THE GLOBAL JOURNEY OF PLASMA

Please note, presenters’ opinions and assessments are their own and are not necessarily that of the Association.

This presentation is not for further distribution cannot be used, shared, or cited without the explicit permission of the Association.
INVESTING ACROSS THE PLASMA VALUE CHAIN

INDUSTRY IS INVESTING ACROSS THE PLASMA VALUE CHAIN TO IMPROVE OUR ABILITY TO MEET PATIENTS' NEEDS
DONOR RECRUITMENT MARKETING CHANNELS

TRADITIONAL MARKETING
- Television & Radio
- Direct Mail
- Billboards
- Print Ads

ONLINE MARKETING
- YouTube
- Facebook
- Twitter
- Email Marketing

IN CENTER MARKETING
- Welcome to Biolife
- Center Posters
- Patient Posters
- Fees Signage

COMMUNITY ENGAGEMENT
- Event Booth/ Volunteering
- Buddy Bonus
- Thank You Cards

DONOR WEBSITE/ PORTAL
- Computer
- Mobile
- Video Gallery
EXPANDING OUR SERVICES TO MEET NEEDS FOR TODAY AND THE FUTURE

ADDRESSING THE GROWING DEMAND FOR PLASMA THERAPIES REQUIRES FOCUSED INVESTMENT IN PLASMA COLLECTION

ATTRACTION NEW DONORS IN THE COMMUNITY
- Reaching new donors
- Increasing community engagement

INCREASING THE SUPPLY OF PLASMA THROUGH NEW CENTERS
1. New Centers
2. Expanding to New Markets
3. Improving Regulations

CREATING AWARENESS AND MESSAGING
1. Awareness of what plasma is
2. Why it’s important to donate
3. What’s in it for the donor

IMPROVING THE DONOR EXPERIENCE THROUGH OMNICHANNEL ENGAGEMENT

- MOBILE APP
- WEBSITE
- DONOR
- SCHEDULING
- INFORMATION
- PAYMENT
THE PLASMA DONATION PROCESS

1. REGISTRATION

2. DONOR QUESTIONNAIRE

3. SCREENING

4. PHLEBOTOMY/DONATION

Community Based Donor Standard
National Donor Deferral Registry® Standard (NDDR®)
Cross Donation Management Standard
Donor Education Standard

Personnel Education and Training Standard Quality Assurance
# General Regulatory Requirements (Plasma) Donor Eligibility - Vital Sign & Lab Testing

<table>
<thead>
<tr>
<th>Vital Signs and Lab Testing</th>
<th>US Source1</th>
<th>US Recovered2</th>
<th>EU Source3</th>
<th>EU Recovered2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Pressure</td>
<td>Systolic 90-180 Diastolic 50-100</td>
<td>Systolic 90-180 Diastolic 50-100</td>
<td>Defined by country</td>
<td>Defined by country</td>
</tr>
<tr>
<td></td>
<td>50-100 BPM</td>
<td>50-100 BPM</td>
<td>Defined by country</td>
<td>Defined by country</td>
</tr>
<tr>
<td>Temperature</td>
<td>&lt;37.5° C</td>
<td>&lt;37.5° C</td>
<td>Defined by country</td>
<td>Defined by country</td>
</tr>
<tr>
<td>Total Plasma Protein</td>
<td>6.0-9.0 g/dL</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Hematocrit (HCT)</td>
<td>Female HCT ≥38% Male HCT ≥39%</td>
<td>Female HCT ≥38% Male HCT ≥39%</td>
<td>N/A</td>
<td>Female HCT ≥38% Male HCT ≥39%</td>
</tr>
<tr>
<td>Weight</td>
<td>≥110 pounds</td>
<td>≥110 pounds</td>
<td>≥110 pounds</td>
<td>&gt;110 pounds</td>
</tr>
<tr>
<td>Age</td>
<td>≥18 (defined as age of majority)3</td>
<td>≥16 (defined by parental consent) Maximum age defined by organization</td>
<td>18-65</td>
<td>18-65</td>
</tr>
<tr>
<td>Syphilis</td>
<td>Negative Tested Initially and every 4 months</td>
<td>Negative Each donation</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Serum Protein Electrophoresis</td>
<td>Protein ≥6.0 g/dl Protein Fractions WNL Tested initially and every 4 months</td>
<td>N/A</td>
<td>Protein &gt; 6.0 g/dl Annual</td>
<td>N/A</td>
</tr>
</tbody>
</table>

1. Required by 21CFR630.
2. Required by European Directive 2002/98/EC.
3. Age of majority may vary by state within the US and is usually defined as 18.
SCREENING AND ELIGIBILITY CRITERIA ARE ESSENTIAL FOR DONORS AND PATIENTS

1. Our strict eligibility and screening standards ensure the safety of donors and patients 1

Strict donation criteria have been established by global regulatory authorities 1.

