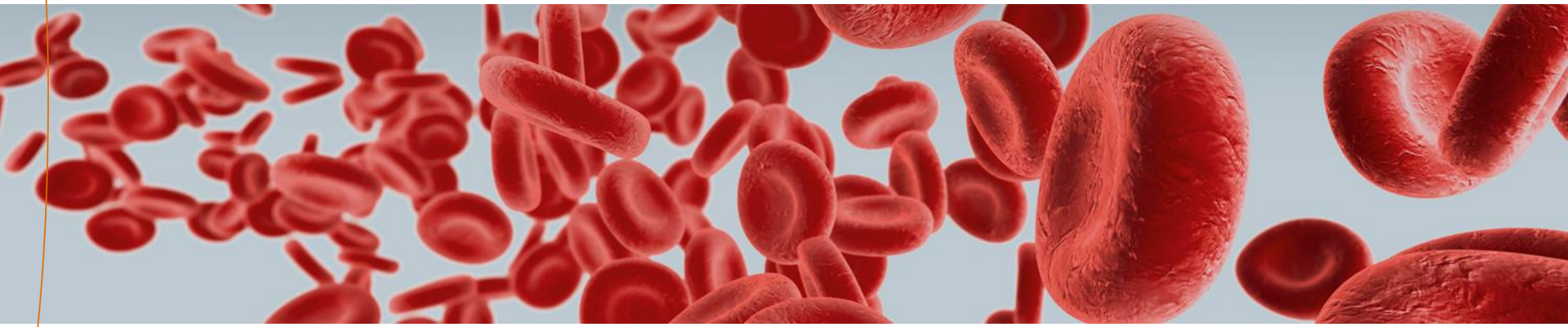
GMP and quality requirements of plasma for fractionation



Dinie Hoentjen

Compliance Officer – QA Department Blood Bank Sanquin - Netherlands

Sanquin Blood Bank

- 1 National organisation for blood collection: Sanquin

- Organisation:
  - 136 collection sites
  - 2 processing locations
  - 1 screenings laboratory (back-up in Belgium)
  - 7 distribution locations

Sanquin Blood Bank - 2019

- Number of donors: 366.000
- Number of donations: 727.4641
  - Whole blood donations: 413.653
  - Plasma Apheresis: 313.811
- Total of 351.913 kg plasma delivered to fractionator

(European) Regulations - Blood collection

(European) Regulations: blood collection

- **Directive 2002/98/EC** of the European Parliament and of the Council of 27 January 2003 setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and amending Directive 2001/83/EC

- **Commission Directive 2004/33/EC** - certain technical requirements for blood and blood components
- **Commission Directive 2005/61/EC** - traceability requirements and notification of serious adverse reactions and events
- **Commission Directive 2005/62/EC** - quality system for blood establishments

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(European) Regulations: blood collection

- **Directive 2002/98/EC** – standards of quality and safety
- **Commission Directive 2004/33/EC** of 22 March 2004 implementing Directive 2002/98/EC of the European Parliament and of the Council as regards certain technical requirements for blood and blood components
- **Commission Directive 2005/61/EC** - traceability requirements and notification of serious adverse reactions and events
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(European) Regulations: blood collection

- **Directive 2002/98/EC** - standards of quality and safety
- **Commission Directive 2004/33/EC** - technical requirements for blood and blood components

- **Commission Directive 2005/61/EC** of 30 September 2005 implementing Directive 2002/98/EC of the European Parliament and of the Council as regards traceability requirements and notification of serious adverse reactions and events

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(European) Regulations: blood collection

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(European) Regulations: blood collection

- **Directive 2002/98/EC** - standards of quality and safety
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- **Commission Directive 2005/61/EC** - traceability requirements and notification of serious adverse reactions and events
- **Commission Directive 2005/62/EC** - quality system for blood establishments

(European) Regulations: blood collection

- **Good Practice Guidelines for Blood Establishment Required to Comply with Directive 2005/62/EC** per Commission Directive (EU) 2016/1214.

  Part of *Guide to the preparation, use and quality assurance of blood components*, containing “best practices”

Recommended document outside Europe:

- WHO Guidance on centralization of Blood donation testing and processing

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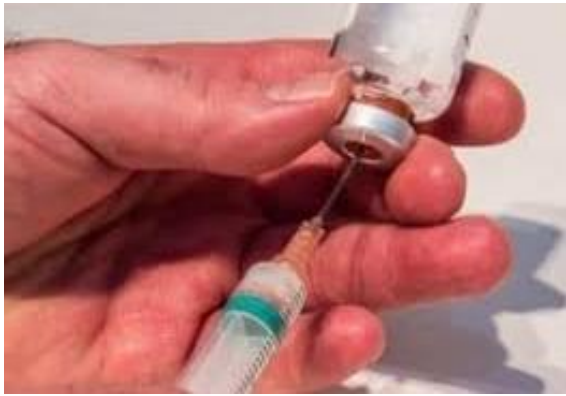
(European) Regulations – Medicine Production



(European) Regulations: Medicine production

- The Rules Governing Medicinal Products in the European Union Volume 4 EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use
  - **Annex 14 Manufacture of Medicinal Products Derived from Human Blood or Plasma**

- Human Plasma for Fractionation Plasma Humanum Ad Separationem **Eur. Pharmacopeia** Monograph **0853**
  - Additional paragraphs mentioned in this monograph on e.g. material for blood bags.

