Canadian Blood Services

BLOOD
PLASMA
STEM CELLS
ORGANS
& TISSUES

DIAGNOSTIC SERVICES

SASKATCHEWAN

YEAR IN REVIEW

JANUARY – DECEMBER 2018

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.

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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 Titre, 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.

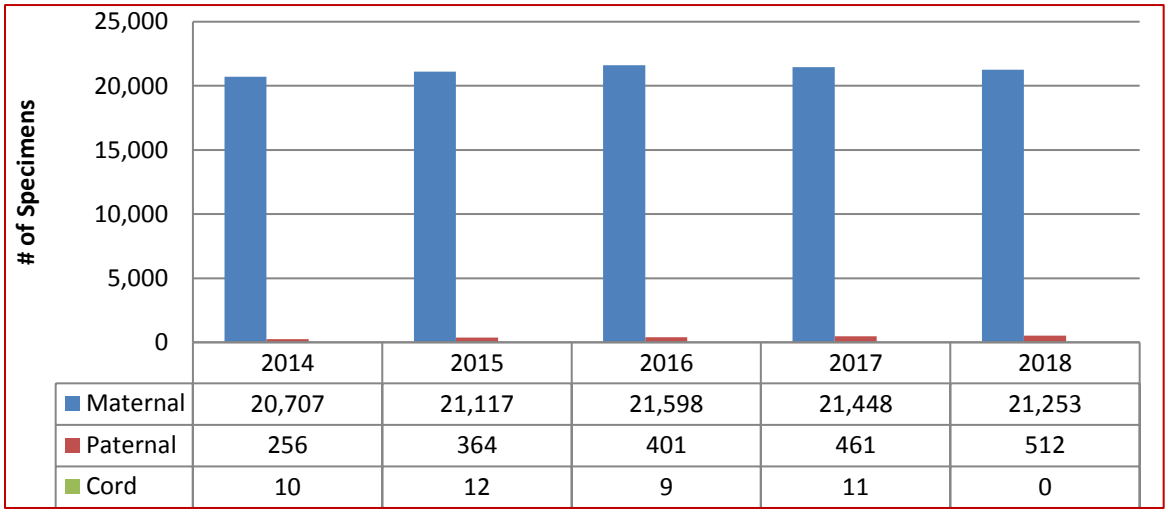
C. Specimens Tested

The data includes all women tested, including referrals.

Table 1: Perinatal Specimens Tested

Specimen Type	Test Type	2014	2015	2016	2017	2018
Maternal	Maternal	20707	21117	21598	21448	21253
Paternal	Paternal	256	364	401	461	512
Cord	Cord	10	12	9	11	0
Total # of Specimens Tested		**20329**	**20973**	**21493**	**22008**	21765
Total # of Patients Tested		**16925**	**17450**	**17631**	**18069**	**17601**

Figure 1: Total Perinatal Specimens Tested



D. Antibodies Identified

In 2018, a total of 135 antibodies were reported (see *Table 2*). This is slightly higher than 2017. One hundred and fourteen women had antibodies identified during their pregnancies, of these; twenty-eight 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 10 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	**2014**	**2015**	**2016**	**2017**	**2018**
Anti-D	16	10	8	7	5
Anti-C	14	10	8	7	4
Anti-E	39	38	28	33	46
Anti-c	16	12	13	15	17
Anti-e	3	5	6	1	2
Anti-Cw	1	3	1	0	3
Anti-K	24	30	37	21	25
Anti-M*	13	10	6	11	8
Anti-S	6	3	2	2	6
Anti-s	1	1	1	0	0
Anti-Fya	9	6	2	3	0
Anti-Fyb	2	1	1	0	0
Anti-Jka	6	8	10	7	9
Anti-Jkb	4	3	1	2	5
Anti-Lua	1	0	1	0	0
Anti-Lub	0	0	0	0	1
Anti-Kpa	2	0	1	1	0
Anti-G	0	1	1	2	1
Anti-Cob	0	1	0	0	1
Anti-Wra	0	1	1	1	2
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	**157**	**143**	**131**	**113**	**135**

*Anti-M – IgG antibody detected

Clinically Insignificant Antibodies	2014	2015	2016	2017	2018
Anti-Le[a]	12	14	9	7	12
Anti-Le[b]	2	2	1	1	2
Anti-N	1	0	1	1	1
Anti-Sda	0	0	0	0	1
Anti-A_1	0	0	3	1	6
Anti-P1	0	0	0	0	4
Passive Anti-D *(not included in total)*	156	178	217	158	183
TOTAL: Clinically Insignificant Antibodies	**15**	**16**	**14**	**10**	**26**