Centers are staffed by medical professionals with specialized training.

Once eligible, donors can participate as often as local regulations permit.
- US: 2x / 7 days (104 donations / year) 2
- Europe: < 50 donations / year, may vary by country 3

Donors receive a medical history screening each time they donate and undergo a physical examination as required by local regulations.

TESTING

Serology Screening (Every Donation)
- HCV, HIV, HBV screening

NAT Screening (Every Donation)
- HCV, HIV, HBV,
- Parvo (B19), HAV Testing

Donor Qualification Testing (3x/Year)
- Syphilis, TP, SPE and ATYA
LOGISTICS: TRANSPORTATION

UPGRADED OPEN CONTAINER

UPGRADED FREEZER TRAILERS

FLEET MANAGEMENT SOFTWARE

SATELLITE TRACKING

CELLULAR/DIGITAL TEMPERATURE MONITORING DEVICES
LOGISTICS: STORAGE FACILITIES

- Freezer (-20 degrees Celsius)
- Cold Room (+5 degrees Celsius)
- Automated Plasma Dispositioning System (APDS) Sorting Line
  - 510 k medical device
LOGISTICS: PRODUCT TRACEABILITY

- Barcode
- RFID Technology
- Inventory Hold
- Single Unit Release Verification
- Unit Traceability
- Batch Building
2. Rigorous plasma screening processes ensure a healthy pool of plasma for therapeutic use

Samples from each donation are sent to a laboratory and rigorously tested for indicators of viral infections

Every plasma donation is screened for:
- HIV
- Hepatitis A, B & C
- Parvo B19

3. Plasma products are further safeguarded by advanced pathogen reduction processes

The plasma undergoes viral inactivation and removal steps that reduce or eliminate any remaining risk of contamination.

1. Solvent / detergent treatment
2. Nanofiltration
3. Incubation and heat treatment

Viral inactivation and removal reduces risk approx. x100,000,000


Reactive donations excluded
## Inspections Schedule (Example)

<table>
<thead>
<tr>
<th>Regulatory Agency</th>
<th>Audit/Inspection Frequency</th>
<th>Why Inspected?</th>
<th>Location(s) inspected?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corporate Audit</td>
<td>Two Years</td>
<td>Provide an independent and documented assessment of compliance to quality requirements</td>
<td>All</td>
</tr>
<tr>
<td>FDA</td>
<td>Two Years</td>
<td>To ensure compliance to Codes of Federal Regulations (CFR)</td>
<td>All</td>
</tr>
<tr>
<td>CLIA (US Only)</td>
<td>Two Years</td>
<td>To ensure compliance with Federal laboratory requirements; CLIA regulation(s) apply because we are considered a laboratory due to the total protein test(s)</td>
<td>All</td>
</tr>
<tr>
<td>State (US Only)</td>
<td>Varies</td>
<td>To ensure compliance with state requirements (as applicable)</td>
<td>Dependent on the State Requirements</td>
</tr>
<tr>
<td>EMA (National Authority)</td>
<td>Two to-Four Years</td>
<td>Required for center approval in centralized Plasma Master File (PMF) Allows plasma to be used in all manufacturing facilities that manufacture product for the EU, Australia, New Zealand and Switzerland</td>
<td>All</td>
</tr>
<tr>
<td>IQPP/PPTA</td>
<td>Three Years</td>
<td>PPTA works cooperatively with patient groups, policymakers, regulatory agencies and other stakeholders to address critical issues that impact the industry and patients who depend on plasma protein therapeutics.</td>
<td>All</td>
</tr>
</tbody>
</table>
INTERNAL AUDITS AND EXTERNAL INSPECTIONS

- Centers, Laboratories, Storage Facilities
- Inspection Types

- On site
- Desk/Document Request Paper Based
- Virtual Video Conference
- Hybrid (limited hours onsite)
IN SUMMARY

Plasma centers are vital contributors to their local communities. Staff committed to the well-being of our donors.

Engaging with donors builds a sense of community.

IQPP Standards ensure donor safety and quality throughout the collection, testing and release process.

Digital Technology is advancing throughout the supply chain.

