

1st Edition, November 2023

**Guidance for
RHD non-invasive
prenatal testing (*RHD*
NIPT)
for fetal RhD blood group
prediction in pregnancy**

Assisting clinical care providers with the safe introduction
of *RHD* NIPT and targeted RhD immunoglobulin therapy



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Disclaimer

Institutions using this guidance document should formulate their own policies according to their patient population and availability of *RHD* NIPT. By necessity, these policies may need to be broader than those in this document.

We acknowledge the limitations and imperfections inherent in terminology and have aimed to use terminology that is as inclusive as possible, and which avoids inadvertent exclusion.

While the advice and information in this guidance is believed to be true and accurate at the time of publication, the authors and the ANZSBT recognise that preferred terminology and language will continue to change over time to reflect diverse and evolving consumer identities and needs.

Guidance for *RHD* non-invasive prenatal testing (*RHD* NIPT) for fetal RhD blood group prediction in pregnancy

Prepared by the:

Steering Committee of the Quality Use of Non-Invasive Prenatal *RHD* Testing Project
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Acknowledgement

The development of the Guidance for *RHD* non-invasive prenatal testing (NIPT) for fetal RhD blood group prediction in pregnancy, a national roadmap for the safe and appropriate introduction of *RHD* NIPT and associated clinical care pathways and brochures was supported by a Quality Use of Pathology Program (QUPP) Grant (4-GZS2YFL) from the Australian Government Department of Health.

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Foreword

The Australian and New Zealand Society of Blood Transfusion (ANZSBT) is pleased to publish the first edition of *Guidance for RHD non-invasive prenatal testing (NIPT) for fetal RhD blood group prediction in pregnancy*.

The project to develop this guidance was funded by a \$352,000 grant from the Australian Government Department of Health 'Quality Use of Pathology Program' (QUPP). The QUPP is a competitive national grants program which aims to improve health and economic outcomes through best practice use of pathology testing and receiving this grant is a significant achievement for the Society.

The guidance document was developed to support the advancement of the recommendation for the introduction of NIPT for fetal *RHD* in all RhD negative pregnant women, complementing the *Guideline for the Prophylactic use of Rh D immunoglobulin in pregnancy care* (NBA, 2021)¹.

In developing the guidance, the project's Steering Committee consulted widely and has produced a national roadmap, clinical care pathways, and complementary materials to support the safe and appropriate introduction of *RHD* NIPT into the clinical setting and enable targeted antenatal RhD immunoglobulin prophylaxis.

On behalf of Council and members I wish to acknowledge the commitment David Roxby (Project Manager) and Kristen Brown (Project Officer) along with the members of the Steering Committee, chaired by Philip Crispin, who provided their time and expertise in developing this excellent and important guidance document.

Simon Benson
ANZSBT President

November 2023

1. National Blood Authority (2021) *Guideline for the prophylactic use of Rh D immunoglobulin in pregnancy care*
<https://www.blood.gov.au/anti-d-0>

Abbreviations

Ab	Antibody
ACM	Australian College of Midwives
ANZSBT	Australian and New Zealand Society of Blood Transfusion
cffDNA	Cell free fetal deoxyribonucleic acid
CVS	Chorionic villus sampling
CHF	Consumer's Health Forum of Australia
DAT	Direct antiglobulin test
EDD	Estimated due date
EDTA	Ethylenediaminetetraacetic acid
FMH	Fetal maternal haemorrhage
GP	General Practitioner
HDFN	Haemolytic disease of the fetus and newborn
Ig	Immunoglobulin
IATA	International Air Transport Association
IUT	Intrauterine transfusion
Lifeblood	Australian Red Cross Lifeblood
LIS	Laboratory information system
MRN	Medical record number
NBA	National Blood Authority
NIPA	Non-invasive prenatal assessment
NIPT	Non-invasive prenatal testing
NPAAC	National Pathology Accreditation Advisory Council
PHN	Primary health network
PTS	Pneumatic tube system
QUPP	Quality Use of Pathology Program
RACGP	Royal Australian College of General Practitioners
RANZCOG	Royal Australian and New Zealand College of Obstetrics and Gynaecology
SOP	Standard operating procedure
TAT	Turnaround time

Glossary

Antenatal record	A unique healthcare record that contains all relevant information from conception and throughout a pregnancy
False-positive	An RhD negative fetus that is incorrectly classified as RhD positive
False-negative	An RhD positive fetus incorrectly classified as RhD negative
Hand-held pregnancy Record	The hard-copy personal record provided to women where clinical pregnancy and postnatal visits are documented
Healthcare Professionals	The term healthcare professionals refer to all clinical care providers, including general practitioner's, midwives, nurses, medical officers and obstetricians
Healthcare record	Documentation unique to the patient, containing transcripts of patient care and progress, investigational data and consultations, which is retained by the managing healthcare professional or health service
Kleihauer-Betke Test	Test used to detect and quantify fetomaternal haemorrhage
Medical Record Number (MRN)	A number used by a hospital or health facility to identify an individual and their health records
My Health Record	The digital health record, unique to each individual, that enables direct uploading of medical and diagnostic reports
Non-Invasive Prenatal Testing (NIPT)	A screening test which analyses fetal DNA obtained from a maternal blood sample
Partial D RhD group	RhD antigen with fewer antigen sites or missing epitopes leading to weak(er) or absent reactions with anti-D sera
Patient	The term patient refers to both woman and infant in the context of healthcare provision and is not intended to imply ill health
Pneumatic Tube System	Transport system comprised of cylindrical tubes which use a vacuum mechanism to transport specimens between laboratory and or hospital departments for processing
Processing pathology/specimen	The pathology or laboratory services that completes the testing and resulting of a laboratory service
Referring pathology/Laboratory service	The laboratory/pathology service that transports a specimen to another pathology/laboratory service for testing. This may be within the pathology service network or an external provider
<i>RHD</i>	The gene symbol for RhD gene (italicised)
RhD	Refers to the RhD blood group system
<i>RHD</i> NIPT	A screening test which analyses fetal DNA obtained from a maternal blood sample, to determine the fetal RhD blood group

Shared care (in the context of pregnancy)	A collaborative agreement for agreed goal/s and treatment plan between a team of health healthcare professionals and the woman throughout the antenatal and postnatal period
Specimen	Means any tissue or fluid (including blood) from an individual that is submitted to the pathology service testing

Summary of Amendments - May 2025

Guideline updated to reflect changes in nomenclature of Variant D phenotypes

- Please refer to the following sections:
 - 2.1 - Indication and timing of *RHD* NIPT during pregnancy
 - FP3 - Flow pathway for *RHD* NIPT for RhD negative women in pregnancy
 - FP5 - Flow pathway for women with a known Variant D (weak or partial D) blood group
 - 4.3.2 Risks of *RHD* NIPT

Introduction

This guidance have been developed to support the introduction of *RHD* non-invasive prenatal testing (NIPT) for fetal *RHD* genotyping, and targeted RhD immunoglobulin (Ig) prophylaxis in pregnant women who are RhD negative.

The guidance recommendations are intended to be utilised in conjunction with existing national guidelines pertaining to RhD Ig prophylaxis; including the Department of Health *Clinical Practice Guidelines: Pregnancy Care*², the National Blood Authority (NBA) *Guideline for the Prophylactic use of Rh D immunoglobulin in pregnancy care*³, and the Australian and New Zealand Society of Blood Transfusion (ANZSBT) *Guidelines for Transfusion and Immunohaematology Laboratory Practice*.⁴ The guidelines have been provided in a format that enables adaption for local context and should be considered with existing processes and resources for maternity care pathways.

The document has been developed from a summary of existing evidence, relevant national guidelines, the international implementation experience and subject matter expert consensus of what is determined to be good practice (see bibliography).

The NIPT method refers only to NIPT for *RHD* status of the fetus. It remains separate from other non-invasive prenatal tests used for genetic screening. For pregnant women with anti-D red cell antibodies detected during pregnancy, the specialised *RHD* NIPT testing for fetal genotyping is provided by Australian Red Cross Lifeblood (“Lifeblood”); this is not included in this guidance document. It is important that the scope of the *RHD* NIPT for fetal RhD prediction is clearly distinguished from all other types of non-invasive prenatal tests, so that pregnant women and clinicians understand the clear purpose of this test.

There are approximately 45,000 women in Australia who are identified to be RhD negative who give birth each year. Of these, approximately two thirds (29,000) will be carrying an RhD positive fetus. If maternal anti-D antibodies are produced, they will be directed against fetal red blood cells that express RhD leading to potential haemolytic disease of the fetus and newborn (HDFN). This can have significant morbidity and mortality as it leads to severe anaemia, causing fetal hydrops (heart failure) and jaundice resulting in kernicterus, long-term disability, or death.

At the time of writing this guidance document, routine practice in Australia was for RhD Ig to be given to all RhD negative women at 28 and 34 weeks gestation, regardless of the RhD blood group of the fetus. This was due to the inability to determine the fetal RhD status except using invasive testing, such as amniocentesis or chorionic villus sampling, or from cord blood typing completed at birth. This universal approach to prophylactic RhD Ig administration means that the approximately 16,000 RhD negative women who are not carrying a RhD positive fetus are receiving RhD Ig unnecessarily. At the

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2. Department of Health (2020) *Clinical Practice Guidelines: Pregnancy Care*
<https://www.health.gov.au/resources/pregnancy-care-guidelines>
 3. National Blood Authority (2021) *Guidelines for the Prophylactic use of Rh D immunoglobulin in pregnancy care*
<https://www.blood.gov.au/anti-d-0>
 4. Australian and New Zealand Society of Blood Transfusion (2016; revised 2020) *Guidelines for Transfusion and Immunohaematology Laboratory Practice*
<https://anzsbt.org.au/guidelines-standards/anzsbt-guidelines>

birth of the baby, a subsequent dose of RhD Ig is given to women who are RhD negative if the baby is RhD positive. The routine use of RhD Ig for all women who are RhD negative creates significant supply challenges, and despite an exceptionally safe blood product supply in Australia, still results in exposure to avoidable risks of blood products.

