Federal Institute for Vaccines and Biomedicines

Paul-Ehrlich-Institut

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Transitioning from Accreditation to Good Manufacturing Practice

European Oversight & Regulatory Framework for Blood Establishments

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Inspection Services for Biological Medicinal Products

IPFA Workshop Stellenbosch - Educational Day

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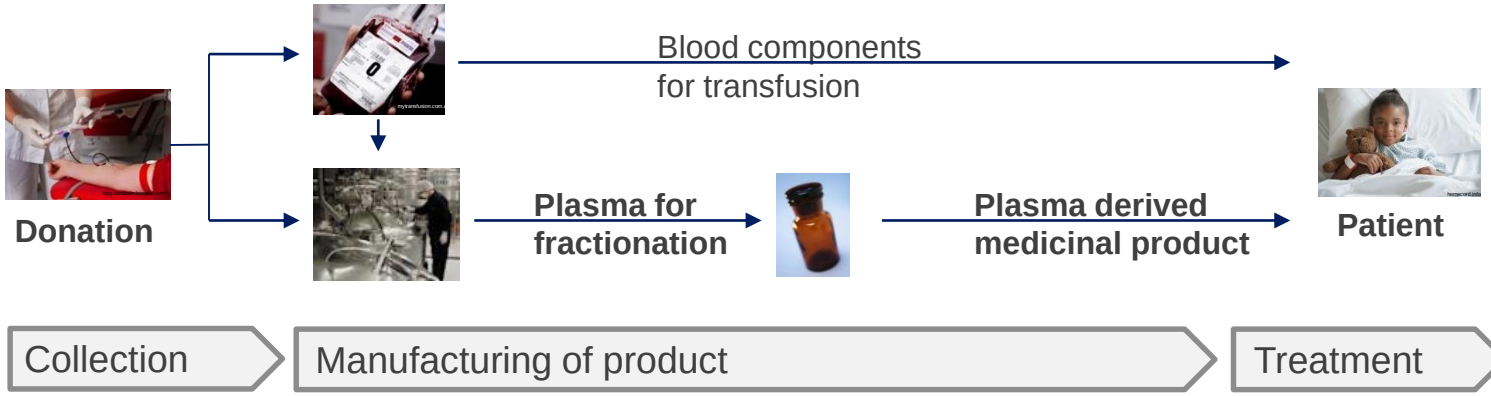
Blood & Blood Products – Challenges

- Biological products of human origin → High variability
- Linked with ethical aspects → Paid vs unpaid donations
- Risk of transmission of communicable diseases
- Life saving → No alternative treatments
- High quality and safety expectations → Influence on further processing

Blood & Blood Products – Goals

- Improving the quality and safety of
  - Plasma for fractionation as starting material
  - Blood components for transfusion
- Optimizing the use of blood donations
  - Less discarded units
  - Increased availability of plasma
  - (Contract) fractionation programs
- Harmonization in the regulation of blood/blood products
- Facilitate international cooperation between National Regulatory Authorities (NRAs)

Blood & Blood Products – How can we get there?



- Robust collection and preparation processes → Smoothens out the high variability
- Quality and process monitoring → Controls the processes
- Defined quality requirements/product specifications → For each intermediate and final product
- Clear identification and complete documentation → To ensure full traceability

Blood & Blood Products – Why GMP?

- Voluntary
- Not harmonized
- Self-regulated system
- Issued by various accreditation bodies

→ Basis & tool for moving towards GMP

- Integral part of quality assurance
- Long established standard for controlling medicines manufacture
- Proactive and reactive manufacturing tool
- Risk-based approach
- Globally accepted regulatory standard
- Common language between blood establishments and fractionator

→ Consistent quality across borders

GMP – What are the main principles?

