

# Strategies for management of manufacturing process for Blood Products

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# Agenda

1. Manufacturing Network Overview
2. Blood Products Manufacturing
3. Supply Chain of Blood Products
4. Life Cycle Management Strategy
5. Case Study: Contract Manufacturing
6. Summary and Conclusions



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# Manufacturing Network Overview

**CSL Plasma**  
Good for You. Great for Life.

**CSL Behring**  
Biotherapies for Life™

**Seqirus™**  
A CSL COMPANY

**VIFOR  
PHARMA**

## Manufacturing Sites



**Marburg, (MRB)  
Germany**

**3.000+**  
employees

Core products:

- Coagulation factors
- Critical care



**Bern, (BRN)  
Switzerland**

**1.700+**  
employees

Core products:

- Immunoglobulins
- Albumin



**Kankakee, (KAN)  
USA**

**1.700+**  
employees

Core products:

- Albumin
- Intermediate pastes



**Broadmeadows,  
(BMW) Australia**

**1.200+**  
employees

Core products:

- Coagulation factors
- Critical care
- Immunoglobulins



**Wuhan,  
China**

**210+**  
employees

Core product:

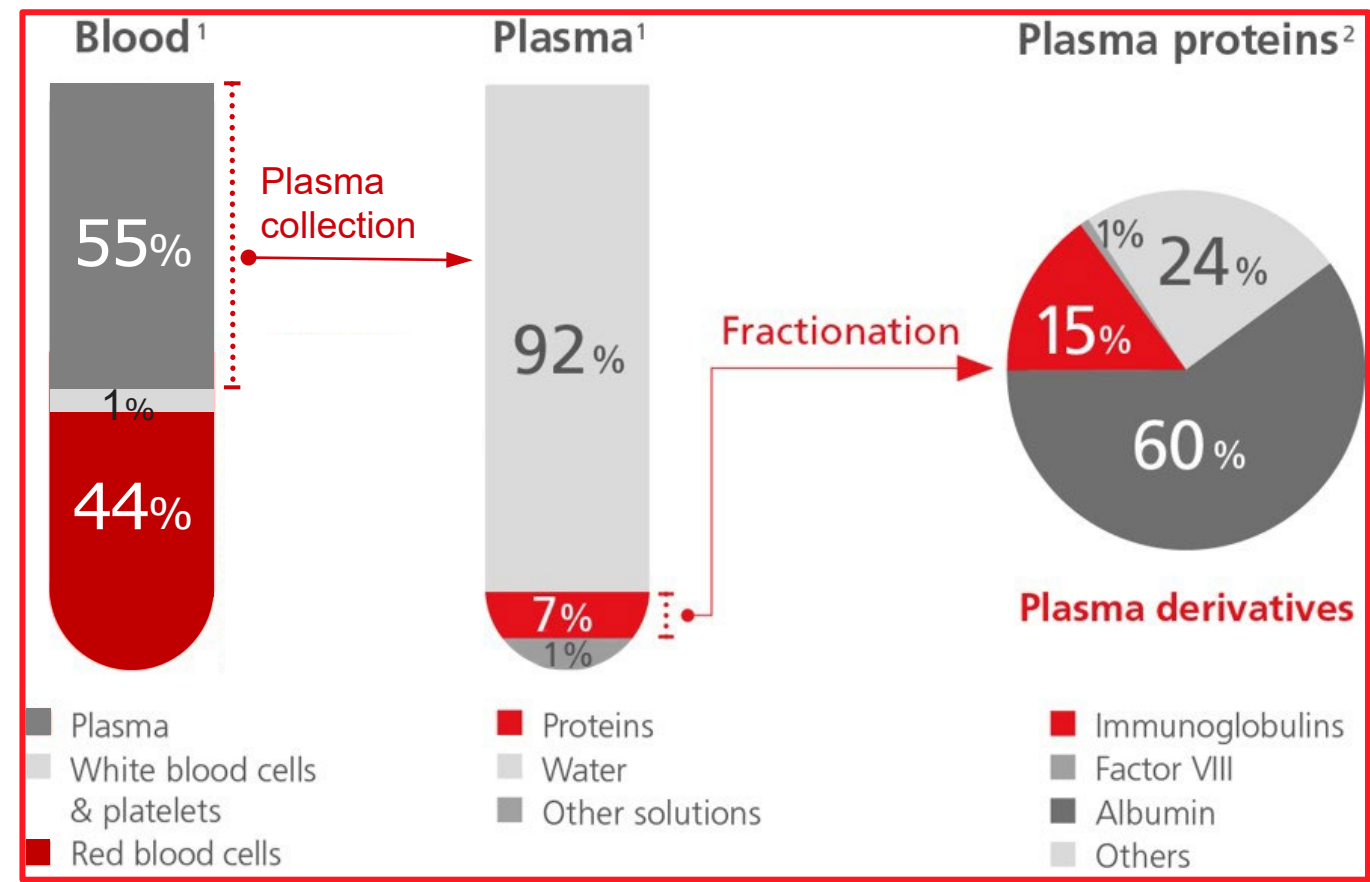
- Albumin
- Immunoglobulins