Recommended document outside Europe:

- WHO Guidance on increasing supplies of plasma-derived medicinal products in low- and middle-income countries

Requirements set by Fractionator

Plasma Requirements and Quality Agreement

Plasma requirements:

- existing regulatory framework in the country
- practical requirements on e.g.:
  - Donor acceptance and deferral criteria
  - Testing
  - Storage and transport conditions
  - Labelling
  - Lookbacks
  - Additional information required for yearly update Plasma Master File

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Plasma Requirements and Quality Agreement

Plasma requirements:

- existing regulatory framework in the country
- practical requirements

Quality Agreement

- how to handle in case of deviations, complaints, intended changes etc.

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Quality of plasma: why and how

Why is the quality of the plasma so important

- It should have the correct composition
  - For a product of Human Origin always some variance
  - Optimal, so minimal loss of labile proteins.
- It should be safe
  - Donor health & testing
  - No contamination from other source
- Traceability
  - In case of e.g.: donor health information received after donation, or recall by supplier on consumables
  - Haemovigilance / Pharmacovigilance

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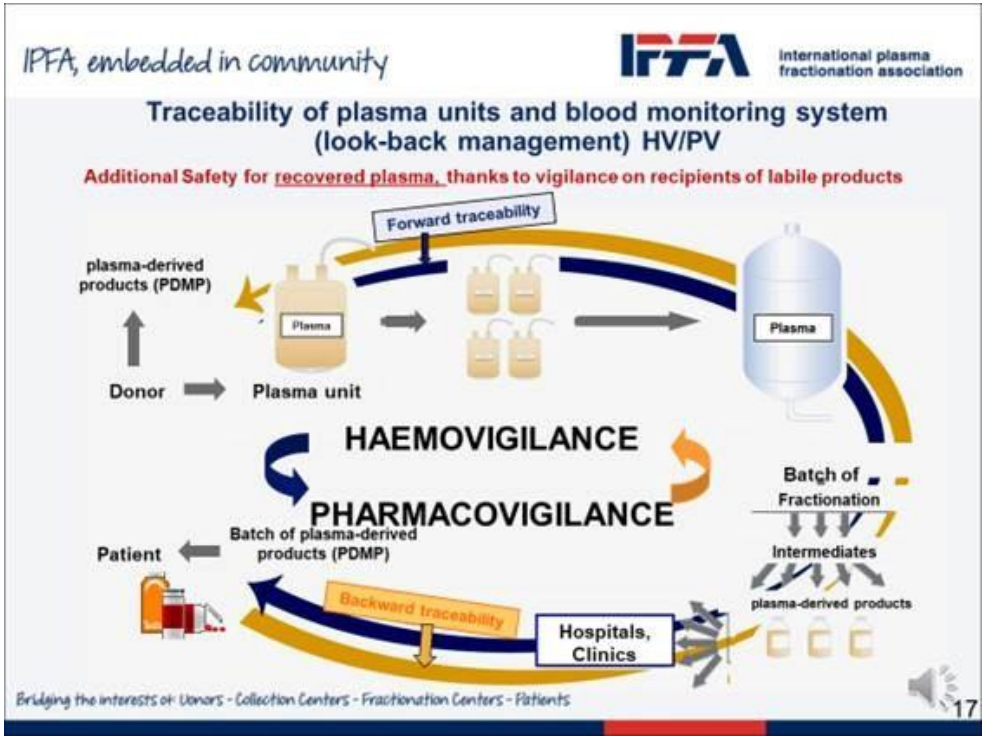

How to assure quality of plasma

- Validated, stable process
- Establish operational process
  - Trained personnel
  - Documentation and registration
  - Premises, equipment and materials
  - Blood collection, testing and processing
  - Storage and distribution

How to assure quality of plasma (2)

Key points for plasma:

- Donor eligibility including testing
- Processing:
  - Time between collection and freezing
  - Speed of freezing process and required end temperature
  - Storage temperature (incl during transportation)
- Traceability / labelling:
  - Unique DIN – product code combination
- Shipment documentation:
  - Electronic file with required information on each plasma, in agreed format

How to assure quality of plasma (3)

- QC tests
  - Process in control, product within specification
- Supplier management
- Lookback system in place

How to assure quality of plasma (4)

- Audits
  - Internal audits, supplier audits, audits by our NCA, audits by fractionator
- Change control procedure
  - As layed down in Quality Agreement => notification prior to implementation
- Annual information
  - Epidemiological data, as required by EMA
  - Inspection / audit status of involved centers

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Summary

- Fractionators need products:
  - that meet agreed criteria (of directives, their PMF etc.)
  - of high quality and constant quality
- Proof must be available
  - Validated process
  - Temperature logging / registration
- Notification in case of
  - deviation
  - change

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Thank you for your attention

d.hoentjen@sanquin.nl

www.sanquin.nl