- Quality Management 

- Personnel 
- Premises 
- Equipment & Materials 
- Calibration 
- Qualification & Validation 

- Change Control 

- Documentation 
- Manufacturing   
- Storage 
- Transport 
- Contract Management 
- Non-conformance 
- Self Inspection/Audits 

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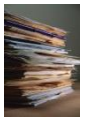
- Documentation 
- Manufacturing   
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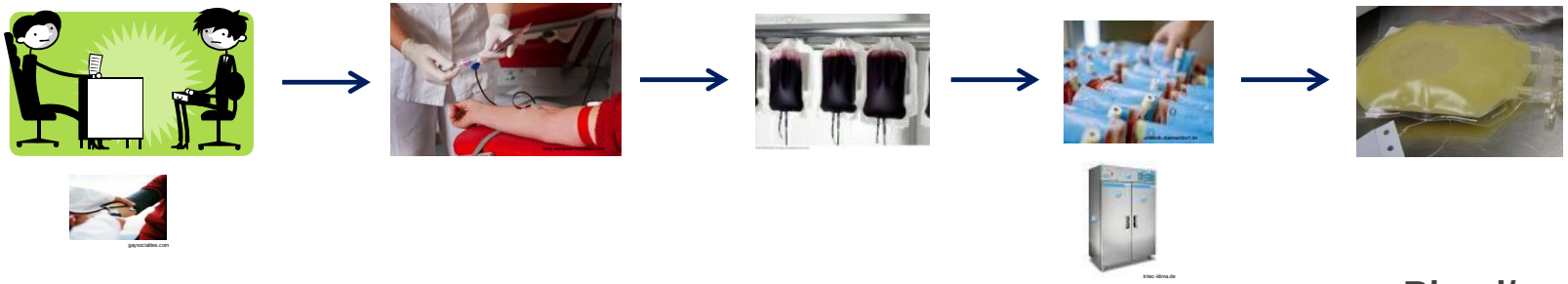
GMP – Main Principles (1)

- Quality Management
  - Coordinated activities to direct and control an organization
    ⇒ quality at all levels
  - Comprises Quality System (QS)
    Quality Assurance (QA)
    Quality Control (QC)
    Quality Risk Management (QRM)
  - Responsibility of all personnel



Donor selection | **Donation** | **Processing** | **Storage** | **Blood/ blood product**

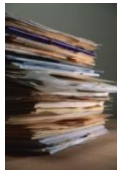
GMP – Main Principles (2)

- Personnel
  - Sufficient numbers
  - Training program & records (initial & continuous training)
  - Organizational chart → Responsibilities: no gaps/unexplained overlaps

- Premises (incl. mobile sites)
  - Must suit the activities to be carried out (e.g. temperature monitored)
  - Easy to maintain and clean
  - Sufficient space to prevent mix-ups & microbial contamination
  - Controlled access
  - Dedicated/separate areas, e.g. donor interviews, laboratory, equipment repairs, waste disposal/biohazard waste, staff rest/changing areas

GMP – Main Principles (3)

- Equipment
  - Qualified → Written protocol
  - Calibrated → Recognized international standard & monitoring plan
  - Maintained to suit intended purpose → Repairs, preventive maintenance
  - Log books → History (e.g. qualifications, repairs, maintenance)



- Documentation
  - Defined documentation system → SOPs, protocols, records, etc.
  - Document control → Drafting, approval, distribution, revision, archiving
  - Should be legible, have unambiguous content & be in orderly fashion
  - Traceability:

    Donor ↔ blood/blood component ↔ sample ↔ recipient/finished product

    Donation ↔ collection (bag/bottle) ↔ processing system

GMP – Main Principles (4)

- Manufacturing
  - Unambiguous donor identification → Donor selection & collection
  - Donor selection → Standardized process, confidential interview, defined donor eligibility & deferral criteria
  - Collection → Donor & product safety (e.g. single-use material, disinfection before venipuncture)
  - Preparation → Validated processes, aseptic conditions, closed systems recommended)
  - Testing → Validated processes, defined algorithms, suitable reagents
  - Labelling → Unique donor & donation identification (numeric, barcode, etc.), clear release status (donations/blood products & materials)
  - Release of products, reagents & critical materials → Defined responsibilities & acceptance criteria

→ Avoid: risk of mix-ups, contamination & microbial growth!






