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Human Medicines Division

Consolidated 3-year work plan for the Haematology Working Party (HWP)

Chairperson: Daniela Philadelphy

Work plan period: November 2022 - December 2024 (with a first review point after one year)

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1. Strategic goals

The area of expertise of the Haematology Working Party (HAEMWP) formerly the Blood Products Working party is in non-malignant haematology and also includes conditions for which medicinal products derived from human plasma and their recombinant analogues are used.

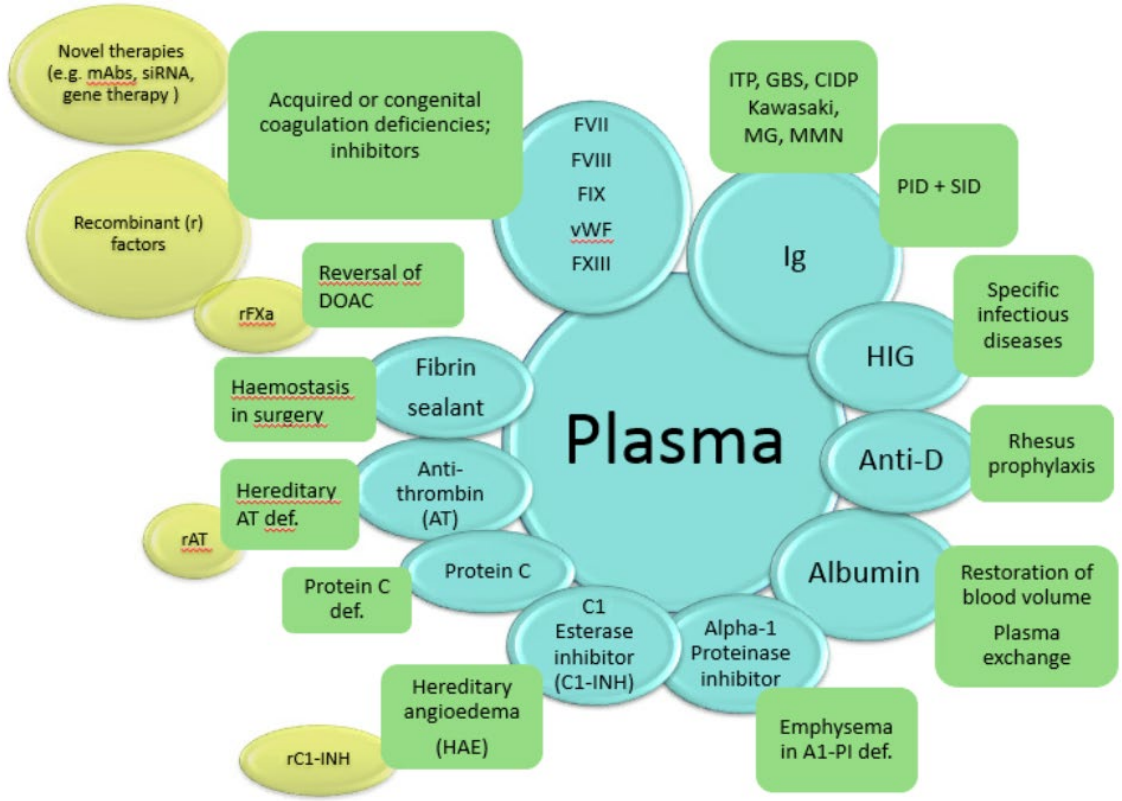
Many new products including gene therapies are being developed for the treatment of different haematological conditions, frequently congenital and hereditary, for some of which there have been few or no satisfactory treatments available. However, these conditions did not fall within the remit of existing working parties. Since there is overlap between the field of expertise of the Haematology Working Party (HAEMWP) and non-malignant haematology it was decided to expand the area covered by the BPWP to non-malignant haematology in general.

The HAEMWP has covered manifold biological products (which were traditionally referred to as blood products) manufactured from plasma, such as immunoglobulins, coagulation factors, human albumin and fibrin sealants and used in a range of indications. It also covered other products with specific therapeutic indications, such as haemophilia e.g. recombinant products (rFVIIa, rFVIII, rFIX, rFX, rFXIII), and novel non-coagulation factor therapies (see figure below).

WHO has classified plasma products as essential medicines and dedication to this field within a working party is therefore considered essential.

Historically, plasma products have been a perturbed field with lasting negative effects e.g. hepatocellular carcinoma from hepatitis C contamination. Although all aspects from donation to production and authorisation of plasma products are better regulated today than ever before, it remains an area of high vigilance and expanding use.

