Canadian Blood Services
Société canadienne du sang

DIAGNOSTIC SERVICES

SASKATCHEWAN

YEAR IN REVIEW

JANUARY – DECEMBER 2016

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.

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, fetal trauma or procedure, IV drug use).

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.

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).

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.

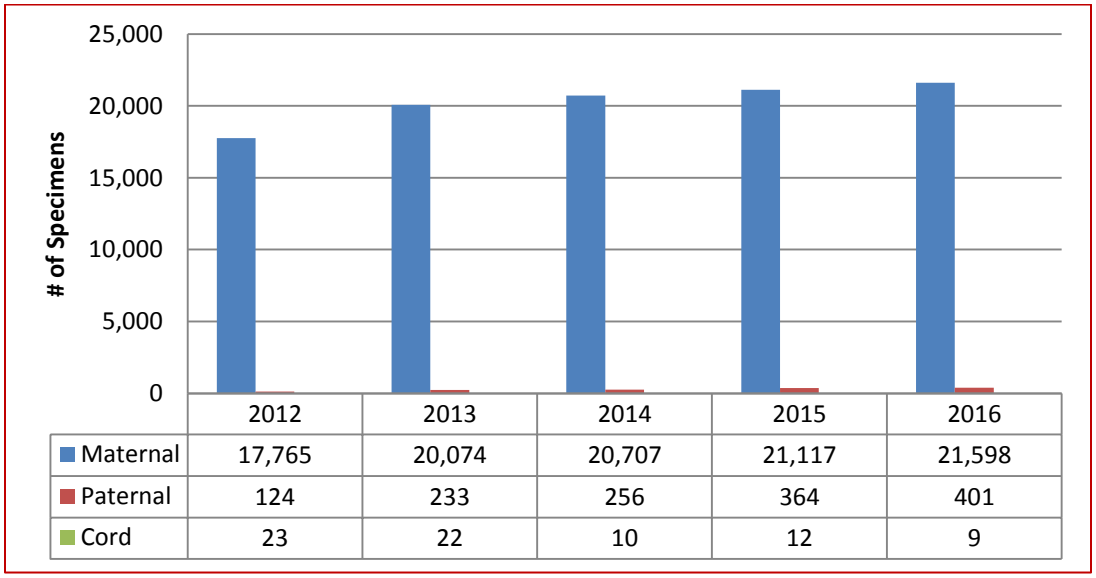
C. Specimens Tested

The data includes all women tested, including referrals.

Table 1: Perinatal Specimens Tested

Specimen Type	Test Type	2012	2013	2014	2015	2016
Maternal	Type and Screen	17,765	20,074	20,707	21,117	21,598
Paternal	ABO/Rh	124	233	256	364	401
Cord	ABO/Rh	23	22	10	12	9
Total # of Specimens Tested		**17,912**	**20,329**	**20,973**	**21,493**	22,008
Total # of Patients Tested		**14989**	**16925**	**17,450**	**17,631**	18,069

Figure 1: Total Perinatal Specimens Tested



D. Antibodies Identified

In 2016, a total of 152 antibodies were reported (see *Table 2*). This is slightly lower than 2015. One hundred and twelve women had antibodies identified during their pregnancies, of these; nineteen women 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-E, anti-K, anti-D, anti-C, anti-c, and anti-Jka which together represented 70% of the total antibodies identified.

Titres for 3 of the clinically significant antibodies increased from non-critical to critical levels during the pregnancy with a total of 25 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

Maternal Antibodies Identified (Including Passive D) – 2016					
Clinically Significant Antibodies - Antibody	**2012**	**2013**	**2014**	**2015**	**2016**
Anti-D	12	9	16	10	8
Passive Anti-D	156	123	156	178	217
Anti-C	8	10	14	10	8
Anti-E	32	33	39	38	28
Anti-c	11	3	16	12	13
Anti-e	4	2	3	5	6
Anti-Cw			1	3	1
Anti-M	14	12	13	10	6
Anti-N					1
Anti-K	20	17	24	30	37
Anti-S	3	4	6	3	2
Anti-s			1	1	1
Anti-Fya	3	2	9	6	2
Anti-Fyb	1	1	2	1	1
Anti-Jka	6	10	6	8	10
Anti-Jkb	1	1	4	3	1
Anti-Lua			1	0	1
Anti-Lub				0	
Anti-Kpa			2	0	1
Anti-G	1			1	1
Anti-Cob				1	
Anti-Wra				1	1
Anti-V					1
Anti-Mit					1
Anti-Dantu					1

Clinically Insignificant Antibodies - Antibody	**2012**	**2013**	**2014**	**2015**	**2016**
Anti-Le[a]	7	10	12	14	9
Anti-Le[b]	1	1	2	2	1
Anti-N		2	1		1
Anti-A_1					3
Anti-M					6