GMP – Main Principles (5)

- Storage
  - Secure, segregated & clearly marked → Quarantine, released, rejected, etc.
  - Defined temperature limits → Controlled and monitored
  - „First-in (or first-expired) first-out“ principle (materials & reagents)

- Transport
  - Validated
  - Packaging → Integrity & storage temperature maintained
  - Defined temperature limits → Controlled and monitored
  - Contracts in case of 3rd party services

Impact of GMP in Blood Establishments

- Supports systematic approach to donor selection → Product safety
- Ensures appropriate testing methods and test kits as well as suitable reagents → Valid test results
- Requires the use of suitable facilities, equipment and materials → Consistent quality
- Reduces errors and technical problems → Consistent quality
- Ensures the existence of validated and robust processes → Consistent quality

Impact of GMP in Blood Establishments

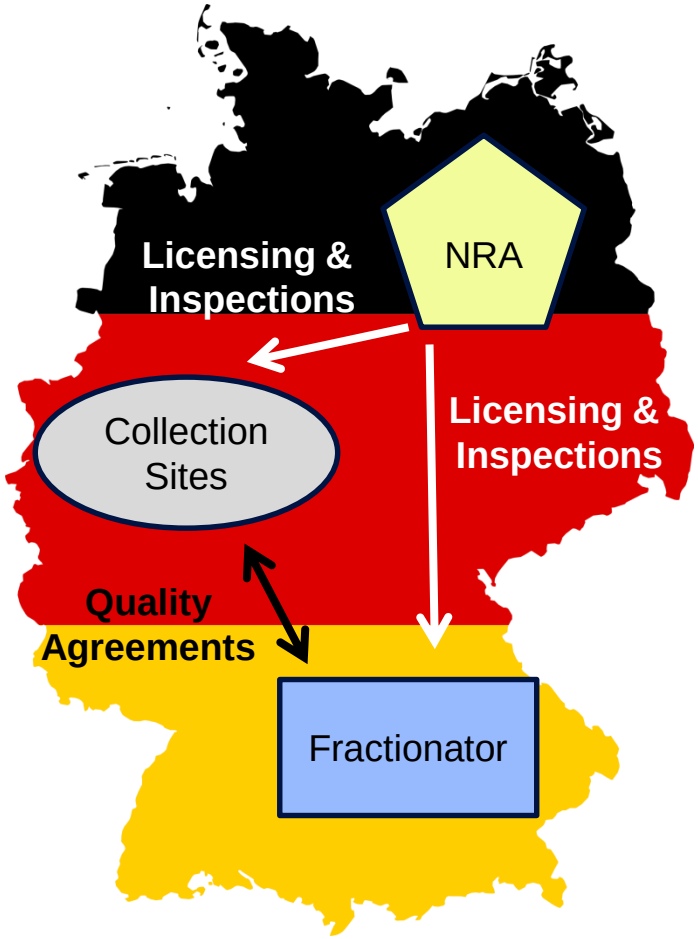
- Guarantees the release of products which comply with safety and quality requirements → Product safety
- Ensures adequate documentation and full traceability for each donation/product (donor ↔ recipient) → Donor & patient safety
- Strengthens the competency of personnel → Product safety
- Promotes continuous improvement → Product safety

