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Regulatory Considerations for Plasma for Fractionation

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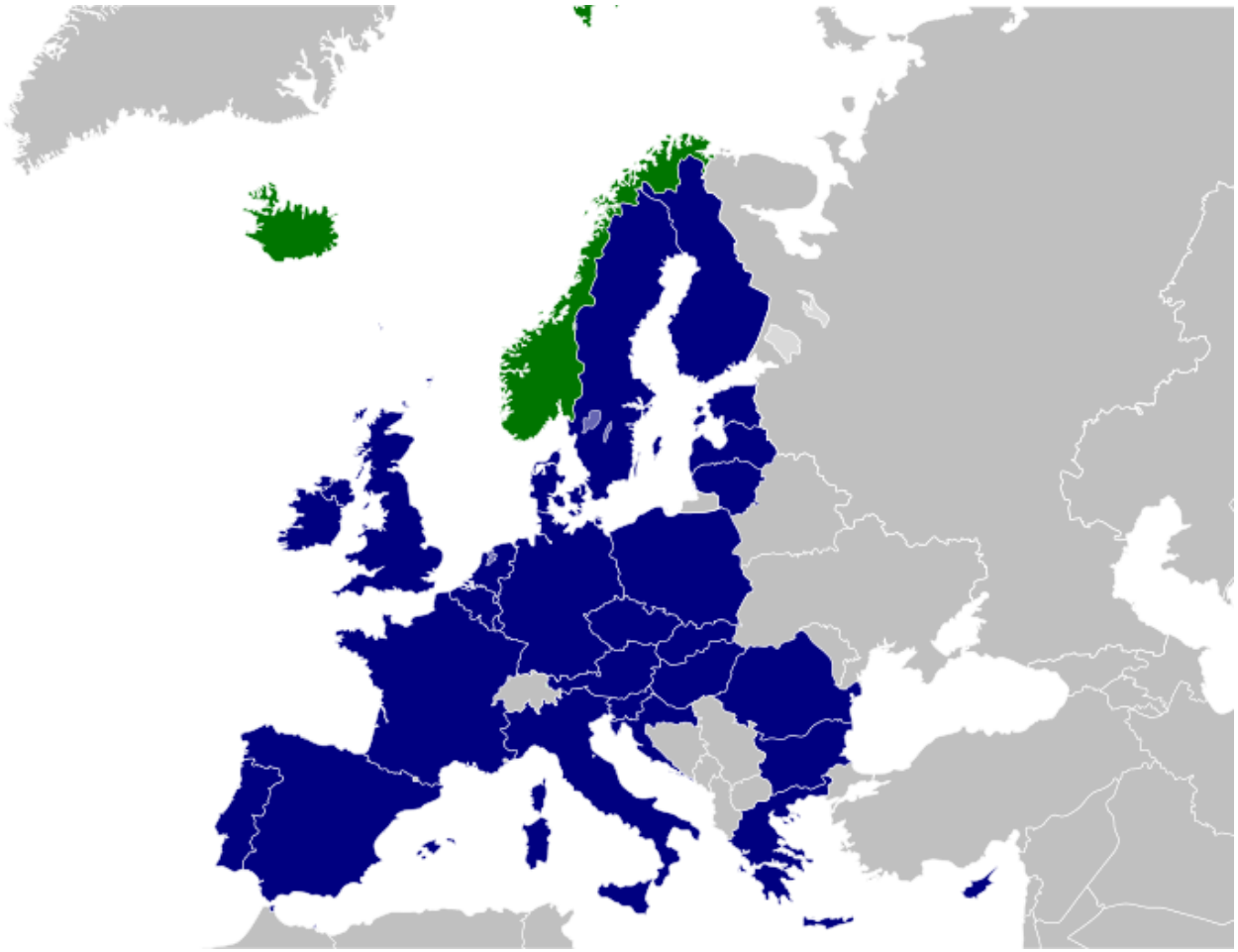
Plasma Master File

- **The EEA and the European Medicines Agency**
- **Reason for the PMF**
- **Benefits of the PMF**
- **Key Points of PMF**
- **Procedure of the PMF**
- **Information provided in the PMF**
- **EU Experience with the PMF**
- **Conclusions**

PMF in the EEA: European Economic Area



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Consists of

- **the EU**
- **Norway**
- **Iceland**
- **Liechtenstein**

The European Medicines Agency (EMA)

Centralised MAA Procedure – EMA Scientific Committees

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Amsterdam
~800 staff
coordinate:
- **formal procedure**
- **evaluation**
- **supervision**
- **pharmacovigilance**

Scientific Working parties e.g. BWP

CVMP
Committees for ...
PRAC
Pharmacovigilance Risk Assessment Committee
PDCO
Paediatric Committee
COMP
Committee of Orphan Medicinal Products
CAT
Committee for Advanced Therapies

CHMP
Committee for Medicinal Products for Human use

National CA
- **4000 experts from**
- **27 member states + 2**

as scientific resource

Experts from each Member State
Scientific evaluation (Q, S, E)
Supported by standing and ad hoc Working parties
CHMP issues Recommendation for Marketing Authorisation to European Commission

