ACM SUBMISSION

Prophylactic use of Rh D immunoglobulin in maternity care

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ACM Submission to the guideline for the prophylactic use of Rh D immunoglobulin in maternity care

Cover Sheet

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Is this submission being made on behalf of an organisation? (Y / N)					Yes
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*** The NBA may include your name, or the name of your organisation with your submission, and/or quotes from your submission in any reports prepared relating to this draft guideline, and/or the final published guideline and its later publications.*

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SUMMARY OF CLINICAL GUIDANCE

Section	Page Number	Comments	Attached documentation Y/N
Summary	pp. 1-5	This is a very good addition to the document and provides useable and accessible information to clinicians. This will assist with clinical decision making around the appropriate and judicious use of Rh D immunoglobulin prophylaxis. The supporting care pathway is also an effective method of supporting clinicians in their decision making.	N
N/A		It is essential that women are provided with information about Rh D immunoglobulin prior to collection of a blood sample at 11 weeks. This should include clear guidance that Rh D immunoglobulin is a blood product and more, that there are important considerations surrounding receiving blood products. This information will give the woman time to consider her vaccine status and to make an informed decision about prophylaxis where she is found to be Rh negative. A standardised consumer pamphlet that outlines the risks/screening scrutiny of blood products, the recommendations reflected in this guideline and associated considerations would be ideal.	N
Summary of clinical guidance	p. 5	The summary is clear about the management and administration of immunoprophylaxis for non-sensitised women. While there is some reference to the woman who has pre-existing sensitivity, a box related to the management of a woman with a pre-existing sensitivity is needed.	N
R4		We request that greater clarity be provided around the definition of 'bleeding' with specific examples of when Rh D immunoglobulin is not required and when bleeding is not likely to result in alloimmunisation. Similarly, it is important that there is clear direction provided to clinicians about the situations where immunoprophylaxis would not be required in the 'summary of clinical guidance on the use and timing of Rh D immunoglobin' p. 5.	N

1. INTRODUCTION

Section	Page Number	Comments	Attached documentation Y/N
Introduction	p. 6	The inclusion of information about Rh D immunoglobulin being a blood product is an important addition to this guideline and should be added to the introduction. This information is often not well known and is an important discussion point when clinicians are providing information to women in order for them to make informed decisions. We	Section 1.2 of the associated evidence review could be utilised to address this suggestion.

		would also like to see a brief overview of how it is sourced such as that provided in the corresponding review document under section 1.2.	
Introduction	p. 6	There should be greater emphasis on the importance of establishing and differentiating between passive and preformed antibodies. This is a concern for practitioners (e.g. new graduates, non-obstetric emergency department personnel) who do not understand the importance of this difference. This poses a risk in that clinicians may progress with the administration of routine immunisation for a woman with existing (non-passive) antibodies and subsequently, cause harm to the baby. Clarity in the summary of recommendations is vital for the safe administration of Rh D immunoglobulin. This document will be read by clinicians who are seeking guidance and making clinical decisions about whether to administer immunoprophylaxis. We suggest that in settings where there is not a clinician with knowledge and education around the use and administration of immunoprophylaxis (e.g. midwife / obstetrically trained care providers), that clinicians are to discuss this decision with a lead maternity care provider. This could be added to the flow chart, section labelled 'antibody screen positive.'	N
Introduction 1.2	p. 6	Section 1.2 states that the Rh D immunoglobulin guidelines were intended to be reviewed within five years of 2003 – did this happen? If not, it would be helpful to understand why this did not happen.	N
Introduction 1.3	p. 7	There is consistent reference to the burden on donors and therefore, the judicious use of prophylaxis throughout the document. In light of this, it would be appropriate for this to be stated in section 1.3. The document will ultimately guide clinical decision making and therefore it is important that clinicians are aware of the many important reasons for understanding the appropriate management of women who are Rh D negative as well as the considerations that need to be made when offering women immunoprophylaxis.	N