02

# Blood Products Manufacturing

# From Blood to Plasma Products

Used % of Blood to Products: ~2%



Modified from: PPTA, 2021

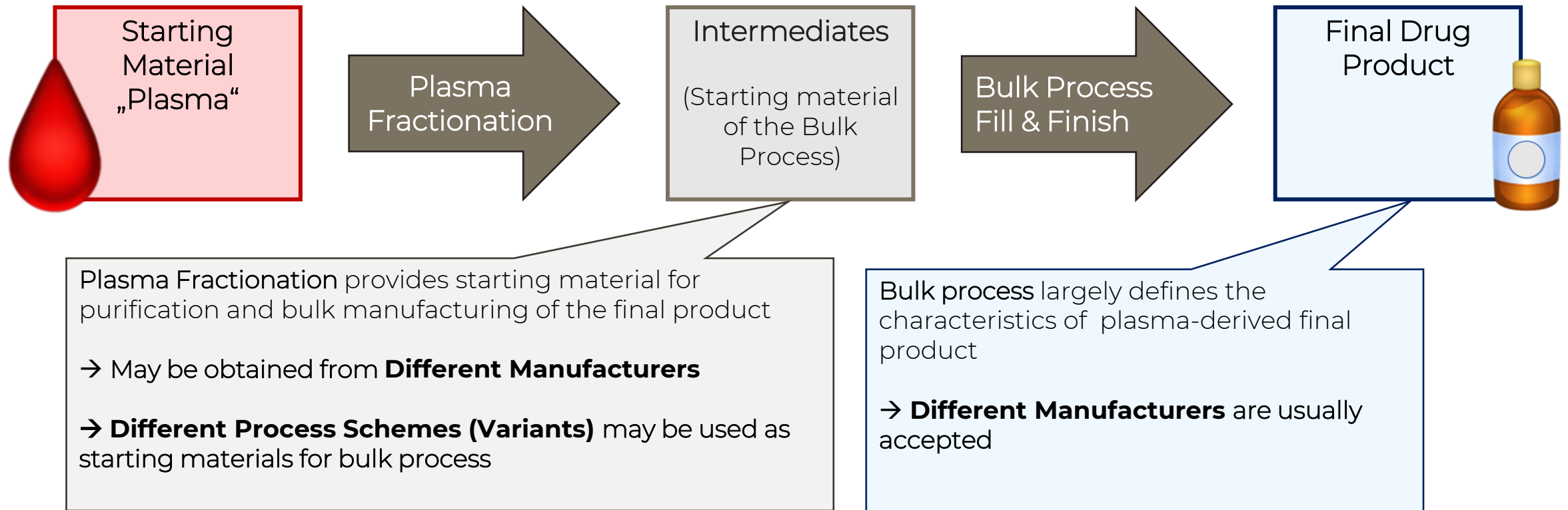
# From Donor to Patient

Total duration: ~9months



# Blood Products Manufacturing

## Principles for one Final Drug Product

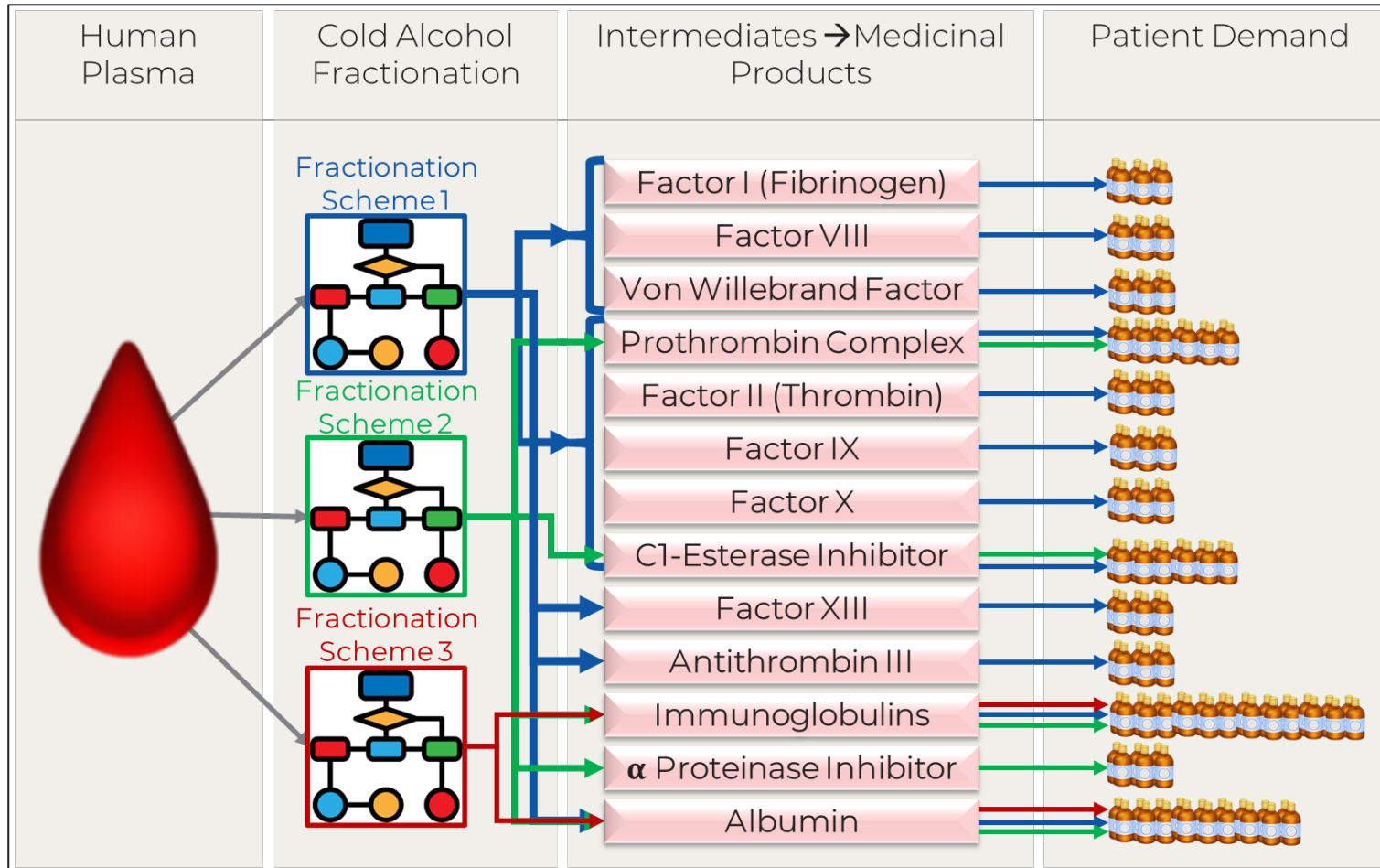


Flexibility is required to best exploit precious plasma to meet patient demands



# Blood Products Manufacturing

## Alternative Fractionation Schemes



(Scheme for illustration of the principles only, not representing actual figures)