To provide targeted RhD Ig therapy for only those women who require treatment (RhD negative mother carrying a RhD positive fetus), *RHD* NIPT is required to determine the fetal RhD blood group. The *RHD* NIPT has proven safety and efficacy as the routine standard of care in several countries (Denmark, Sweden, France, Germany, Netherlands and the UK), with many of these countries adopting this approach more than 10 years ago.

As pregnancy progresses, there is an increasing amount of cell-free fetal DNA (cffDNA) [3-30% depending on gestational age] circulating in the maternal blood. *RHD* NIPT uses cffDNA obtained from a maternal blood specimen to predict the fetal RhD status, thereby allowing targeted therapy with RhD Ig prophylaxis for women who are RhD negative. To ensure adequate amounts of cffDNA, it is recommended that *RHD* NIPT is not performed prior to 11⁺ weeks gestation.

The test is very accurate, with a small chance that the results will report a RhD positive fetus when the fetus is identified as negative at birth. Of clinical significance is the potential for a very small chance of RhD positive fetuses to be reported incorrectly as RhD negative. This may lead to alloimmunisation of the mother affecting the baby and future pregnancies. The risk of this occurring remains low, as these babies will be identified as RhD positive following cord blood sample testing at birth and the mother offered RhD Ig to minimise the risk.

RHD NIPT should be offered as standard care for all women who are RhD negative with no preformed RhD antibodies (as per NBA Guidelines). The *RHD* NIPT must not be confused with non-invasive prenatal analysis (NIPA) for women identified at high risk of HDFN with preformed red cell antibodies such as anti-D, K or Fy (testing performed by Lifeblood's Red Cell Reference Laboratory, Queensland). The present guideline does not change this pathway.

Scope

This guidance document supports safe practices for services and organisations wishing to introduce *RHD* NIPT as part of the pregnancy care pathway. The intention is to ensure that RhD negative women who require RhD Ig receive the intended prophylaxis throughout their pregnancy and at the birth of their baby. The guidance refers to fetal *RHD* NIPT recommended for RhD negative women who have no preformed red cell RhD antibodies. Women with preformed clinically significant antibodies (for example anti-D, -c, -C, -E, -K, -k, -Fy^a, -Fy^b) or variant D (weak/partial D) groups will require specific testing (see Section 2.2 clinical pathways).

It is acknowledged that service variation may require local adaptation of resources and policies, with the aim of the guideline to provide a generalised approach to practice that can be applied to all maternity care models, regardless of their location in Australia and the patient population for whom they provide care.

Terminology

The guidance is primarily informative and reflect what the Project Steering Committee believes is the minimum acceptable level of practice. Guidance is provided in the form of recommendations, the strength of which is indicated by the following (modal) terms:

Must Indicates a strongly recommended practice where compliance would be expected.

- Should** Indicates a recommended practice where compliance would be expected but alternative practices may be acceptable.
- May** Indicates a practice that is permitted within the context of the guidance.⁵

5. Ginige, S, Daly, J, Hyland, C, Powley, T, O'Brien, H, Moreno, A, Gardener, G and Flower, R. (2022) The role of non-invasive prenatal testing (NIPT) for fetal blood group typing. *Australian and New Zealand Journal of Obstetrics and Gynaecology*, 62: 33-36 <https://obgyn.onlinelibrary.wiley.com/doi/10.1111/ajo.13446>

1 Roles and responsibilities

1.1 Clinical care providers

It is the responsibility of all healthcare professionals (midwives, general practitioners (GPs) and medical officers) providing antenatal care at any time point during the antenatal period to follow the procedure in this guidance and ensure that following processes occur where indicated:

- Provide information
- Informed consent:
 - Consent for *RHD* NIPT (verbal)
 - Consent for RhD Ig (written)
- Documentation of the results and management completed in the individual health record/clinical records
- Request of correct test type, specimen collection and follow up results of blood tests
- Documentation of results and management completed in the individual health record/clinical records
- *All adverse events are reported according to local and/or national requirements*

1.2 Laboratory and pathology staff

Laboratory and pathology staff have the responsibility to provide accurate, safe and reliable test results for *RHD* NIPT and ensure accessibility of the results to the woman and the healthcare providers. This includes:

- Ensuring minimum specimen requirements are met or provide notification to the requesting clinician when the specimen does not meet the minimum requirements for processing
- Reporting of results and entry within the relevant laboratory information system (LIS)
- Uploading of the *RHD* NIPT report to My Health Record
- Adhering to all local standard operating procedures (SOPs) relating to the specimen collection, transport, tracking, analysis, resulting and reporting

2 Indication and timing of *RHD* NIPT during pregnancy

2.1 Indication

All pregnant women must have their blood group (ABO and RhD) and antibody screen completed prior to ordering *RHD* NIPT. Where the blood group testing has been completed by an external/private pathology laboratory, a copy of the report must be available and should be entered into the woman's healthcare record.

All pregnant women with a RhD negative blood group with no preformed anti-D red cell antibodies should be offered *RHD* NIPT between 12 weeks and 26 weeks gestation for each individual pregnancy (see simplified flow pathway FP1; page 11). This includes women with a singleton or multiple pregnancy as the *RHD* NIPT will identify if at least one of the fetuses is RhD positive and RhD Ig prophylaxis will be recommended if there is a positive result.

Women with other preformed clinically significant red cell alloantibodies, D Variant (weak/partial D) (other than weak D group 1, 2, 3, 4.0, 4.1, Asian DEL [RHD*1227A]) will require specific testing (see Section 3. Clinical care pathways).

If a woman presents after 26 weeks gestation, routine RhD Ig prophylaxis at 28 weeks should be recommended as well as *RHD* NIPT, as the *RHD* NIPT results may not be available by 28 weeks gestation due to transport and specimen processing delays.

Completing *RHD* NIPT may be considered up to 32 weeks as this would still prevent the dose of RhD Ig at 34 weeks gestation for women carrying an RhD negative baby.

Local care pathways should also consider women who have not had antenatal care prior to birth, present late (after 26 weeks) or for those women who decline to have the test.

2.2 Timing of *RHD* NIPT

Evidence supports testing beyond 11 weeks gestation, however *RHD* NIPT assays should focus on a careful design that ensures adequate levels of cffDNA that ensures high sensitivity to avoid false-negative results. This guidance recommends *RHD* NIPT testing from 12 weeks gestation to align with current antenatal schedule of care although individual laboratories may wish to validate from 11 weeks gestation.

Testing should be completed at or after 12 weeks and prior to 26 weeks gestation to align with current antenatal care schedules. This optimises result accuracy and allows for transport, processing and reporting of results prior to the 28 weeks appointment should the woman require RhD Ig.⁶

A woman may still be considered for *RHD* NIPT testing up to 32 weeks, as RhD Ig would not be required at 34 weeks and for sensitising events if the fetus was predicted to be RhD negative (refer to FP1-4).

⁶ National Blood Authority (2021) *Guideline for the prophylactic use of Rh D immunoglobulin in pregnancy care*
<https://www.blood.gov.au/anti-d-0>

2.2.1 Late presentation

For women who have not had antenatal care prior to 26 weeks of pregnancy, the care pathway should continue as per the current universal approach for routine prophylaxis as outlined in the RANZCOG 2019 *Guidelines for the use of Rh(D) Immunoglobulin (Anti-D) in obstetrics*.⁷

For women who have missed *RHD* NIPT prior to 26 weeks gestation, the woman may still be considered for *RHD* NIPT up to 32 weeks to further reduce unnecessary RhD Ig prophylaxis requirements.

7. Royal Australian and New Zealand College of Obstetrics and Gynaecology (2019) *Guidelines for the use of Rh(D) Immunoglobulin (Anti-D) in Obstetrics (C-Obs 6)*
<https://ranzocg.edu.au/resources/statements-and-guidelines-directory>

3 Clinical care pathways

3.1 Transition of Care

Clinical care during pregnancy spans multiple parts of Australian medical systems. Many patients will transition between these systems during their pregnancy. For instance, many patients receive GP care during early pregnancy and then transition to the care of a maternity service. This transition occurs at variable gestations across Australia. Furthermore, some patients may participate in a shared care program where GPs and midwives provide antenatal care alongside hospital colleagues. Such arrangements are not currently supported by a single inter-operable clinical record, but rather separate clinical records with the need for periodic communication, correspondence, information sharing and mechanisms to acknowledge results and management decisions.

Transitions of care and sharing of care across multiple medical systems with separate clinical records, marks the greatest time of risk in the loss of crucial clinical information, medical error, and inadvertent service delivery gaps. Both clinical transition periods and shared care arrangements need clear local processes and procedures to ensure clarity about roles and responsibilities, closed loop communication for the provision and acknowledgement of results and management decisions.

The RACGP's Position Statement, titled *Shared Care Model between GP and non-GP specialists for complex chronic conditions*⁸ highlights several safety issues in this area including (but not limited to):

- communication
- clarity around healthcare provider roles
- the need for implementable shared clinical protocol development

This clinical guideline needs to be implemented with clear local processes that facilitate safe, closed loop communication between all maternity care providers, and the provision of, access to, and acknowledgement of both results and management decisions. Implementation will require activities to develop these processes to reflect local resourcing and arrangements.

3.2 Flow pathways

Clinical care pathways have been developed to support clinical care providers and laboratory staff in navigating the recommended care for women with an RhD negative blood group, where additional considerations may require variation to standard care.

