Study on Competitive Market Analysis of the Plasma Industry for Strategic Decision Making

By

Manu Bhardwaj

Dissertation submitted in partial fulfillment of the requirements of the degree

MBA Hospital and Health Management

Academic year, 2018-2020

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CERTIFICATE BY SCHOLAR

This is to certify that the dissertation titled **"A study on competitive market analysis of the Plasma Industry for Strategic decision making " at PharmaACE, Analytics Center of Excellence, Pune** and submitted by **Dr. Manu Bhardwaj,** Enrolment No **0771** under the supervision of **Dr. Dhirendra Kumar, Professor** for award of MBA in Hospital and Health of the University carried out during the period from **3rd Feb 2020** to **3rd May 2020** embodies my original work and has not formed the basis for the award of any degree, diploma associate ship, fellowship, titles in this or any other institute or other similar institution of higher learning.

Dr. Manu Bhardwaj

PharmaACE

The certificate is awarded to

Dr. Manu Bhardwaj

In recognition of having successfully completed his Internship in the department of

Competitive Intelligence

and has successfully completed his Project on

A competitive market analysis report on the Plasma Industry for Strategic decision making.

starting from

February 03, 2020 to May 03, 2020

at

PharmaACE Analytics LLP

He comes across as a committed, sincere & diligent person who has a strong drive and zeal for learning

We wish him all the best for future endeavors.

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I. ACKNOWLEDGMENT

This employment opportunity with PharmaACE, Pune is once in a lifetime chance for learning, understanding and professional development. It has helped me in learning my duties as a professional working in a multinational consulting setup. It has carved some wonderful memories in my life and has helped me to develop as a management professional. I am also grateful for having a chance to work with wonderful people and professionals who are among the most acknowledged names in the industry. This period has helped me in honing my skills.

I am extremely indebted and would like to convey my deepest warm gratitude to, Mr. Dinesh Pandey, Chief of staff and Mrs. Pratima Chaudhary, Practice Head, PharmaACE, who in spite of being extraordinarily busy with their duties, took time out to hear, guide and kept me on the correct path. And I would also like to thank from the core of my heart Mr. Amit Pharande, Team Lead, and my mentor who worked tirelessly with me and for arranging all facilities to make my life easier which allowed me to carry out my projects during this period. I would also like to express my heartfelt thanks to Dr. Dhirendra Kumar, Professor, IIHMR University, for his constant support and guidance during this project. I choose this moment to acknowledge their involvement thankfully.

I see this opportunity as a huge step in my career development. And I will strive to use my gained skills and knowledge in the best possible way to shape my career and use the best of my knowledge to help others in need as a token of appreciation for those who helped me gain these skills.

Sincerely,

Dr. Manu Bhardwaj

MBA-HM (2018-2020)

Date: 2020-05-03

II. ABBREVIATIONS

Bn	Billion
CAGR	Compound Annual Growth Rate
CI	Competitive Intelligence
CSL	Commonwealth Serum Laboratories
EMA	European Medicines Agency
EU	European Union
FD & C	Federal Food, Drug and Cosmetic Act
FEIBA	Factor eight inhibitor bypass activity
GMP	Good manufacturing practice
IgG	Immunoglobulin G
IVIG	Intravenous immunoglobulin
NBA	National Blood Authority
NRA	National Regulatory Authority
PDP	Plasma-derived products
PDT	Plasma-derived therapies
PHS	Public Health Service Act
SCIG	Subcutaneous immunoglobulin
US	United States

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1. SECTION-A (Executive Summary)

The Blood Plasma Market is expected to exceed more than US$44.0 billion by 2024 at a CAGR of 9.3% in the given period as the need for plasma products will continue to grow.

- **Plasma-Collection & Fractionation:**
  Plasma is moving from nascency towards a whole therapeutic expertise, and is going to positively affect both the pharma industry and the recipients
  U.S. commercial blood establishments supply the largest proportion of source plasma used for fractionation
  Source plasma is also collected in significant quantities in China, Germany, Austria, Czech Republic, and Hungary
  The south-east Asian region is also making progress in terms of plasma fractionation and might assume a significant role in plasma production in the coming years

- **Economics & Key Players**
  The Blood Plasma Market which includes product, application and regional segments is expected to exceed more than US$44.0 billion by 2024 at a CAGR of 9.3% in the given period
  The key players according to market share in 2019 are:
  CSL Behring (~37%); Grifols (~22%); Octapharma (~12%); Takeda (~11%)
  The commercial sale of all the major products obtained from 1 liter of plasma generates around US$ 696 in 2019

- **Regulations & Remunerations**
  The leading nations allowing remunerations are US ($30-50), Germany ($30), China (ranging from several dollars, along with paid leaves for employees and credits for college students), Austria ($28), certain provinces of Canada ($30-50) and Russia ($5.5/plasma donation if donated 60 times annually)
  Countries that are in the process of developing a national blood program could benefit from taking some aspects of the U.S. regulatory approach to expand their donor base of source plasma for manufacturing, beyond aiming to accept plasma only from voluntary unpaid donors

- **Challenges & Hurdles**
  The amount of domain expertise and capital required, are the major hurdles for a new player or competition to venture into this industry
  The regulatory scenario of the industry will keep on tightening because of the abusable nature of the raw material and new mutated viral infections coming into play

Due to the increasing number of patients who are suffering from diseases that can effectively be treated with plasma products, the need for these products will continue to grow and the demand for plasma will increase equally

2. SECTION-B (Main text)

2.1 Background

Basic role of the Competitive Intelligence team is to provide knowledge on the subject matter that is required by the approaching clients so they could take better strategic decisions based on sound knowledge, deciding the future for their firm . These could include market assessment reports, product analyses, review of the current product universe, therapeutic area intelligence reports, etc. Nature of the work largely depends upon the requirement of the client.

Hence, a well-known name in Pharma Industry multinational giant approached PharmaACE's Competitive Intelligence team to understand business development opportunities.

I was fortunate enough to work with the Competitive Intelligence team of PharmaACE on this Project.

To tackle such a task, the requirements of the client are understood through a formal meeting, the sole agenda of this preliminary meeting is to set the expectations with the upcoming project. In which the approaching client shares their expectations/requirements with the CI Team. And same was true for this project as well, a meeting was undertaken, and expectations were understood and prioritized.

The approaching client wanted to understand what the current scenario is globally in the plasma industry to better craft their next steps for expansion

This is followed by numerous internal meetings to organize thoughts and workflow of the whole team during the project.

Plasma industry stands on the shoulders of plasma derived products which are used to treat or aid various disease that are either unmanageable or treatable by the current conventional pharmaceutical medicines. These plasma derived products help many suffering patients with illness previously thought to be an end, lead a better and fuller life. It takes more than 1000 plasma donations to derive a 1-year therapy for 1 patient.

2.2 Aim

To analyse the competitive market of Plasma Industry for Strategic decision making

2.3 Research Question

What is the competitive scenario in Global plasma industry?

2.4 Objective

i. To study the Competitive Landscape of plasma industry
ii. To analyze the Opportunities in Plasma industry
iii. To determine the key products and players in the Plasma Industry

2.5 Methodology

- Study design- Descriptive and Exploratory research
- Study type- Secondary research
- Period of Study – February 2020 to May 2020
- Study Area- Global plasma industry

2.6 Data-collection

Secondary data: A rigorous secondary research was done with inference concluded from different databanks, research papers, books, journals, and websites to collect the data. Plasma industry market was assessed, and the data was extracted and analysed to arrive at conclusions.

2.7 ROL (Review of Literature)

1. A descriptive study on Plasma-derived Industry and Plasma-Derived Medicinal Products in the Italian National Blood Transfusion Service

The study carried out in 2018-2019 concluded that 50,000 kg of plasma were collected, in 1990 in Italy with an 453,000 kg increase from 1990 to 2000, which was further up to 786.000 kg from 2000 to 2013. After 2014 saw a decrease, plasma collection has increased again up to 839,000 kg in 2018. The present situation of PMP demand warrants a dependence on the free market of 23% for IVIG. If the demand continues, a provision of over 1,160,000 kg should be requested to guarantee IVIG self-sufficiency.

1. A study on Modern Plasma Fractionation

The study carried out in 2018-2019 concluded that the plasma industry has been targeting mostly proteins, the obvious candidates for replacement therapy, it can also be hoped that they will invest into developing new products because plasma turns out to be a unique source of potential therapeutic proteins. Finally, one should understand that plasma protein therapies are expensive and inaccessible to the developing world.

2. A study on Stability of Plasma Proteins and Factors in Chinese Universal Pooled Plasma

There were notable differences in plasma protein levels in single units of freshly frozen plasma. Therefore, after different pooling protocols, the mean value of plasma proteins did not change. However, with a greater number of pooled samples, plasma proteins were more stable with a smaller standard deviation. Acceptable standards for Chinese universal pooled plasma was achieved with storage for 1 day at 22°C, 4 days at 4°C, and 3 months at -20°C.

3. A study on Plasma-derived Medicinal Products: Demand and Clinical Use

The study concluded that the increasing demand for IgG is the main challenge for the future for all the stakeholders involved in PDP industry. In fact, over the recent decade, scientific literature on PDMP has been increasingly published bringing about new evidence and new therapeutic indications, even though the levels of supportive evidence are sometimes controversial. Moreover, the increased use of polyvalent immunoglobulin for subcutaneous administration suggests including this preparation in the toll fractionation contract

2.8 Plasma and Plasma-derived products (PDP's)

More than 3,000 plasma proteins control balance in a human body, some with health promoting effects and others with disease associated effects.