**Alternative Fractionation Schemes** are used to obtain Plasma Products:

- Interchange of Intermediates
- Varying cold alcohol fractionation conditions like: pH, temperature, alcohol %
- Combining of fractionation steps
- Various adsorption steps can be used

**Alternative Fractionation Schemes** are needed to address the demands for high and low volume products

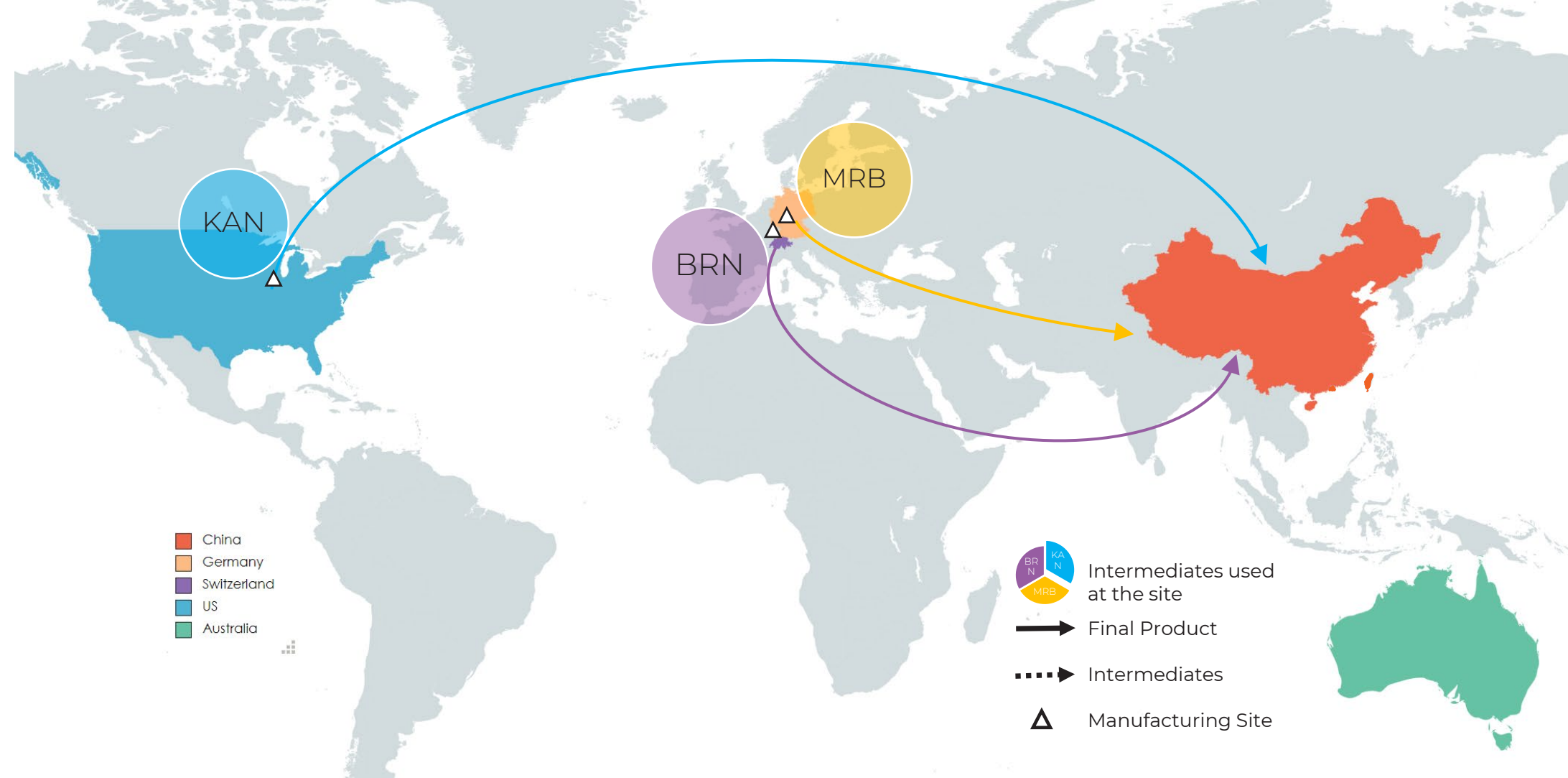


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# Supply Chain of Blood Products