- FP1 Simplified flow pathway for RhD negative women with no alloantibodies
- FP2 Flow pathway for *RHD* NIPT in pregnancy
- FP3 Flow pathway for *RHD* NIPT for RhD negative women in pregnancy

8. The Royal Australian College of General Practitioners (2023) *Shared Care Model between GP and non-GP specialists for complex conditions*
<https://www.racgp.org.au/advocacy/position-statements/view-all-position-statements/clinical-and-practice-management/shared-care-model-between-gp-and-non-gp-specialist>

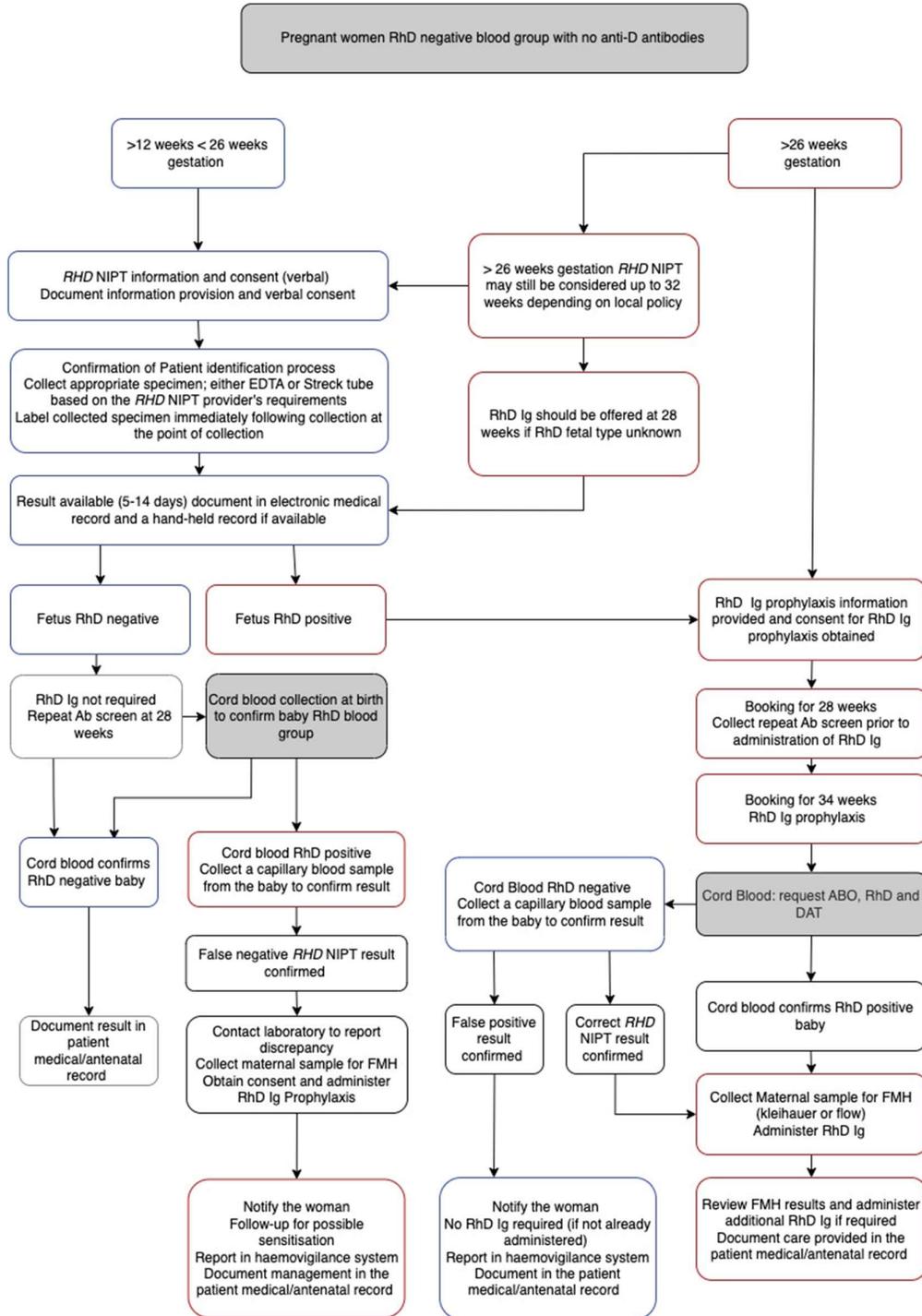
- FP4 Flow Pathway for RhD Ig prophylaxis with the introduction of *RHD* NIPT (including sensitising events)
- FP5 Flow Pathway for women with D variant (weak or partial D) RhD blood group
- FP6 Flow pathway for women with potentially clinically significant red cell alloantibodies or a history of fetal anaemia / haemolytic disease of the fetus and newborn (HDFN)
- FP7 Flow pathway for laboratory / pathology for *RHD* NIPT specimen management

Each care pathway should be applied based on the clinical history, pathology results, test timing and the woman's preferred treatment option following provision of information.

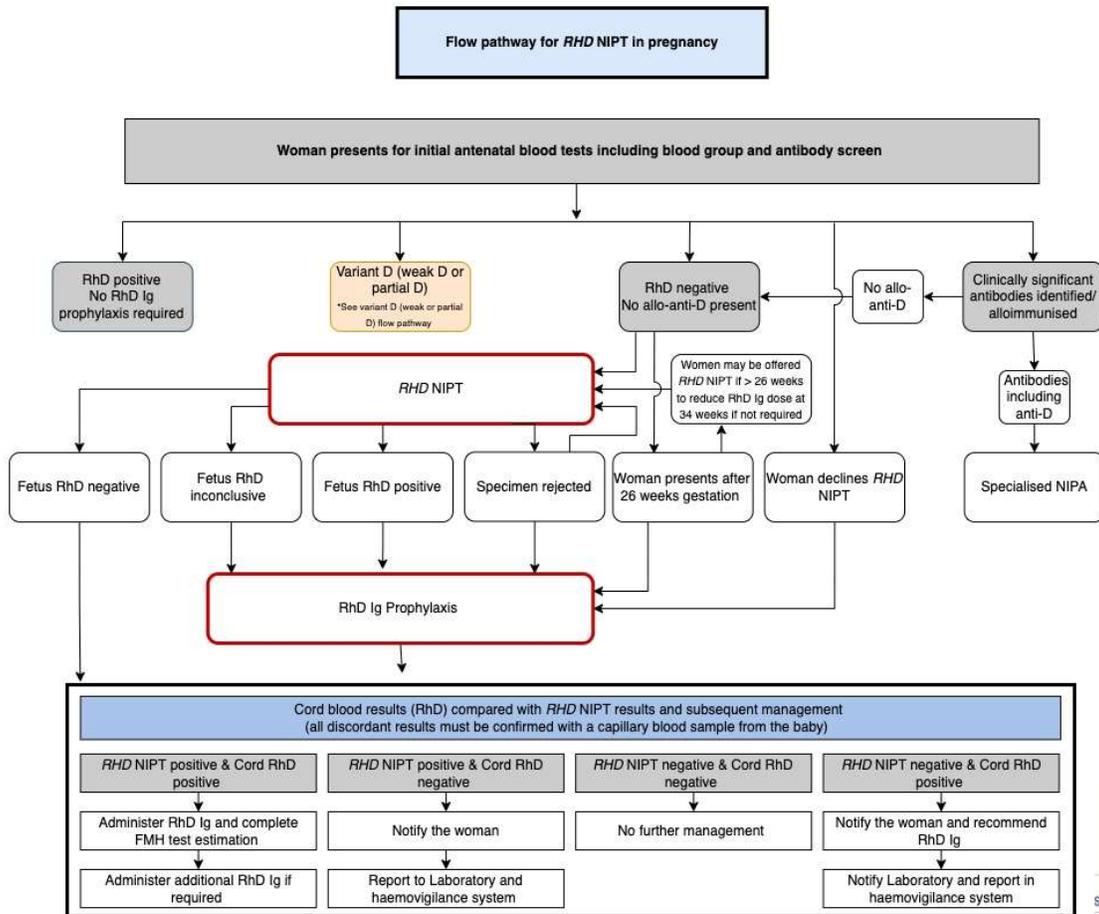
The intent of these flow pathways is to provide context for the application of *RHD* NIPT testing across a number of clinical care settings and environments. The flow pathways are designed as a guide only and may be utilised as a template to develop local flow pathways.

Where testing is declined or there are unavailable or uncertain results that cannot be clarified, RhD Immunoglobulin prophylaxis should continue as part the recommended clinical care pathway.

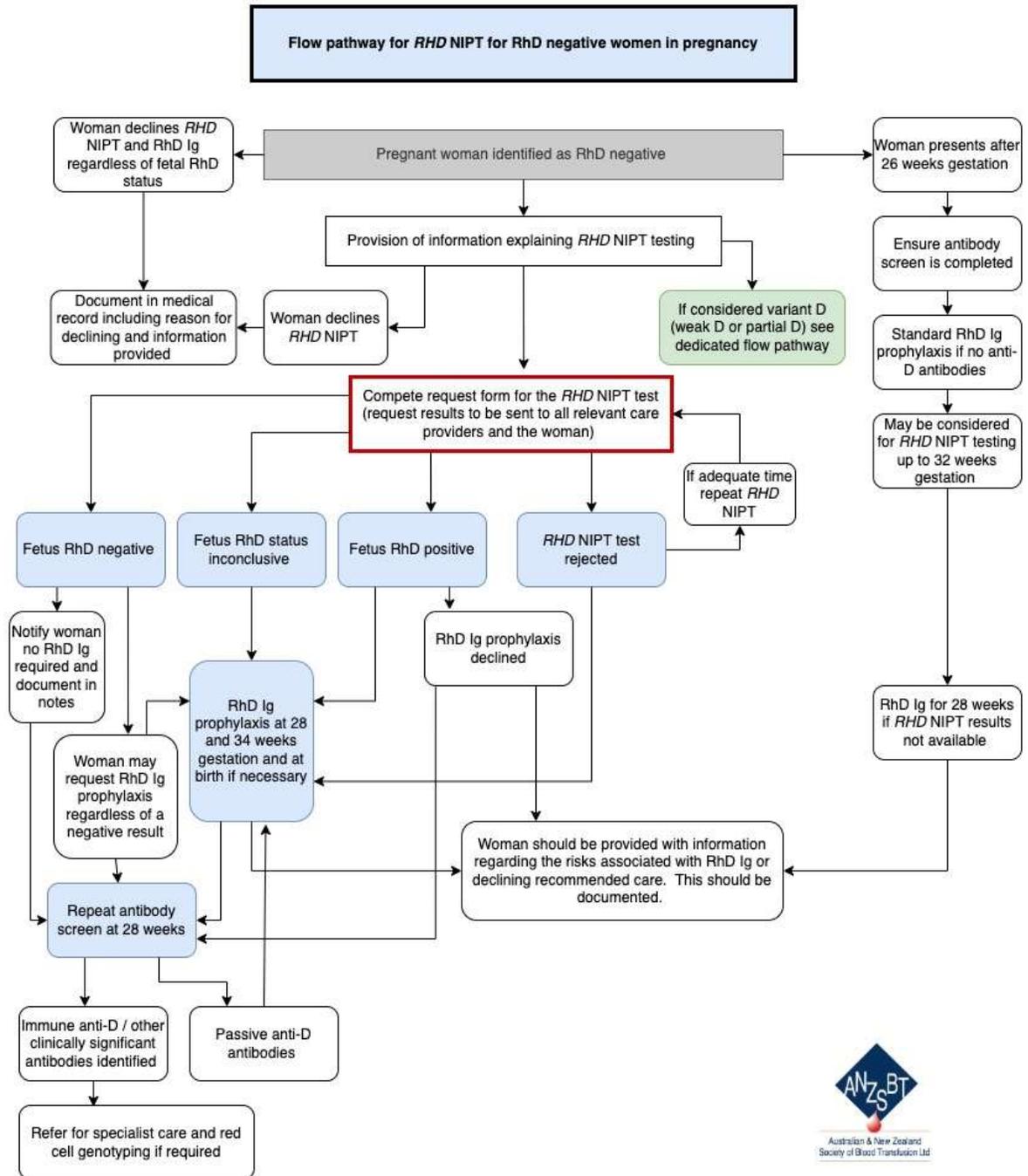
FP1 Simplified flow pathway for RhD negative women with no alloantibodies



