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

London, 13 July 2007
Doc. Ref. EMEA/CHMP/BPWP/72151/2007

OVERVIEW OF COMMENTS RECEIVED ON THE CORE SPC FOR HUMAN ANTI-D IMMUNOGLOBULIN FOR INTRAMUSCULAR USE CPMP/BPWG/574/99 REV1.

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

	Name of Organisation or individual	Country
1	PPTA	Belgium
2	IPFA	Netherlands
3		
4		
5		
6		
7		
8		
9		
10		
11		
12		
13		
14		
15		
16		
17		
18		
19		
20		
21		
22		
23		
24		

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 74 18 85 45
E-mail: mail@emea.europa.eu http://www.emea.europa.eu

Table 2:Discussion of comments

GENERAL COMMENTS - OVERVIEW		
SPECIFIC COMMENTS ON TEXT		
GUIDELINE SECTION TITLE		
Line no.[1] + paragraph no.	**Comment and Rationale**	**Outcome**
Line 9-13 Par. 4.4	A product specific warning has been included for products containing "small quantities" of IgA; this is inconsistent with the current version of the relevant monograph, which does not address the IgA content, and with paragraph 2 of the cSPC (Qualitative and quantitative composition) which does not require to report the IgA content	This criticism is per se correct. The Monograph for intramuscular immunogloblin (338) does not require IgA content to be labelled. However, the information on IgA in 4.4. may still be relevant and helpful to the treating physician. EMEA will liaise with the European Pharmacopoeia on this matter.
	Analysis of anti-D products had shown anti-C levels that might have clinical implications. Ireland had raised the issue with Group 6B of the European Pharmacopoeia.	There is no indication of clinical consequences.
4.2.	<u>Prevention of Rh(D) immunisation in Rh(D) negative women</u> RE: Post natal prophylaxis, second paragraph: For post-natal use, the product should be administered as soon as possible within 72 hours of delivery... The 72 hours is the acceptable delay for IV anti-D immunoglobulin. The maximum acceptable delay should be determined according to the bioavailability of the IM product, determined by the specific PK studies.	From Bowman (Volume 43, December 2003 TRANSFUSION): It has been shown experimentally that at least partial protection is afforded by giving RhIg up to 13 days after exposure to D+ RBCs. Rh prophylaxis therefore is recommended up to 28 days after delivery, with the understanding, however, that the longer prophylaxis after delivery is delayed, the less likely it is to be effective.

[1] Where applicable

4.4.	Special warning and special precautions for use RE: 5th paragraph: [Product specific] < Invented name ... after administration of blood components products containing IgA. ... hypersensitivity reactions.> The words 'blood components' should be replaced by 'plasma-derived medicinal'.	Revision implemented
5.1.	Pharmacological properties RE: 4th paragraph: During pregnancy ... and may cause haemolytic disease of the subsequent Rh(D) positive newborn. The wording 'subsequent Rh(D) positive' should be deleted.	Is implemented in the text released for consultation.
5.2.	Pharmacokinetic properties RE: Human anti-D immunoglobulin for intramuscular administration is available in the recipient's circulation after a delay of 2-3 days. Should this not be <Product specific>, according to the PK and bioavailability studies ?	This is not likely to vary greatly and is not critical for clinical use. Therefore, the general statement has been kept but the wording modified to be more scientifically correct.