Part VI: Summary of the risk management plan

S**ummary of risk management plan for Fibrinogen concentrate, human (human blood coagulation factor I)**

This is a summary of the risk management plan (RMP) for Fibrinogen concentrate, human (FCH). The RMP details important risks of FCH and how more information will be obtained about FCH risks and uncertainties (missing information).

The summary of product characteristics (SmPC) and package leaflet of FCH give essential information to healthcare professionals and patients on how FCH should be used.

I. The medicine and what it is used for

FCH is authorized as Haemocomplettan R for treatment of bleeding in patients with congenital hypofibrinogenaemia, dysfibrinogenaemia or afibrinogenaemia and also for the treatment of bleeding in patients with acquired hypofibrinogenaemia. Riastap/ RiaSTAP is authorized for the treatment of bleeding in patients with congenital hypofibrinogenaemia or afibrinogenaemia with bleeding tendency. Please see the Summary of Product Characteristics (SmPC) for the full indication description. Haemocomplettan R and RiaSTAP are both administered by injection/ infusion.

II. Risks associated with the medicine and activities to minimize or further characterize the risks

Important risks of FCH, together with measures to minimize such risks and the proposed studies for learning more about risks that may be associated with FCH, are outlined below.

Measures to minimize the risks identified for medicinal products can include:

- Specific information, such as warnings, precautions, and advice on correct use of the product, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorized pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimize its risks.

In addition to these risk minimization measures, information about adverse reactions is collected continuously and regularly analyzed, so that immediate action can be taken as necessary should an important safety event be identified. In addition, a Periodic Safety Update Report (PSUR) is prepared and submitted to health authorities according to pre-specified timelines after FCH has been granted authorization for use in a country. This report provides an evaluation of the benefit:risk profile of FCH. These measures constitute routine pharmacovigilance activities.

If important information that could potentially affect the safe use of FCH is not yet available, it is listed under 'missing information' below. CSL continuously gathers information in the post-marketing data collection system, for pediatric and elderly populations, as well as in pregnant and nursing women, to more fully characterize the safety profile of FCH.

II.A List of important risks and missing information

Important risks may require special risk management activities to further investigate or minimize the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of FCH. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine);

List of important risks and missing information	
Important identified risks	• Anaphylaxis and Hypersensitivity/Allergic Reactions • Thromboembolic Events
Important potential risks	• Transmission of infectious agents
Missing information	• Paediatric Population • Pregnancy and Breastfeeding • Elderly Population

II.B Summary of important risks

Anaphylaxis and Hypersensitivity/Allergic Reactions	
Evidence for linking the risk to the medicine	Hypersensitivity and anaphylaxis are known risks associated with the use of blood components. Hypersensitivity is an adverse reaction that is highly variable with respect to frequency and severity. It is of great concern because serious forms of hypersensitivity reactions, such as anaphylaxis , can be quite severe, life threatening and even fatal. Information captured from literature reporting, clinical trial and post-marketing data collection contribute to the strength of evidence. Hypersensitivity and anaphylaxis are important identified risks that may occur with the use of FCH.
Risk factors and risk groups	Individuals who have had a previous anaphylactic or severe systemic reaction to human plasma products/ preparations are at a high risk of further episodes of hypersensitivity/anaphylaxis.

	The risk increases with use of multiple doses or with exposure to other plasma products.
Risk minimization measures	Routine risk minimization measures: CCSI Section 4.3 and 4.4 USPI Section 5 and 6 SmPC Section 4.4 and 4.8 Additional risk minimization measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Participation in EUHASS

Thromboembolic Events	
Evidence for linking the risk to the medicine	Thromboembolic events (TEEs) are a common risk with the use of systemic hemostatic agents. Information captured from literature reporting, clinical trial and post-marketing data collection of thromboembolic events, which may range from non-serious to life threatening or fatal, contribute to the strength of evidence. The risk of TEEs is considered an important identified risk associated with FCH use.
Risk factors and risk groups	Risk factors for thrombosis include: smoking, immobility, congestive heart failure, hypertension, age, diabetes, prior TEEs and concomitant medications that may have impact on blood coagulation (e.g., oral contraceptive). Patients with cardiovascular risk factors are at increased risk.
Risk minimization measures	Routine risk minimization measures: CCSI Section 4.3 and 4.4 USPI Section 5 and 6 SmPC Section 4.4 and 4.8 Additional risk minimization measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Participation in EUHASS

Transmission of infectious agents	
Evidence for linking the risk to the medicine	When medicinal products which have been prepared from human blood or plasma are used, there is a potential risk of transmission of infectious agents. This risk is reduced by screening plasma donors, incorporation of specific virus inactivation/removal steps in the manufacturing process for viral clearance, and adherence to good manufacturing practice. There are no confirmed case reports of transmission of infectious agents associated with use of FCH in clinical studies or from post marketing data collection. This risk is considered an important potential risk for FCH.
Risk factors and risk groups	Exposure to blood products increases the risk for acquiring infectious agents such as HAV, HBV, HCV. Risk is also increased in IV drug users and same sex partners.
Risk minimization measures	Routine risk minimization measures: CCSI Section 4.4 USPI Section 5

	SmPC Section 4.4 Additional risk minimization measures: None
Additional pharmacovigilance activities	Additional pharmacovigilance activities: Participation in EUHASS

Limited experience in paediatric population	
Risk minimization measures	Routine risk minimization measures: As described in CCDS Section 4.2, and USPI section 8. Additional risk minimization measures: No additional risk minimization measures.

Limited experience in pregnancy/lactation	
Risk minimization measures	Routine risk minimization measures: As described in CCDS Section 4.6, USPI Section 8, and SmPC Section 4.6. Additional risk minimization measures: No additional risk minimization measures.

Limited experience in elderly population	
Risk minimization measures	Routine risk minimization measures: As described in USPI Section 8. Additional risk minimization measures: No additional risk minimization measures.

II.C Post-authorization development plan

II.C.1 Studies which are conditions of the marketing authorization

At this time, there are no studies required as a condition of marketing authorization.

II.C.2 Other studies in post-authorization development plan

There are no other studies in the post-authorization development plan for Human Plasma Fibrinogen Concentrate.