NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE
Health Technology Appraisal

Routine antenatal anti-D prophylaxis for women who are RhD negative (review of NICE technology appraisal guidance 41)

The table contains summaries of comments received in response to consultation on the ACD and received via the NICE website and in writing from the public.

Comment from	Nature of comment	Response
Baxter Healthcare	Section 2.6: The ACD states that 'recent survey evidence suggests that the single-dose regimen is increasingly preferred for logistical reasons.' From reading the Assessment Report, this appears to be based only on anecdotal evidence. Baxter believes this statement misleadingly favours the single-dose regimen without mention of there being no evidence of difference in efficacy between the two regimens or of previously stated concerns from the Royal College of Nursing (RCN), and that it should be removed or amended to reflect a more balanced point of view.	Comment noted. Section 2.6 of the FAD has been amended accordingly.
Baxter Healthcare	Section 3.4: The word 'autoimmune' is incorrect and should be replaced either by 'immune' or 'idiopathic'. Baxter also requests that the fact that WinRho SDF is marketed in the UK *solely* for the treatment of idiopathic/immune thrombocytopenic purpura be made more explicit, preferably at the start of the section.	Comment noted. Section 3.4 of the FAD has been amended accordingly.
Baxter Healthcare	Section 3.6: The final sentence should be amended to 'Costs are likely to vary…' as locally negotiated procurement discounts will mean prices will invariably differ from list price.	This is standard wording in the FAD and therefore section 3.6 of the FAD remains unchanged.
Baxter	Section 4.1.6: Baxter believes that the phrase '…and no evidence of a difference in	Comment noted. Section

Comment from	Nature of comment	Response
Healthcare	efficacy between these regimens' should be removed, or re-worded as per the Assessment Report which states that the studies 'do not provide any evidence to suggest that two 500 IU doses of anti-D at 28 and 34 weeks are more, or less, effective than a single dose of 1500 IU at 28 weeks.'	4.1.6 of the FAD remains unchanged. The statement in the FAD essentially states the same message as the assessment report.
Baxter Healthcare	Section 4.3.8: In the Assessment Report, there was mention of concerns by the RCN regarding protection at 28 and 39 weeks. However there is no mention of such concerns within the ACD. Baxter believes that this section also gives a misleading impression in favour of the single-dose regime and that the RCN concerns are valid and important for consideration in this section. Also within this section, Baxter believes that the paragraph on supply constraints is of such importance that it should be addressed in its own separate section and that the concluding statement again should be addressed as a separate paragraph.	Comment noted. Section 4.3.8 of the FAD has been amended. Comment noted. Section 4.3.8 of the FAD includes the discussions that the Committee had around this issue.
BPL	On page 6 of 26 in the Appraisal document and on page 7 of 18 under the third tab of the Evaluation Report the licensed indications for the various products are given: • D-Gam 500 IU is also licensed for potentially sensitising events after 20 weeks of gestation.	Comment noted. Section 3.1 of the FAD has been amended accordingly.
CSL Behring	Section 2.6 (page 6 of ACD), fourth line: please remove the words "at least" since 1500IU of both of the one dose regimens in this technology is indicated for antepartum prophylaxis, the words "at least" implies that a minimum of 1500IU or higher doses need to be used. It should therefore read "..... single dose of 1500IU at 28 weeks gestation...."	Comment noted. Section 2.6 of the FAD has been amended accordingly.