GMP in Blood Establishments
- Oversight in the EU (1) -

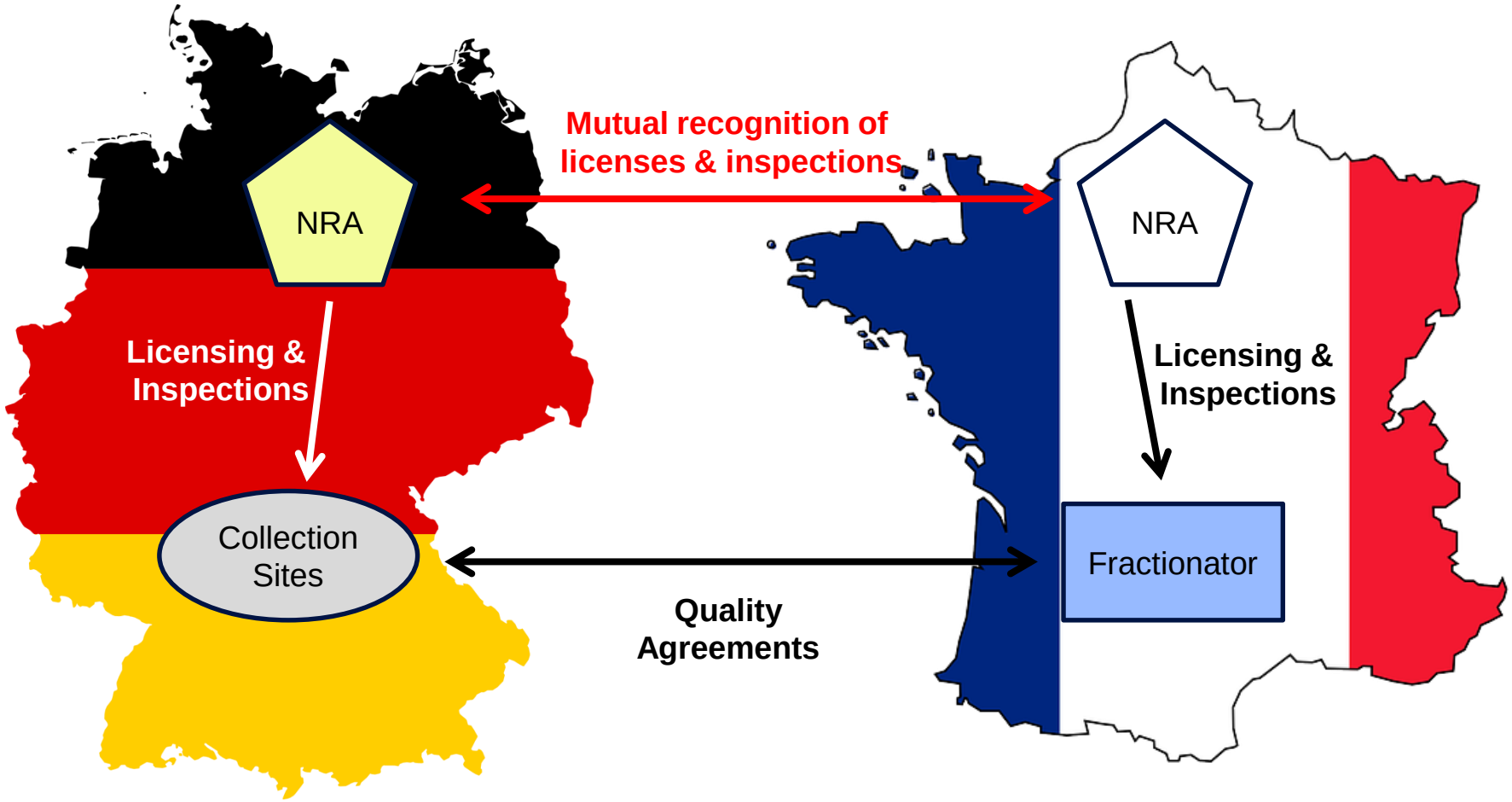
- National Regulatory Authority (NRA):
  - Ensures the implementation of GMP and adherence to it
  - Conducts appropriate control measures, e.g. inspections every 2 years
  - Licenses blood establishments
    testing laboratories
    manufacturers/fractionators
  - Revokes licenses in case of non-compliance with regulatory requirements

- Manufacturer/fractionator
  - May define additional quality requirements with the blood establishment
  - May perform audits at the collection sites