- **What's Plasma?**

Blood is made up of four main components: Red blood cells, white blood cells, platelets, and plasma. Plasma, also known as blood plasma, appears light-yellowish or straw-colored. It serves as the liquid base for whole blood. Plasma contains 92% of water and 8% to 9% of solids. Plasma mainly comprises:

i. Coagulants, mainly fibrinogen, aid in blood clotting
ii. Plasma proteins, such as albumin and globulin, that help maintain the colloidal osmotic pressure at about 25 mmHg
iii. Electrolytes like sodium, potassium, bicarbonate, chloride, and calcium help maintain blood pH
iv. Immunoglobulins help fight infection and various other small amounts of enzymes, hormones, and vitamin

- **Plasma's Development**

Plasma is formed from water and salts absorbed through the digestive tract. Plasma proteins, on the other hand, have distinct organs that produce them based on an individual's stage of development. In Embryo, the mesenchymal cells are responsible for the plasma cell production. The first protein to be synthesized is albumin, followed by globulin and the other plasma proteins. In Adults, the reticuloendothelial cells of the liver oversee plasma protein synthesis. Gamma globulins originate from B lymphocytes, which in turn form immunoglobulins

- **Role of Plasma**

More than 3,000 plasma proteins control balance in a human body, some with health promoting effects and others with disease associated effects. They help to carry out many important functions in the human body, including clotting blood, fighting diseases, and other important jobs.

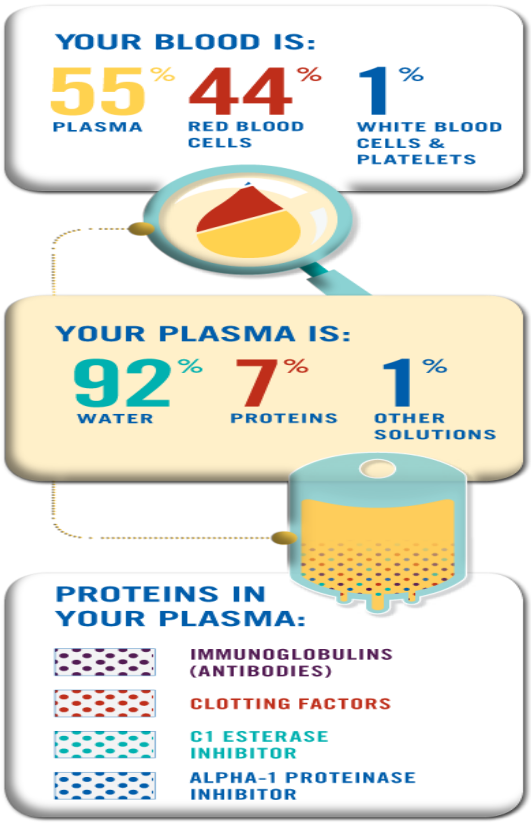


Fig 1.: This figure indicates the relative percentages of components of blood, plasma and subsequently the proteins forming plasma.

The protein concentration in plasma is approximately 60–80 mg/mL and these proteins are isolated to create life-saving plasma protein therapies

Plasma Protein	Normal Level	% in plasma	Function
Albumins	3-5 g/dl	60%	Maintains colloid osmotic; transports insoluble molecules
Globulins	2-3 g/dl	38%	Participate in immune system
Fibrinogen	0.3 g/dl	7%	Blood coagulation
Clotting factors		<1%	Conversion of fibrinogen into fibrin
Regulatory proteins		<1%	Regulation of gene expression

Table 1.: This table indicates the various protein concentration in plasma and their functions.

- **Why are plasma proteins therapies important?**
  Plasma contains hundreds of proteins covering a myriad of physiological functions.
  The protein concentration in plasma is approximately 60–80 mg/mL of which most abundant proteins, albumin and immunoglobulin (Ig) G, are present representing about 80% of all plasma proteins and less abundant proteins include the protease inhibitors, like a1-antitrypsin (AAT) and antithrombin (AT), and the coagulation factors such as factor VIII (FVIII) which exhibit potent physiologic activity.
  Plasma proteins are used to treat many conditions including immune deficiencies, autoimmune disorders, neurological & bleeding disorders, and shocks and burns
  These proteins are isolated to create lifesaving plasma protein therapies

- **Can't these proteins be replicated to treat rare conditions?**
  Due to the specific qualities of some of these proteins, they cannot be replicated by recombinant approaches. Factors such as histocompatibility or post-translational modifications enforce that these proteins can be considered irreplaceable. This is the case in particular with immunoglobulin that, because of its unique structural features and polyvalence, will be very difficult to replicate by recombinant means and therefore plasma therapy is likely to remain the only treatment for immune deficiency or immunomodulation in the foreseeable future.

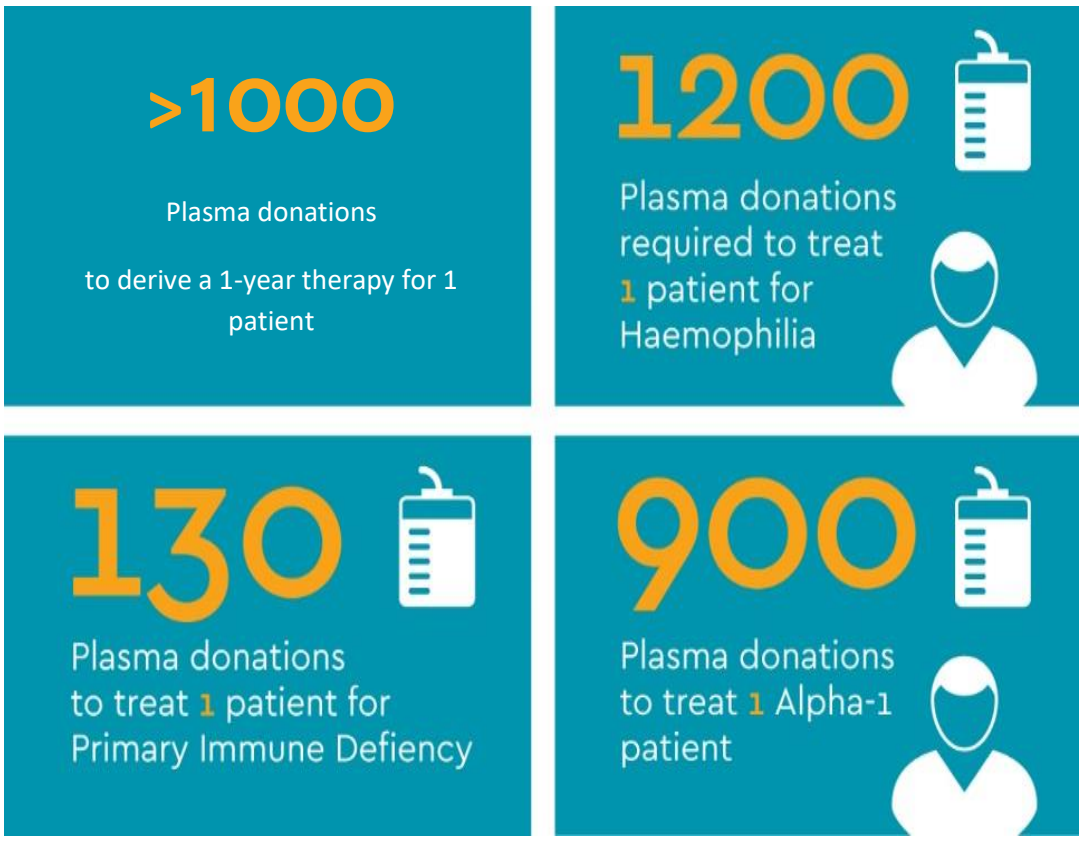


Fig 2.: This figure indicates the amount of plasma donations required to treat a patient.