# Plasma Intermediates from single manufacturing site

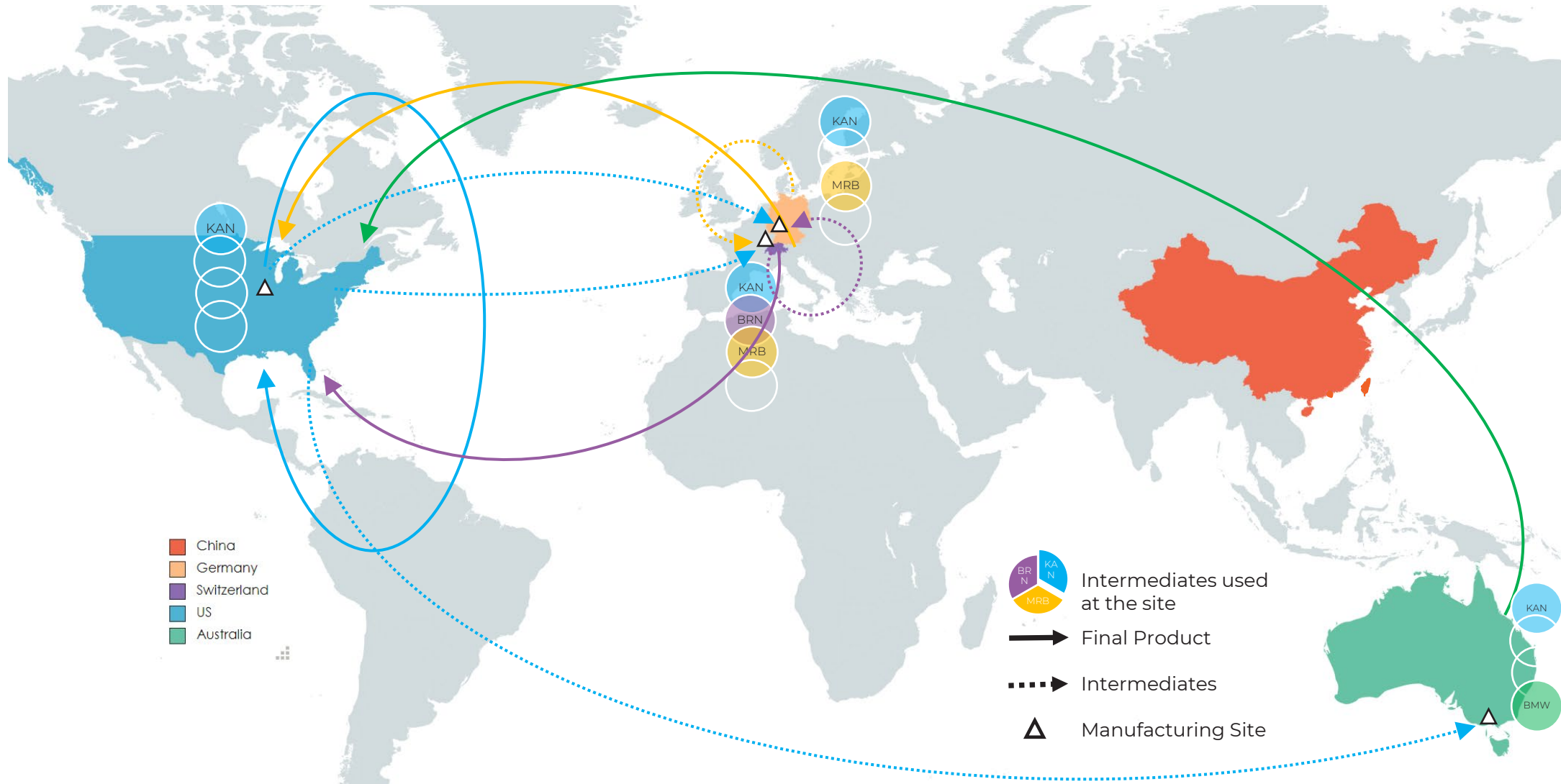
## Inflexible supply approach



Modified from: <https://www.mapchart.net/world.html>