Table 3: Perinatal Patient Antibody Titres

Antibody	Critical Level	Non-Critical Level	Non-Critical to Critical
Anti-D	5	2	-
Anti-C	-	5	-
Anti-E	-	22	-
Anti-c	-	7	-
Anti-e	-	2	-
Anti-DC	-	-	-
Anti-DE	-	-	-
Anti-Ec	5	2	-
Anti-Ce	2	1	-
Anti-G	-	1	-
Anti-K	11	11	2
Anti-Fya	-	2	-
Anti-Fyb	-	1	-
Anti-Jka	1	9	1
Anti-Jkb	-	1	-
Anti-M	-	6	-
Anti-S	1	1	-
Anti-s	-	1	-

Figure 2: Total Number of Perinatal Antibodies

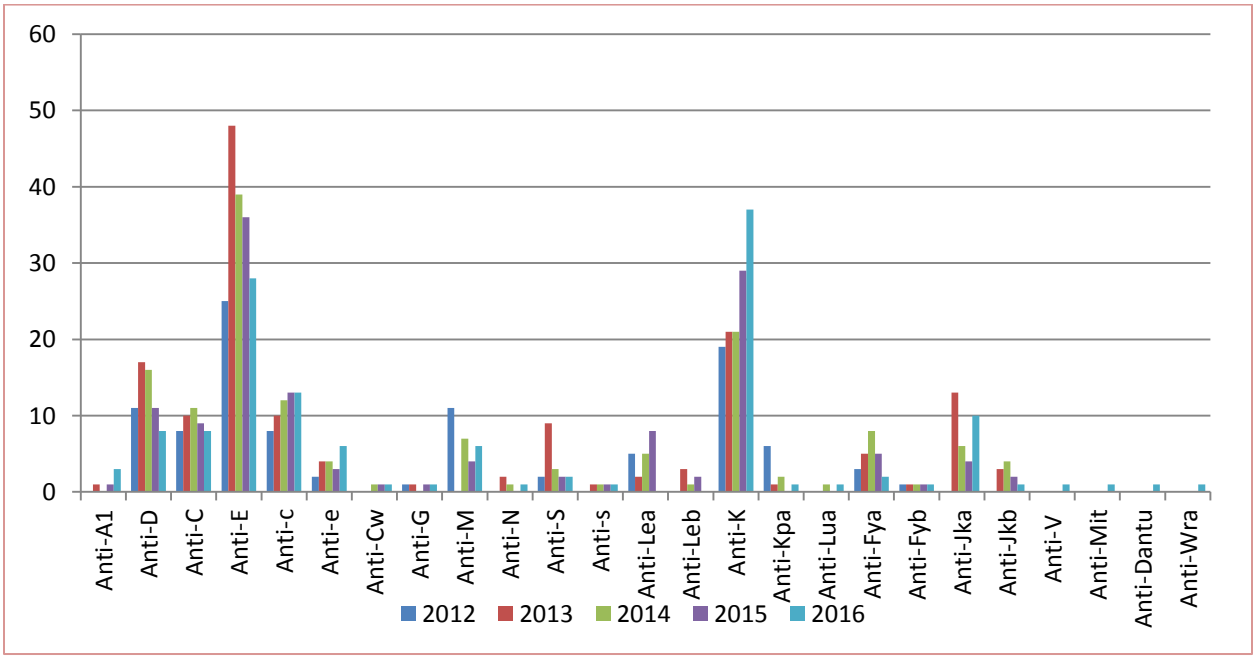


Figure 3: Frequency of Clinically Significant Antibodies

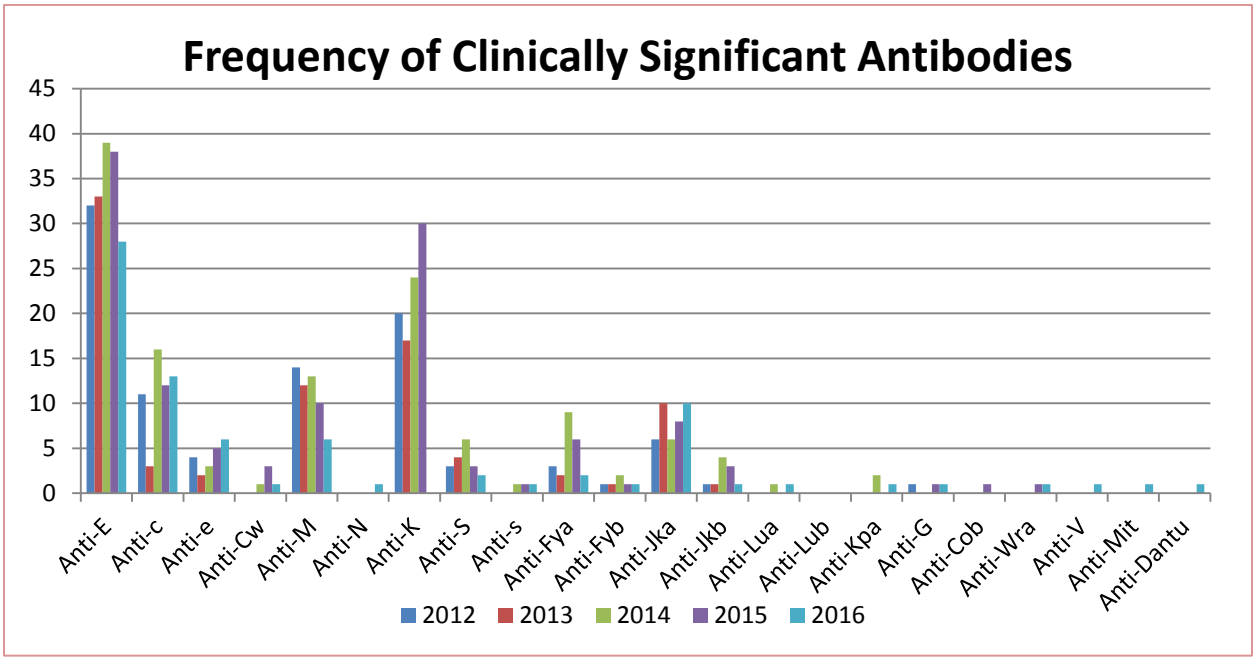


Table 4: Combination Antibodies

Antibodies	Number in 2016
Anti-C, Anti-D	2
Anti-c, Anti-E	6
Anti-C, Anti-e	4
Anti-c, Anti-E, Anti-Fya, Anti-K, Anti-s	1
Anti-C, Anti-G	1
Anti-c, Anti-Jka	1
Anti-Dantu, Anti-Mit, Anti-Wra	1
Anti-E, Anti-Jka	1
Anti-Fyb, Anti-V	1
Anti-K, Anti-Kpa	1
Total	19

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.

Testing Performed

The Crossmatch/Reference Laboratory routinely performs the following tests:

- ABO/Rh blood type
- Screen for red blood cell antibodies
- Antibody Identification, if antibodies are detected