Plasma products are further safeguarded by advanced pathogen reduction processes.

THANK YOU!
THE GLOBAL JOURNEY OF PLASMA
FROM FRACTIONATION TO PACKAGING

MICHAEL SCHROEDER
GENERAL MANAGER AND SITE HEAD, MARBURG
CSL BEHRING GMBH MARBURG

CSL Behring
CSL AT A GLANCE

35+ Countries worldwide

9.2 bio. US $ annual Revenue

8 Manufacturing Sites

Australia
China
Germany
Switzerland
UK
USA

27.000+ Employees worldwide

R&D Investments of 3.7 bio. US $ in 5 years drive promising new products forward

1.700+ R&D Employees

270+ Plasma donation centres throughout Europe and North America

CSL is a leading global biotechnology company that develops and delivers innovative biotherapies that save lives, and help people with life-threatening medical conditions live full lives.
CSL BUSINESS

CSL BEHRING
20,000+
GLOBAL EMPLOYEES

Develops, manufactures & markets biotherapies for:
- Coagulation disorders
- Immunological disorders
- Pulmonary therapies
- Wound healing therapies
- Critical care therapies
- Operates one of the world’s largest plasma collection networks

SEQIRUS
2,000+
GLOBAL EMPLOYEES

- Second-largest influenza vaccine provider in the world.
- Provides influenza vaccine to both the Northern and Southern hemispheres, protecting Australia, the UK and the US from the ever-present threat of an influenza pandemic.
- Our broad portfolio of influenza products are sold in more than 20 countries around the world.

RESEARCH & DEVELOPMENT
1,700+
GLOBAL EMPLOYEES

Develops new & improved protein-based therapies for treating serious illnesses.
- Haemophilia
- Immunoglobulins
- Speciality plasma products
- Breakthrough medicines
One of the world’s largest and most sophisticated plasma collection networks.

- 270+ collection centers located in the US and Europe
- 12,000+ employees

Testing laboratories in Knoxville, US and Göettingen, Germany.

Logistics centers in Indianapolis (Indiana) and Mesquite (Texas), US and Schwalmstadt, Germany.
THE MANUFACTURING PROCESS
FROM FRACTIONATION TO PACKAGING

1. PLASMA COLLECTION
2. PLASMA PREPARATION
3. BASE FRACTIONATION
4. BULK MANUFACTURING
5. ASEPTIC FILLING
6. VISUAL INSPECTION
7. PACKAGING
8. DISTRIBUTION
9. TREATMENT
THE COHN FRACTIONATION PROCESS

The Cohn process is a series of purification steps with the purpose of extracting albumin from blood plasma. (Initial treatment target were soldiers suffering shocks and burns in World War II.)

The original process is based on pH, the ethanol concentration and temperature settings to precipitate the plasma into five fractions.

EDWIN JOSEPH COHN
1892 - 1983
Cohn became famous for his work on blood fractionation during WWII.
In base fractionation, physical and biochemical processes are used to separate the human plasma into different fractions.

1st purification of proteins.

This step is fundamental to the production of our medications.
PLASMA FRACTIONATION PROCESS

- CRYOPRECIPITATE
- FACTOR IX INTERMEDIATES
- INHIBITOR INTERMEDIATES
- IMMUNOGLOBULIN PASTE
- FRACTION IV1 - IV4 INTERMEDIATES
- ALBUMIN INTERMEDIATES
- WASTE

Reference: Preparation of Plasma Derivatives, chapter 19; Rossi's Principles of Transfusion Medicine 4th edition
In bulk manufacturing, the intermediates produced in the base fractionation are further processed into the active ingredient.

Multiple methods/techniques are used to further purify the target proteins.

Another important process step is the virus inactivation.

Final formulation before filling.
PLASMA FRACTIONATION

Processes used for purification of proteins and final formulation of final products.

- Plasma
- Cryodepleted Plasma
- 8% Precipitation (Fraction I)
- 25% Precipitation (Fraction II + III)
- 40% Precipitation (Fraction V)
- Precipitation
- Adsorption
- Chromatography
- Virus inactivation
- Filtration
- Zentrifugation
- Fibrinogen Factor VIII
- Factor IX
- C1 Inhibitor
- Antithrombin III
- Immunoglobuline
- Albumin

Reference: Preparation of Plasma Derivatives, chapter 18; Rossi's Principles of Transfusion Medicine 4th edition
Filling of the products – either in liquid or in freeze-dried form – and sealing of the vials are performed in a clean and aseptic environment.