2. METHODOLOGY

Section	Page Number	Comments	Attached documentation Y/N
Methodology	p. 9-12	Methodology is appropriate for the purpose of sourcing evidence. A systematic approach was used, informed by the Cochrane handbook reflecting a rigorous process to the sourcing of evidence to inform the guidelines. The	N

		supporting review documents provide evidence of the process undertaken.	
Box 2.1	p. 10	Questions outlined are appropriate and useful with respect to informing the content and updates of the guidelines. The answers provide appropriate clinical guidance under relevant sections and headings.	N
Box 2.2	p. 11	The labelling of the recommendations may be perceived as confusing. That is, four definitions use the term 'weak.' We would suggest that they would be better labelled as 'Conditional, discretionary etc' with 'weak' in parentheses.	N
2.5	p. 11	There appears to be rigour to the review process. The document states that consensus was reached by at least two reviewers and a third where necessary. This increases validity and reliability and therefore, interpretation of the results. Further to this, the review excluded papers that were not undertaken in settings comparable to Australia. This increases applicability of results to the Australian context.	N
2.6	p. 12	Strengths and limitations are outlined and how evidence was rated against five domains. Can you specify the 'risk of bias assessment tool' that was used? The document states that the 'most appropriate' was used. This is vague.	N

3. CLINICAL GUIDANCE

3.1 Routine antenatal Rh D immunoglobulin immunoprophylaxis

Section	Page Number	Comments	Attached documentation Y/N
3.1	p. 13	Language throughout the document could be improved to reflect women's choice and autonomy including in this particular section. For example, the use of 'given' implies that women do not have a choice. We would like to see the term 'offered' used to reflect the woman's ability to exercise informed decision making following full disclosure of all relevant information. This is line with the recommendations and enablers of the new *Woman-centre care: strategic directions for Australian maternity services* released in November 2019.	N
3.1.1	p. 13	The research and results of the review reflect no difference in the use of single versus multiple dose regimes. While there is discussion as to why a two-dose regime is recommended, we feel that with judicious use of Rh D immunoglobulin based on the recommendations in the	N

		guideline, these challenges and burdens will be reduced. Therefore, it is reasonable to suggest a single dose may be a viable alternative until further research can confirm one option is better than the other. The implications related to cost, convenience for the woman and the woman's preference with respect to regime should also be considered.	
3.1.3	p. 18	Page 18 highlights that the 'interpretation of the results should be made with caution.' We feel this needs to be emphasised and supported with a comment that the current research suggests that there is benefit to offering women anti-D prophylaxis where they are known to be Rh D negative and without preformed antibodies.	N
Burden on donors	p. 21	The rationale provided in this section is stronger with regards to the two-dose regime however, judicious use and better screening would mean that prophylaxis is only used where necessary and therefore this alone could reduce the burden on donors and ultimately, increase supply. The concerns around compliance are not supported by evidence and are likely to be overcome by thorough information provision at the time of screening and ongoing throughout the pregnancy. However, it is important to note that woman have the right to decline this treatment.	N
3.1.4	p. 21	For greater clarity, we advise that you include information as to the rationale for the extra 250IU in the single dose preparation and on what evidence this is based, if any.	N
3.1.4 Resources and other considerations	p. 21	We note that there are challenges related to the supply and manufacture of a single-dose option however, in section 5.1, this appears to be already available. Could you please clarify in more detail, the challenges to provide more weight to the recommendation of continuing with the two-dose regime?	N
N/A		Our members raised concerns about access to electronic pathology results for the non-invasive tests and how this has and could potentially impact decision making. Limited access to results prior to offering the woman immunoprophylaxis could result in women being offered immunoprophylaxis when they do not need it. While this may be viewed as a jurisdictional/institutional responsibility, it would be advantageous for there to be a clear statement about the importance of access to this information for the purpose of making clinical decisions. Further to this, there were concerns raised about the omission of a discussion and/or guidance on what to do in the event that a woman:	N

		• experiences a sensitising event around the time of the routinely offered doses (28 week / 34 week / post 42-week pregnancy) • received the routine dose at an alternative gestation (e.g. 30 weeks) date. We recommend that this guidance be included in the guidelines to address these concerns.	