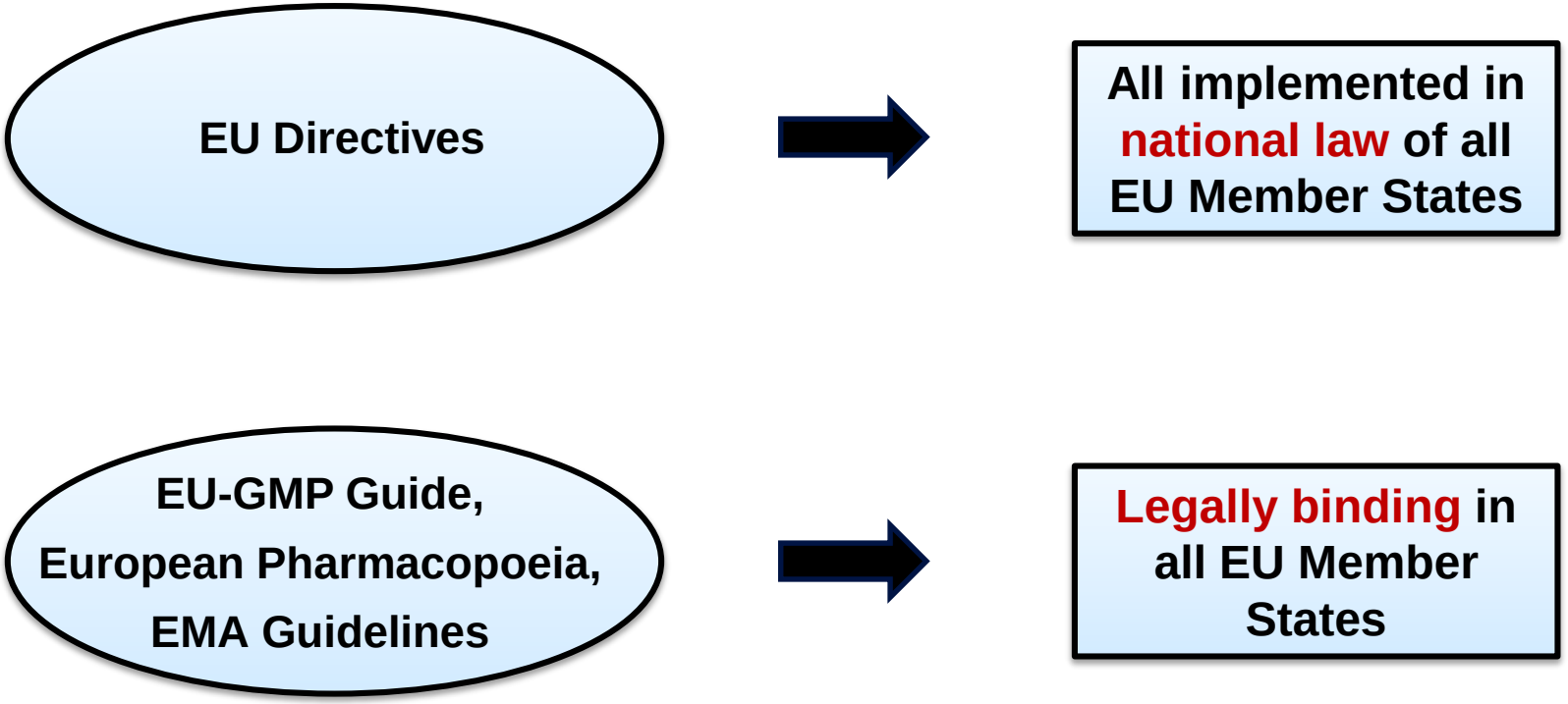
GMP in Blood Establishments
- Oversight in an EU Member State (1) -



