



**COMMITTEE FOR MEDICINAL PRODUCTS FOR HUMAN USE
(CHMP)**

**CONCEPT PAPER ON THE NEED FOR A GUIDELINE ON THE CLINICAL
INVESTIGATION OF SPECIFIC IMMUNOGLOBULINS**

AGREED BY THE BLOOD PRODUCTS WORKING PARTY	June 2009
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1. INTRODUCTION

Both guidelines on the core SmPC for human plasma-derived hepatitis B immunoglobulin, i.e. for intramuscular use (CPMP/BPWG/4222/02) and for intravenous use (CPMP/BPWG/4027/02), have been in operation since November 2006.

Other specific guidelines on core SmPC, i.e. Core SmPC for human rabies immunoglobulin for intramuscular use (CPMP/BPWG/3728/02), Core SmPC for human tetanus immunoglobulin for intramuscular use (CPMP/BPWG/3730/02) and Core SPC for human varicella immunoglobulin for intramuscular use (CPMP/BPWG/3726/02) have been in operation since February 2006.

Nevertheless, no guideline on the clinical investigation of these human specific immunoglobulins is currently available.

As the regulatory experience from the marketing authorisation applications, especially for human plasma-derived hepatitis B immunoglobulin has been developing during the past decades, the development of a guideline appears appropriate.

2. PROBLEM STATEMENT

Due to the recent increase of submission of marketing authorisation applications for human plasma-derived hepatitis B immunoglobulin (HBIG), several questions regarding the required clinical data arise. Furthermore, compliance to the current available Core SmPC being recommended, a specific guidance relating to the clinical investigation of HBIG products appears appropriate. The expansion of this NfG to all specific immunoglobulins¹ needs to be considered.

3. DISCUSSION (ON THE PROBLEM STATEMENT)

Considering the similar content of the Core SmPC for human plasma-derived hepatitis B, human rabies, human tetanus and human varicella immunoglobulin, elaborated during a single wave, and the similar pharmacological properties, a single approach can be followed to elaborate the NfG relating to the clinical investigation of specific immunoglobulins. This guideline can address the differences in the clinical requirements of these immunoglobulins and the aspects that could be common for all of them.

As a consequence of considering the data necessary to support the safe and effective use of the specific immunoglobulins, the current guidance on Core SmPCs may need to be revisited in order to ensure their compliance to the NfG.

4. RECOMMENDATION

The Blood Products Working Party (BPWP) recommends preparing a guideline on the clinical investigation of specific immunoglobulins as no European guidance exists in this area.

It is suggested first to address the common aspects of these specific immunoglobulins.

Indeed, the clinical approach can be based on three pillars:

- Product compliance with relevant Ph.Eur monographs,
- PK data should show expected characteristics of an immunoglobulin,
- Confirmatory data (for example for HBIG: anti-HBs levels >100IU/l, recurrence rates).

Then, some points pertaining to the specific management of the pathology should be addressed.

Notably, the following aspects should be studied and taken into account:

- The therapeutic indications (kind of prophylaxis, combination with the vaccine),
- The posology and the method of administration.

¹ Except human anti-D immunoglobulin where a guideline is already available.

5. PROPOSED TIMETABLE

This guideline will be discussed during the meetings of the BPWP in 2009 and 2010. It is anticipated that a draft CHMP document will be released for external consultation during 2010. The period for external comments for the draft text of the guideline will be 6 months.

6. RESOURCE REQUIREMENTS FOR PREPARATION

There will be two Rapporteurs involved in the preparation of the guideline. The draft will be discussed during the meetings of the BPWP.

7. IMPACT ASSESSMENT

A harmonised regulatory approach will encourage a more consistent assessment of products by regulators, and set clear standards and expectations for Industry. In addition, this will provide physicians and patients with reassurance about the safe and effective use of these products. The resource implications for preparation of the guideline are considered justified by the fact that application of guidance will make assessment easier and will result in less resources being needed during assessment.

8. INTERESTED PARTIES

Interested parties with specific interest in this topic will be consulted during the preparation of this guideline including IPFA, PPTA and WHO.² Other EMEA Working Parties including Efficacy Working Party and Vaccine Working Party will be involved during the preparation.

² IPFA: International Plasma Fractionation Association
PPTA: Plasma Protein Therapeutics Association
WHO: World Health Organisation