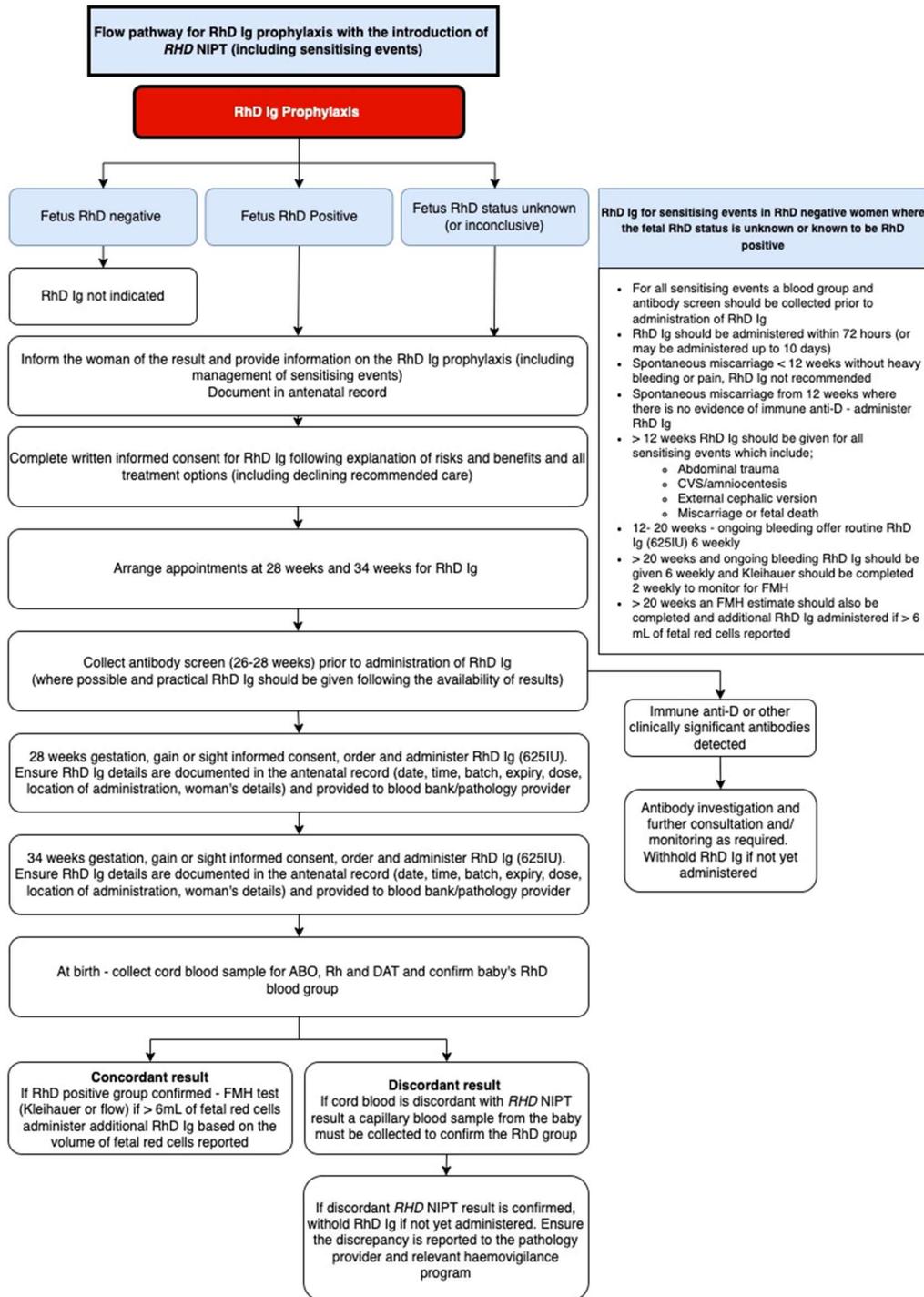
FP2 Flow pathway for *RHD* NIPT in pregnancy



FP3 Flow pathway for *RHD* NIPT for RhD negative women in pregnancy



FP4 Flow Pathway for RhD Ig prophylaxis with the introduction of *RHD* NIPT (including sensitising events)



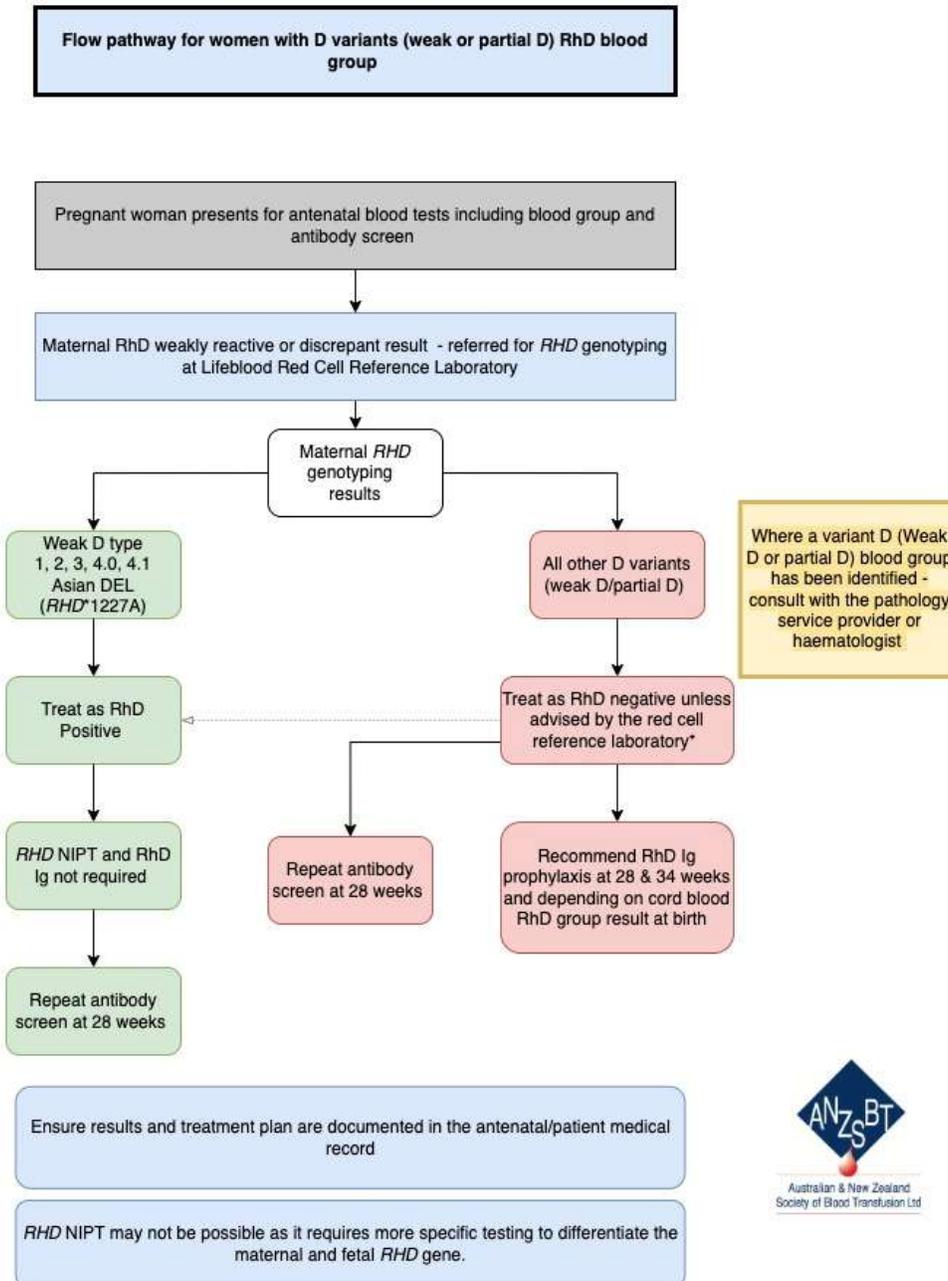
Notes

Ideally the *RHD* NIPT should be completed as close to 12 weeks gestation as possible to reduce the number of women who may require RhD Ig prophylaxis for sensitising events prior to the availability of *RHD* NIPT results being available.