Table 3: Perinatal Patient Antibody Titres (2018)

Antibody	Critical Level	Non-Critical Level	Non-Critical to Critical
Anti-D	1	7	
Anti-C		2	
Anti-E	5	29	3
Anti-c	1	9	
Anti-Ec	3	2	1
Anti-CG		1	
Anti-Fyb		1	
Anti-Jka		6	
Anti-Jkb		4	
Anti-M		6	
Anti-S		2	

Figure 2: Total Number of Perinatal Antibodies (2018)

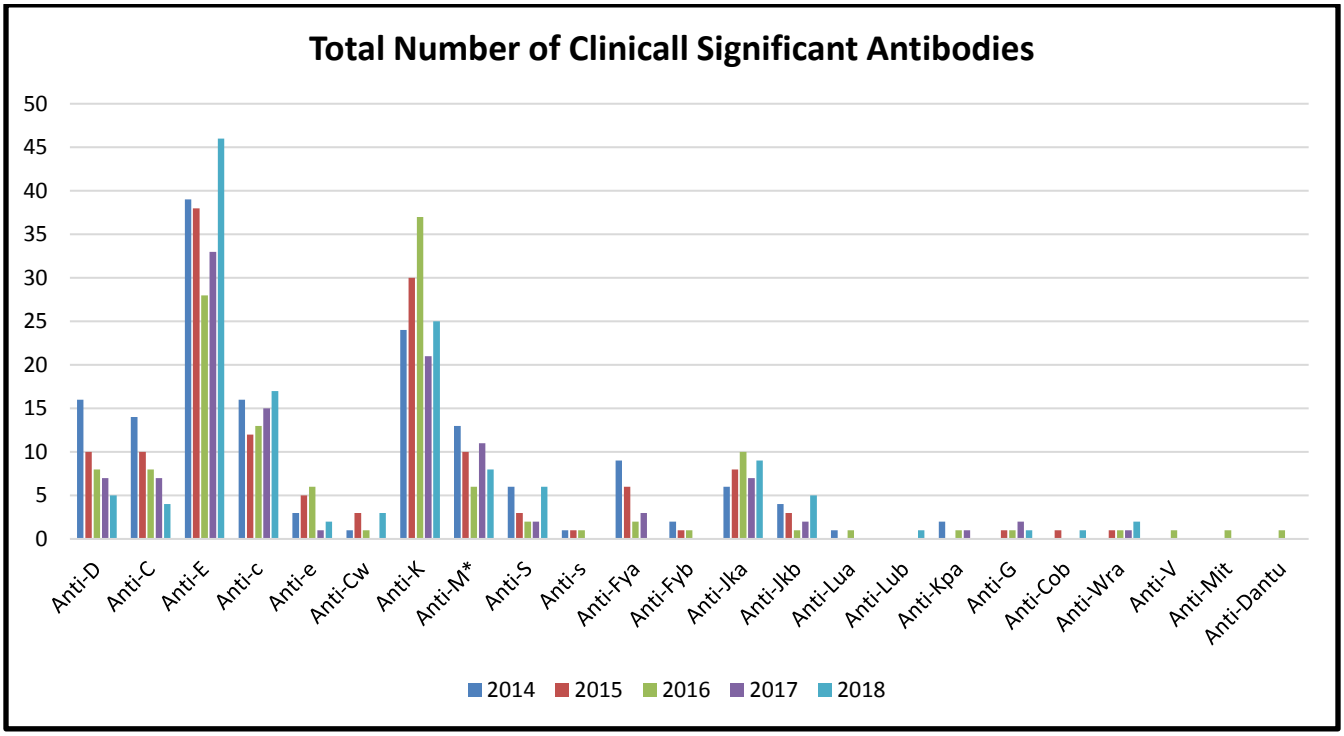


Figure 3: Frequency of Clinically Significant Antibodies (2018)