# Plasma Intermediates from multiple manufacturing sites

## Flexible supply approach



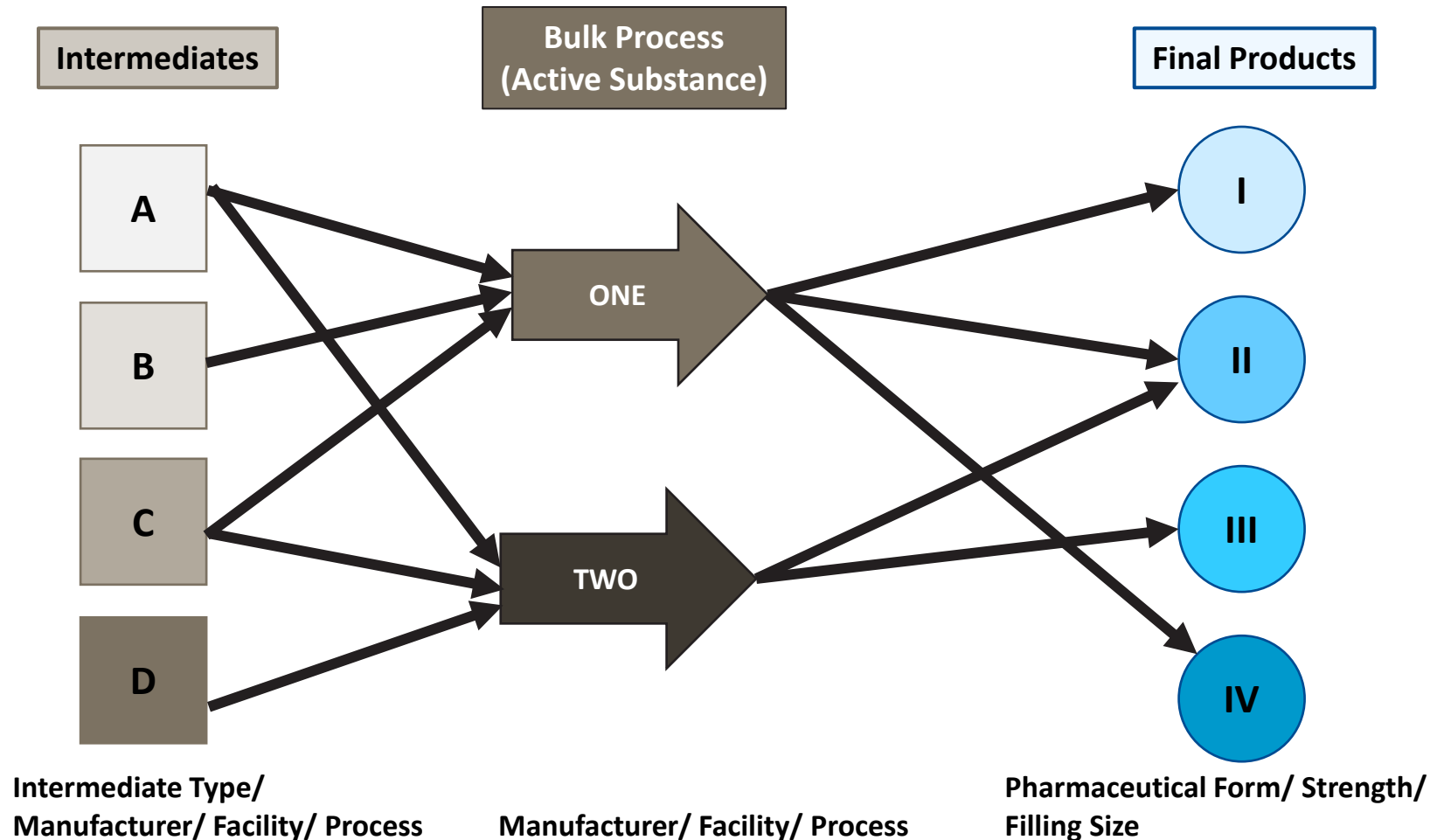
Modified from: <https://www.mapchart.net/world.html>