If the *RHD* NIPT fetal RhD type has not yet been completed, or results are not available, the woman should be treated with RhD Ig prophylaxis as per the *NBA Guidelines for the Prophylactic use of Rh D immunoglobulin in pregnancy care*⁹ and the current Royal Australian and New Zealand College of Obstetrics and Gynaecology (RANZCOG) *Guidelines for the use of Rh(D) Immunoglobulin (Anti-D) in Obstetrics*.¹⁰

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9. National Blood Authority (2021) *Guideline for the Prophylactic use of Rh D immunoglobulin in pregnancy care*
<https://www.blood.gov.au/anti-d-0>
 10. Royal Australian and New Zealand College of Obstetrics and Gynaecology (2019) *Guidelines for the use of Rh(D) Immunoglobulin (Anti-D) in Obstetrics (C-Obs 6)*
<https://ranzcof.edu.au/resources/statements-and-guidelines-directory>

FP5 Flow Pathway for women with a known Variant D(weak or partial D) blood group



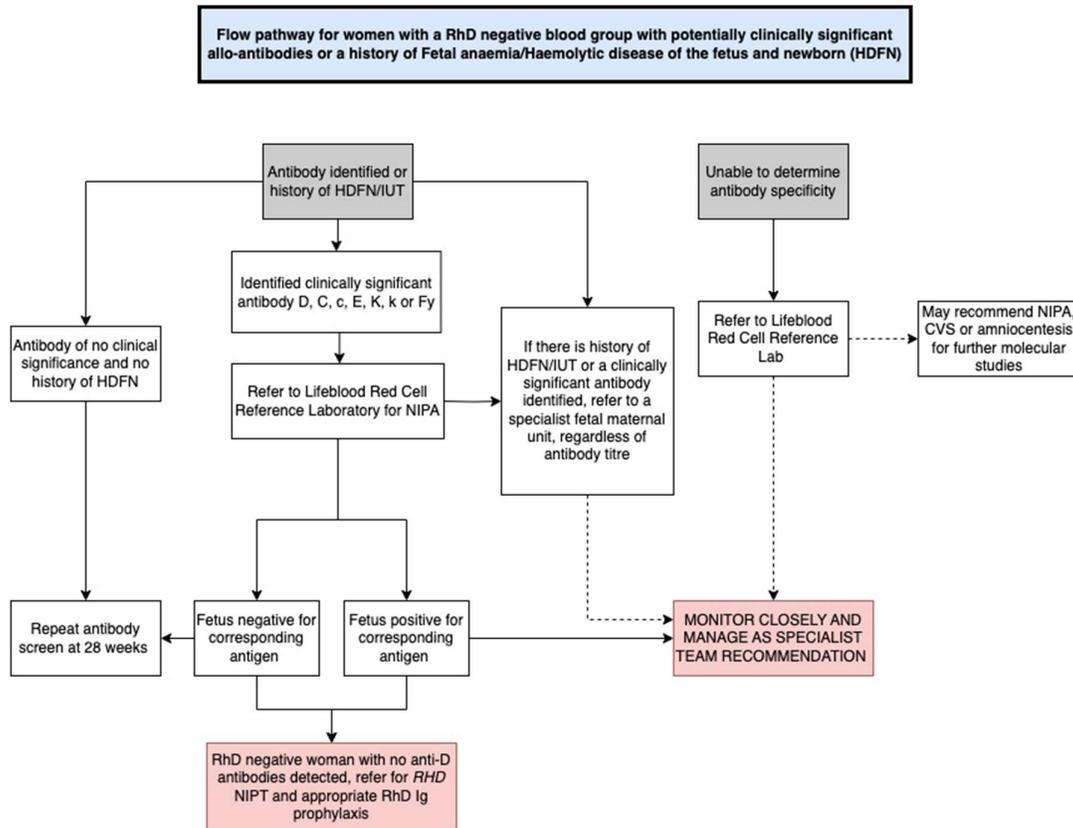
Notes

Women with known variant D (weak/partial D) types may or may not require *RHD* NIPT:

- Where the woman is known to be a Weak D type 1, 2, or 3, the woman should be treated as RhD positive and does not require RhD Ig.

- Women with all other *RHD* variants should be treated as advised by the red cell reference laboratory. In general these groups are treated as RhD negative and recommended RhD Ig prophylaxis, however there are some rare D variants that are recommended to be managed as RhD positive in pregnancy, including Weak D type 4.0, 4.1 and Asian DEL [*RHD**1227A(*RHD**01EL.01)]. In most cases *RHD* NIPT will not be informative for women with D variants as it is usually not possible to differentiate the fetal and maternal *RHD* gene.
- Where a woman is identified as having a partial D type, consultation with the pathology service provider is recommended. The pathology service provider may also recommend consultation with a haematologist to determine whether further investigation and / monitoring is required.

FP6 Flow pathway for women with potentially clinically significant alloantibodies or a history of fetal anaemia/haemolytic disease of the fetus and newborn (HDFN)



Notes

For pregnant women with an RhD negative blood group who are known to be alloimmunised (performed anti-D) the testing pathway will continue with the current established treatment pathway and may require specialised testing by Lifeblood's Red Cell Reference Laboratory and consultation with a haematologist or fetal medicine specialist to manage pregnancy care if indicated.

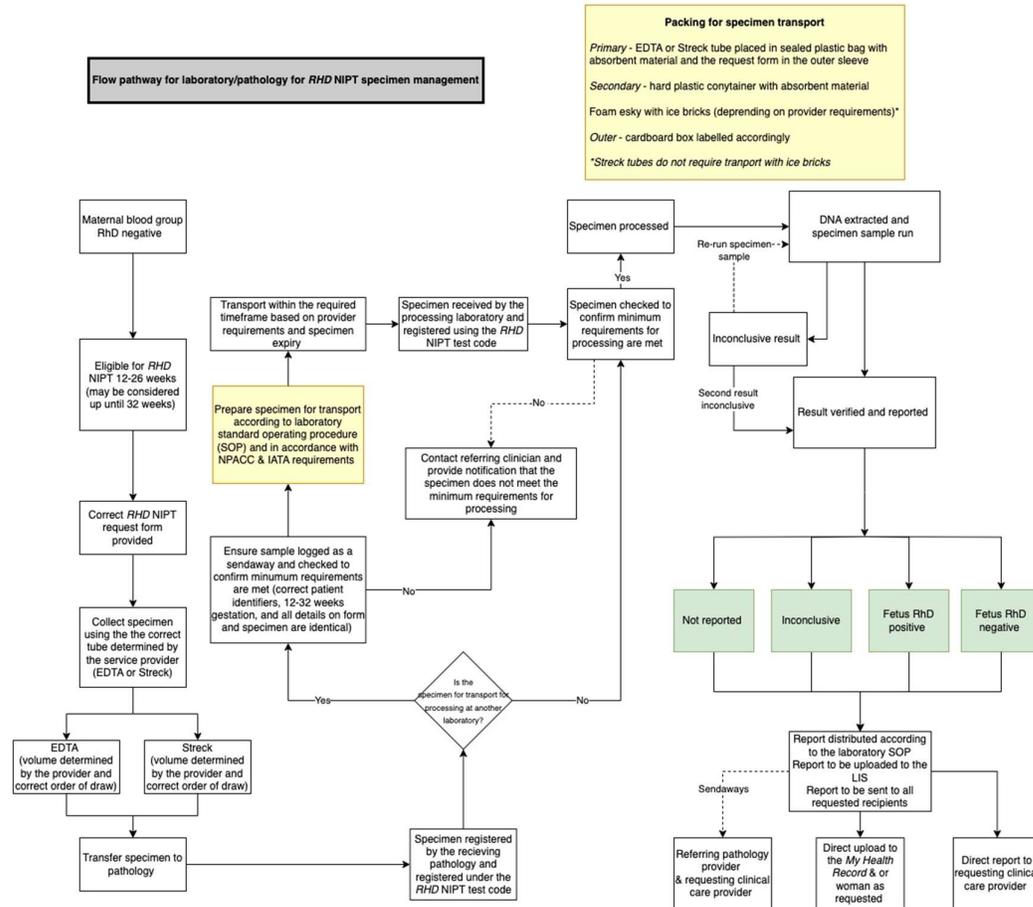
Women with detectable, clinically significant antibodies should be referred for further testing according to the antibodies which are detected:

- Anti K is considered clinically significant at any titre
- Other red cell antibodies may be clinically significant if there is any prior history of HDFN or at titres ≥ 32 (or anti-D quant $\geq 4\text{IU/mL}$ or anti-c quant $\geq 7.5\text{IU/mL}$) or if the titre is rising 2 more dilutions on serial testing).
- Women with detectable antibodies (anti-D, -c, -C, -E, -K, -k, -Fya, -Fyb): Specialised non-invasive prenatal analysis (NIPA) provided by Lifeblood's Red Cell Reference Laboratory is recommended.

- Women with red cell antibodies of unidentified specificity:
Refer a specimen to Lifeblood's Red Cell Reference Laboratory for further investigations to determine antibody specificity and clinical significance.

The Lifeblood Red Cell Reference Laboratory Request form and further information can be obtained from the [Red Cell Reference](#) page of the Lifeblood website.