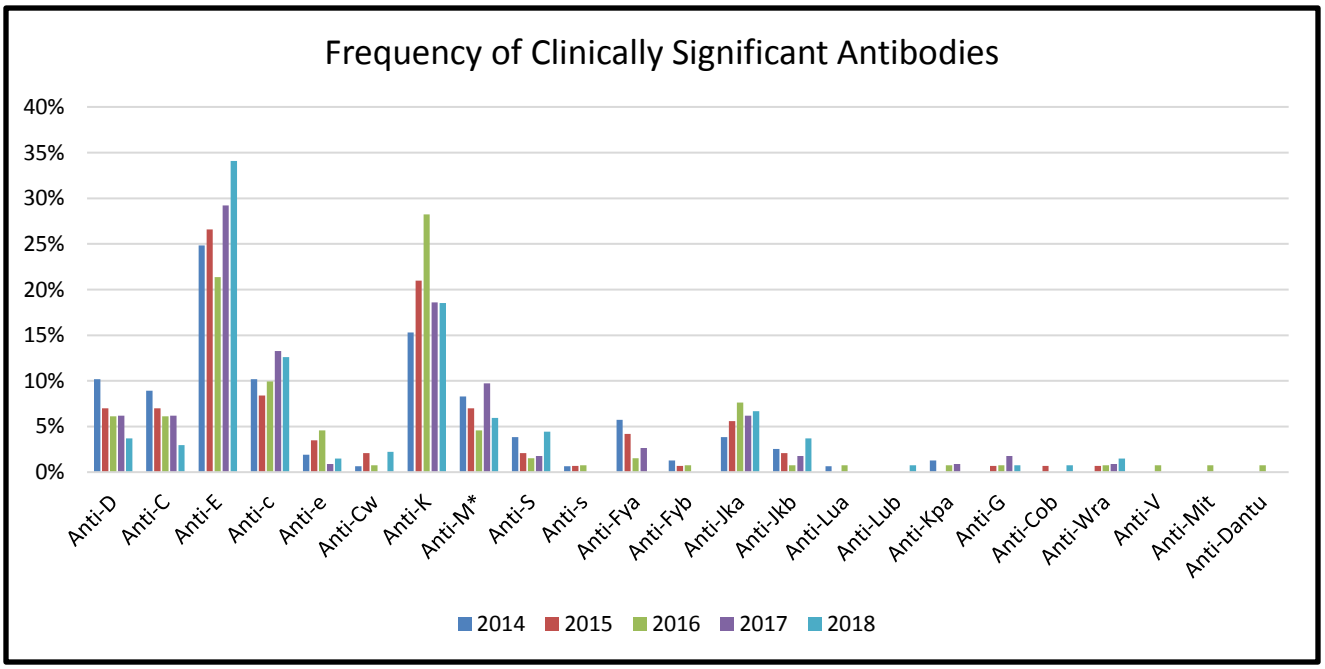


Table 4: Combination Antibodies (2018)

Antibodies	Number in 2018
Anti-E Anti-c	5
Anti-E Anti-c Anti-K	2
Anti-E Anti-K	1
Anti-E Anti-Jka	1
Anti-E Anti-Wra	2
Anti-E Anti-Jka	1
Anti-E Anti-Cob	1
Anti-E Anti-Jkb	1
Anti-E Anti-Lea	1
Anti-D Anti-C	2
Anti-c Anti-Jka	2
Anti-c Anti-K	2
Anti-K Anti-Cw	1
Anti-K Anti-Fyb	1
Anti-e Anti- Lea	1
Anti-M Anti-P1	1
Anti-N Anti-S	1
Anti-Lea Anti-Leb	2

CROSSMATCH / REFERENCE LABORATORY

The Crossmatch/Reference Laboratory within Diagnostic Services provides transfusion medicine services and reference testing to 37 hospitals within 13 Health Regions in Saskatchewan. **As of 2017-06-19, Crossmatching Services were repatriated from Canadian Blood Services to two Saskatchewan hospital sites.**

In 2018 there were no red cell antibody investigations referred to BC Diagnostic Services

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

	2018
Total samples sent	4
# of patients tested	4
# of patients not requiring MFM follow-up. (Tested negative for the corresponding antigen)	1

Patient	Maternal Antibody	Predicted Fetal Phenotype negative for the corresponding antigen	Follow-up required?
3	Anti-K	K inconclusive	Yes
8	Anti-K	K Pos	Yes
18	Anti-D	RhD Pos	Yes
21	Anti-K	K Neg	No

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 6: Patient # - RHD Type/Result (2018)

# of Patients	RHD Genotype	Predicted Phenotype	RHD Sequencing	Rh(D) Group
10	Possible D *	D variant	NO	NEG
12	Possible D	D positive	NO	POS
1	not done - too old. New sample requested			
14	weak D type 1	weak D	NO	POS
6	Weak D type 2	weak D	NO	Pos
2	weak D Type 3	weak D	NO	POS
5	weak D type 4.0 or 4.3	weak D	NO	NEG
50	**Total number tested**			

Possible D* = Rh neg (prior to 2018-04-16).
Possible D = Rh pos (after 2018-04-16).