- Crossmatch, electronic and serological
- Phenotyping (patient and donor units)
- Transfusion Reaction Investigation
- Direct Antiglobulin Test
- Elution and Absorption

Antibody screening and identification is routinely performed by tube testing using PEG for enhancement.

Crossmatched blood components are distributed through the Diagnostic Services Laboratory to those hospitals which receive all of their transfusion medicine services from Canadian Blood Services. Hospitals which provide transfusion medicine services directly receive all of their blood components through the Product and Hospital Services area at Canadian Blood Services.
As a Reference Laboratory, the Crossmatch Laboratory performs complex antibody investigations and distributes crossmatch compatible (or least incompatible) red cell units.

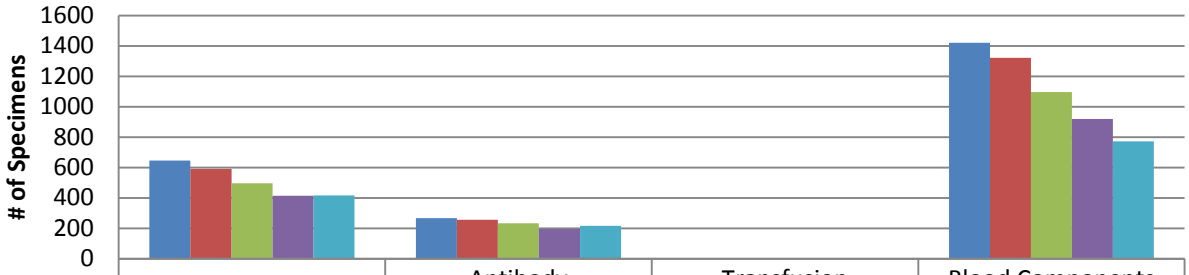
A. **Specimens Tested**

The data in this report reflects a calendar year period to enable better correlation to other government statistical data. The total number of crossmatch specimens tested has shown a slight increase over the past year.

