Assessment Group Comments on the ACD of routine antenatal anti-D for RhD-negative women

This document provides comments on the ACD of RAADP for RhD-negative women. Our main comments are provided in Section 1.

Section 1: Main comments

Comments on Section 4.1

- Section 4.1.1: We would suggest changing 'Only this RCT' to 'This new RCT' in the last sentence of this paragraph.

- 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).

Comments on Section 4.2

- 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 1995 prices. It should also be noted that the ICERs presented for Chilcott *et al.* exclude the valuation of stillbirths and grief.

- 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.

- 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.

- 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.

- 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 on Section 4.3

- 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.

- 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.

- 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.

Appendix A: Valuation of foetal loss as reported in HTA report

Because the valuation of a foetal loss is subjective, according to how the individual may value the QALYs lost associated with the foetus and the QALYs lost by the parent(s), a threshold analysis has been carried out to investigate the impact of different valuations associated with foetal loss. The results are presented in Table 31 below.

Table 31: Implied QALY differential per foetal loss avoided

	Threshold	**£20K**	**£25K**	**£30K**	**£35K**	**£40K**	**£45K**	**£50K**
RAADP given to RhD-negative primigravidae versus no RAADP	D-Gam	17	13	10	8	6	5	4
	Partobulin	24	18	14	12	9	8	7
	Rhopylac	12	8	6	5	3	3	2
RAADP given to all RhD-negative women versus primigravidae	D-Gam	36	26	20	16	13	10	8
	Partobulin	50	38	30	24	20	16	14
	Rhopylac	25	18	13	10	7	5	4

These results show that RAADP given to RhD-negative primigravidae compared to no RAADP would be considered cost-effective at a threshold of £30,000 per QALY gained if a

foetal loss is assumed to be worth 10, 14 and 6 QALYs lost for D-Gam, Partobulin and Rhopylac respectively. Similarly, RAADP given to all RhD-negative women compared to RhD-negative primigravidae only would be considered cost-effective at a threshold of £30,000 per QALY gained if a foetal loss is assumed to be worth 20, 30 and 13 QALYs lost for D-Gam, Partobulin and Rhopylac respectively. These QALY losses are a combination of both the parental QALYs lost and those QALYs lost as a result of the death of the foetus itself. Since a lifetime lost with life expectancy of 79 years is equal to 24 QALYs after discounting, Partobulin would be considered cost-effective for all RhD-negative women compared to RhD-negative primigravidae at a threshold of £30,000 per QALY gained if the loss of a foetus was assumed to be equal to the loss of a life with average lifetime expectancy and 6 QALYs lost by the parent(s).