Comment from	Nature of comment	Response
CSL Behring	Section 3.3 (page 7 of ACD) first sentence: please replace adsorption chromatography with cation-exchange column chromatography. This method was discussed in paper by Stucki M et al. Characterisation of a chromatographically produced anti-D immunoglobulin product. Journal of Chromatography B. 700 (1997) 241-248. (Included in CSL Behring submission).	Comment noted. Section 3.3 of the FAD has been amended accordingly.
Royal College of Paediatrics and Child Health	The College believes that this document addresses the question of efficacy and cost effectiveness and has reached a clear conclusion. The introduction regarding the process of sensitization and the hazards to the baby have been written in very simple English and yet the description of the economic modelling provides no comparable explanation. The College is puzzled that the ICER is defined as a ratio and yet appeared to be presented in units of £. It would be helpful to include perhaps a simple table with on one side the cost of prophylaxis and the cost of care of sensitised pregnancies and affected babies, compared with the costs of the obstetric & neonatal/paediatric care if no prophylaxis is undertaken. This could be presented per 1000 deliveries so that individual PCTs could use it to calculate costs and savings when adopting the policy. The College will be interested to see the supporting information when the policy is launched.	Comments noted. The incremental cost effectiveness ratio (ICER) is the ratio of the benefits (measured in quality adjusted life years [QALYs]) gained to the costs incurred. Therefore it is presented as the cost per QALY i.e. how much a technology will cost for a patient to gain one additional quality adjusted life year. Costing, audit and implementation tools will be produced to accompany the final guidance..
Royal College of Paediatrics and Child	4.3.9 The College believes that 4.3.9 is unworkable in practice, and as such may continue to leave a group of women unprotected. While clearly fully informed consent is required before immunisation can be offered, the fact that the woman is for instance in a "stable" relationship with a RhD negative partner at that time should not be a	Comment noted. The Committee suggests that in some cases RAADP may not be of benefit and that

Comment from	Nature of comment	Response
Health	contraindication to receiving this immunisation.	women must be given an opportunity for discussion of the risks and benefits involved so that they can make an informed decision whether to use anti-D immunoglobulin or not.
Royal College of Pathologists and Royal College of Physicians	Do you consider that all of the relevant evidence has been taken into account? Yes	Comment noted.
Royal College of Pathologists and Royal College of Physicians	Do you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence and that the preliminary views on the resource impact and implications for the NHS are appropriate? Yes	Comment noted.
Royal College of Pathologists and Royal College of Physicians	Do you consider that the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS? Yes, but in addition we would suggest that Audit form part of the formal recommendations in order to provide better information on effectiveness for the purposes of future reviews	Comment noted. Audit criteria will accompany the final guidance.
Royal College of	Are there any equality related issues that may need special consideration? No	Comment noted.

Comment from	Nature of comment	Response
Pathologists and Royal College of Physicians		
NHS Blood and Transplant	We are a little concerned that the cost effectiveness analysis has not made any consideration of the fact that approximately 60% of women will also need anti-D at delivery. Delivery is probably the most important time for sensitisation and this aspect of the cost should not be separated from RAADP Using the prices quoted in the document (BNF 2007) D-Gam costs £27 per 500-IU vial Rhophylac costs £46.50 per 1500-IU prefilled syringe If you take 100 women 1. To give 100 of them two doses of D-Gam 500iu at 28 and 34 weeks costs 100x 2x 27 = £5400 To also give the 60 who deliver a D+ fetus D-Gam 500iu costs 60x27 = £1620. Total 5400+1620 = £6820. By sticking to one preparation the donor exposure will be limited. 2. Give 100 women one dose of Rhophylac 1500iu at 28 weeks costs =£4650 and to give 60 of them a further vial at delivery costs 60x46.5 = £2790 Therefore the total cost of using this preparation is £7440. Once again donor exposure would be limited by using the same preparation. 3. To be as cheap as possible you could give Rhophylac 1500iu at 28 weeks and D-	Comments noted. Section 4.3.7 of the FAD states that anti-D immunoglobulin will be given at times other than RAADP. The cost of anti-D immunoglobulin for other indications will remain the same in comparator group and intervention group and therefore will not affect the incremental cost-effectiveness.