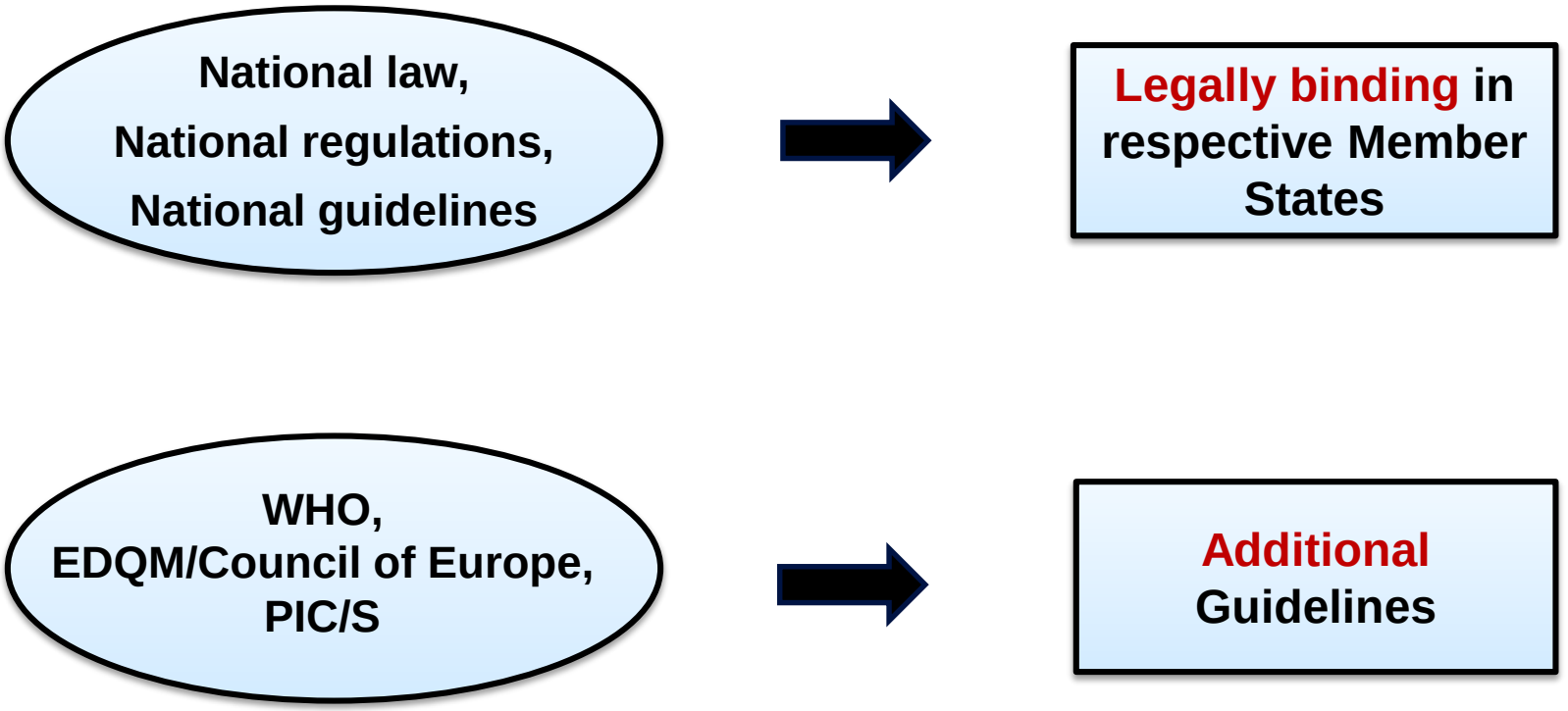
GMP in Blood Establishments
- Oversight between EU Member States (2) -



GMP in Blood Establishments
- EU Regulatory Framework (1) -



GMP in Blood Establishments
- EU Regulatory Framework (2) -



GMP in Blood Establishments – What are the benefits?

- Impact on availability
  - Quality is ensured → plasma, as a precious starting material, could be used for fractionation
  - More plasma would be available and less plasma would be discarded → increase in the availability of blood products

- Impact on cooperation
  - Building up a common language → confidence for regional/ international cooperation between NRAs in the regulation of blood products
  - Enhancing a common understanding → better collaboration between NRAs, blood establishments and fractionators

Conclusion

- GMP is a beneficial tool to improve blood & plasma quality
- Strict adherence to GMP in collection, preparation, manufacturing, testing and distribution is essential
- Enforcement of GMP by the competent NRA allows the NRA to ensure quality and safety of blood products
- Helps to increase the availability of plasma
- Helps to successfully implement plasma fractionation programs across borders

Thank you for your attention!

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Section 1/1 – Inspection Services for Biological Medicinal Products