Overview of products and indications which were already within the remit of the BPWP:



Numerous interactions take place with the EC SOHO (substances of human origin) team, the plasma industry organisations PPTA/IPFA and the European Blood Alliance concerning the security of blood and plasma supply in light of increasing demand for plasma products. The long-standing contact with patients' organisations, through which the HAEMWP is aware that there is increasing anxiety about possible shortages of essential plasma products (e.g., immunoglobulins), will be continued.

In haemophilia the expertise in the HAEMWP can be used efficiently for novel therapies. The HAEMWP had already successfully liaised with the CAT/SAWP on gene therapy products and contributed to the RP on gene therapies for haemophilia to be used by clinical assessors and will be drafting a Reflection Paper on non-replacement therapies.

For the mid- to long term goals, the scope of the HAEMWP can cover products, which may include gene therapies, monoclonal antibodies and small molecule substances for disorders such as anaemias (e.g. congenital and hereditary anaemias: beta-thalassemia, sickle cell disease, erythrocyte enzyme deficiencies), thrombotic microangiopathy, bone marrow failure syndromes and thrombocytopenia. Current HAEMWP members can provide input on these products, and additional expertise will be sought as needed. The need to develop guidelines in some of these indications has been highlighted by industry in business pipeline meetings.

2. Tactical goals: activities/projects to deliver the strategic goals

2.1. Guideline activities

Revision of existing EU Guidelines:

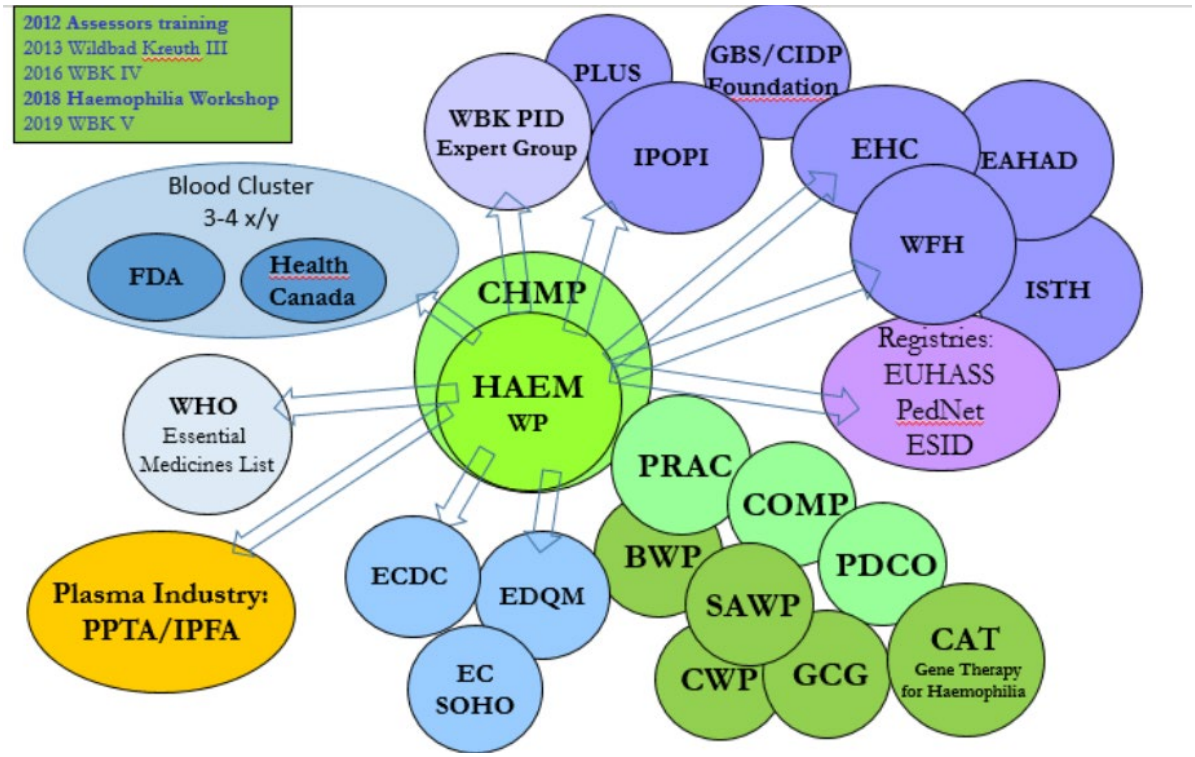
- Guideline and core SmPC on Immunoglobulins (SC/IM) (SCIg/IMIg) (CHMP/BPWP/410415/2011 Rev. 1)
- Guideline and core SmPC on fibrin sealant (EMA/CHMP/BPWP/741603/2015, replacing CPMP/BPWP/1089/00), EMA/CHMP/BPWP/598816/2010 rev. 1)
- Guideline on FIX and core SmPC (EMA/CHMP/BPWP/144552/2009 rev. 2 Corr. 1) and (EMA/CHMP/BPWP/1625/1999 rev. 3)
- Reflection Paper on the Clinical Investigation of Activated Recombinant Human Coagulation Factor VII (rFVIIa) products (EMA/CHMP/BPWP/99228/2014)