Comment from	Nature of comment	Response
	Gam 500iu at delivery. This would cost (100 x 46.5) + (60x27) ie £6270 but this would mean guaranteeing the mother is exposed to donors from two different sources (CSL-Behring donor plasma and BPL donor plasma) and quite possibly different countries plus the added complexity of stocking two preparations. We thought it would be worth the health economics team considering this and perhaps making some reference to it in the document rather than presenting the costs of RAADP without reference to the delivery dose We have not included figures on the 86.5% compliance with the 2 dose regime - this would reduce its effectiveness (and cost). Receiving 1500iu at delivery in option 2 which may reduce the number of sensitisations compared with 500iu at delivery.	Comment noted. Compliance with both dosing strategies was assumed by the Committee to be the same.
NHS QIS Reviewer 1	Whether you consider that all the relevant evidence has been taken into account. *I consider that most of the relevant evidence has been considered. I do consider that the new technologies involving non invasive pre natal diagnosis (NIPD) should be carefully considered when the results of ongoing studies are published*	Comment noted.
NHS QIS Reviewer 1	Whether you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence.. *Cost effectiveness calculations assume that the implementation is cost neutral to the maternity service delivering the recommendations. This is incorrect as Maternity services have to make special arrangement eg set up dedicated anti-D clinics in order to deliver RAADP.*	Comment noted. This is discussed in section 4.3.8 of the FAD.
NHS QIS Reviewer 1	Whether you consider that the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS.	Comment noted.

Comment from	Nature of comment	Response
	The provisional recommendations are sound	
NHS QIS Reviewer 2	Whether you consider that all the relevant evidence has been taken into account. *Yes.*	Comment noted.
NHS QIS Reviewer 2	Whether you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence.. *Yes. Acknowledging that I have no experience of cost-effectiveness modelling the figures quoted in 4.2.4 seem lower than one would expect both for minor and major developmental problems. I think that it is correct to highlight in 4.3.3 the reasons why this underestimate might be the case.*	Comments noted.
NHS QIS Reviewer 2	Whether you consider that the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS. *Yes* *The research recommendations are also appropriate and important*	Comment noted.
NHS QIS Reviewer 3	Whether you consider that all the relevant evidence has been taken into account. *The limited evidence base seemed to have been considered – the majority from the previous appraisal*	Comment noted.
NHS QIS Reviewer 3	Whether you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence. *The Committee had not received any economic models, considered there were problems with some of the costs in the model developed, combined multigravidae women with primigravidae women, unlike the previous appraisal. However the discussion as reported highlighted some reasons for the cost and combination groups and therefore it was possible to trace the argument.*	Comments noted.
NHS QIS Reviewer 3	Whether you consider that the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS.	Comment noted

Comment from	Nature of comment	Response
	My concern is that there appears to be much uncertainty regarding cost and possibly benefit, but with the evidence presented and the inclusion of the final statement about choice (not currently included in the recommendation), the recommendations could be the basis for guidance.	
NHS QIS Reviewer 4	Whether you consider that all the relevant evidence has been taken into account. *Yes. The methodology and evidence base used is appropriate and comprehensive for the purpose.*	Comment noted.
NHS QIS Reviewer 4	Whether you consider that the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence. *Yes.*	Comment noted.
NHS QIS Reviewer 4	Whether you consider that the provisional recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS. *Yes.*	Comment noted.
PCT	Do you consider that all of the relevant evidence has been taken into account? Yes, there has been an extensive and comprehensive review of the literature, and engagement with patients, clinicians and other stakeholders. Do you consider the summaries of clinical and cost effectiveness are reasonable interpretations of the evidence and that the preliminary views on the resource impact implications for the NHS are appropriate? The resource impact implications for the NHS are likely to be appropriately covered. There are two areas where we would wish to comment on clinical and cost effectiveness which may indicate that benefits to patients and the NHS are more limited than suggested in the ACD.	Comments noted.
PCT	**Benefit and Harm**	Comments on the