Currently there are more than 20 Protein-derived products (PDPs) in the market and Immunoglobulin G (IgG) has been the driver of plasma fractionation volumes for the past twenty years

Immunoglobulin products	Clotting factors and other products	Albumin Products
✓ Intravenous immunoglobulin (IVIG) ✓ Subcutaneous immunoglobulin (SCIG) ✓ Normal human immunoglobulin ✓ Hyperimmune immunoglobulin products	✓ Factor VIII ✓ Factor IX ✓ Factor VIIa ✓ FEIBA ✓ Protein C ✓ Prothrombin complex ✓ Antithrombin III ✓ Fibrogammin ✓ Factor XI and factor XII ✓ C1 esterase inhibitor	✓ 4% human albumin solution ✓ 20% human albumin solution

Table 2.: This table indicates the major products that can be manufactured from source plasma

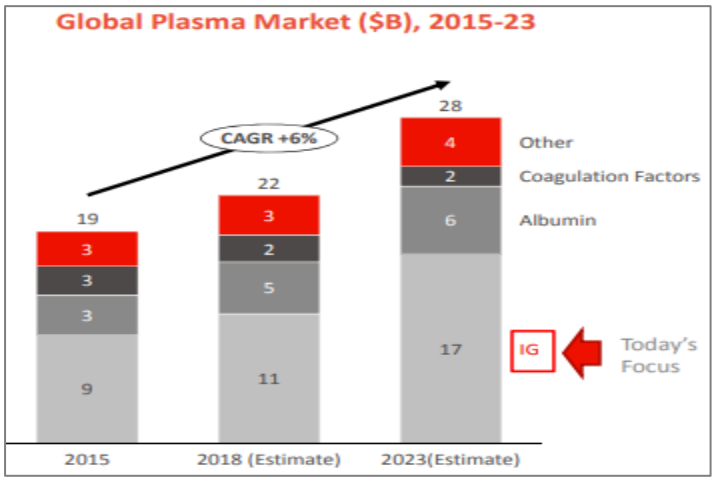


Fig 3.: This figure indicates the estimated rise of the global plasma market from $19 bn in 2015 to $28 bn in 2023

PDPs treat well-defined medical conditions, replacing missing or deficient proteins found in plasma, to allow their recipients to lead healthier and more productive lives. The patient populations that rely upon plasma protein therapies generally require regular infusions or injections for the duration of their lives

The most important biological medicines which can be prepared from human plasma are albumin, Immunoglobulin G (IgG), coagulation factor VIII and IX, α1-antitrypsin, anti-thrombin III, ceruloplasmin, and plasminogen

Today, more than 20 different protein products, and more if one considers the variety of hyperimmune IgG preparations, can be extracted through large-scale fractionation of human plasma

IgG has been the driver of plasma fractionation volumes for the past twenty years

Prior to that, factor VIII was the driving protein for fractionation. At present, IgG and albumin are sold from every litre of plasma fractionated, and factor VIII is still sold from nearly all the litres fractionated.

There is a growing need for Plasma derived products led by Immunoglobin and by 2018, CSL, Takeda and Grifols are the top 3 companies in terms of product revenues

Fig 4.: This figure indicates the percentage of immunoglobulin products sold by region

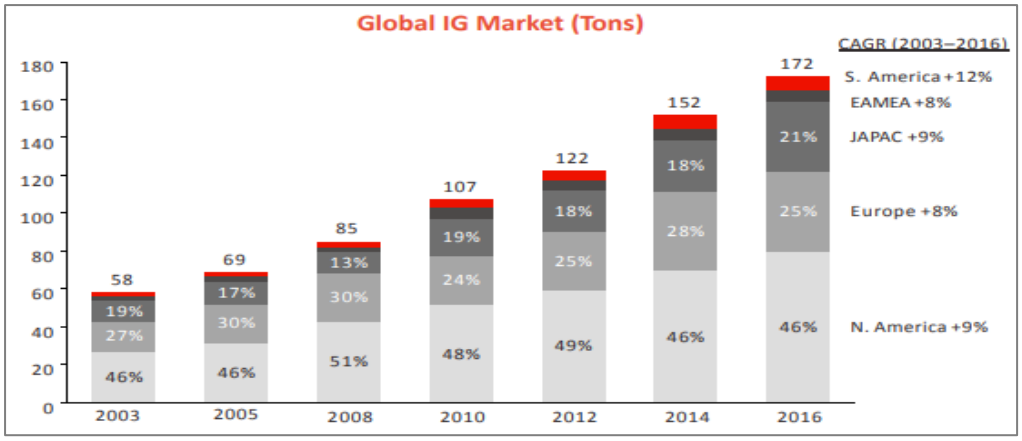


Fig 5.: This figure indicates the steady rise in the global immunoglobulin market since 2003

- Large amounts of plasma derived products are exported from the U.S. and Europe to countries in Asia Pacific, South America, Middle East, and Africa
- **IgG has been the driver of plasma fractionation volumes for the past twenty years due to improved diagnosis rate and disease awareness**
- There is a growing need for Plasma derived products led by Immunoglobin and by 2018, CSL, Takeda and Grifols were the top 3 companies in terms of product revenues
- North America and Europe hold major worldwide IVIG/SCIG unit sales for the year 2017
- Prior to that, factor VIII was the driving protein for fractionation. At present, **IgG and albumin are sold from every liter of plasma fractionated**, and factor VIII is still sold from nearly all the liters fractionated

The U.S. PDPs market represents close to half of the world's total in value, as well as in volume for some products

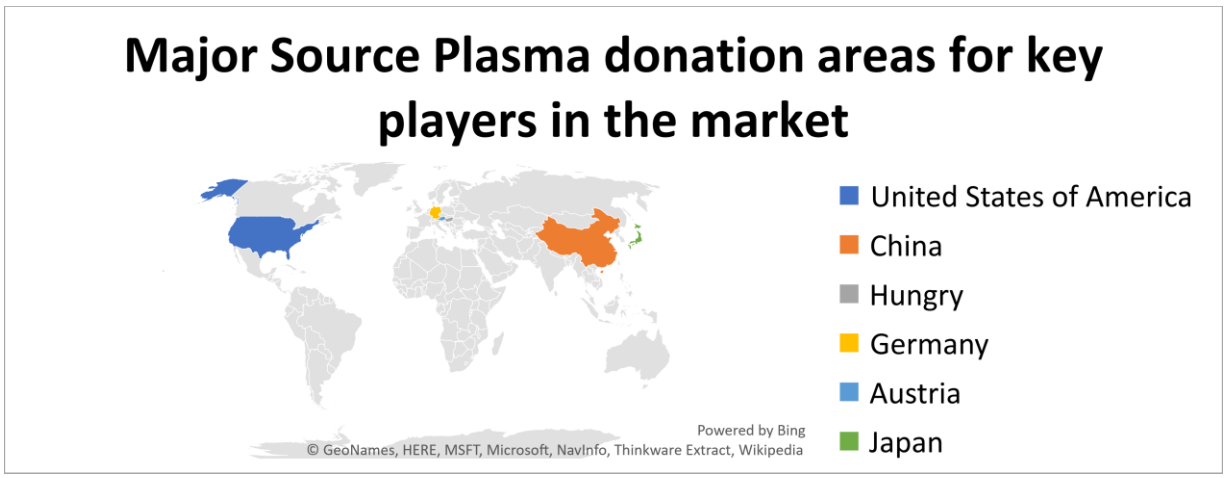


Fig 6.: This figure indicates major source plasma donation areas for key players in the market

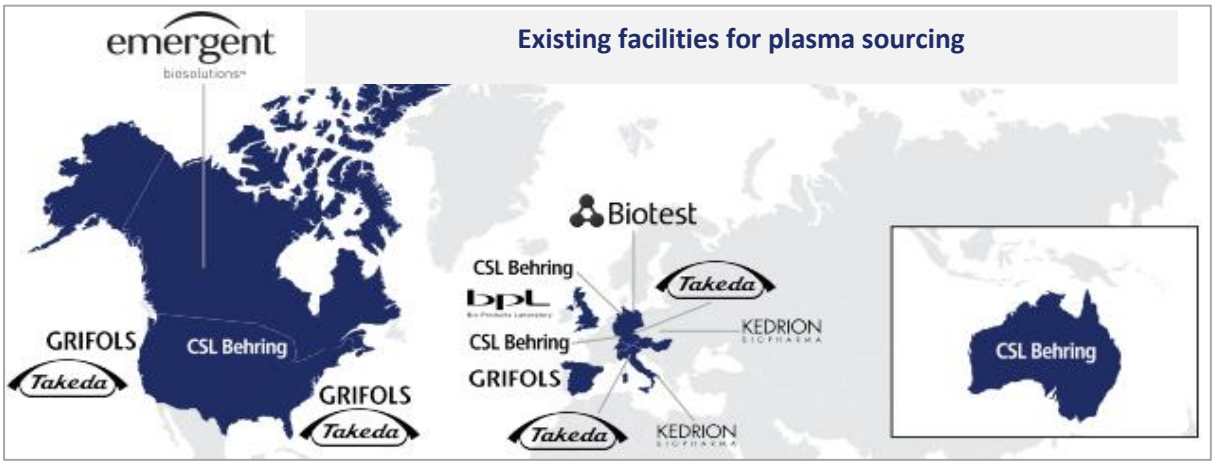


Fig 7.: This figure indicates the major plasma sourcing facilities location for major players

Plasma Sourcing

US is the major exporter responsible for more than 40% of world's source plasma feed, which is worth more than $2bn in terms of plasma and related products

China has begun to impact the global plasma proteins industry through its mergers and acquisitions of plasma companies outside China

In order to operate multiple production sites, about half of the plasma collected in the U.S. for fractionation is shipped abroad, mainly to Europe

In 2018, 22 million liters of U.S. plasma transfers to foreign countries were recorded by the U.S. Department of Commerce and 144,000 liters came from 24 countries into the U.S.