FP7 Flow pathway for laboratory/pathology for RHD NIPT specimen management



Packing for specimen transport

Primary - EDTA or Streck tube placed in sealed plastic bag with absorbent material and the request form in the outer sleeve

Secondary - hard plastic container with absorbent material

Foam esky with ice bricks (depending on provider requirements)*

Outer - cardboard box labelled accordingly

*Streck tubes do not require transport with ice bricks

Results			
Not Reported	Inconclusive	Fetus RhD positive	Fetus RhD negative
<p>Where the specimen does not meet the minimum requirements, the specimen should not be processed and the requesting pathology service or clinical care provider should be notified.</p> <p>A specimen may be rejected for the following reasons:</p> <ul style="list-style-type: none"> - minimum identification requirements are not met or are incorrect - specimen has been opened prior to processing - specimen haemolysed - incorrect tube or form - gestation < 12 weeks or > 32 weeks gestation <p>If time permits, a repeat RHD NIPT may be offered, or RhD Ig prophylaxis should be recommended.</p> <p>A cord blood test should be completed at the birth of the baby to confirm the baby's ABO and RhD blood group. If the baby's RhD blood group is confirmed to be RhD positive, RhD Ig is recommended</p>	<p>If a specimen returns an inconclusive result, the specimen should be run through the analyser again. If the second result is also inconclusive this should be the final result reported.</p> <p>This may occur if the quality or amount of the specimen sample is inadequate, or the maternal blood group is a weak D or partial D.</p> <p>Where the result is inconclusive, RhD Ig prophylaxis should be recommended and a cord blood test completed at the birth of the baby to confirm the baby's ABO and RhD blood group</p>	<p>Where the fetus is predicted to be RhD positive, the woman should be recommended RhD Ig prophylaxis at 28, 34 weeks and for all sensitising events. A cord blood test should be performed at the birth of the baby to confirm the RHD NIPT results</p>	<p>Where the fetus is predicted to be RhD negative, RhD Ig prophylaxis is not recommended.</p> <p>A cord blood test should be performed at the birth of the baby to confirm the RHD NIPT results</p>

4 Consent

4.1 Consent for *RHD* NIPT

The consent process and treatment decision should be clearly documented in the antenatal/clinical records and be available for all clinical care providers involved throughout the pregnancy. This should include the information provided, treatment preferences, care pathway and any further management. Women may decline parts or all of the recommended care, and this should be clearly documented in the antenatal record, along with treatment preferences. Women should also be made aware that they may withdraw or change consent at anytime.

Agreement to have the *RHD* NIPT for determination of fetal RhD status following informed discussion, assumes consent for the specimen collection and associated reporting. Written consent is not required for *RHD* NIPT testing.¹¹

4.2 Provision of information

All women with an RhD negative blood group should receive information explaining treatment pathways aimed at reducing the risk of HDFN. This includes the risks and benefits associated with *RHD* NIPT and RhD Ig prophylaxis if required, and treatment options which are available.

4.2.1 Translation of Information

Information should be sufficient to enable an informed decision, and this may require translation of information through the support of a translation service or the use of translated resources for consumers where English is not a person's first language.

4.2.2 Resources available for *RHD* NIPT

Information should be provided in a way that is meaningful and explains the risks, benefits and available care pathways and treatment options relating to *RHD* NIPT. Information should be sufficient to enable informed decision-making with the support of the clinical care provider. Resources, including an interactive consumer resource and consumer information brochures, are available on the [ANZSBT website](#).

4.3 Risks and benefits of *RHD* NIPT

4.3.1 Benefits of *RHD* NIPT

The expected benefits of routine *RHD* NIPT for RhD negative pregnant women are:

11. National Pathology Accreditation Advisory Council (2023) *Requirements for medical testing for human genetic variation (3rd ed)*
<https://www.safetyandquality.gov.au/publications-and-resources/resource-library/requirements-medical-testing-human-genetic-variation-third-edition>

- Prevention of unnecessary RhD Ig prophylaxis and risks associated with administration of blood products
- Avoiding painful injections when the fetal *RHD* genotype is predicted as RhD negative
- Reduced appointments and time to attend for administration of RhD Ig where it is not required.
- Increased availability of RhD Ig for those women who require it
- Reduced anxiety associated with potential sensitising effects for women where the fetus is predicted as being Rh negative

4.3.2 Risks of RHD NIPT

4.3.2.1 Inconclusive result

There is a small risk that the results may be reported as inconclusive. Inconclusive results may be provided where the maternal specimen is collected from a woman with variant D blood type, where the specimen quality is poor, or where there is inadequate fetal DNA.

In the instance of an inconclusive result, the report will indicate that an accurate result cannot be provided and that the woman should be treated as per standard of care with prediction of an RhD positive fetus. This would result in a risk level equivalent to the current risks of current standard of care (i.e. unnecessary administration of RhD Ig).

4.3.2.2 False positive RHD NIPT results

There is a small risk that the fetal RhD blood group will be incorrectly resulted as RhD positive. This would result in a risk level equivalent to the risks of current standard of care (i.e. unnecessary administration of RhD Ig).

A cord blood specimen will be collected at the birth of the baby and RhD Ig will be withheld if the fetal RhD blood group is confirmed to be RhD negative.

4.3.2.3 False negative RHD NIPT results

There is a very small risk (0.5 -1.0%) of a false negative result, meaning that the fetus is incorrectly predicted to be RhD negative. This may result in the woman developing anti-D antibodies that may be of significance for this pregnancy, but more likely subsequent pregnancies.

In the event of a false negative result, the percentage of women who develop anti-D antibodies remains small with alloimmunisation estimated to be 0.8-1.5%, providing the woman has RhD Ig administered at the birth of the baby.

Should a *RHD* NIPT result predict a RhD negative fetus followed by a cord blood result showing a RhD positive baby, a repeat capillary blood sample from the baby should be collected and tested to confirm the baby's RhD blood group.

Where the baby is confirmed to be RhD positive, the mother should receive RhD Ig within 72 hours and a repeat blood group and antibody screen completed. This must be investigated and reported through the appropriate haemovigilance reporting system and the processing laboratory notified of the discordant result. Consultation with a haematologist should be considered.

The woman should be notified of the incorrect results and information provided relating to implications for future pregnancies.¹²

4.4 Consent for RhD Ig prophylaxis

Although considered to be a very safe treatment, RhD Ig is derived from human blood and has risks associated with blood-derived products. If the RhD negative woman is determined to be carrying a RhD positive fetus, and RhD Ig is to be part of the treatment plan, this will require a written consent form. This should be accompanied by further information relating to the risks and benefits of RhD Ig administration.

4.4.1 Resources for RhD Ig prophylaxis

Lifeblood and CSL Behring have developed the [Important Information for Rh \(D\) negative women](#) and [You and your baby: Important information for Rh\(D\) negative women](#) consumer resources that explain the process, risks and benefits of RhD Ig therapy.

4.5 Women who decline RHD NIPT

There are several reasons that a woman may decline to have the *RHD* NIPT for prediction of fetal RhD status. These include desire not to have antenatal testing, or women who decline blood products based on preference or religious beliefs regardless of the fetal RhD status, where there are no future pregnancies intended or where the father of the baby is known to have an RhD negative blood group.

If the woman declines the *RHD* NIPT and RhD Ig prophylaxis, it is important that the woman is provided adequate information relating to associated risks and potential outcomes for the current and future pregnancies. This should be clearly documented in the woman's antenatal record/clinical care record.

For RhD negative women who decline the recommended care, further consultation may be required. Any further advice, consultation and/or treatment care plan should be clearly documented in the antenatal record.¹³

Where a woman declines to have *RHD* NIPT, RhD Ig prophylaxis is recommended at 28 and 34 weeks gestation, with an additional dose of RhD Ig at the birth of the baby if the cord blood specimen determines the baby to be of RhD positive blood group.

13. Australian College of Midwives (2021) National Midwifery Guidelines for Consultation and Referral <https://midwives.org.au/Web/Web/About-ACM/Guiding-Documents.aspx?hkey=5f46e7ad-8ffa-4abb-ad31-e127157eceb2>

5 Specimen collection

5.1 Specimen collection

All specimens for *RHD* NIPT must be collected in accordance with the requirements as outlined in the *NPAAC Requirements for Transfusion Laboratory Practice (5th ed 2022)*¹⁴ and *ANZSBT Guidelines for Transfusion and Immunohaematology Laboratory Practice (2020)*.¹⁵

In addition to these guidance, each pathology provider may have preferences and/requirements for the *RHD* NIPT specimen as outlined in their standing operating procedure (SOP) manual.

It is the responsibility of the collecting person to ensure that they are familiar with these, including the minimum patient identification requirements and patient identification processes.

5.2 Patient identification

Prior to the collection of the *RHD* NIPT blood specimen, the woman's FULL NAME and DATE OF BIRTH (DOB) must be verified, preferably by the woman from whom the specimen is being collected. These details should be visually compared to those on the request form to ensure they are an identical match, and again on the specimen label following collection.

5.3 Specimen and request form requirements

The specimen must contain a minimum of 2 patient identifiers for the mother for the specimen (preferably 3) and a minimum of 3 patient identifiers for the mother for the request form [FULL NAME, DATE OF BIRTH (DOB) and MEDICAL RECORD NUMBER (MRN) if known]. The request form and specimen label details must match exactly.

The appropriate specimen tube types (EDTA or Streck 'Cell-Free DNA BCT®') must be collected according to the specific requirements as outlined by the test provider. The specimen must contain adequate blood volume for processing, the signature of the collector and must be labelled at the time of collection with the confirmed patient details.

There are several specific requirements necessary to ensure that the fetal DNA remains stable and reduce the likelihood of an inconclusive result or sample rejection.

These include:

- The specimen must not be reopened or used for other testing purposes, with *RHD* NIPT requiring a dedicated specimen
- The specimen must be collected in the specified order-of-draw depending on the type of tube utilised (EDTA or Streck) and provider preference

14. National Pathology Accreditation Advisory Council (2022) *Requirements for transfusion laboratory practice* (5th ed) <https://www.safetyandquality.gov.au/publications-and-resources/resource-library/requirements-transfusion-laboratory-practice-fifth-edition>

15. Australian and New Zealand Society of Blood Transfusion (2016; revised 2020) *Guidelines for Transfusion and Immunohaematology Laboratory Practice* <https://anzsbt.org.au/guidelines-standards/anzsbt-guidelines>

- The EDD must be used to confirm pregnancy weeks gestation

5.3.1 RHD NIPT request form

It is recommended that a dedicated *RHD* NIPT request form be utilised, reducing the potential omission of the information necessary for specimen processing.