New EU Guidelines:

- Reflection paper on non-replacement therapies for haemophilia
- Guideline or RP on sickle cell disease
- Guideline on beta-thalassemia

2.2. Communication and Stakeholder activities

General Overview of HAEMWP's Working Relationships:



- Cooperation with Registry Holders to coordinate data collection and evaluation (this is part of the RSS 2025).
    - Organise workshops (e.g., Haemophilia Registry Workshop in 2018) to support guidelines development. In this regard, a dedicated follow-up meeting could be organised jointly with CAT and PRAC as a follow-up of the haemophilia registry workshop in 2018. This could facilitate the implementation of an international data collection system, which is expected to deliver post-authorisation information in support of regulatory decision making.
- Work on regulatory research projects: the uniqueness of the HAEMWP is that it brings people and knowledge together from the EU MS that otherwise is difficult to achieve in particular in this field where substantial national diversity exists.
    - Support patients' data evaluation using data from registries
- Participate in the Joint EMA/Industry Task Force (JEIF) meeting (in conjunction with BWP if relevant) on pandemic preparedness.
- Provide support (as relevant) on the increase of plasma donation and supply and liaise accordingly with SPOC working Party, the EC SOHO team and relevant stakeholders (PPTA/IPFA), BWP (e.g. updating the eligibility donor criteria; collaboration concerning PMFs).
- Organise annual meeting with PPTA and IPFA to further continue discussing regulatory and scientific matters relating to plasma collection, inspections of blood establishments and guidelines. Liaise with industry on recombinant/biotechnological products.
- EMA to organise and chair on a rota basis the Blood cluster TCs with FDA (CBER) and Health Canada to discuss specific and identified issues from pre and evaluation products, global plasma issues as well as guidelines with the aim of achieving regulatory convergence in the clinical

development of medicines under development, supervision and regulatory actions (safety issues).

- Cooperation with learned societies (ISTH SSC FVIII/FIX working groups, EAHAD), Wildbad Kreuth (WBK) immunologists group, in future it is proposed to expand the interactions with EHA (European Haematology Association).
- Cooperation with the EC SOHO team, EDQM and ECDC.
- Cooperation with relevant patients' organisations (EHC, WFH, IPOPI, PLUS, GBS/CIDP Foundation International, TIF).
- Participate in conferences as speakers/chair persons to promote guidelines and share regulators' positions.
- Publish articles on product evaluation as well as in areas of interest, set up a publication plan agreed by HAEMWP.

2.3. Multidisciplinary collaboration

(See also section above 2.2)

Given the broad spectrum of indications for immunoglobulins and their possible further expansion into other medical areas, interaction with other WPs (e.g. respiratory drafting group, oncology WP and infectious diseases WP) and clinical experts may arise. For the novel products and gene therapy in haemophilia we are already engaging in "cross-domain" activities with CAT, patient organisations and leading experts – this work will continue.

3. Operational goals: medicinal product-specific activities

3.1. Pre-Authorisation activities

- Contribute to reviewing SA and PA when requested by SAWP/CHMP;
- Contribution to paediatric investigation plans (PIP) upon request of PDCO. Of note, this area could be further strengthened;
- Respond to consultations arising from the CHMP/PDCO/PRAC/CAT.

3.2. Evaluation and supervision activities

- Discuss and review marketing authorisation applications and post-authorisation evaluation procedures to understand issues which should be addressed in new or revised guidelines;
- Address issues related to the evaluation of the safety and benefit/risk of plasma derivatives used as ancillary substances in medical devices;
- Work with BWP and the EDQM on efficacy and safety issues linked to quality;
- Support, as requested, to inspections activities, quality defects, sampling and testing and address issues of supply (i.e. plasma and blood donations);
- Contribute to risk management plans for products in non-malignant haematological indications, input into discussion of pharmacovigilance issues and contribute to referral discussions upon request from CHMP/PRAC;
- Respond to consultations arising from the CHMP/PDCO/COMP/PRAC/CAT as requested.