Much of the plasma that left the U.S. for Europe comes back about 10 months later in the form of various PDPs

The U.S. PDPs market represents close to half of the world's total in value, as well as in volume for some products

Throughout South-East Asia, there is certainly a strong regional will to contribute to the world's supply of plasma for fractionation and could even be a more active contributor

2.9 Plasma Collection and Fractionation

Collection of source plasma (obtained through dedicated plasmapheresis) in the U.S. has expanded rapidly over the past few years to meet increasing demand

Plasma Collection

- Plasma can be obtained in two primary forms: **recovered plasma** (obtained from the "by-product" of whole blood collection) and **source plasma** (obtained through dedicated plasmapheresis, a process where plasma is separated from red blood cells and other cellular components of blood which are then returned to the donor)
- In a **regulated environment**, **plasma is collected by licensed blood establishments** (blood centers and apheresis collection centers) that are inspected by the relevant National Regulatory Authorities (NRAs)
- **Collection of source plasma in the U.S. has expanded rapidly** over the past few years to meet increasing demand, especially for immunoglobulins
- Source plasma is also collected in significant quantities in China, Germany, Austria, Czech Republic and Hungary
- By 2019, China had 263 plasma collection centers drawing some 2.9 million qualified plasma donors across 650 counties

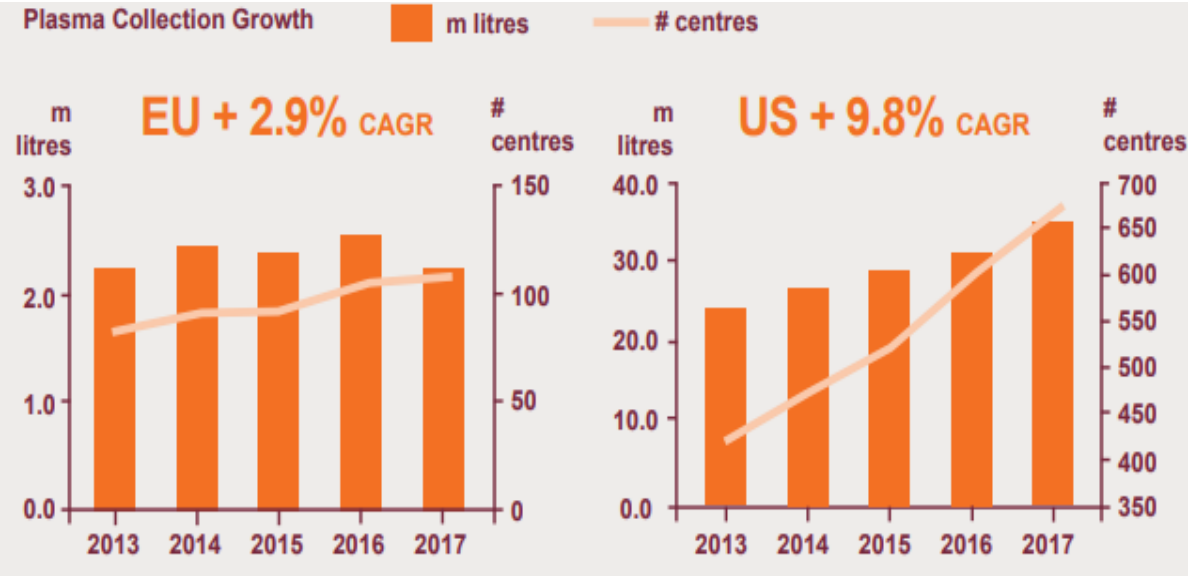


Fig 8.: This figure indicates the growth in plasma collection and number of collection centres over the years from 2013-2017

Both the collection centers and plasma collected in U.S. have increased vastly with 9.8% CAGR in the period of 2013-2017 whereas EU had registered only 2.9% CAGR for the same period

Australia: In 2018/19, for the first time, the AUSTRALIAN RED CROSS collected more units of plasma than whole blood, approximately 61,000 vs. 60,000 units, respectively. This contrasts with over 100,000 whole blood donations and ca. 25,000 plasma donations 10 years previously

Regarding Asia and Pacific countries,

- Some countries have achieved good manufacturing practices (GMP) compliance and are involved in (contract) manufacturing (like Japan, Australia, New Zealand, Singapore, Malaysia, Hong Kong, Taiwan, South Korea)
- While some countries are improving their blood transfusion organizations with the aim of conforming with GMP standards and optimizing the quality of plasma (e.g. Indonesia, Thailand, Vietnam, Sri Lanka), other countries (in particular India) have a long way to go

Plasma Industry Process: Plasma that comply with quality and testing requirements are only used for fractionation and this production cycle takes a few weeks to several months

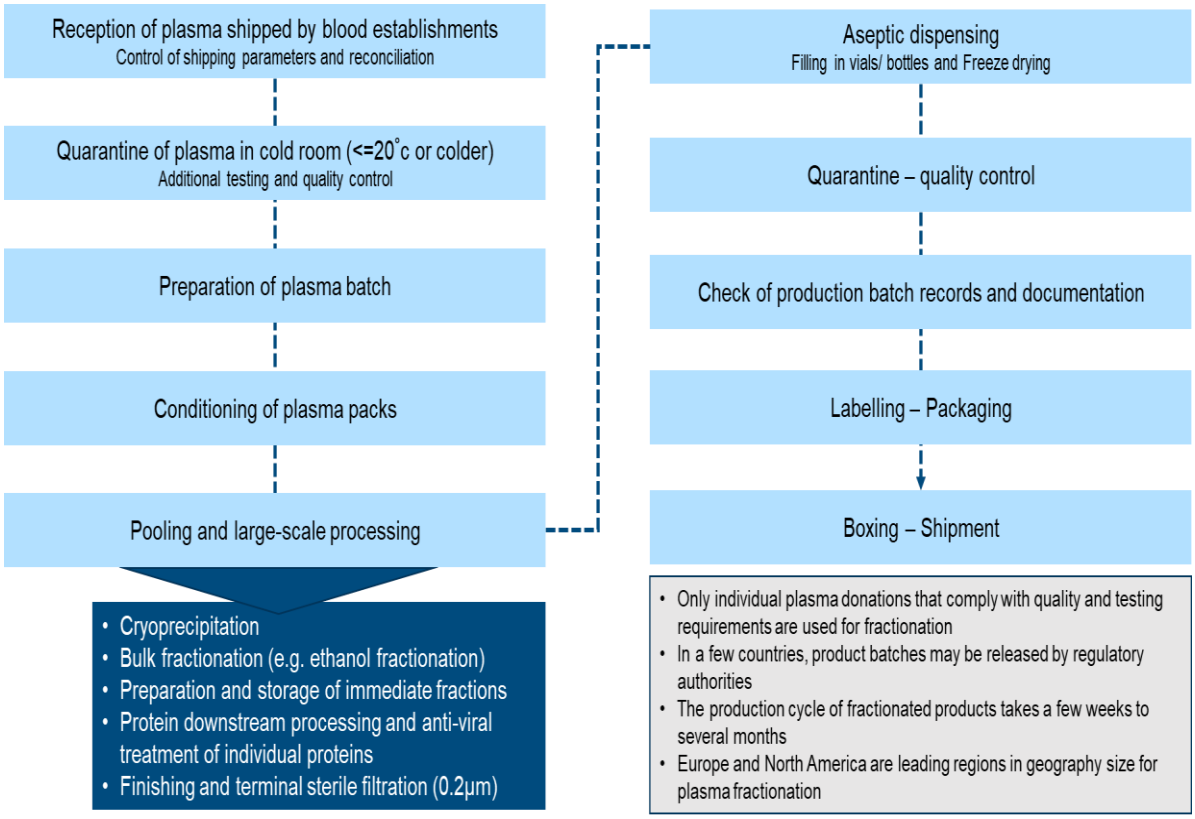


Fig 9.: This figure indicates process flow from receiving sourced plasma to shipment of the desired component manufactured because of this process

Manufacturing a therapy often takes 7 to 12 months from donation to final product release and most of the larger manufacturers conduct fractionation and purification processes on fractions equivalent to pooled plasma volumes of 3,000 liters - 20,000 liters

Manufacturing

The manufacture of plasma proteins is characterized by high capital costs, complex manufacturing processes, and a considerable regulatory burden

The economic and regulatory pressures require that high-quality manufacturing facilities be designed and maintained

Source and recovered plasma is the starting material used to manufacture lifesaving therapies

Cohn and co-workers developed plasma protein separation process which allowed the establishment of large-scale commercial fractionation enterprises and this process remains the technological basis of the industry to this day

In fractionation, plasma is pooled and processed that employs time, temperature, pH, and alcohol concentrations to extract specific therapeutic proteins

These are then subjected to various purification methods and viral inactivation and removal processes to further ensure their safety and efficacy

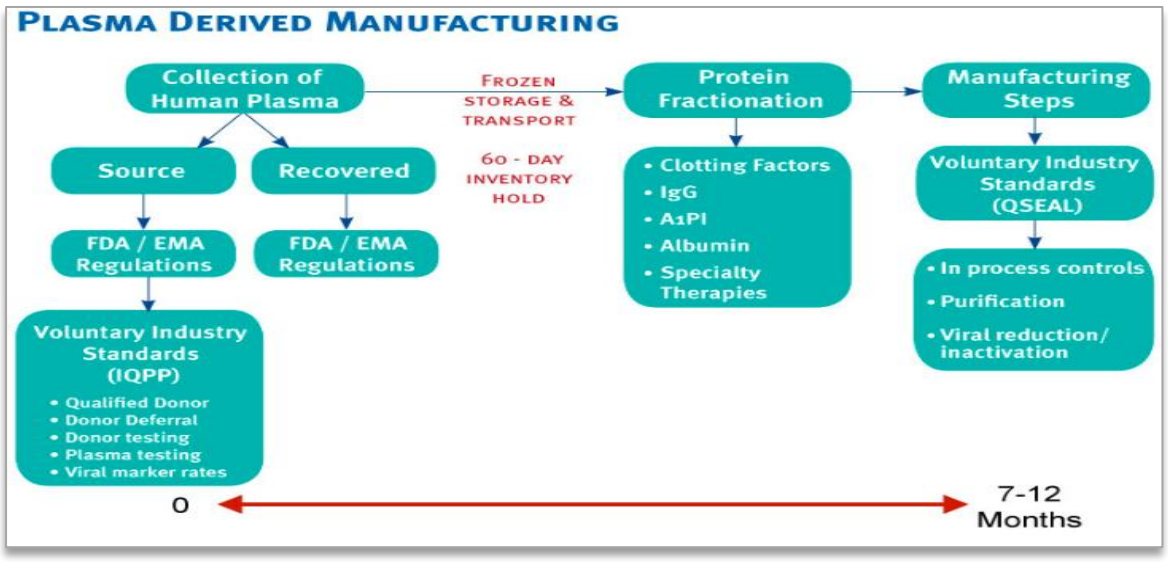


Fig 10.: This figure indicates the timeline and various activities required in the manufacturing process