Table 5: Crossmatch/Reference Specimens Tested

Specimen Type	Test Type	2012	2013	2014	2015	2016
Crossmatch/Reference	Type and Screen	645	590	497	413	416
	Antibody Investigations	267	257	232	196	217
	Transfusion Reaction Investigations	1	0	1	2	2
	Blood Components Distributed	1420	1321	1096	919	772
Test Totals (excluding components distributed)		**913**	**847**	**730**	**611**	**635**
Number of Patients Tested		**346**	**328**	**262**	**242**	**214**

Figure 4: Total Crossmatch Specimens Tested



	Type and Screen	Antibody Investigations	Transfusion Reactions	Blood Components Distributed
2012	645	267	1	1420
2013	590	257	0	1321
2014	497	232	1	1096
2015	413	196	2	919
2016	416	217	2	772

B. Antibodies Identified

In 2016, a total of 70 antibodies were reported (*see Table 6*). The total number of antibodies detected is slightly lower than 2015 but similar to 2012 to 2014. The distribution of the most common antibodies remains consistent.

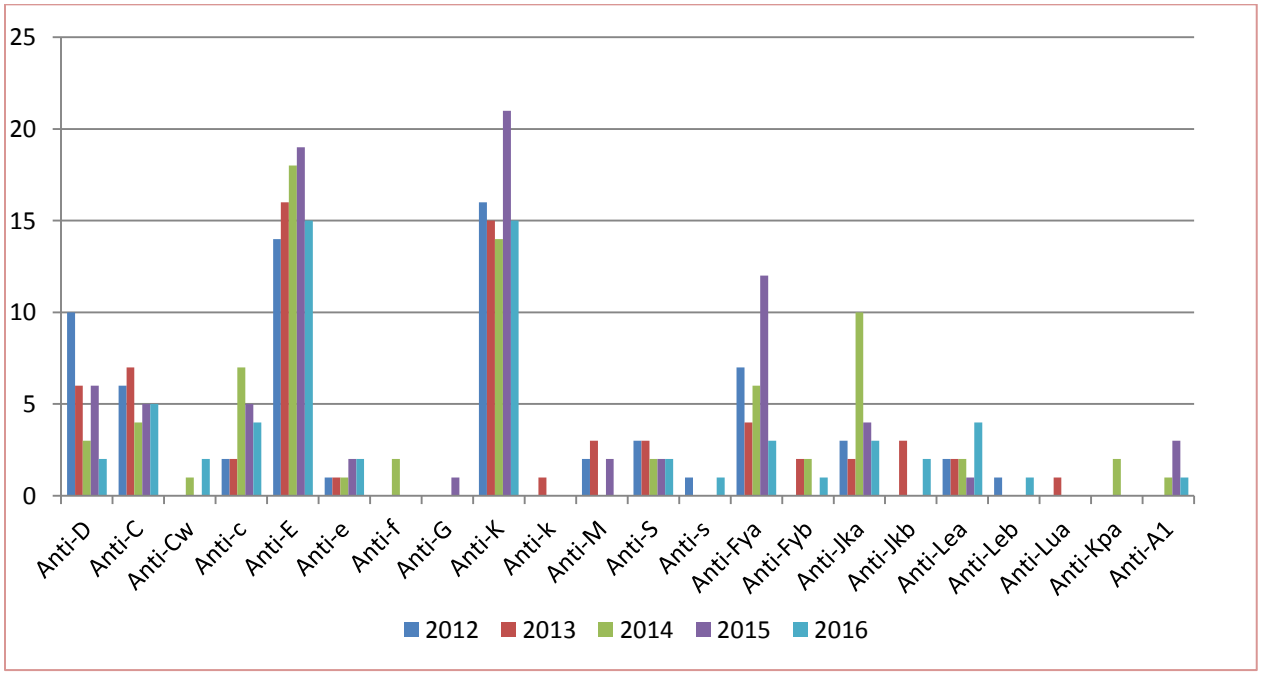
Antibodies identified were considered to be clinically significant if they have been reported to cause acute or delayed hemolytic transfusion reactions. The most common clinically significant antibodies identified were anti-E, anti-K, Anti-c and anti-C (*see Figure 5*) which together represented 64% of the total antibodies identified.

Table 6: Total Number of Crossmatch Antibodies Detected

Antibody	Number Detected 2012	Number Detected 2013	Number Detected 2014	Number Detected 2015	Number Detected 2016
Anti-D	10	6	3	6	2
Anti-C	6	7	4	5	5
Anti-Cw			1		3
Anti-c	2	2	7	5	7
Anti-E	14	16	18	19	19
Anti-e	1	1	1	2	2
Anti-f			2		
Anti-G				1	
Anti-K	16	15	14	21	14

Anti-k		1			
Anti-M	2	3		2	
Anti-S	3	3	2	2	2
Anti-s	1				1
Anti-Fya	7	4	6	12	3
Anti-Fyb		2	2		1
Anti-Jka	3	2	10	4	3
Anti-Jkb		3			2
Anti-Lea	2	2	2	1	4
Anti-Leb	1				1
Anti-Lua		1			
Anti-Kpa			2		
Anti-A1			1	3	1
Total	68	68	75	83	70

Figure 5: Total Number of Crossmatch Antibodies



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.