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 well 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 Winnipeg 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.

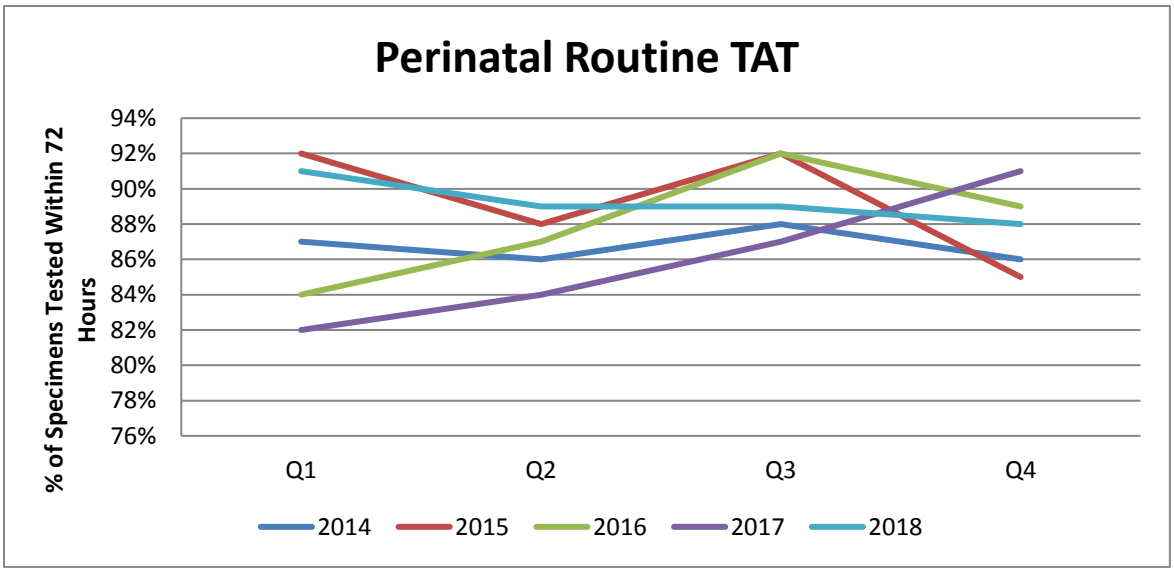
Table 7: Turnaround Time – Routine Criteria by Specimen Type

Specimen Type	Expected Turnaround Time	Expected % of Specimens Which Meet or Exceed Expected TAT
Routine Perinatal Specimens	< 72 hours	85%
Routine Crossmatch Specimens	< 24 hours	85%
Reference Specimens	< 72 hours	85%

Table 8: Turnaround Time – Routine Perinatal Specimens

Turnaround Time (TAT)	2014	2015	2016	2017	2018
% of Specimens Tested within 72 hours	87%	90%	87%	85%	89%
% of Specimens Tested > 72 hours	13%	10%	13%	15%	11%

Figure 5: Perinatal Routine TAT (2018)



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.

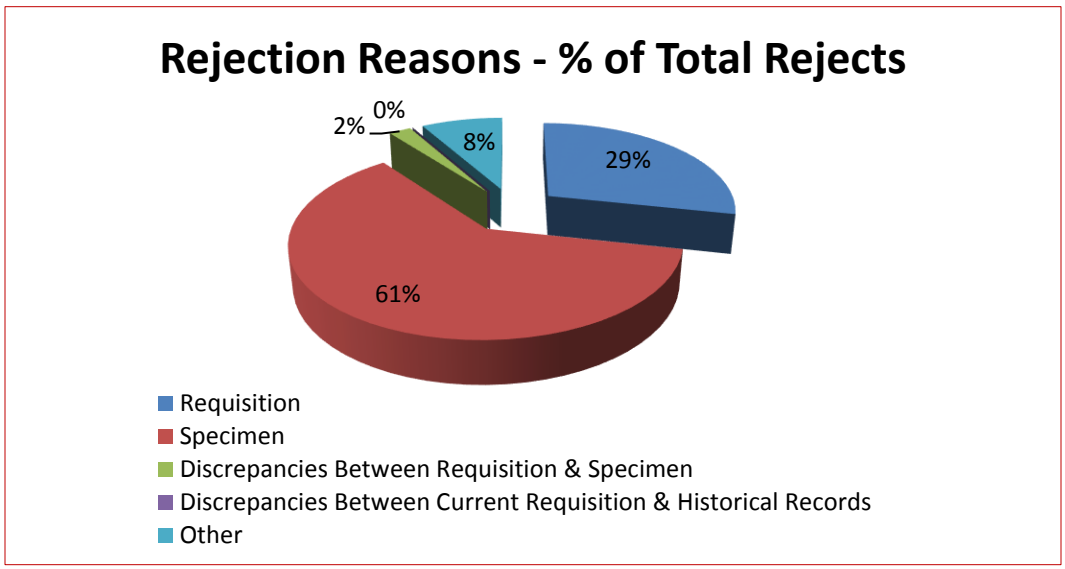
As described in *Table 9*, the reasons for rejecting specimens in the Perinatal Laboratory are distributed similarly between problems with requisitions and discrepancies between the requisition and the specimens. Also, a number of samples fell outside of the testing criteria, having been tested within 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 9: Quarterly Rejection Rates – Perinatal Specimens (2018)