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# Life Cycle Management Strategy

# Complexity of lifecycle activities

## Mitigation through various approaches



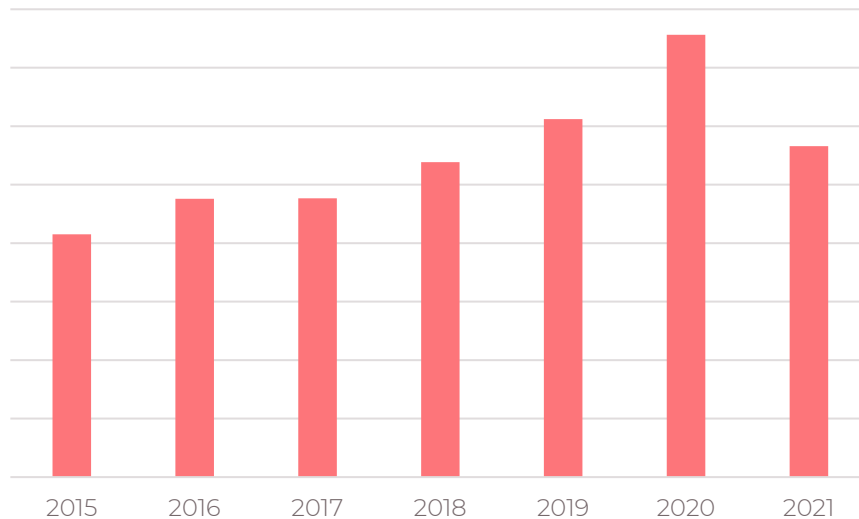
## Streamlined Approaches for LCM are necessary:

- Regulatory Submission Strategies through *Post Approval Change Management Protocols* (PACMPs)
- Science-Based approaches aligned with ICH Q12 *i.e. definition and proposal of EC*
- Risk-Based classifications of *Post Approval Changes* (PACs) with collaboration between Regulatory, R&D and Operations
- Continuous Optimization of information in Dossier

# Complexity of lifecycle activities

## Mitigation through Annual Report

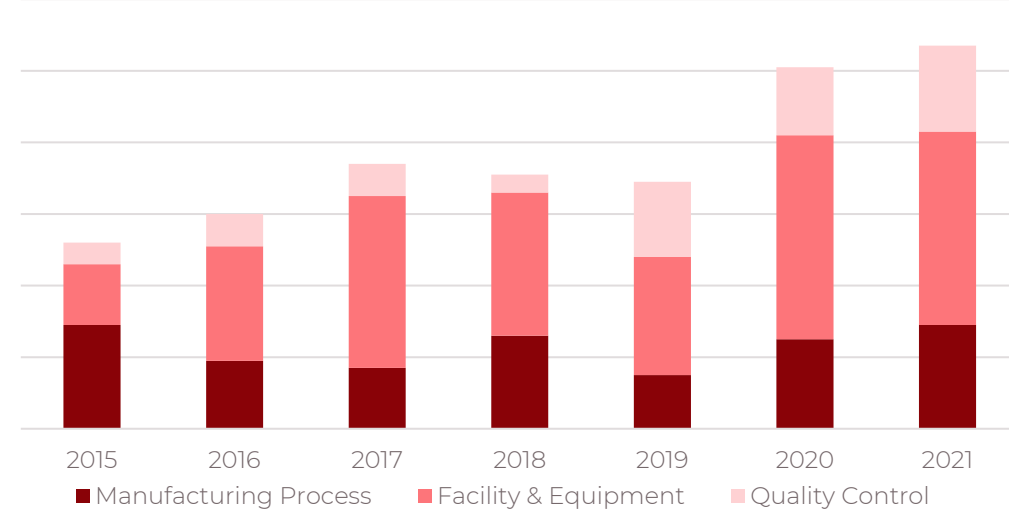
Variation submissions worldwide at CSL Behring