Preparing a therapy often takes from seven to twelve months between donation and final product release. Continuous improvements to increase yield and throughput are important factors in the therapeutic plasma protein manufacturing environment, as is the adoption of new technologies. Most of the larger manufacturers conduct fractionation and purification processes on fractions equivalent to pooled plasma volumes of 3,000 liters - 20,000 liters

Over the years, the Cohn fractionation process was improved and complemented by new technologies in order to maximize production yields

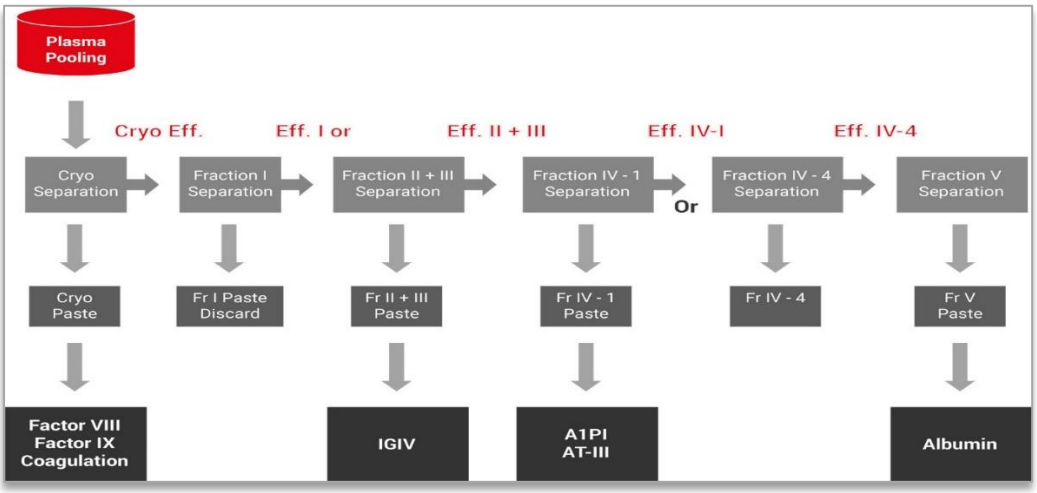


Fig 11.: This figure indicates the various steps to extract various components of plasma

No. of Fraction	% Protein	Components
I	5-10	Fibrinogen
		Clotting factor VIII
II+III	25	IgG
		IgA
		IgM
IV-1	5-10	α-and β-globulins
		α_1-antitrypsin
		Antithrombin III
IV-4	5-10	Complement components
		Ceruloplasmin
		Haptoglobin
		Transferin
V	50-60	Albumin

Fig 12.: This figure indicates the percentages of the main proteins in different fractions

Fractionation

Validated dedicated steps inactivate and/or remove infectious agents potentially present in the starting plasma pool

In Cohn's method of fractionation, five fractions could be obtained by the adjustment of pH, the concentration of ethanol, ionic strength, temperature, and concentration of protein

Over the years, the Cohn fractionation process was improved and complemented by new technologies. Using chromatography processes to purify specific proteins, the industry has significantly increased production yields, in particular Intravenous Immunoglobin

More recently, some companies, such as Prometic and Evolve Biologics are using ligands to extract and purify plasma proteins achieving higher yields, but they have not yet introduced any product on the market. Companies continuously endeavor to maximize their production yields so as to get the most from human plasma and generate more revenues from a liter of plasma. This sophisticated industrial process is performed under highly hygienic conditions in licensed facilities (plasma fractionation plants) that are operated in compliance with good manufacturing practices and following quality assurance principles

Around 85% of plasma fractionated worldwide is obtained by source plasma. CSL Behring, Takeda and Grifols dominate world's plasma fractionation market with 75% share

Fig 13.: This figure indicates in litres the amount of plasma being sourced from different part of the world.

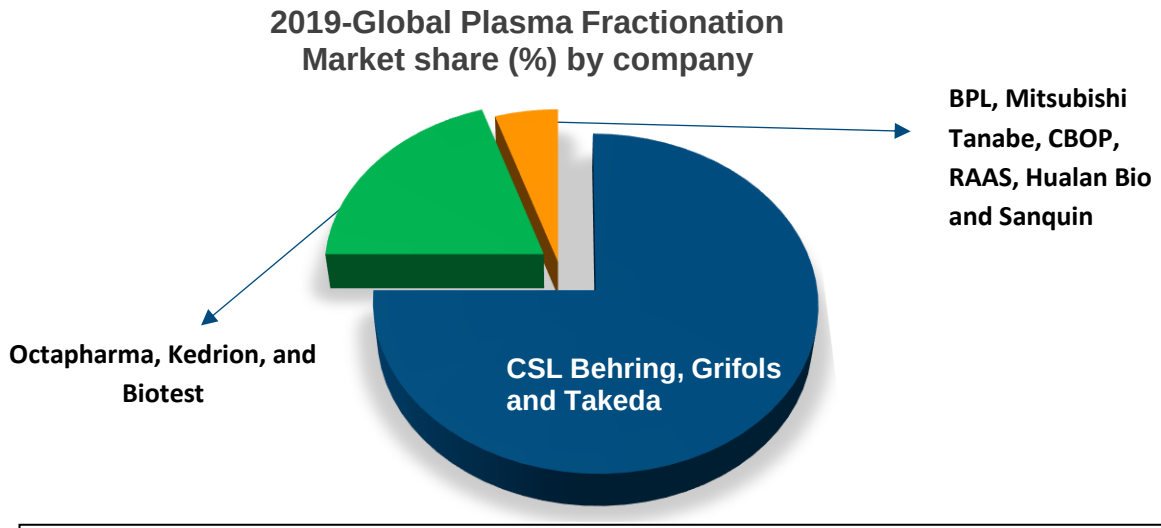


Fig 14.: This figure indicates global plasma fractionation market share by percentage for companies

85% of the plasma fractionated worldwide is obtained by source plasma and the rest is the recovered one

U.S. commercial blood establishments supply the largest proportion of the source plasma used for fractionation

For the year 2018, total source plasma (SP) collections for fractionation in U.S. - 48,721,545 L and in EU – 2,888,390 L

For the year 2017, Europe has the highest portion of recovered plasma (RP) been fractionated. Despite of huge collection of RP, Europe is dependent on U.S. source plasma

In Thailand, 28,334 liters of recovered plasma is collected for fractionation in 2015 and 108,193 liters in 2018

The three dominating plasma fractionation companies in the world are CSL Behring, Grifols Therapeutics and Takeda with a 75% of the market - roughly 25% or 10 million liters of yearly fractionation capacity for each one; A second tier of companies, including Octapharma, Kedrion, and Biotest account for a further 8 million liters of plasma fractionation capacity

Nowadays millions of liters of plasma are fractionated in one year with an estimated global business worth $30.9 billion by 2024 including a CAGR of 6.9% in the forecast period 2019 to 2024

2.10 Plasma Industry Economics and Supply Chain

Higher production costs of plasma industry is majorly due to the involvement of large work force, complex logistics, strict regulations and donor compensation