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 2016, the following results were obtained in patients using one of the two Red Cell antigen genotyping platforms available at CBS:

Figure 6: Rh D Testing Algorithm

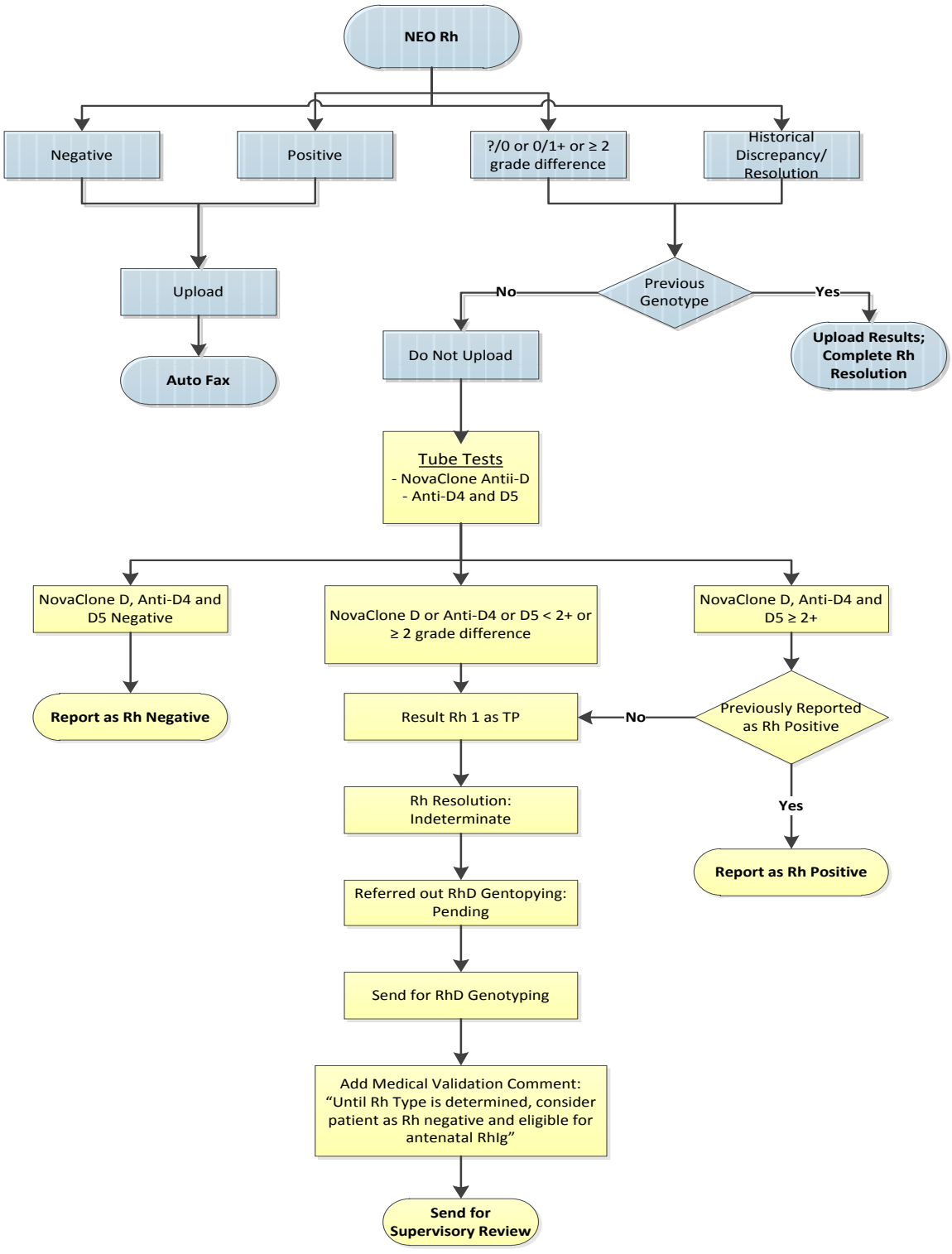


Table 7: Patient # - RHD Type/Result

Number of Patients	RHD Genotype	Predicted Phenotype	RHD Sequencing	Rh Group
17	Sample does not contain any of the RHD polymorphisms interrogated by the kit	Possible D Variant	No	Negative
2	Sample does not contain any of the RHD polymorphisms interrogated by the kit	Possible D Variant	No	Positive
5	Weak D Type 4.0 or 4.3 (RHD*09.03 or RHD*09.05)	Weak D	No	Negative
2	Weak D Type 3 (RHD*01W.3)	Weak D	No	Positive
1	DAR (RHD*09.01)	May form Alloanti-D	No	Negative
1	DHMi (RHD*19)	May form Alloanti-D	No	Negative

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. TAT data for Platelet Immunology will be available commencing in 2014.