3.2 Universal sensitising event immunoprophylaxis in the first 12 weeks of pregnancy

Section	Page Number	Comments	Attached documentation Y/N
N/A		Recommendations are reasonable given the evidence reviewed.	N

3.3 Targeted routine antenatal or sensitising event immunoprophylaxis

Section	Page Number	Comments	Attached documentation Y/N
3.3	p. 27	The use of a non-invasive fetal RHD genotype test is strongly supported and will ultimately result in more judicious use of prophylaxis which will in turn reduce the burden on donors. We support a targeted approach that will ensure improved outcomes for women and babies but also reduce cost and logistical burdens.	N
3.3.1 R8	p. 28	We strongly support recommendation 8 – using a targeted approach to antenatal immunoprophylaxis. This will ensure that prophylaxis is held where the baby is Rh D negative which will again have the benefit of reducing the unnecessary use of immunoprophylaxis. Use of available technology such as a non-invasive test is a positive step and is welcomed as a more readily available option. Our concern is that at present, not all women are able to access this testing due to the financial cost and this presents an issue of equity, particularly where this guideline strongly recommends a targeted approach. Based on this recommendation, could you specify if there are planned steps to make the non-invasive test more readily available to women to ensure this recommendation can be upheld and equity in service provision is addressed.	N
3.3.4	p. 36	We note that some women who have an RH D negative baby will still, at times receive immunoprophylaxis where they screen as 'inconclusive' however, any reduction in use where it is not required is welcomed. Particularly given that modelling has estimated a reduction of over 30% in	N

		prophylaxis and a reduction in the percentage of women receiving unnecessary prophylaxis to under 10%.	
3.3.4 Benefits and harms	p. 37	We strongly support the inclusion of counselling for women around the testing and specifically that the test will not be used to screen genetic profiles or other information. We strongly advocate for this information to be included in any written information that is provided to women.	N
3.3.4 Preference and values		A consideration that needs to be raised is the cost burden of these non-invasive tests to women. Will this be subsidised as while offered, women may decline on the basis of financial reasons. This is particularly pertinent where the test may be inconclusive and a subsequent test is offered/recommended. Steps towards making this test an equitable and accessible option are needed and should be addressed in this guideline or at least, acknowledged as a potential barrier to uptake.	N

3.4 Risk of failure of Rh D immunoglobulin administration due to increased body mass index (BMI)

Section	Page Number	Comments	Attached documentation Y/N
3.4.1 EOP2	p. 37	How will EOP2 be supported? - should there be some guidance around this particular recommendation in terms of clinicians choosing the most appropriate site of administration where women are of high BMI? Given the available evidence, we agree that there be no change to the current regime of immunoprophylaxis for women with a higher BMI but that there be attention paid to ensuring that there is guidance around appropriate injection site to ensure that the immunoglobulin is administered to the deep intramuscular tissue. The Australian Red Cross Blood Service recommend the deltoid muscle or anterolateral thigh as the best site for administration of Rh D Immunoglobulin, with avoidance of the buttocks. We would strongly suggest including guidance about this particular point in the guidelines.	N

3.5 Guidance transferred from the 2003 *Guidelines on the prophylactic use of Rh D immunoglobulin (anti-D) in obstetrics*

Section	Page Number	Comments	Attached documentation Y/N
3.5	p. 42	The expert opinion points outlined in this section are reasonable given the findings presented in prior sections. Could you specify when and how any reviews will be undertaken to ensure that this guidance remains informed	N

		by emerging evidence? Will there be someone dedicated to this and will there be an opportunity for stakeholders and industry etc. to alert the National Blood Authority to any updates that might be worthy of consideration?	