Liquid products are closed with stoppers and crimped immediately after filling.

After filling, freeze-dried products are transferred to the freeze dryer, and vials are stoppered after the drying-process and crimped accordingly.
Controlling of all filled units – automatically, semi-automatically or by hand.
After the visual inspection, the product is stored in the warehouse. From there, it is prepared for labeling and packaging in accordance with the respective country requirements, taking into account the specified quality aspects.
PLASMA FLOWS ON A GLOBAL LEVEL: WHY IT TRAVELS SO FAR

MATTHEW HOTCHKO
PRESIDENT
MARKETING RESEARCH BUREAU
METHODOLOGY

The data used to develop the charts and tables shown in this presentation have been compiled from surveys conducted by the Marketing Research Bureau in over seventy countries and published in various syndicated reports.

All the data and information originate from sources generally available to the public. Their accuracy is not guaranteed, and the Marketing Research Bureau assumes no liability for their use. © 2021
OVERVIEW

Where is plasma for fractionation collected around the world?

After plasma is collected, where is it sent globally?

Plasma products are used around the world, meaning they must travel from where they are produced to the countries where the patients use them.
PLASMA IS SOURCED GLOBALLY, BUT IT IS NOT EQUALLY BALANCED AS THE U.S. IS THE DOMINANT SUPPLIER

Origin of Plasma for Fractionation - 2019

- North America: 67%
- Asia & Pacific: 18%
- Europe: 14%
- Latin America: 1%
- Middle East & Africa: 0%

*United States represents over 99% of the North America total

**China represents over 75% of Asia & Pacific total

Total Plasma Collection volume 2019: 69 M liters.
REGIONAL DISTRIBUTION OF FRACTIONATION PLANTS 2018

NORTH AMERICA: 9
LATIN AMERICA: 3
EUROPE: 21
MIDDLE EAST: 4
AFRICA: 4
ASIA + PACIFIC: 39

TOTAL NUMBER OF FRACTIONATION PLANTS: 76
REGIONAL DISTRIBUTION OF FRACTIONATION THROUGHPUT 2018

GLOBAL FRACTIONATION THROUGHPUT 2018:
61.4 MILLION LITERS
TRANSFERS OF PLASMA FROM THE U.S. TO OTHER COUNTRIES 2019

Total Volume Shipped - 21.5 million liters (includes plasma for transfusion)
Source: US Department of Commerce 2019
CLINICAL NEED FOR IG IS GLOBAL, WITH NORTH AMERICA USING MORE PRODUCT THAN ANY OTHER REGION

Origins of Plasma Fractionation - 2018
- North America: 66%
- Europe: 18%
- Asia & Pacific: 1%
- Latin America: 1%
- Middle East & Africa: 1%

2018 IgG Usage by Region (>200 metric tons)
- North America: 20%
- Europe: 40%
- Asia & Pacific: 10%
- Latin America: 20%
- Middle East & Africa: 6%

Most plasma is collected in the U.S., but Ig use is more globally distributed than plasma collection.
THE SITUATION IN 2018 SHOWS THAT THE US SUPPLIES EXTRA PLASMA FOR THE REST OF THE WORLD

2018 REGIONAL PLASMA USAGE OF IG VS. PLASMA COLLECTED
PLASMA TRANSFERS FROM THE U.S. TO OTHER COUNTRIES

INTERNATIONAL PRODUCT TRANSFERS 2018

CANADA

EUROPE

AFRICA + MIDDLE EAST

ASIA + PACIFIC

LATIN AMERICA

GLOBAL PLASMA FRACTIONATED — 62.0 MILLION LITERS

GLOBAL MARKET VALUE — $24.0 Billion

MRB
CLINICAL NEED FOR ALBUMIN IS GLOBAL, WITH ASIA (MAINLY CHINA) USING MORE PRODUCT THAN ANY OTHER REGION
CONCLUSIONS

- Most of the plasma collected globally for fractionation comes from the United States
- Almost half of the plasma collected in the United States is sent overseas (mostly to Europe) for fractionation
- The immunoglobulin products made from plasma fractionated in the United States and Europe is sent around the world for use by patients, with much of it sold in the United States
- Much of the albumin which comes from United States plasma is sold in Asia (particularly China)
Thank you!

MARKETING RESEARCH BUREAU,

Office Phone: +1-425-502-6265
Email: info@marketingresearchbureau.com
mhotchko@marketingresearchbureau.com

www.marketingresearchbureau.com
THE GLOBAL JOURNEY OF PLASMA