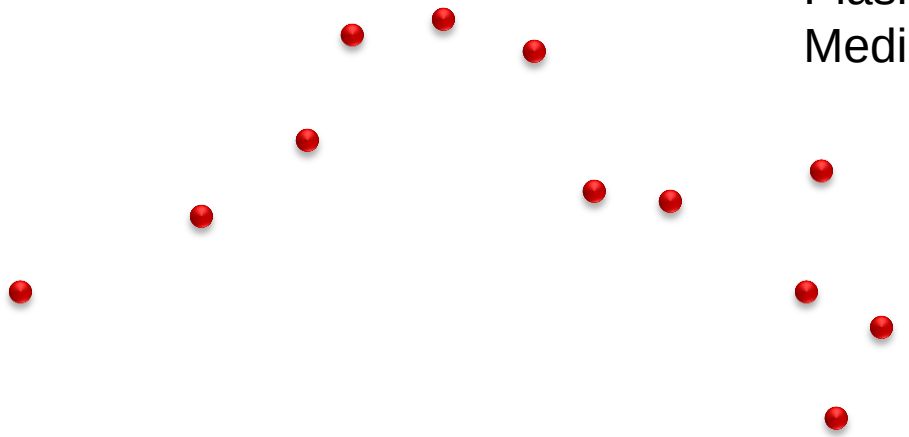
BWP – Biologics **W**orking Party, concerned with Quality Aspects of Biological Medicinal Products

Photo: Rob Acket

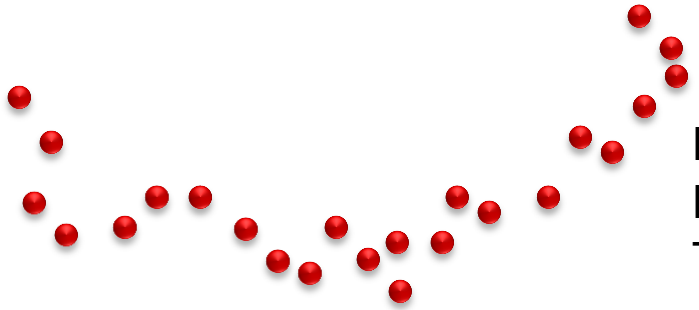
Reason for PMF

- **Plasma is variable Starting Material, the following Changes may apply:**
  - **Change of Blood Establishments (BE)**
  - **Change of Countries of Origin**
  - **Changes of the Epidemiological Situation of the BEs**
  - **Inspection Status of BEs**
  - **Changes of the Testing Laboratories / IVD Kits**
  - **Changes of Regulatory Requirements**
  - **Changes of Address, Blood Bags used, Transport and Storage facilities, …**
- **Plasma is also starting material for a large amount of Medicinal Products**
- **Usually, each change, requires a variation application for each Medicinal Product**

Reason for PMF



Plasma-derived
Medicinal Products



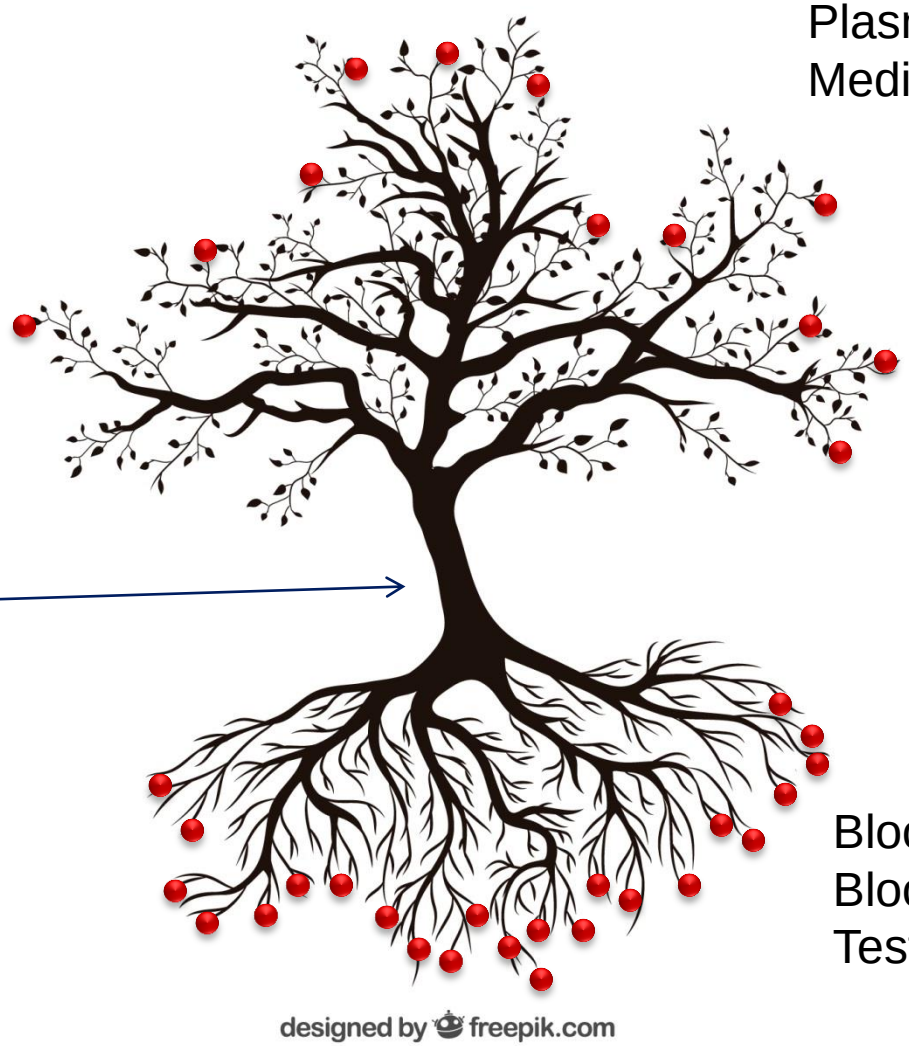
Blood Donation Sites /
Blood Establishments /
Testing Laboratories