4. COST CONSIDERATIONS

Section	Page Number	Comments	Attached documentation Y/N
4		ACM members reiterated the burden of cost to women accessing and choosing to have the non-invasive testing. They have asked for this to be bulk-billed and argue that any fee for service is unethical and will result in access inequity. We strongly support this view and suggest that this be of high importance in light of the recommendations made throughout this document.	N
4	p. 45	The use of 'compliance' and 'patient preference' in close proximity is an interesting combination of words. Compliance reflects the fact that women are required to engage and therefore, do not have the ability to decline immunoprophylaxis where it may be offered to them. Consider words that are supportive of respectful care. Compliance could be replaced with 'uptake' or similar. We would also like to see the term 'patient' removed and replaced with 'woman' throughout the entire document. This is line with the recommendations and enablers of the new *Woman-centre care: strategic directions for Australian maternity services* released in November 2019.	N

5. SUPPLY CONSIDERATIONS

Section	Page Number	Comments	Attached documentation Y/N
5.1 Products currently available	p. 46	The availability of a single dose in table 5.1 suggests that this could be a reasonable alternative to the two-dose regime currently recommended particularly given there is no difference noted in the available evidence. Women's preferences should ultimately be considered.	N
5.2 Supply trends	p. 46	This section states that 'details of clinical use, inventory levels and wastage are not recorded nationally.' Would it be reasonable to recommend that this occurs? If there is no way to track this and there is concern around overuse and burden to donors, it would seem a logical step to have greater rigour and consistency around recording of these key indicators of availability and uptake.	N

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6. SAFETY OF Rh D IMMUNOGLOBULIN

Section	Page Number	Comments	Attached documentation Y/N
6.2	p. 48	The understanding of Rh D immunoglobulin as a blood product is often not well known and therefore, greater information should be provided to woman where administration is offered and/or recommended. This includes information about the potential for blood-borne, viral or infectious diseases to be transmitted despite strict requirements and steps taken during manufacturing. This will ensure that women are fully informed about the risks and benefits and therefore, able to make educated and autonomous decision about the immunoprophylaxis. Further to this, there is also the need for information about the potential for hypersensitivity to be provided to women and also to clinicians. In the event of an adverse event, information and guidance should be available to clinicians to ensure that they are aware of how to appropriately manage the situation. Is there any existing guidance that could be linked or included within this document? This would be advantageous.	N

7. CHALLENGES

Section	Page Number	Comments	Attached documentation Y/N
7.1 Donors	p. 50	Further to our point against section 5.2, it would seem reasonable to consider a more rigorous approach to the management and supply of Rh D immunoglobulin in reducing unnecessary burden. In turn, this may save on wastage etc.	N
7.2 Care Pathways	p. 50	We strongly support the provision of information to women about immunoprophylaxis. This will ensure that women are able to exercise choice and autonomy, free from influence, harassment or coercion.	N
7.3 Compliance	p. 51	Compliance is a value-laden word and suggests that women do not have a choice. As recommended, this could be changed to something like 'uptake' or 'use.' There may be very good reasons as to why there was 'around 70% compliance.'	N
7.4	p. 52	Refusal is a strong word and implies that the woman is non-compliant rather than free and able to exercise	

Consent or refusal to treatment		informed decision making. This needs to be replaced with 'Consent and the choice to decline Rh D immunoglobulin prophylaxis'? This would align with the guidance and enablers of the recently released 'Woman-centred care: Strategic directions for Australian maternity services' plan.	