Comment from	Nature of comment	Response
	From the evaluation (page 83 and 84) the number needed to treat to prevent one foetal loss with this intervention is 5,790 (range of 5,730 to 8,690 given in the previous evaluation) with the benefit almost exclusively falling in subsequent rather than current pregnancies. This is an absolute risk reduction of 0.017% of a RhD negative mother having a foetal loss due to Rhesus incompatibility, which is an extremely small benefit. There is an additional obvious benefit of having a child unaffected by HND, but prevention of foetal loss appears to be associated with the greatest benefit according to the evaluation. At the same time, for a mother, the number needed to cause (significant) harm can be calculated as 140,000 for one preparation, and for any harm as 69,000 for another, though there is usually marked under reporting of adverse events and the numbers needed to harm are almost certainly worse (page 40 of the evaluation). There are also observable changes in babies that cannot benefit from the intervention, but there is no apparent harm from this (also page 40). There must be very few interventions that a patient would give informed consent to for such a small chance of possible future benefit. However, pregnancy may be one area of practice where this would happen, and the risk of harm appears significantly smaller than the chance of benefit. *The likelihood of the expected benefit being realised for an individual patient should be made more explicit in the ACD. The number needed to treat to prevent one foetal loss is 5,790.*	assessment report are noted. The cost effectiveness analysis takes account of the avoidance of sensitisation and HDN of the newborn as well as foetal loss. The rarity of an outcome is taken in to account when calculating the cost effectiveness.
PCT	**Cost Effectiveness** While the analysis in the evaluation is generally handled on a population basis there is one significant area, as indicated in the sensitivity analysis, that is calculated on individual events and this inconsistency feeds through into the conclusions in the ACD.	Comments on the assessment report are noted. The Committee considered that the 79 YLL in the

Comment from	Nature of comment	Response
	Specifically, the years of life lost (YLL) for each foetal loss are calculated on an individual basis, at 79 (average life expectancy). However, most couples will have further pregnancies until the planned family size is achieved and there will therefore be no overall years of life lost to the population. While desired family size may unfortunately not be fully obtainable for an individual mother following foetal loss due to haemolytic disease, for RhD negative mothers overall the average family size should not be significantly affected by this intervention given the small absolute risk of foetal loss due to haemolytic disease prevented. This does not detract from the intense grief and devastating effect on families having a late foetal loss, but there is an attempt in the supporting evaluation to account for this elsewhere. In all official national statistics of years of life lost, deaths in children under the age of one are specifically excluded. While the current explanation in the definition is that the causes of death under one are unique to that age group, this is true at other ages also and previous definitions have included the consideration that planned family size tends to be maintained after an infant death. Given the general exclusion of infant deaths in the calculation of years of life lost, it is difficult to see why foetal loss due to Rhesus disease should contribute to years of life lost in the supporting evaluation. There is also no other situation in which years of life lost are attributed to foetal loss at any stage of pregnancy, and it appears inappropriate that Rhesus disease should be such a special case. This contradicts the last bullet point (page 109 of the evaluation) which asserts otherwise. Internationally, the World Health Organisation, which arguably has a particular focus on infant mortality, also gives reduced weights to YLL in childhood and additionally discounts subsequent YLL to give a total of 33 YLL for an infant death. No YLL are	assessment report (24 QALYs) was an overestimate. The Committee discussed this in detail and gave this comment careful consideration. The Committee did not feel that it was able to assign any particular disutility to foetal loss but accepted the 10 QALY figure from the previous appraisal (equivalent to 13 YLL), see section 4.3.4 of the FAD.

Comment from	Nature of comment	Response
	included for foetal loss in their statistics. This would also suggest that attributing 79 YLL gained for a foetal loss prevented by this intervention is questionable. *The cost per QALY in section 4.2.1 to prevent HDN associated foetal loss appears to be to low because 79 YLL have been allocated for a foetal loss. This appears to be inconsistent with national and international approaches.*	
PCT	Do you consider the recommendations of the Appraisal Committee are sound and constitute a suitable basis for the preparation of guidance to the NHS? The response for question ii) on cost effectiveness would produce a different assessment of cost effectiveness for the intervention and would probably result in a different conclusion if this was taken into account. There are two other areas on which we would wish to comment.	Comment noted.
PCT	**Service Delivery** The assessment concludes that there is a lack of evidence to support either a single dose or dual dose regimen for Anti-D in RhD negative mothers-to-be and makes no recommendation as to which should be implemented. This is unhelpful operationally and the appraisal may consequently add little to practice. While accepting the lack of evidence, a decision on which regimen to implement does have to be made. A consistent national approach would be beneficial, particularly considering the likelihood of systems failure when pregnant women or clinicians move between areas that use different regimens. Where there is no evidence on which to base a preference, either regimen could be recommended on other grounds until there is sufficient evidence from research.	Comments noted. The Committee had no evidence placed before it upon which to base a recommendation for one or the other regimen or any particular product, see section 4.3.8 of the FAD for the Committee's considerations on this issue.