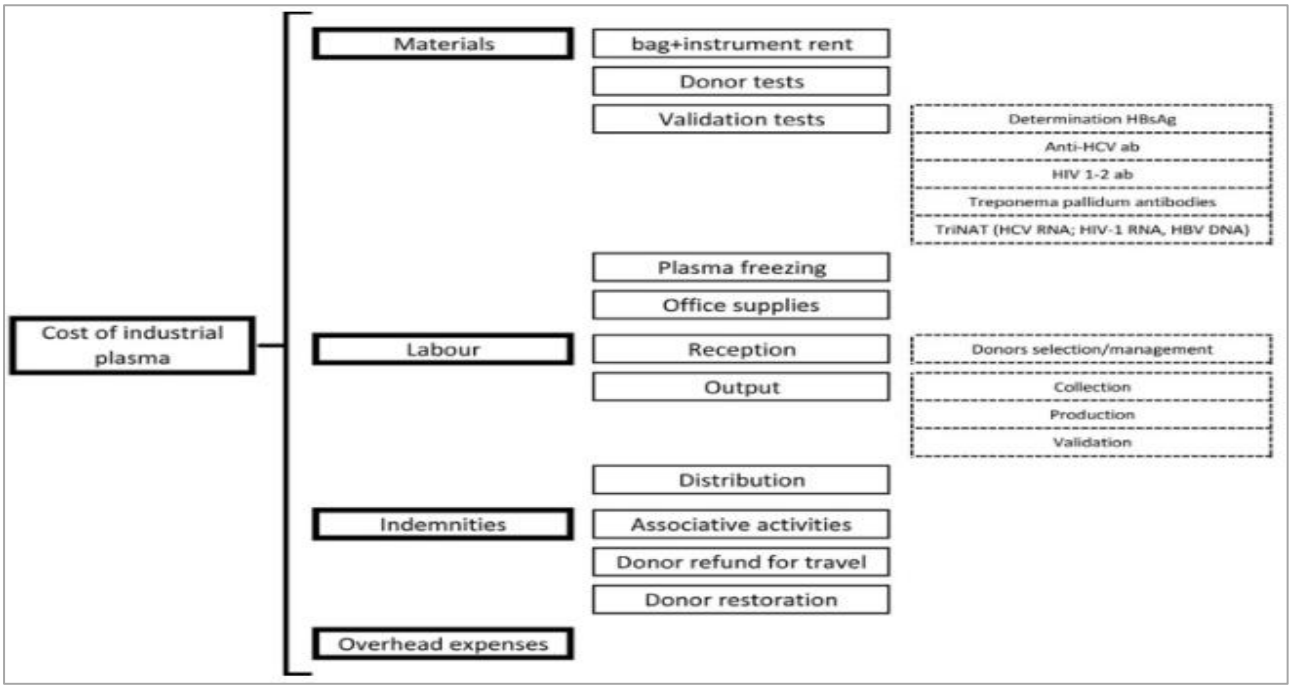


Fig 15.: This figure shows the major cost incurring points in plasma production and manufacturing

Plasma Industry Economics

It is generally estimated that plasma, the raw material, represents roughly 50% of the total cost to produce plasma-based therapeutic proteins

Plasma is expensive because collecting plasma is a complicated and delicate operation, involving a large work force due to the need to collect plasma from thousands of people

Components of this cost include plasmapheresis equipment and highly qualified staff, donors must donate plasma frequently and many donors are needed by the companies, complex logistics, strict regulations, and donor compensation

The commercial sale of all the major products obtained from 1 liter of plasma generates around US$ 696 in 2019

Therefore, a fully operational mid-size plasma fractionation plant processing 35 tons of plasma per week on a 46-week production schedule would generate US$ 1,120 million every year. The Blood Plasma Market which includes product, application and region is expected to exceed more than US$44.0 billion by 2024 at a CAGR of 9.3% in the given period

Different blood plasma supply chains: In countries like U.S., the plasma supply is collected, processed and distributed by private industry whereas in most of Europe, Pacific countries, plasma supply is controlled by government owned blood establishments

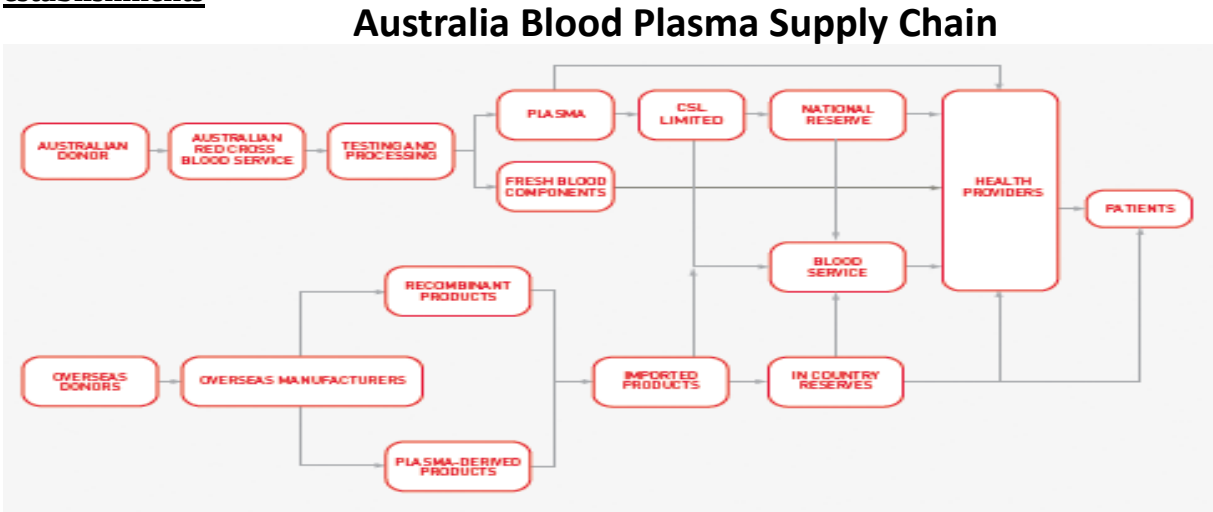


Fig 16.: This figure indicates the journey of donated plasma in Australia from donor to patient

In Australia, the National Blood Authority (NBA) manages the national planning and purchasing of blood and blood products

- Australian Red Cross Blood service collects plasma and delivers it to CSL Limited for manufacture of PDPs
- **For the year 2018, Australian Red Cross blood service has delivered 675.3 tons of plasma to CSL for fractionation for use in plasma products**

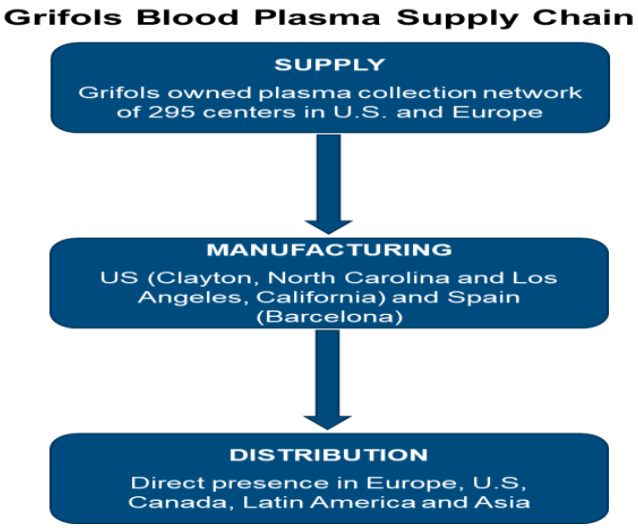


Fig 17.: This figure indicates how Grifols a U.S and Europe based firm manages its supply, manufacturing, and distribution.

2.11 Global regulatory system for plasma fractionation

U.S. regulations permit more frequent donations and greater total volume withdrawn per year than other countries within a favorable regulatory climate

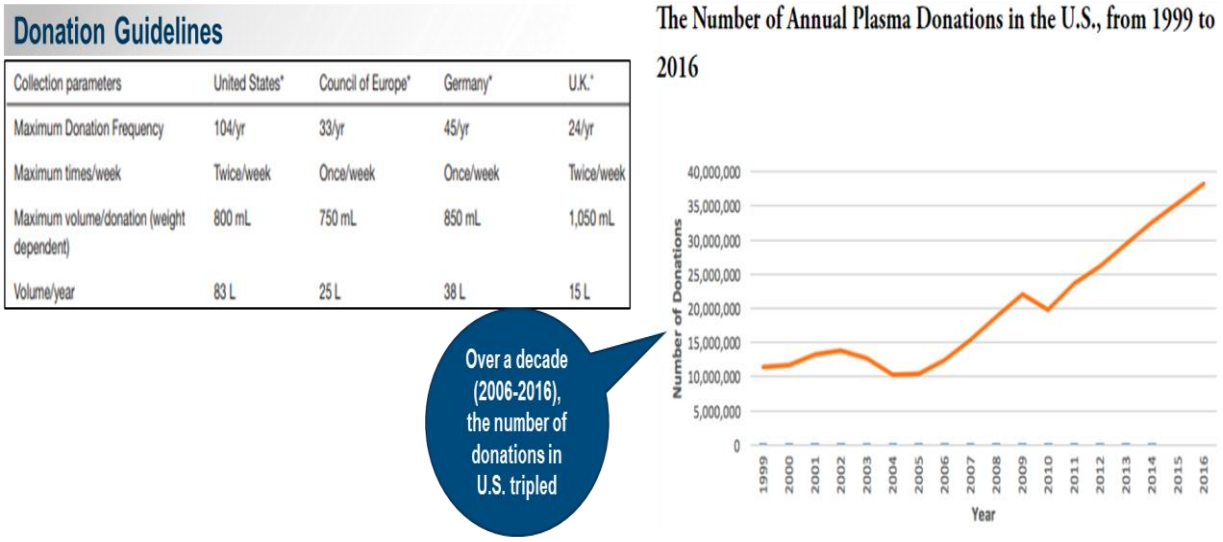


Fig 18.: This figure indicates the guidelines in various countries and in increase in plasma donation in the U.S. from 1999 to 2016

U.S. blood and plasma are collected, processed and distributed by private industry that is regulated by the FDA under two national laws: the Public Health Service (PHS) Act, and the Federal Food, Drug and Cosmetic (FD & C) Act and European Medicines Agency (EMA) regulates in Europe

Donors eligible to donate plasma for fractionation are individuals who meet donation criteria (such as age and donation frequency), do not present risk factors of blood-born infectious agents, and comply with requirements defined by the plasma fractionator and the NRAs of the country of plasma collection and of use of the products