8. MONITORING THE USE OF Rh D IMMUNOGLOBULIN

Section	Page Number	Comments	Attached documentation Y/N
8.2 Adverse event reporting and monitoring	p. 53	Further to our point above, is there guidance on the appropriate management of an adverse reaction and if so, could it be linked to this document? This guidance is important for clinicians to appropriately manage adverse reactions.	N
8.3	p. 53	This speaks to our point about ensuring that greater rigor in recording and monitoring of use should be undertaken.	N

9. IMPLEMENTING, EVALUATING AND MAINTAINING THE GUIDELINE

Section	Page Number	Comments	Attached documentation Y/N
		Please see comments raised again section 3.5 with respect to updates and reviews.	

A communication and education strategy will be developed to support effective implementation.

We welcome your suggestions on target audiences, key messages, strategies, and tools and resources that should be considered in the communication and education strategy.

Further to comments throughout the document, please find some suggestions:

- A useable and accessible version of the guidelines is useful for clinicians at the coalface including midwives, nurses and obstetricians as examples. The summary of recommendations is welcomed in this regard and will help inform clinical decision making as well as information provision.
- Communication about immunoprophylaxis is welcomed and this includes clinicians and women receiving user-friendly information about the latest guideline and what it means for them. Wide dissemination and education sessions should be offered. Information should include that fact that Rh D immunoglobulin is in fact a blood product and therefore it should be managed and discussed as such. This includes information about the risk of adverse reactions and how they should be managed.
- Education and guidance around the most appropriate site of administration of Rh D immunoprophylaxis for women with a high BMI is welcomed.

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- Education and guidance around the management of an adverse reaction is not included in the guideline and while there is some research available about how best to do this, this information is not easily accessible. It is advantageous to include this information in the guideline or provide a direct link to this information as well as to provide education around this point.
- The provision of information through social media channels and professional associations would be an appropriate approach to disseminating information.

APPENDIXES

Appendix A1 Abbreviations and acronyms

Section	Page Number	Comments	Attached documentation Y/N
N/A		Nil suggestions.	

Appendix A2 Terminology

Section	Page Number	Comments	Attached documentation Y/N
N/A	p. 63	Rh D negative women defines the woman by the fact that she is Rh D negative. This needs to be changed to 'a woman who is Rh D negative'	

Appendix B Research priorities

Section	Page Number	Comments	Attached documentation Y/N
N/A	p. 64	We support the inclusion of woman's preferences in considering the move to a single dose option.	
	p. 64	The research foci are appropriate and important given the findings of the review and the contents of the guidelines. How will these questions be addressed and how will any research which attempts to answer these questions, be funded, particularly given that many are specific to the Australian context?	

Appendix C Dosing of Rh D immunoglobulin following fetomaternal haemorrhage quantification

Section	Page Number	Comments	Attached documentation Y/N
N/A		Nil comments.	

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Appendix D and Appendix E Development process

Section	Page Number	Comments	Attached documentation Y/N
		Nil comments however, transparency in who was involved in the development and review is helpful.	

ADDITIONAL COMMENTS

Section (if applicable)	Page Number (if applicable)	Comments
		We strongly advocate for and suggest that the woman's preference be forefront and consistently reiterated throughout this document, particularly given the recently published Strategic directions for Australian maternity service. A woman should: • Receive all necessary information which should be underpinned by the current evidence base. • Be offered the opportunity to discuss risks, benefits and alternatives, if any, alongside of any recommendation to immunoprophylaxis • Be given information about the implications of declining immunoprophylaxis • Have time to consider the above information and subsequently, be free to exercise informed decision making, free from coercion, bias, harassment or bullying. This will support individualised care provision for all women.
		We suggest that you replace 'patient' with 'woman' throughout the entire document. This is line with the recommendations and enablers of the new *Woman-centre care: strategic directions for Australian maternity services* released in November 2019.

VOLUME 1 – EVIDENCE REVIEW

Section	Page Number	Comments	Attached documentation Y/N
		Comprehensive review undertaken and results are reflected in the guideline.	

VOLUME 2 - APPENDIXES

Page Number	Section Number	Comments	Attached documentation Y/N
		Nil comments.	