Comment from	Nature of comment	Response
	In this instance, the balance of comments made in the report and received from consultees would suggest the two dose regimen was to be preferred because of a wider period of protection. However, the cost effectiveness acceptability curve (page 121 of the evaluation) would suggest that a single dose regimen for all RhD negative pregnancies is most cost effective. *The recommendations would be more useful operationally if it were specified which of two possible regimens should be implemented.*	
PCT	**Reassurance and Multigravidae** Paragraph 4.3.2 indicates that one of the benefits to pregnant women is reassurance and 4.3.5 suggests that it would be difficult not give an intervention in a subsequent pregnancy if it had been given in the first. This is a difficult consideration as the grounds for reassurance may be known to be either misplaced or limited. Generally, it is more appropriate to provide unbiased information to individual patients on the evidence based balance of risks and benefits so that they (with their clinicians) may make informed choices. An obvious example of this issue would be antibiotics for sore throats which historically have provided misplaced reassurance. Also, the ICER associated with the intervention in multigravidae is considerably above the upper threshold usually used for NICE. NICE routinely makes decisions on the use of interventions in subgroups and the following of previous clinical practice would not normally be sufficient reason to disregard NICE's usual approach. *Reassurance and existing practice seems to be given as the reason in the ACD for recommending the intervention to multigravidae where the ICER is between £46,000*	Comment on the assessment report are noted. The Committee based its decision on additional analysis which considered all pregnant women as a group and compared them to no RAADP. See sections 4.2.8, 4.3.5 and 4.3.6 of the FAD.

Comment from	Nature of comment	Response
	and £52,000. This is appears to be inconsistent with NICE's general attempt at following an evidence based approach and an upper threshold of £30,000 for ICER, and may have significant resource implications if applied to future technology appraisals.	
PCT	Are there equality related issues that may need special consideration? Paragraph 2.5 of the appraisal consultation document would suggest that the recommendation was largely based on the effect on the white population. In fact, the evaluation report indicates that benefits are greater to the non white population (page 110 of the evaluation) because if fathers are from the same ethnic group more pregnancies in RhD negative mothers are likely to be affected. The implication of implementation is one of a reduction in inequalities because of a disproportionate benefit for pregnancies in non-white mothers, and it would be helpful to acknowledge this in the ACD	Comments noted. The recommendation is for the use of anti-D immunoglobulin in all pregnant women therefore there is no equality issue.
Assessment group	Section 4.1.1: We would suggest changing 'Only this RCT' to 'This new RCT' in the last sentence of this paragraph.	Comment noted. Section 4.1.1 of the FAD has been amended accordingly.
Assessment group	Section 4.1.3: We would suggest changing the wording of the sentence beginning 'All studies' to 'Two of these studies' (studies which reported sensitisation rates at, or 6 months after, delivery would have included women who did not go on to have further pregnancies).	Comment noted. Section 4.1.3 of the FAD has been amended accordingly.
Assessment group	Section 4.2.1: The choice of which results are reported from the economic evaluations which have been identified by the literature review is unclear. Four (unnamed) studies have been reported. Since it has been stated that only 2 evaluations were applicable to the NHS it would seem most appropriate to report the results of these two studies. When reporting the results from Vick et al. it should be clear that these are based on	Comments noted. This is a summary of the evidence and therefore details of results have not been included.

