Supervisor, EDM Diagnostic Services) and Lhevinne Ciurcovich (Technical Supervisor, BCY Diagnostic Services). **DARA and more... a Transfusion Medicine Case Study,** Lunch N Learn Presentation (EDM / BCY CBS Centres) April 3, 2019.