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%
Routine Crossmatch Specimens	24 hours	85%
Reference Specimens	72 hours	75%

Figure 7: Perinatal Routine TAT

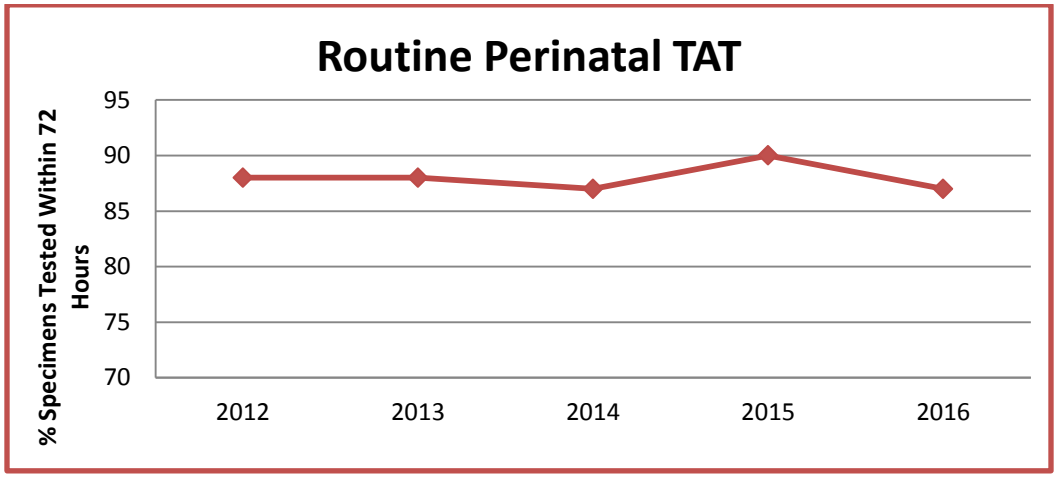


Table 9: Turnaround Time – Routine Perinatal Specimens

Turn Around Time (TAT)	2012	2013	2014	2015	2016
% of Specimens Tested within 72 hours	88%	88%	87%	90%	87%
% of Specimens Tested > 72 hours	13%	13%	13%	10%	13%