Special criteria may exist for the collection of hyperimmune plasma (used to make hyperimmune IgG preparations), such as procedures for donors' immunization and minimal antibody titer

U.S. regulations permit more frequent donations and greater total volume withdrawn per year than other countries

The leading nations allowing remunerations are USA ($30-50), Germany ($30), China (ranging from several dollars, along with paid leaves for employees and credits for college students), Austria ($28), certain provinces of Canada ($30-50) and Russia ($5.5/plasma donation if donated 60 times annually)

Several countries, including Austria and Germany have adopted more flexible rules that enable them to collect more plasma than other European countries

Additionally, in contrast to most European countries, the U.S. does not regulate marketing activities and incentives to recruit and retain plasma donors

The European standards for temperature of freezing have become industry standards for both source plasma and recovered plasma as stringent European parameters are science-based

U.S. standards for components of plasma for fractionation

Processing elements	Source plasma	Recovered plasma
Collection method	Plasmapheresis	Whole blood or apheresis
Time from collection to freezing	immediately	Undefined
Freezing conditions, temperature	≤–20 °C	Undefined
Storage expiration	≤–20 °C, 10 yr	Undefined
Shipping temperature	≤–5 °C	Undefined
Allowable deviation	Can exceed <–20 °C for <72 hr total; never >–5 °C, always frozen	Undefined

EU standards for components of plasma for fractionation

Processing elements	European Pharmacopoeia			Council of Europe	
Purpose	Labile proteins for fractionation	Non labile protein for fractionation		For transfusion	
Collection method	Plasmapheresis or plasma from whole blood	Plasmapheresis	Plasma from whole blood	Whole blood plasma	Apheresis
Time from collection to freezing	≤24 hrs	≤24 hrs	≤72 hrs	≤18 hrs (≤6 hrs optimal); if 20–24 °C, then ≤24 hrs	≤6 hrs; if 20–24 °C, then ≤24 hrs
Freezing conditions, temperature	Frozen to a core temp of ≤–25 °C in ≤12 hr	Chamber at ≤–20 °C		To <30 °C within 1 hr	
Storage	≤–20 °C			If –18 to –25 °C, 3 months; if <–25 °C, 36 months	
Shipping temperature	≤–20 °C			–18 to –25 °C for 3 months storage; <–25 °C, for 36 months storage	
Allowable deviation	Exceeds –20 °C not more than 72 h total; one time >–15 °C; never >–5 °C			None	

Fig 20.: This figure indicates EU standards for components of plasma for fractionation

Source plasma and recovered plasma must meet standards of collection, freezing, storage, and shipping

The European standards for temperature of freezing have become industry standards for both source plasma and recovered plasma, which is one factor that makes Plasma for fractionation derived from these plasmas suitable for marketing in Europe as well as the U.S.

Placing Source Plasma in the freezer "immediately after filling" is a more problematic requirement

Separating plasma from cells by plasmapheresis and freezing it rapidly is the optimal way to preserve protein activity and recovery

This requirement, however, limits the ability of non-commercial blood establishments to collect apheresis plasma for manufacturing on mobile units because mobile units often cannot return to a central facility in time to freeze plasma

Although recovered plasma does not have any required standards in practice, most blood facilities in the U.S. follow the European Pharmacopoeia standards for recovered plasma

Countries that are in the process of developing a national blood program could benefit from taking some aspects of the U.S. regulatory approach to expand their donor base of source plasma for manufacturing, beyond aiming to accept plasma only from voluntary unpaid donors (VUDs)

- Source plasma from paid U.S. donors will continue to be the major source of Plasma for Fractionation (PF) for many years to come
- The voluntary standards of the fractionation industry significantly enhance the minimal requirements of the FDA
    - These voluntary standards are measures to recruit and keep healthy donors, and to exclude those who are intent on gaming the system. Although paid Qualified Donors of Source Plasma still have a modestly higher prevalence of transmitted infections than VUDs, their donations will not compromise the safety of PDPs because of the overwhelming effectiveness of viral clearance in the manufacturing of PDPs
- In addition to the stringent regulations and good manufacturing procedures imposed by healthcare regulatory agencies, Plasma Protein Therapeutics Association (PPTA) sets and monitors certain additional voluntary standards which further document the safety and quality of plasma collection for both the plasma donor and the receiving patient

Challenges faced in plasma industry due to stringent regulations on donations

In most countries, the collection of blood is reliant on voluntary blood donors, and it is not remunerated for. Many of these countries are importers of plasma from those few countries that allow remunerating plasma donors

Canada bans source plasma collections from compensated donors in all but two provinces based on a decades-old perception that plasma from such donors is not without certain risks

In Europe, some countries believe that plasma from compensated donors is not safe and plasma for therapies should only come from recovered plasma from uncompensated donors. Yet these same countries import therapies made from U.S. source plasma

Current European regulations require at least one physician on site to provide medical expertise as well as donor oversight, evaluation, and management. These positions are generally difficult to fill, mainly due to the numerous competing career paths for new physicians

The consequences of a lower number of physicians means limitations on plasma center operations and may reduce opportunities for people to donate in European countries

Many variables could be impacting patient access to therapies, including growing clinical need, global regulatory policies, issues with distributors and/or manufacturers, as well as physician, hospital, or pharmacy protocols

Overreliance on one source like the United States for plasma exposes the supply chain to significant risks. Europe is a significant importer of plasma, and it has been suggested that plasma collection within the region must be increased to mitigate the supply chain risks.

PESTEL Analysis of Plasma Industry

- **Political**:
    - Governments all over the world are encouraging submissions from the industry in technological as well as operational aspects.
    - Government and private organizations support blood donation camps and programs to meet the rising demand of plasma

- **Economical**:
    - The Blood Plasma Market is expected to exceed more than US$44.0 billion by 2024 at a CAGR of 9.3% in the given forecast period
    - Sales of blood therapeutics were $30.9 billion in 2017. By 2024, these products will reach $57.5 billion, reflecting a five-year CAGR of 8.2%
    - High complexity and cost associated with the collection of blood plasma
    - Preparing a therapy often takes seven to twelve months, between donation and final product release

- **Social:**
    - An increase of 11.6 million blood donations from voluntary unpaid donors from 2008 to 2015 has been reported by 139 countries. The highest increase of donations is in the South-East Asian Region (83%) and the Americas (70%)

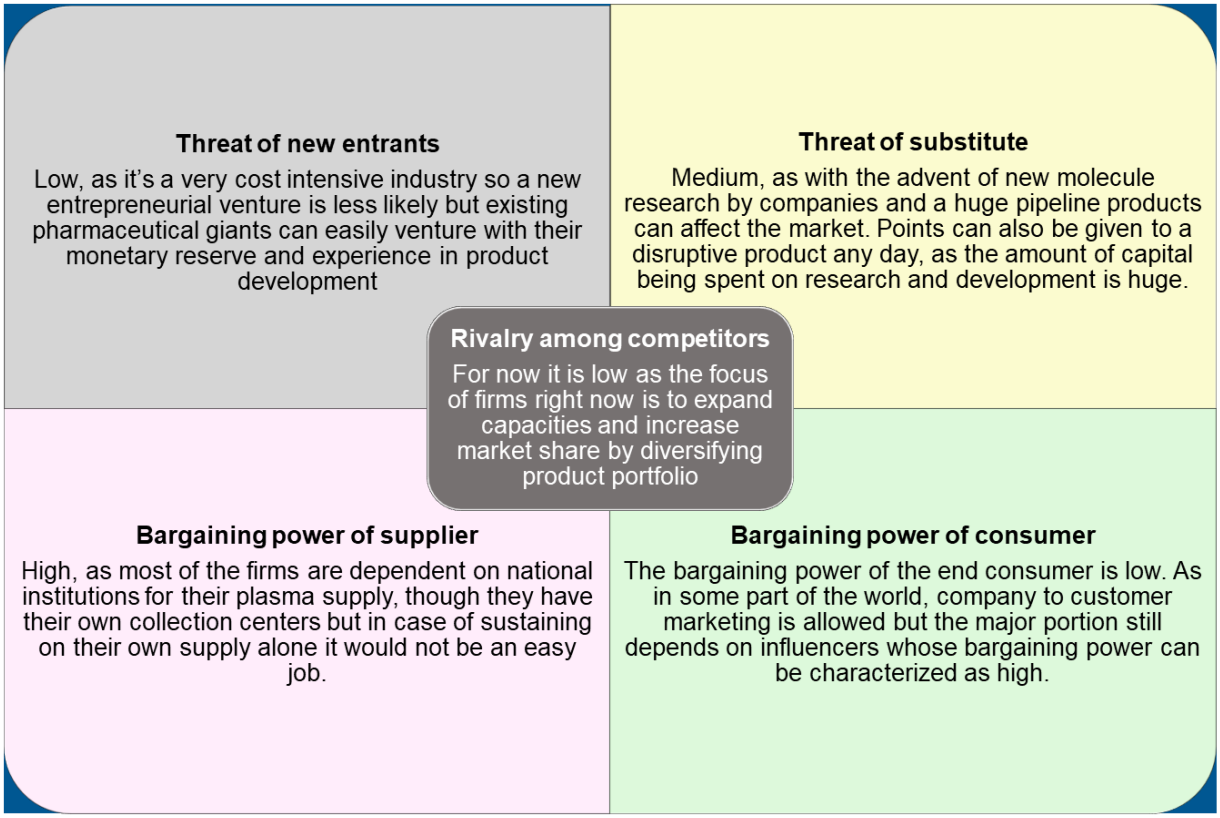
- About 78 countries collect more than 90% of their blood supply from voluntary unpaid blood donations
- Initiatives to raise awareness of the unique nature of plasma protein therapies and the value they provide to patients

