Response on behalf of Royal College of Physicians and the Royal College of Pathologists to the **Technology Assessment Report '*Routine antenatal anti-D prophylaxis for RhD-negative women (review)*', commissioned by the NHS R&D HTA Programme on behalf of the National Institute for Health and Clinical Excellence.**

Coordinated by: [redacted]

The report provides a detailed assessment of the various issues involved in both the implementation of the technology and the consequences of failure to provide appropriate prophylaxis for pregnant Rh-D negative women. In general, we agree with the data presented and their interpretation, and feel the conclusions drawn from the assessment are appropriate, with the following comments:

Published data and quality of evidence

The report confirms that there has been little information published regarding implementation of RAADP either in relation to the regimen used, compliance with treatment or clinical effectiveness as measured by reducing sensitization events. Also there have been no studies to directly compare the clinical effectiveness of a two dose versus one dose treatment schedule, but what data there are suggests that both treatment schedules appear to be equally effective.

We agree that the quality of included research is not high, there being only one RCT, but also that the community based studies by MacKenzie et al and Mayne et al offer the best information on the likely efficacy of RAADP in a real life setting, and do demonstrate a reduction in the number of women found in subsequent pregnancy to be sensitized.

BCSH recommendations

The report states on Pg 37 3.3, para 2, 2nd that "The BCSH recommends the use of the two dose regimen, noting that more evidence is required to establish the

comparative efficacy of a single dose of 1500IU at 28 weeks. BCSH guidelines actually state (section 3.1) "This section takes account of the publication of the NICE guidance which recommends that RAADP is offered to all D negative non-sensitised pregnant women at 28 and 34 weeks gestation at routine antenatal visits (NICE 2002). A dose of at least 500IU, im is recommended on each occasion"

No specific BCSH recommendation is actually given in the BCSH guidelines, and so the statement in the report is incorrect. The BCSH wording actually refers (incorrectly) to the original NICE guidance TA41, which does not specify the two dose regimen. This highlights the point made in our earlier report that the original TA guidance 41 was somewhat ambiguous and open to interpretation in respect of the most appropriate dose and schedule of anti-D.

Continuing cases of sensitization

The report makes the point that despite the increased compliance with RAADP, some women continue to be sensitised, and suggests four possible reasons for this. A fifth additional reason could be:

- Failure to implement RAADP regime at all by some Trusts and incomplete adherence to advice ie poor compliance with 2nd dose

Implementation issues:

a) Importance of the Blood Transfusion laboratory for successful implementation

The report does not consider the reasons for failure to implement TA41 by some organizations, and suggests that implementation should have no particular resource or logistical implications apart from the cost of the technology.

The submission by RCP/RCPath highlighted the importance of a multidisciplinary approach to implementation, and stressed the need for laboratory input and expertise for interpretation of results. This aspect is not really covered by the report. Also, the importance of communication between all healthcare

professionals and clients is only mentioned very briefly in relation to midwives, with no reference to liason between the clinical area and the laboratory. The importance of the laboratory contribution to successful implementation of the guidance is not covered by the report. The details contained in the "practical guide to implementation" (Appendix 1 of the RCP/RCPath submission) help identify potential reasons why implementation may be less than ideal.

b) Resources

3.3.4 Anticipated costs associated with intervention

The use of RAADP does impose additional clerical and administrative burden on Blood Transfusion laboratory personnel where this is the site of issue for anti-D. There are also some additional reagent costs associated with the antibody screening required to exclude the presence of additional allo-antibodies post RAADP administration, although these costs are likely to be offset by the dropping of the 28 week antibody tests.

Targeted AADP

The report acknowledges the potential contribution of foetal genotyping technology, but states that it must yield no false negatives in order to be feasible in practice. This would seem to be an unrealistic goal as no test will be able to guarantee 100% no false negatives. However the technology will be more applicable for implementation if the specificity of the test is improved, and its optimal timing is determined. Further studies will be needed to determine its effectiveness, its associated costs and the potential cost savings, mainly in reduced use of anti-D.

Implementation and compliance data

The report confirms the need for a national co-ordinated audit to assess implementation and compliance issues, and to study sensitization rates in order to answer the question of why continued sensitization is occurring despite an increase in implementation of RAADP.

Further research

We agree with the recommendations for future research:

- Compare the efficacy of the different RAADP regimens. Issues relating to compliance and safety may also influence the efficacy of the different regimens of RAADP, and hence further research would also be useful in these areas;
- Confirm or disprove the preliminary findings that protection against sensitisation provided by RAADP in primigravidae extends beyond the first pregnancy;
- Aim to improve non-invasive genotyping of the foetus.