Figure 8: Crossmatch Routine TAT

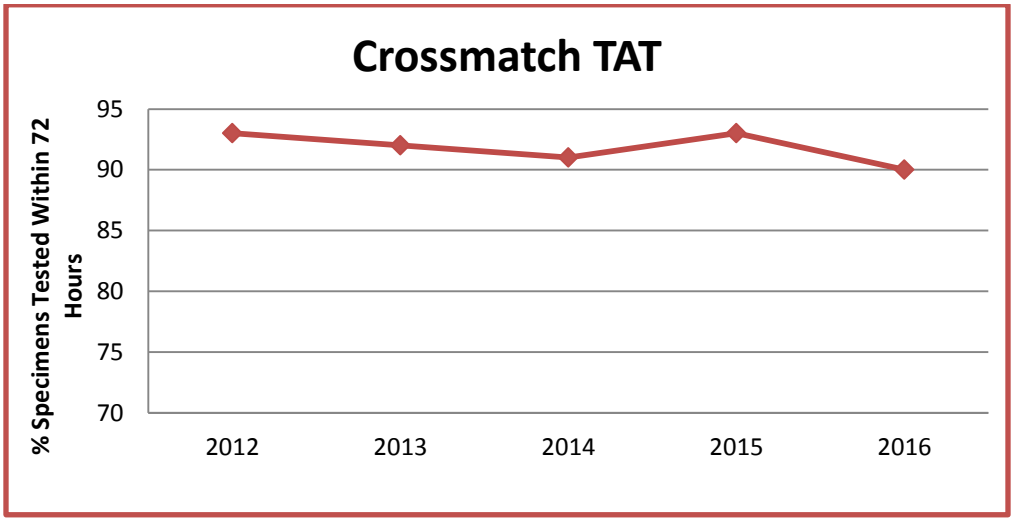


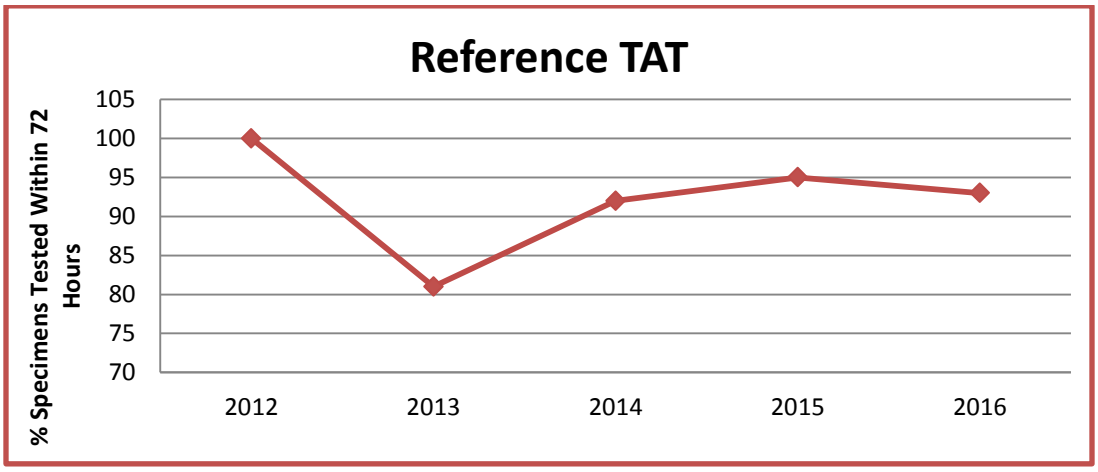
Table 10: Turnaround Time – Routine Crossmatch Specimens

Turn Around Time (TAT)	2012	2013	2014	2015	2016
% of Specimens Tested within 24 hours	93%	92%	91%	93%	90%
% of Specimens Tested > 24 hours	7%	8%	9%	7%	10%

Table 11: Reference TAT

Turn Around Time (TAT)	2012	2013	2014	2015	2016
% of Specimens Tested within 72 hours	100%	81%	92%	95%	93%
% of Specimens Tested > 72 hours	0%	2%	1%	5%	7%

Figure 9: Turnaround Time – Reference Specimens



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 12*, 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% from Q1 to Q4.

Table 13 describes the reasons for rejecting specimens in the Crossmatch Laboratory. Cancellation of the crossmatch (Other category) is the only rejection code used in 2016. Problems with requisitions and specimen labelling are rare occurrences in the Crossmatch Laboratory.

Table 12: Quarterly Rejection Rates – Perinatal Specimens

Rejection Category	Q1	Q2	Q3	Q4
Requisition	26	18	22	24
Specimen	21	12	25	30
Discrepancies Between Requisition & Specimen	0	1	5	10
Discrepancies Between Current Requisition & Historical Records	24	10	22	14
Other (Duplicates, etc.)	24	10	22	14
Total # specimens rejected	106	84	111	92
Total # specimens received	5374	5720	5274	5340
Rejections as a % of total	**2%**	**2%**	**3%**	**2%**