Comment from	Nature of comment	Response
	1995 prices. It should also be noted that the ICERs presented for Chilcott et al. exclude the valuation of stillbirths and grief.	
Assessment group	Section 4.2.1: The analysis incorporated QALY losses for a fetal loss rather than QALY gains for avoiding fetal loss. In addition, although an example of multigravidae only has been provided in the report by Chilcott et al., this would impact upon the ICER for both multigravidae and primigravidae.	Comment noted. In the analysis in the Assessment report, QALYs, are incorporated for foetal loss. However QALYs are gained by avoiding such a loss through the use of the intervention (RAADP).
Assessment group	Section 4.2.3 and Section 4.2.8: Each regimen of RAADP is not compared with no RAADP in the model as stated. This is correct for primigravidae, but RAADP given to multigravidae is compared against RAADP given to primigravidae rather than no RAADP. We would request that you delete Section 4.2.8 as this was an analysis which was requested at the time of the first committee meeting, but which we have suggested is inappropriate as it is not an incremental analysis of the comparators stated in the scope. Comparing RAADP for all women against no RAADP could be misleading since many of the benefits of giving RAADP to all women may be achieved by giving RAADP to primigravidae. By comparing the additional costs and benefits of giving RAADP to all women with giving RAADP to primigravidae alone, we can assess whether RAADP given to multigravidae in addition to primigravidae is likely to be considered cost-effective or whether the additional resources required for giving RAADP to multigravidae could produce more benefit if used for another need elsewhere.	Comments noted. The Committee discussed this and decided that considering all women together, regardless of whether it was their first, second, third etc pregnancy, compared to no RAADP was an appropriate approach. See sections 4.3.5 and 4.3.6 of the FAD.
Assessment group	Section 4.2.3: It should be stated that the sensitisation rates presented in the description of the model are based on RAADP given to all women.	Comment noted, this is covered in section 4.1.5 and 4.2.3 of the FAD.

Comment from	Nature of comment	Response
Assessment group	Section 4.2.5, Section 4.3.4 and Section 4.3.5: We would request that you present the results of the analysis assuming that a fetal loss is associated with 79 life years lost which equates to 24 discounted QALYs lost (as in the original analysis) and also the results of a threshold analysis which we have carried out following the first committee meeting to investigate the impact of different assumptions (see Appendix A for the analysis included in the HTA report). Given that the valuation of a fetal loss is complex and highly uncertain, we would request that you include this (see Section 4.2.5) rather than assuming that a foetal loss is associated with a loss of 10 QALYs given that this was assumed only to be a minimum at the previous RAADP assessment based on the threshold analysis which had been carried out at that time. The threshold analysis for this review suggests that in order for RAADP to be considered to be cost-effective at a cost per QALY gained of £30,000, for primigravidae a fetal loss would have to be valued at a minimum of 6 QALYs and for all women a fetal loss would have to be valued at a minimum of 13 QALYs.	Comments noted. The Committee accepted the 10 QALYs loss in line with the previous appraisal, see section 4.3.4 of the FAD.
Assessment group	Section 4.3.3 and 4.3.6: Within the first committee meeting, the clinical experts suggested that the cost of IUT was underestimated. However, because this makes up such a small proportion of the management of sensitisations, the impact on the cost of the management of sensitisations is extremely minimal.	Comment noted.
Assessment group	Section 4.3.6: It should be noted that a review of the literature in this area was carried out by the Assessment Group and it would be very difficult to demonstrate that parents/ carers of a disabled child have a lower quality of life.	Comment noted.
Assessment group	Section 4.3.8: The economic model included 2 administration costs of £5 for the 2-dose regimens and only 1 for the single dose. I think the committee were suggesting that the costs may be higher if RAADP could not be supplied within a routine visit. Our clinical expert suggested that RAADP would be supplied within routine appointments more often than not.	Comment noted.
Web comments		