### Complexity of lifecycle activities:

- Number of Post Approval Changes is increasing
- Multi-facility/multi-modules production cycles
- Worldwide submissions

Annual reportable changes in US



### Solution:

- Extensive and extended use of Annual Reports
- Risk based approach for lifecycle

### Result:

- Increase in the lifecycle efficiency
- Better access to the quality products for the patients

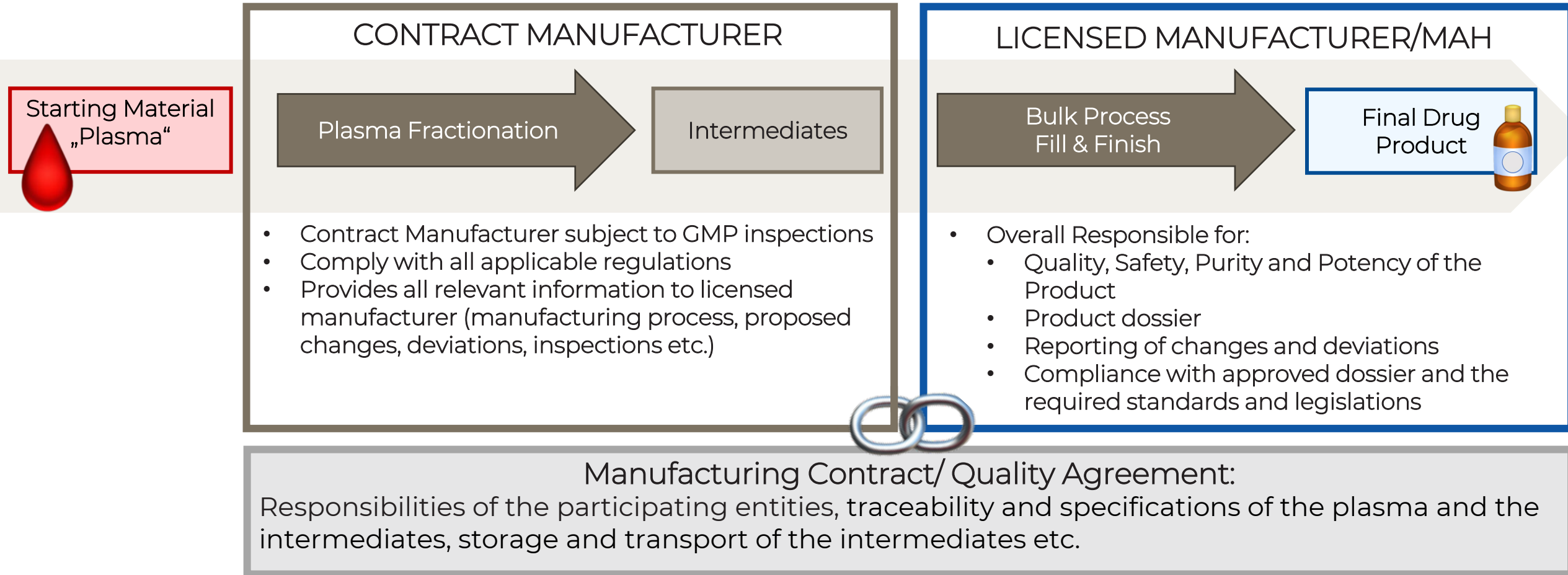


**05**

## Case Study: Contract Manufacturing

# Case Study: Contract Manufacturing

## Responsibilities for MAH and CMO: Intermediates and Final Product



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## Summary and Conclusions

## Blood Products Manufacturing, Supply and Control

### Manufacturing

- Network of Manufacturing Sites to utilize precious plasma in most effective and efficient way
- Alternative Fractionation Schemes to optimize range of products derived from plasma
- ICH and risk based approaches for Lifecycle Management to accommodate its complexity

### Supply

- Exchange of Intermediates from different fractionation sites to reduce drug shortage risk and increase product availability to the patients

### Control

- Use of international standards, regulations and agreements assures Quality of the product on each manufacturing step including operations at CMOs



**Thank You for your attention !**