Figure 10: Perinatal Rejection Reasons

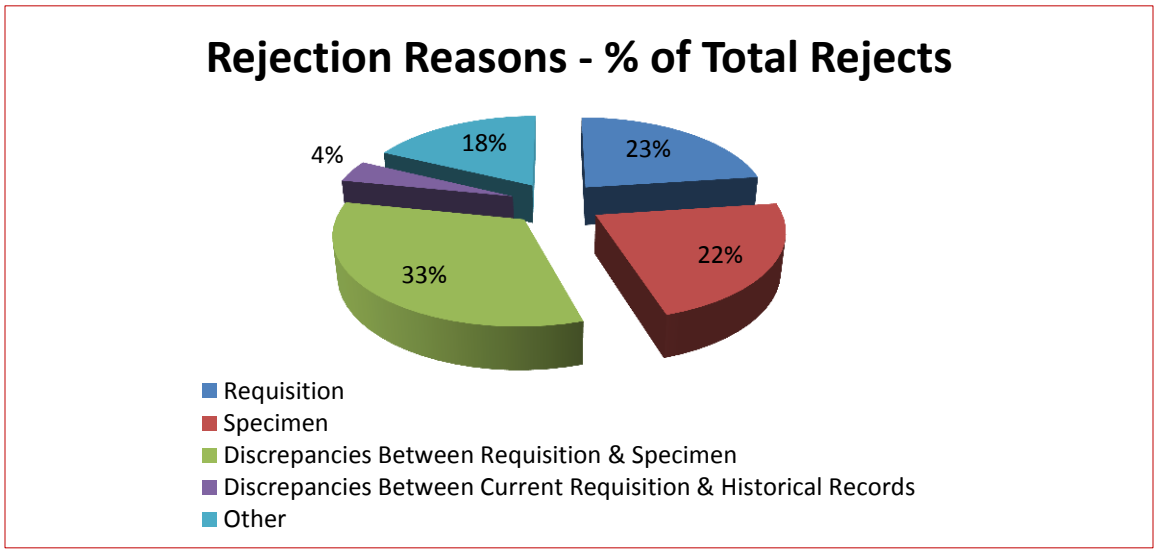


Table 13: Quarterly Rejection Rates – Crossmatch Specimens

Rejection Category	Q1	Q2	Q3	Q4
Requisition	0	0	0	0
Specimen	0	0	0	0
Discrepancies Between Requisition & Specimen	0	0	0	0
Discrepancies Between Current Requisition & Historical Records	0	0	0	0
Other (Duplicates, etc.)	3	0	0	0
Total # specimens rejected	3	0	0	0
Total # specimens received	98	102	43	63
Rejections as a % of total	**3%**	**0%**	**0%**	**0%**

ACCOMPLISHMENTS IN 2016

A. Restructure Laboratory Services

Participate with MOH, 3S Health and Regional Health Authorities in discussions related to restructuring provincial laboratory services. Discussions will include transfer of the crossmatch services to RHAs and potential relocation of the perinatal testing program.

B. Perinatal Advisory Committee

The Perinatal Advisory Committee for 2016 was held on June 13th and 14th. This year, the PNAC meeting was hosted in Winnipeg and was held in conjunction with a Grifol's Transfusion Science Education Course, which followed the PNAC meeting on June 15th and 16th.

The PNAC meeting covered a range of topics relevant to the CBS diagnostic and perinatal laboratories. Our agenda included a review of laboratory internal audits which allowed us to compare practice across laboratories and identify areas for improvement and standardization. Specific standardization initiatives related to the antibody investigation algorithm for prenatal patients, the strategy and algorithm used for assessment of serological weak D patients through genotyping, and recommendations related to standard timing for prenatal sample testing were discussed. We developed a strategy for investigation of anti G in prenatal patients and discussed the feasibility of enhanced automated testing.

Results of projects from the prior year were also reviewed. These included the results of an audit amongst hospital transfusion services regarding the feasibility of using Kell negative phenotyped red cell units for transfusion to female patients of child bearing potential, as well as the results of a study into the utility of a new monoclonal anti Mia antibody.

In follow up to the 2016 meeting several projects have been selected for additional work. These include continued work on alignment of the algorithm for assessment for weak and partial D antigens by RHD genotyping. The second involves additional work on development and standardization of automated testing for passive anti D evaluation and the third major initiative chosen for additional work was the agreement on timing of sample testing for perinatal patients.

The PNAC meeting was followed by a one and one half day Grifol's Transfusion Science Education course. The course included a distinguished panel of speakers who covered diverse topics related to both blood group serology and the utility afforded by blood group genotyping. The education day was well attended by both local transfusion medicine staff and transfusion professionals from across Canada.

The annual Perinatal Advisory Committee meeting for 2016 is planned for June 13 and 14 2016 in Winnipeg MB. The PNAC meeting will be followed by an Educational Event sponsored by Grifols. Attendees will include Laboratory Directors, Associate Directors and Managers as well as perinatal supervisory staff and laboratory physicians who oversee perinatal testing. We will also welcome some hospital colleagues, both technologists and physicians, who are involved with perinatal testing laboratories. Ongoing work on standardization among our laboratories is a theme for this year. Our meeting plan and ongoing work plan for the remainder of 2016 will include:

- Discussion and consensus on appropriate follow up for perinatal patients with inconclusive antibodies.
- Planning for investigation of patients with possible antibodies to low prevalence antigens in the perinatal setting. We will discuss the development of a standard “low prevalence” panel of cells that will allow for investigation of antibodies to low prevalence antigens which may be clinically significant in pregnancy.
- Discussion and consensus on the timing of repeat samples for patients with clinically significant or potentially significant antibodies in the perinatal setting.
- We will discuss the functionality of our standardized antibody investigation algorithm, including any necessary changes following one year of use.
- We will optimize and standardize the use of our algorithm used for RHD genotyping in perinatal patients with weak or variable Rh D serological typing.
- We will discuss the optimal serological evaluation for anti G, especially in the presence of passive anti D.
- We will discuss the results of an audit of Kell negative donor unit availability in transfusion of Kell negative (or Kell unknown) females of child bearing potential.

We will have some updates and final discussions on completed projects including a study of anti Mia antisera in the BC perinatal testing lab as well as an update of testing and labeling strategies for platelet products in fetal/neonatal alloimmune thrombocytopenia.

GOALS FOR 2017

A. Crossmatch Repatriation

CBS is working with the Saskatchewan Ministry of Health and the Regional Health Authorities to repatriate crossmatch services that have been provided by the Canadian Blood Services, Regina to the provincial laboratories. Transition of these services is underway and will occur in 2017.