Where a generic request form is utilised for *RHD* NIPT, pathology providers should consider education which specifically targets additional information required for the *RHD* NIPT and inclusion of additional dedicated sections for specific *RHD* NIPT information.

The specimen must be accompanied by the specified request form which contains the following information:

- correct patient details (a minimum of 3 unique patient identifiers)
- date/time of collection
- name and signature of the collector
- estimated due date (EDD)
- the requesting clinician's name and contact details and where copies of results are to be sent (it is recommended that the woman should be included to receive a copy of the results/report). It is important that the requesting clinicians' details are included in the event that the specimen cannot be processed.
- any potential sensitising events and relevant clinical information

5.4 Urgent processing of specimens

If urgent processing of the *RHD* NIPT specimen is required, this should be indicated on the form and the processing laboratory contacted to confirm expected turnaround time.

5.5 Specimens which do not meet minimum requirements for processing

Specimens that do not meet the minimum acceptance requirements may be rejected and require a repeat collection or result in an inability to complete the *RHD* NIPT testing and/default to routine RhD Ig prophylaxis.

The laboratory will notify the clinician if the specimen is rejected. Facilities must have processes in place to manage rejected specimens. This should include documentation requirements, and consideration given as to whether repeat collection of the specimen may be accepted or if care defaults to routine RhD Ig prophylaxis.

6 Transport and storage of specimens

6.1 General principles

Once collected, the specimen and request form should be sent directly to the laboratory to enable specimen registration and processing. Each provider may have additional requirements which are specific to their processes and the tube utilised as these will change the storage conditions necessary to maintain the integrity of the specimen.

Collection centres and pathology services must have processes in place to enable safe transport of specimens to the processing laboratory from locations that are a long distance from the laboratory. This should also include times and days the specimen collection may be completed if there is a limited service for *RHD* NIPT, to reduce rejection of expired and/haemolysed specimens.

6.2 Specimen registration

Each specimen should be registered in the Laboratory Information System (LIS) using the test code for *RHD* NIPT. This is important to ensure that the specimen can be tracked, processed, and reported.

Once registered the specimen may be tracked to reduce the risk of the specimen being lost and for improved visibility of the specimen for referring pathology services and requesting clinicians, particularly for results not received within the expected timeframe.

6.2.1 *Sending specimens on to another laboratory for processing*

Specimens received by a referring pathology service must be registered in the LIS and then managed according to the local SOP for sending specimens away to another pathology service for processing, whether within or external to the referring service provider. This additional process must ensure that the integrity and storage condition of the specimen is maintained, minimising delays in delivery to the processing centre to avoid expiry of the specimen.

Specimens which require transport to another laboratory for processing must be packed and transported in accordance with the *RHD* NIPT requirements and NPAAC *Requirements for the packing and transport of pathology specimens and associated materials*.¹⁶

If there is a delay in transferring the specimen to the processing laboratory, the specimen must be stored according to the processing laboratory's requirements until it can be transferred. Specimens must be received at the processing laboratory within the validated time from collection otherwise it will not be processed.

16. National Pathology Accreditation Advisory Council (2022) *Requirements for the packing and transport of pathology specimens and associated materials* (5th ed)
<https://www.safetyandquality.gov.au/publications-and-resources/resource-library/requirements-packaging-and-transport-pathology-specimens-and-associated-materials-fifth-edition>

The referring laboratory should provide contact details to assist with potential issues with specimen requests that may lead to specimen rejection so that appropriate follow up and notification may be made to the requesting clinician. This is essential to ensure reports are received by the intended pathology service and requesting service/clinician.

6.3 Pneumatic tube system (PTS)

Where the pneumatic tube system (PTS) is used for specimen transport, it must be validated for its suitability to maintain specimen integrity for *RHD* NIPT testing prior to use.¹⁷

17. Streck Cell-Free DNA BCT® Product Instructions for Use (2020)
<https://www.streck.com/products/stabilization/cell-free-dna-bct/>

7 Reporting and accessibility of results

7.1 Reporting of results

Results should be reported in a timely manner to allow for clinical interpretation of results and associated treatment recommendations. The results should be concise and clearly distinguish the results applicable to the mother and those of the fetus.

It is recommended that results are reported in a prompt and uniform manner to enable standardisation of language for *RHD* NIPT results and reduce potential errors associated with misinterpretation:

Table 7.1 Example of reported result outcomes

Fetal RhD result	Management
RhD Positive	Offer routine RhD Ig prophylaxis at 28, 34 weeks and at birth
RhD Negative	No RhD Ig required
Not reported (Not tested)	Offer repeat test if < 26 weeks. If declined or >26 weeks offer routine RhD Ig prophylaxis (Repeat test may be considered up to 32 weeks gestation at the discretion of the treating clinician); or offer routine RhD Ig prophylaxis and treat as per RhD positive fetus
Inconclusive result	Offer routine RhD Ig prophylaxis and treat as per RhD positive fetus

There must be clear processes and policies in place which determine the responsibility of report receipt by the intended recipient/s and secure transfer of results. This is especially important where the processing laboratory is separate from the referring pathology service (see 6.2.1).

Laboratories should have an agreement with external laboratories which outlines tracking, reporting and receipt responsibilities, to minimise lost reports or those not received by the requesting clinical care provider. This is especially important to avoid the need to administer prophylactic RhD Ig unnecessarily, to recollect or the potential for a woman to become alloimmunised to anti-D if the results are not actioned.

Where the requesting clinician is no longer involved in the care of the woman, the requestor should provide the results to the current clinical or treating care providers. It remains the responsibility of the person ordering the test to follow up the results and inform the woman of the RhD status of the fetus and clinical implications associated with the results.

Where there is anticipated transfer or shared care arrangements at the time of request form completion, the details of the additional clinical care providers should be included as result recipients.

It is recommended that the woman be included as a result recipient on the request form and that the results are uploaded to the *My Health Record* to minimise the risk of results being lost within complex care environments and promoting inclusion of the woman in the pregnancy care pathway.

7.2 Result report outcomes

7.2.1 RhD positive fetal blood group

Where a fetus is predicted to be RhD positive, the recommended care is to administer RhD Ig prophylaxis as per the NBA *Guidelines for the Prophylactic use of Rh (D) immunoglobulin in pregnancy care*.¹⁸

This should be clearly documented in the antenatal/healthcare record and arrangements made by the clinical care provider to ensure that the woman receives the intended treatment throughout the pregnancy and at the birth of their baby.

7.2.2 RhD negative fetal blood group

Where the fetus is predicted to be RhD negative, RhD Ig therapy is not recommended. The woman should be notified, and this should be clearly documented in the antenatal/healthcare record.

7.2.3 Inconclusive results

There may be occasions where the results are reported as inconclusive where an accurate result cannot be obtained due to a weak D or partial D type, poor specimen quality or insufficient ccfDNA. In these instances, the result should be reported as “inconclusive” and provide information for the clinician on further management. The report should include clear guidance of whether the woman is recommended to have routine RhD Ig prophylaxis and administration of RhD Ig for sensitising events.

7.2.4 Results not reported

Where the specimen does not meet the minimum requirements, the specimen should be rejected and registered as not reported. This is to prevent potential wrong blood in tube (WBIT) and the risk of a false result. It is recommended that the requesting clinician is notified as soon as possible to enable a reorder for *RHD* NIPT if time permits, and/or administration of RhD Ig prophylaxis therapy.

Specimens sent to an external provider for processing should be thoroughly checked prior to transport to the processing laboratory to minimise the number of specimens transported unnecessarily and the delay in time to enable repeat testing if this is an option.

7.3 Accessibility of results

It is well understood that the pregnancy care environment is complex and frequently involves multiple clinical care providers with limited interface between clinical information systems and software. This creates difficulty in safe transfer of care and limits the safety for shared-care arrangement.

The *RHD* NIPT test is indicated and interpreted in the context of several blood tests and the clinical history of the woman in pregnancy. Accessibility of the results is crucial in ensuring that the woman

18. National Blood Authority (2021) *Guidelines for the Prophylactic use of Rh (D) immunoglobulin in pregnancy care* <https://www.blood.gov.au/anti-d-0>

receives the intended care, and in reducing the risk of anti-D alloimmunisation and associated consequences.

It is recommended that *RHD* NIPT results be provided to all women to minimise the risk of results being inaccessible or lost through transfer of care. This may be achieved through inclusion of the woman as a result recipient on the request form, uploading of results to the My Health Record and/ documentation of the results in a hand-held pregnancy care record. Accessibility of the results is important for subsequent pregnancies to assist with interpretation of antibody screening and understanding the level of risk for development of HDFN. Each result must be carefully and clearly matched against each individual pregnancy.

Where there is transfer of care or a shared-care model throughout the pregnancy, the results should be provided to other clinical care providers throughout the antenatal period to ensure that all clinical staff providing antenatal care are aware of the RhD status of the fetus. Instances where results are received after referral has already been made, require processes to ensure the provision, acknowledgment, and associated management of these results by other providers should be implemented.

7.3.1 Hand-held pregnancy care record

It is recommended that for services utilising hand-held antenatal records, that these are adapted for the purpose of recording *RHD* NIPT related information.

Including:

- information provision for *RHD* NIPT and the associated risk, benefits, and treatment options
- referral for *RHD* NIPT if eligible (date completed) or alternate testing if indicated (i.e. NIPA genotyping for women with clinically significant antibodies)
- result for fetal RhD group – the maternal and fetal RhD results should be clearly distinguished to prevent confusion of maternal and fetal RhD blood groups
- if the woman is eligible and declines *RHD* NIPT, this should be indicated along with the reason the test was declined
- administration of RhD Ig prophylaxis and indication – RhD negative mother and fetal RhD blood group positive, inconclusive, or unknown
- where the antenatal record may also be utilised to guide recommended antenatal screening, services should consider inclusion criteria for *RHD* NIPT and a request for a copy of results to be sent to the woman and uploaded in *My Health Record*.

7.4 Specimen turnaround time (TAT)

The specimen turnaround time (TAT) should be within 10 days; however this will vary depending on specimen transport time and the processing laboratory.