Priorities for 2023

4. Guidelines

4.1. EU Guidelines

Action: Lead

Reflection paper on non-replacement therapies for haemophilia

Target date Draft guideline to be released for public consultation Q2 2023
Consultation with PDCO and COMP

Action: Lead

Clinical investigation of human normal immunoglobulin for subcutaneous and/or intramuscular administration (SCIg/IMIg) (CHMP/BPWP/410415/2011 Rev. 1) and core summary of product characteristics for human normal immunoglobulin for subcutaneous and/or intramuscular administration (EMA/CHMP/BPWP/143744/2011 rev. 1)

Target date Draft guideline to be released for public consultation Q4 2023

Action: Lead

Guideline on the Clinical Investigation of Human Recombinant Factor IX Products (EMA/CHMP/BPWP/144552/2009 rev. 2 Corr. 1) and Guideline on the Core SmPCs for Human plasma-derived and recombinant coagulation Factor IX products and (EMA/CHMP/BPWP/1625/1999 rev. 3)

Target date Final guideline to be released for public consultation Q1 2023

Action: Lead

Fibrin sealant core SmPC and clinical investigation guideline (EMA/CHMP/BPWP/741603/2015, replacing CPMP/BPWP/1089/00), EMA/CHMP/BPWP/598816/2010 rev. 1

Target date Draft guideline to be released for public consultation Q4 2023

Action: Lead

Reflection paper on Factor VIIa products (EMA/CHMP/BPWP/99228/2014)

Target date Draft guideline to be released for public consultation Q4 2023

Action: Lead

Reflection paper on sickle cell disease

Target date Draft guideline to be released for public consultation Q1 2024

Action: Lead

Reflection paper on beta thalassemia

Target date Draft guideline to be released for public consultation Q1 2024

5. Training for the network and knowledge building

- Organise online internal training via the EUNTC platform
- Organise one virtual training session per year (within a HAEMWP meeting) on a regulatory topic concerned with plasma or other relevant products in the field of non-malignant haematology. Organise online internal training via the EU NTC platform.

6. Contribution to dialogue and engagement with stakeholders and external parties

6.1. Workshops

- The Haemophilia Registry Workshop was organised in 2018 to support guidelines development. In this regard, a dedicated follow-up meeting could be organised jointly with CAT and PRAC as a follow-up of the haemophilia registry workshop in 2018. This could facilitate the implementation of an international data collection system, which is expected to deliver post-authorisation information in support of regulatory decision making. Cooperation with Registry Holders to coordinate data collection and evaluation (this is part of the RSS 2025).

6.2. Collaboration with Interested parties and other stakeholders

- Organise annual meeting with PPTA and IPFA to further continue discussing regulatory and scientific matters relating to plasma collection, inspections of blood establishments and guidelines. Liaise with industry on recombinant/biotechnological products.

7. European collaborations

- Provide support (as relevant) on the increase of plasma donation and supply and liaise accordingly with the SPOC working Party, the EC SOHO team, EDQM and relevant stakeholders (PPTA/IPFA), BWP (e.g. updating the eligibility donor criteria; collaboration concerning PMFs).
- Cooperation with learned societies (ISTH SSC FVIII/FIX working groups, EAHAD), Wildbad Kreuth (WBK) immunologists group. Expoan collaboration with EHA (European Haematology Association).
- Cooperation with the EC SOHO team, EDQM and ECDC on any plasma related matters.
- Participation of EMA to the joint meetings of the Competent Authorities on Blood and Blood Components, Tissues and Cells and Organs as needed.
- Participation of EMA to ECDC SoHONet meetings as observer.
- Cooperation with relevant patients' organisations (EHC, WFH, IPOPI, PLUS, GBS/CIDP Foundation International, TIF).

8. International activities

- EMA to organise and chair on a rota basis the Blood cluster TCs with FDA (CBER) and Health Canada to discuss specific and identified issues from pre and evaluation products, global plasma issues as well as guidelines with the aim of achieving regulatory convergence in the clinical development of medicines under development, supervision and regulatory actions (safety issues).

Abbreviations

BCP	Business Continuity Plan
DOAC	Direct-acting oral anticoagulants
EAHAD	European Association for Haemophilia and Allied Disorders
ECDC	European Centre for Disease Prevention and Control
EDQM	European Directorate for the Quality of Medicines
EHA	European Haematology Association
EHC	European Haemophilia Consortium (46 national patients' organisations of people with rare bleeding disorders from 27 Member States)
EMRN	European Medicines Regulatory Network
EUHASS	European Haemophilia Safety Surveillance
FDA	Food and Drug Administration
IPFA	International Plasma and Fractionation Association
IPOPI	International Patient Organisation Primary Immunodeficiencies
ISTH	International Society on Thrombosis and Haemostasis
JEIF	Joint EMA/Industry Task Force
Kreuth group	A voluntary group of European Immunologists who originally convened at Wildbad Kreuth in 2013 and have since provided expert support on GL/core SPCs for immunoglobulins
PLUS	Plasma Users Coalition
PMF	Plasma Master File
PPTA	Plasma Protein Therapeutics Association
RSS	Regulatory Science Strategy
SOHO	substances of human origin
SSC	Scientific and Standardization Committee
WFH	World Federation of Hemophilia