European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

London, 13 July 2007
Doc. Ref. EMEA/CHMP/BPWP/72096/2007

OVERVIEW OF COMMENTS RECEIVED ON DRAFT GUIDELINE ON THE CLINICAL INVESTIGATION OF HUMAN ANTI-D IMMUNOGLOBULIN FOR INTRAVENOUS AND/OR INTRAMUSCULAR USE CPMP/BPWG/575/99 REV. 1

Table 1: Organisations that commented on the draft Guideline as released for consultation

Add name followed by link to individual received comment (upon publication by Web Services)

	Name of Organisation or individual	Country
1	PPTA	Belgium
2	IPFA	Netherlands
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Table 2:Discussion of comments

GENERAL COMMENTS - OVERVIEW		
Although not different from the previous version of the guideline, the number of patients to be enrolled in the efficacy study seems to be rather high. One of our member companies has recently investigated the possibility to conduct such a study, and found some difficulties. (see also comment below)		
Outcome: Historically out of 100 pregnancies approximately 8 women were at risk of sensitisation (8%). The first anti-D studies (Bowman, Herman, Huchet, Tovey, Trolle) showed that due to postnatal prophylaxis this rate could be reduced to approximately 1.6%. Additional antenatal prophylaxis reduced this further to 0.08% in the Bowman study. Using the postnatal rates as a base (as antenatal prophylaxis is not common procedure in all EU states) one can state that in 200 patients there is a 95% probability that at least one sensitisation would occur. Therefore, if this is not seen in the clinical trial, the product is deemed to have a ≤1.6 sensitisation rate. Alternative approaches may be possible, provided that they are adequately justified and provide sufficient evidence to demonstrate that efficacy is not inferior to existing products. However, the experience in an MR-procedure showed that going below 200 patients was fraught with difficulty in developing meaningful statements on efficacy, considering that im and iv, ante-and postpartum efficacy had to be shown. The company concerned was then able to fulfil the requirements with relative ease in a resubmission procedure.		
SPECIFIC COMMENTS ON TEXT		
GUIDELINE SECTION TITLE		
Line no.[1] + paragraph no.	**Comment and Rationale**	**Outcome**
1.1.	Clinical Use Antenatal prophylaxis should not mentioned, according to the Core SPC and the clinical development proposed (2.2 and 3.2)	Indications in the clinical guideline and in the core SPCs have been harmonised.
2.2.1.	Prevention of Rh(D) immunisation RE: The study should investigate at least 200 patients and should ... All data on further pregnancy should be reported. What is the scientific rational for such a number? Does it come from a specific product study? Others have done better! The number of included patients should be according to the possible proof of no or acceptable immunisation level (incidence of anti-D antibodies at 3-6 months).	See general comment and response above. The last sentence in 2.2.1 "All data on a further pregnancy should be reported" has been deleted as it could be misunderstood that data from a further pregnancy was a requirement. The original intention of this sentence, that had been added to the consultation draft guideline, was that a company should not withhold any available information.

[1] Where applicable