Urgent specimen requests may be available sooner depending on the location of the referring laboratory and the number of specimens being processed. If a RhD negative women presents

following a sensitising event prior to result availability, RhD Ig prophylaxis should be administered as per the NBA *Guidelines for the Prophylactic use of Rh D immunoglobulin in pregnancy care*.¹⁹

7.5 Results not received

If the *RHD* NIPT result is not received within the expected TAT, the requesting clinician should contact the *RHD* NIPT service provider to follow up the result.

If the specimen has been lost or rejected, the woman should be contacted for a follow up:

- If the woman is < 26 weeks gestation, a repeat specimen collection may be offered.
- If > 26 weeks gestation, *RHD* NIPT should still be considered up to 32 weeks gestation with RhD Ig prophylaxis recommended at 28 weeks gestation and this must be clearly documented in the antenatal record.

19. National Blood Authority (2021) *Guidelines for the Prophylactic use of Rh D immunoglobulin in pregnancy care* <https://www.blood.gov.au/anti-d-0>

8 Postnatal confirmation of *RHD* NIPT results using a cord blood specimen

A cord blood specimen should be collected following the birth of the baby from all RhD negative women (prior to administration of RhD Ig if required) to confirm the baby's RhD group and the *RHD* NIPT results.

Where the cord blood RhD group is discordant with the *RHD* NIPT testing, a capillary blood sample should be collected from the baby to confirm the baby's RhD blood group. If a false negative result is confirmed the woman should have a repeat antibody screen and RhD Ig recommended. Discrepant results between *RHD* NIPT and cord blood results must be reported to the *RHD* NIPT provider and the local and or national haemovigilance system.

False positive results must also be reported to provide both ongoing validation of the test accuracy and as a cause of unnecessary administration of RhD Ig.

The woman should be made aware of the baby's blood group following cord blood testing, even in the absence of discrepant results.

9 Education and training

9.1 General principles

It is recommended that clinical care providers and laboratory staff be provided with adequate education and training prior to the introduction of *RHD* NIPT as part of the complete pregnancy care pathway. There must be processes in place to support safe transition from the current pathways of care, to prevent errors which may result in the development of anti-D antibodies and associated poor fetal outcomes.

Education and training should become a standard inclusion for current pregnancy care education opportunities in the future, as *RHD* NIPT becomes the standard of care for all RhD negative pregnant women in Australia.

9.2 Resources

There are several tools and resources available for clinicians, consumers, laboratory staff and pathology services to assist with the application of *RHD* NIPT in the pregnancy care (see resources list).

Clinicians should have a clear understanding of the RhD blood group system, clinical implications of the blood group system during pregnancy and the clinical management pathways.

Education should incorporate an ability to understand and interpret the reports of the *RHD* NIPT results for both the clinical care providers and the pathology staff.

9.3 Education for consumers

It is recommended that consumers be provided with accessible and meaningful information to reduce the risk of adverse outcomes with the introduction of *RHD* NIPT in the pregnancy care setting, and to enable shared decision-making between the woman and the care provider/s. Resources for the consumer are available through the [ANZSBT website](#).

10 Adverse events and haemovigilance reporting

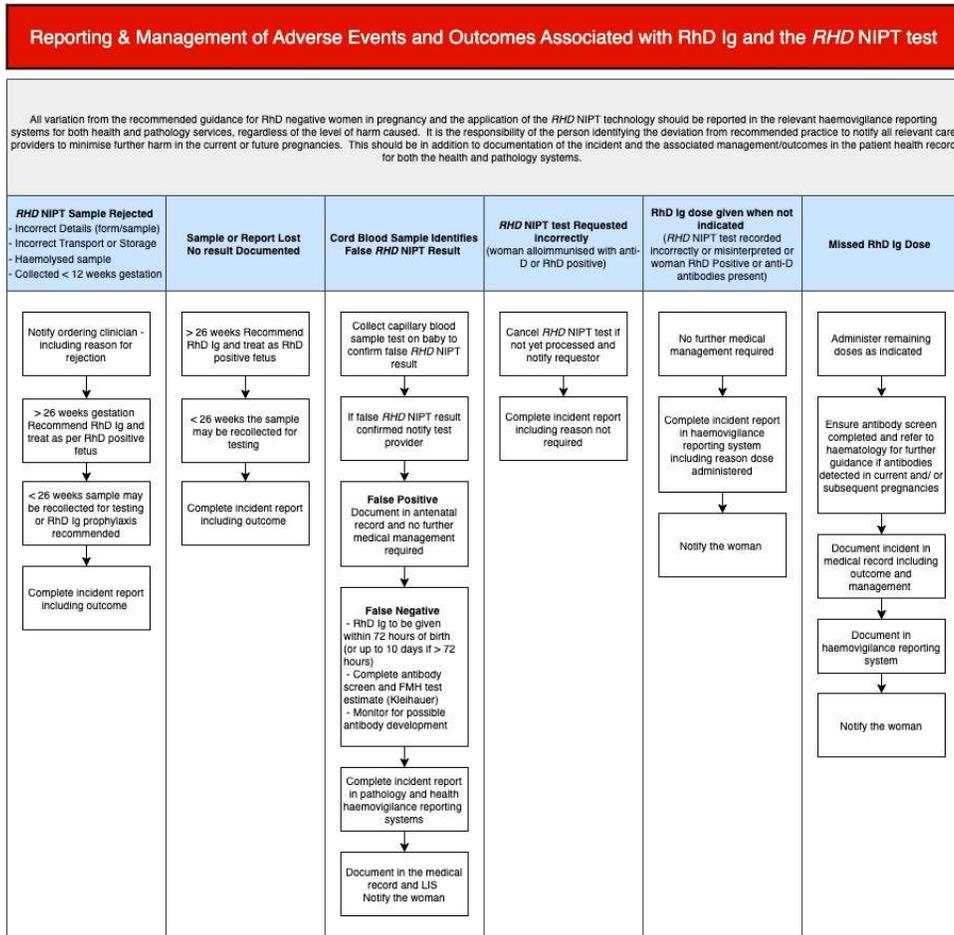
All adverse events associated with the *RHD* NIPT, RhD Ig prophylaxis (incorrect or omitted dose), reactions or discordant blood results should be reported to local, state and or the national haemovigilance or clinical incidence systems (*Figure 1: Example Haemovigilance Reporting and Management for RHD NIPT and Incident Types*).

These should include specimen rejections (including reason e.g. incorrect patient identifiers), lost specimens, incorrect results, wrong blood in tube (WBIT) and incorrect collection time (outside of 12 to 32 weeks).

Where a report is lost or misinterpreted this should also be reported and include the outcome for the woman and or baby. Delays in RhD Ig prophylaxis, failure to complete a consent, incorrect dose, and unnecessary administration of RhD Ig must be reported regardless of the resulting level of harm.

Reporting of adverse events must be monitored to identify trends in areas that may require local practice change, education, or support to improve safety of the *RHD* NIPT and RhD Ig prophylaxis. This information is important in evaluating the successful implementation of *RHD* NIPT as part of the complete pregnancy care pathway and identify areas that may require further information and or support.

Figure 1: Example haemovigilance reporting and management for RHD NIPT and incident types



Incident Types		
The following incidents should be reported when identified to monitor and evaluate the safe introduction of the RHD NIPT. This must be in accordance with Local, State and National reporting requirements.		
Sample	Results and Reporting RHD NIPT	RhD Ig
Sample collected prior to 12 weeks gestation and rejected/not reported	RhD negative woman not offered RHD NIPT (this does not include women who decline the test)	Administered when RHD NIPT result indicates a RhD negative fetus (this does not include where the woman requests RhD Ig regardless of result)
Sample haemolysed or transported incorrectly	Results lost or not documented in the antenatal record	Administered to a woman with known anti-D antibodies or woman who is RhD positive
Sample labelled incorrectly - including incorrect or missing details	Cord blood indicates false RHD NIPT result (test provider and woman must be notified)	Administered to a RhD negative mother with RhD negative fetus due to misinterpretation of results or administered where the RHD NIPT test result is then found to be incorrect at the birth of the baby
Incorrect request form or form details missing/incorrect	Results delayed or misinterpreted (RhD Ig dose missed or administered unnecessarily due to clinician misinterpreting results)	Dose missed due to misinterpreted results or failure to document results in the health record
Sample and form details do not match		
Sample and/or form lost		
Sample requested and not required (woman RhD positive or alloimmunised with anti-D antibodies and Red Cross Lifeblood NIPA indicated)		

11 Quality and safety

There must be clear local guidelines and processes to support safe care of pregnant women identified to be RhD negative in the context of *RHD* NIPT and targeted RhD Ig therapy. These guidelines must include education requirements, communication of changes to practice and access to resources to assist with transition from universal RhD Ig prophylaxis to targeted RhD Ig for pregnant women. These should also include provision of additional support during the transition phase, and consideration of a staged implementation to minimise adverse events.

All organisations should have processes in place to monitor and evaluate the quality and safety of *RHD* NIPT and its application in the clinical setting.

All adverse events must be reported, monitored, and managed as part of local haemovigilance and pharmacovigilance systems, which contributes to state and national haemovigilance monitoring.

These should be incorporated within existing systems for haemovigilance monitoring and reporting and reviewed by the institutional Blood Management Committee or local equivalent.

In the primary care setting, GPs and practice centres should consider implementing practice-based audit, utilising existing clinical data and extraction tools, including POLAR® and Pencs® software, to review and improve clinical care. Such data-driven quality improvement activities may occur at a practice level, or at a larger pooled level (such as local primary health networks [PHN]), depending on resource availability.

These data-driven quality improvement activities may be further supported through local PHNs to enable targeted evaluation and practice improvement support that is consistent with the recommendations within this guidance document.

In future, subject to the availability of resourcing, oversight and expertise, use of national data assets such as, Primary Health Insights or the planned National Primary Health Care Data Asset may provide an avenue for systematic data-driven quality improvement activities at a larger scale.

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