Rejection Category	Q1	Q2	Q3	Q4
Requisition	4	9	8	17
Specimen	14	7	11	50
Discrepancies Between Requisition & Specimen	2	0	0	1
Discrepancies Between Current Requisition & Historical Records	0	0	0	0
Other (Duplicates, etc.)	3	2	2	4
Total # specimens rejected	23	18	21	72
Total # specimens received	5153	5169	4880	5709
Rejections as a % of total	0.4%	0.3%	0.4%	1.3%

Figure 6: Perinatal Rejection Reasons (2018)



ACCOMPLISHMENTS IN 2018

A. Perinatal Advisory Committee

The PNAC continues to collaborate throughout the year and at an annual November meeting. In 2018 several initiatives were finalized including a strategy for automated testing of passive anti D on the NEO analyzer, a standardized and updated investigation algorithm for patients with weak serological reactivity with anti D reagents and a standardized algorithm and repeat testing strategy for prenatal patients with anti M. These initiatives will be implemented in early 2019 with the final versions of the new Work Instruction format at all CBS perinatal testing labs.

The group reviewed and discussed recent national and international guidelines concerning recommendations for testing all prenatal patients with a repeat antibody investigation in mid pregnancy. Cost estimates were presented along with the calculated rate of new antibodies in this prenatal population. The group agreed to additional studies and collaboration with hospitals related to risks of antibody development in this group – possibly with feedback to the SOGC group based on the results. Additional research and collaboration regarding a change in titration strategy to include titration of multiple antibodies as combined titers was also planned – with prospective studies to proceed in the future.

PNAC had a wide-ranging discussion related to the investigation strategies for referral samples.

Ongoing work over the coming year will include concentrated efforts to update and standardize work instructions and to continue with plans for integrating NIRL donor and patient testing into the Brampton antibody investigation laboratory.

B. Revised Diagnostic Services Web Pages

All Diagnostic Services sites (Vancouver, Edmonton, Regina, Winnipeg, and Brampton) and National Immunohematology Reference Laboratory (NIRL) collaborated in a project to redesign and refresh the current Diagnostic Services webpages on www.blood.ca. The new "Laboratory Services" webpages features includes (Test Catalogue and Quick Links) and information to make the site more user friendly for hospital customers. The new web-section https://blood.ca/en/hospital-services/laboratory-services launched June 25, 2018.

C. Saskatchewan Perinatal Testing

With the closure of the Saskatchewan (SK) Diagnostic Services in October 2017, BC and Yukon Diagnostic Services was assigned testing of SK perinatal patients samples to provide continuity of services to the healthcare providers of SK. Under the scope of the perinatal program, BC provides routine testing, antibody identification, titrations and report results to SK healthcare provider. The SK perinatal program will be reverted back to Saskatchewan under the direction of SK Health in the near future.

GOALS FOR 2019

A. Perinatal Testing Transition

Canadian Blood Services will continue to hold planning discussions with Saskatchewan Ministry of Health officials and stakeholders to ensure a smooth transition process of perinatal testing from the Vancouver Diagnostic Services Laboratory to Saskatchewan hospital testing sites.

B. *MMA* Testing

When serologically compatible red blood cells are not available for a patient with several or rare alloantibodies, the *Monocyte Monolayer Assay (MMA)* can help predict the survival of serologically incompatible red blood cells in vivo. Canadian Blood Services will be determining the feasibility of implementing the *MMA* in Edmonton, and the potential for offering it as referral test to transfusion medicine clinicians and facilities. A thorough assessment of the methodology and required equipment and reagents will be performed, and the viability of this project will be determined.