Comment from	Nature of comment	Response
NHS professional 1	6.1 When will this test be available?	The date of commercial availability of such a test is unsure. A review of this appraisal would take the availability of this test into account.
NHS professional 2	We are the Regional Maternity Unit for N.Ireland and had 5,300 deliveries in 2007. We implemented routine antenatal Anti-D prophylaxis for all Rhesus negative women in 2004 using 2 doses of Anti-D - to be given at 28 and 34 weeks during their hospital appointment. We have one midwife allocated during the clinics, am and pm, Mon-Fri to deal with, not only the administration of Anti-D but also the counselling and consent issues. It would be of great benefit to us to have clarification and clear direction from NICE that one single dose of Anti-D can be given at 28 weeks. This would help to reduce the amount of time that a midwife would need to spend dealing with Anti-D administration etc. We are also planning to limit the 35 week hospital appointment to hospital care only women. As we have no arrangements in community for administration of Anti-D one single dose at 28 weeks would be more appropriate for us. It would be more cost effective for our unit to use one-dose Anti-D at 28 weeks. For our unit the one-dose regime would be simpler, more convenient and less prone to errors and omissions than two-dose regimen. It would benefit our service if there was clinical evidence to support the single-dose regimen.	Comment noted. The Committee were unable to recommend one regimen over the other see section 4.3.8 of the FAD. Sections 3.1, 3.2, 3.3 and 3.4 of the FAD state the summary of the product characteristics for each for the anti-D immunoglobulins.
Patient	As a RhD negative woman married to an RhD negative man, I feel very strongly about point 4.3.9. When I gave birth to my second son, the hospital staff would not let me leave hospital before having the anti-D injection, even though my husband was in possession of a blood donor card with his blood type listed. The only reason I could	Comment noted.

Comment from	Nature of comment	Response
	think that the staff were being so obstinate was that they thought there was a possibility that the baby was not his child. Eventually I was able to have my sons blood typed - this was arranged	
Health Economist 1	In 2.5, it is not clear to me what the 37 deaths refers to: presumably it is for anti-D admin at birth only. It is not clear how many of these deaths would be averted by the administration of anti-D at 28 and 34 weeks. Ditto for children with development problems. Since anti-D is already being recommended, these figures (for anti-D at 28, 34 and 40 weeks) should be part of the story for current practice.	Comments noted. These are deaths that occur with the use of anti-D immunoglobulin for indications other than routine antenatal prophylaxis. While a proportion of these deaths can be prevented by rigorously following guidelines for the use of anti-D immunoglobulin, the assessment assumes that a further proportion of these could be prevented by the use of RAADP.
Health Economist 1	1 Partobulin is not on emc and D-gam has only a PIL on emc. It is therefore not possible to check the adverse reactions to these two products as advised in the draft guidance. 2 Additionally, no details of batch size of any products are given. If there is a very large batch size and the batch were to be contaminated by a new and hitherto unknown virus, it could easily lead to a catastrophic outcome that could lead to the loss of the lives of many women. In the past 40 years, at least 4 such viruses/prions have led to deaths through blood contamination, most notably of many haemophiliacs	Comment noted. Risk of blood borne infections with unknown pathogens cannot be quantified. The Committee was aware of the potential risks but considered that these were

Comment from	Nature of comment	Response
	in this country alone. It is not clear that the committee has factored this element into its discussion sufficiently. As a minimum, use of the product in a woman unlikely to ever become pregnant again should not be advised. However, for smaller batch sizes the problem should be correspondingly smaller, as long as the existence of the new disease can be recognised within a few months.	outweighed by the benefits. In section 4.3.8 of the FAD the Committee note the importance of limiting a women's exposure to different anti-D immunoglobulins.
NHS professional 3	Highly support the single dose from practical point of view. One area which doesn't seemed to have been factored in is that most Rh neg women request that their partners blood group is tested and this has lead to a small but significant workload and additional risk factor with a different persons blood group filed in the maternity notes eg Mrs Black is O neg but Mr Black is O Pos and it is too easy when the chart is read at a busy clinic not to pick up that you are looking at the man's blood result. Different risk management protocols have had to be introduced but it remains problematic	Comment noted.

Responses from consultees and commentators of no comment were received from:
The Department of Health
The Royal College of Nursing