Designed by Freepik

Idea from Eva Lindberg

Reason for PMF

Plasma-derived
Medicinal Products



Plasma
Master
File

Blood Donation Sites /
Blood Establishments /
Testing Laboratories

Designed by Freepik

Idea from Eva Lindberg

Benefits of PMF

- **Reduction of Work load for both Pharmaceutical Companies and Regulatory Authorities**
- **Certificate is valid throughout EU – easier access to starting material**
- **Improvement of the Regulatory Consistency in the EU – unified Requirements for PMF Holder**
- **Information on Epidemiology, Inspections, etc annually updated – Ability to increase Patient Safety**

(Within EEA, Inspection Results are mutually agreed between Member States)

Regulatory Basis of the PMF:

- **Legal Basis established in 2003 (Commission Directive 2003/63/EC, Part III)**
- **Use of PMF Certification is optional**
- **PMF Certificate valid in all EU member states**
- **Stand-alone document, independent from MA documentations**
- **A PMF can be linked to several medicinal products and medical devices**
- **One medicinal product dossier can reference to several PMFs**
- **Detailled information on human plasma used as starting material of active substances or excipients from collection to plasma pool**
- **Initial Licensure of PMF Certificate by EMA**
- **Followed by mandatory Annual Updates for re-certification**

Procedure of the PMF (Re-) Certification

- Centralised Procedure organised by EMA
- Evaluation by coordinator 1 and coordinator 2
- Certificate of Compliance with EU legislation issued by EMA
- Evaluation Report is provided
- Annual Update (AU) to be applied for on fixed date
- Evaluation of AU by coordinator 1 and 2
- Discussed in the PMF group of BWP to ensure consistency
- Variation Application are possible outside of AU evaluation

Informations provided in PMF

General Information

- **Plasma-derived Products list**
- **Overall Safety Strategy**
- **General Logistics**

Technical Information

- **Plasma Origin**
- **Plasma Quality and Safety**
- **Interaction Between Manufacturer and BE**

Informations provided in PMF

General Information

- **Plasma-derived Products list**
- **Overall Safety Strategy**
- **General Logistics**

Technical Information

- **Plasma Origin**
  - BEs, Inspections, Epidemiology, Residual Risk Assessment, Characteristics of Donation
  - Test Labs, Inspection Status
  - Donor Selection/Exclusion criteria
  - Traceability, Look-Back Procedure
- **Plasma Quality and Safety**
- **Interaction Between Manufacturer and BE**

Informations provided in PMF

General Information

Plasma-derived Products list

Overall Safety Strategy

General Logistics

Technical Information

Plasma Origin

Plasma Quality and Safety

- Compliance with Ph. Eur.
- Testing single Donations, mini-pools and plasma pools (Serology + NAT)
- Technical Characteristics of blood bags
- Conditions of Storage and Transport
- Inventory Hold
- Characterisation of plasma pool

Interaction Between Manufacturer and BE

Informations provided in PMF

General Information

- **Plasma-derived Products list**
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Technical Information

- **Plasma Origin**
- **Plasma Quality and Safety**
- **Interaction Between Manufacturer and BE**
  - Contracts
  - Notification System

EU Experience with PMF Certification

- **Well-Established Clear Procedure, well accepted by Applicants**
- **Majority of Companies uses PMF System – currently 10 PMF holders according to EMA homepage***
- **Data provided in a harmonised way, simplifying Assessment**
- **PMF System provides detailed information and good overview on Plasma used for manufacture in EU**
- **Application and related issues discussed by a BWP sub group on monthly basis**
- **A lot of Inspection-related issues, necessitate close communication with inspectorates**

***) https://www.ema.europa.eu/en/human-regulatory/overview/plasma-master-file-pmf-certification/plasma-master-file-certificates**

Conclusions

- **In EU Centralised PMF Procedure provided mutliple Benefits for Regulatory Authorities, Manufacturers and Patients**
- **Process implemented in 2003 as optional Procedure**
- **Centralised Procedure orchestrated by EMA,**
- **Leading to a stand-alone Document accepted in the EEA Region**
- **Concept may also be beneficial for other Regions**

Thank You !!

Our Focus is on Health