- **Technological:**
  - A new red blood cell testing technology aimed at patients with illnesses that require frequent transfusions
  - FDA laboratory is evaluating this new technology which identifies the genetic characteristics of a patient's red blood cells so they can be more precisely matched to a donor
  - Companies are working to develop oxygen carriers that could substitute for red blood cells

- **Environment:**
  - Holding plasma, freshly harvested from Citrate phosphate dextrose (CPD)-whole blood, at ~ 4°C for up to 24hrs before freezing at -20°C for 4 months was shown to induce close to 25% loss of FVIII activity compared to plasma frozen immediately
  - Can be environmentally very toxic if spilled or not managed properly
  - Donated blood or plasma can have infectious pathogens. So, having proper discarding process is of utmost importance

- **Legal**:
  - It’s one of the heavily regulated industry both at national and international level
  - Stringent regulatory standards on the import and export of plasma product

Porter's five forces



2.12 Overview of key players in the plasma industry

CSL together with Grifols currently hold more than 50% share in the global plasma market. Other key players are Takeda, Octapharma, etc..

CSL holds 1st position with ~37% share in the global plasma market

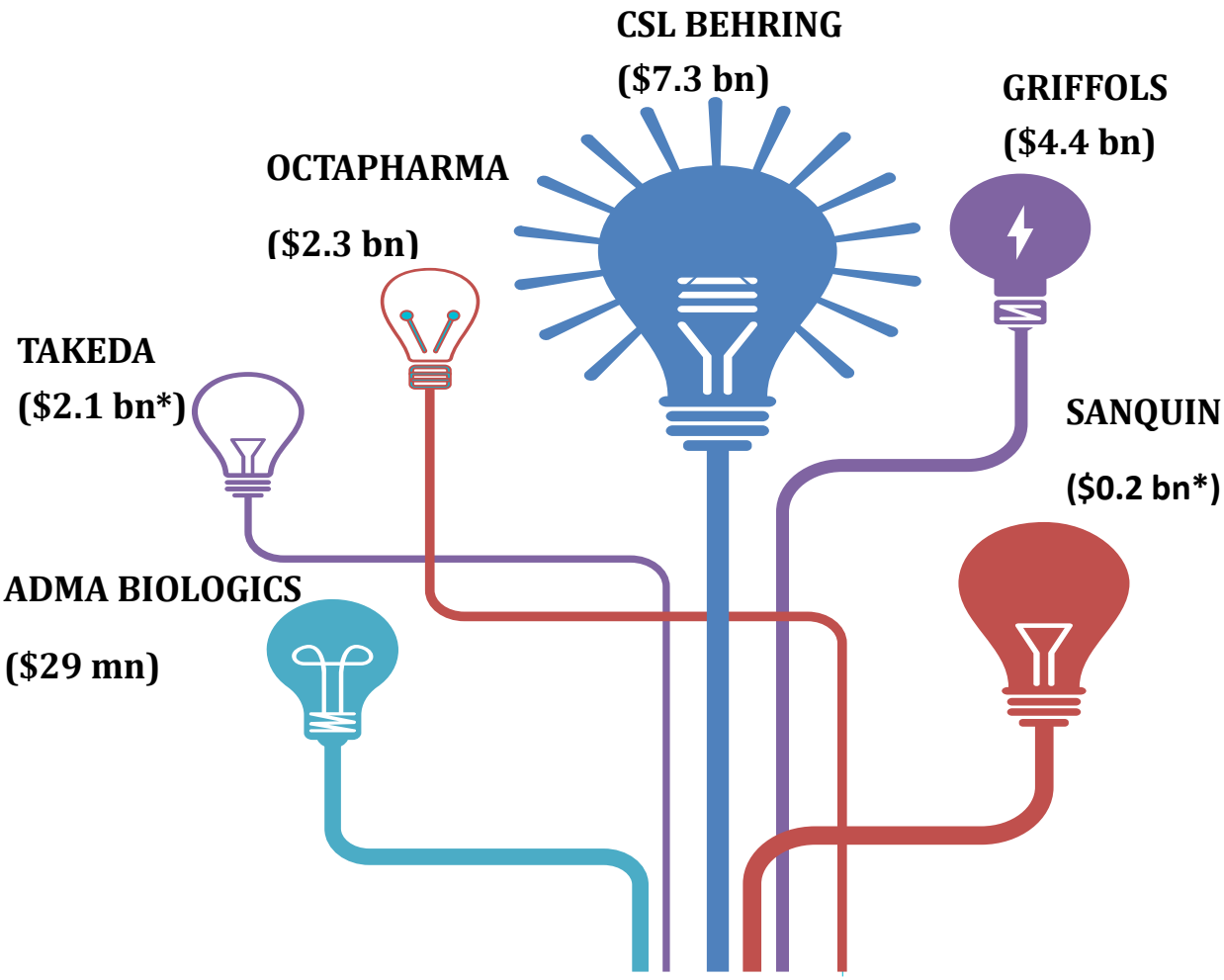


Fig 21.: This figure indicates major players in the plasma industry according to market share

1. *CSL Behring*

CSL holds 1st position with ~44% share in the global plasma market

CSL Behring is a biopharmaceutical company, manufacturing plasma-derived and recombinant therapeutic products and related services

Company Overview

CSL Limited was incorporated in 1991 and listed on the Australian Securities Exchange (ASX) in 1994 with specialization in the treatment of rare and serious diseases such as Immunology and Neurology, Hematology and Thrombosis, Cardiovascular and metabolic, Transplant, Respiratory and Vaccines

CSL Plasma a subsidiary of CSL Behring, is the largest collector of human blood plasma in the world, sourcing plasma from hundreds of thousands of donors globally to produce a range of life-saving medicines for critically ill patients.

Pipeline Product Portfolio

Research/Pre-clinical: Improved Fibrinogen, CSL787 Nebulised Ig, P. gingivalis POD* OH-CRC, Discovery Projects

Clinical Development: Hizentra®, Privigen®, HAEGARDA®, CSL730, CSL312 anti-FXIIa, CSL334 IL-13r, CSL324 anti-G-CSFr, Mavrilimumab anti-GM-CSFr, CSL889 hemopexin, CSL200, CSL630, CSL312, CSL311 anti-beta common, CSL346 anti-VEGF-b, CSL112 Apo-A1, CSL964, CSL842 C1-INH AMR, Clazakizumab Anti IL-6 Vitaeris

Registration/Post-Launch: Hizentra® CIDP, Privigen® PID, Privigen® CIDP, CSL830 C1-INH Subcut, Haegarda®, Kcentra®, Idelvion®, Afstyla®, Zemaira®

Leadership Team

Paul Perreault

CEO and Managing Director

David Lamont

Chief Financial Officer

Andrew Cuthbertson

Chief Scientific Officer and R&D Director

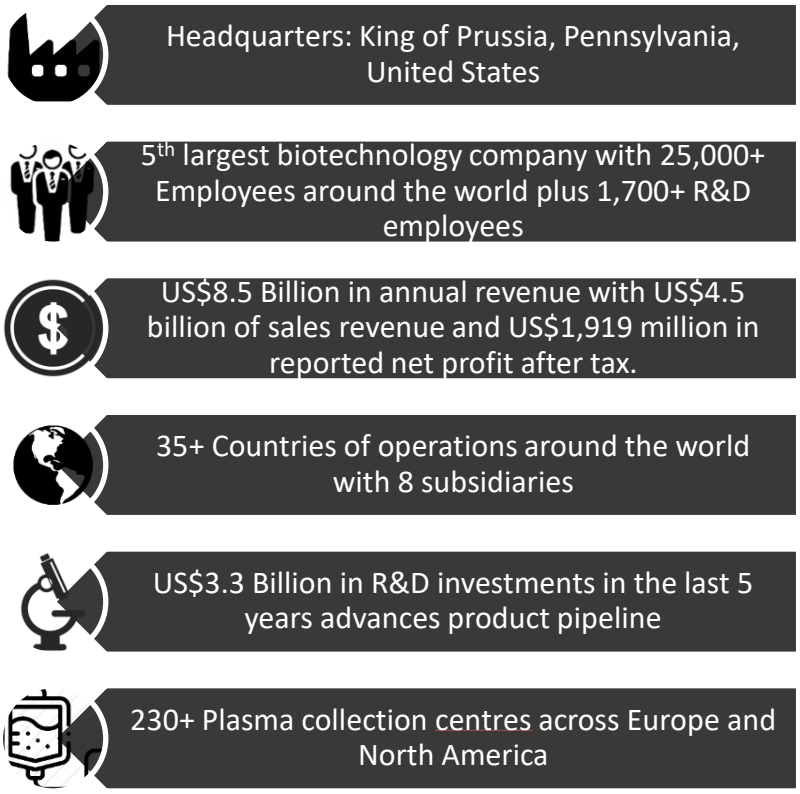


Fig 22.: This figure indicates the summary of CSL Behring's company profile.

Inline Products Portfolio

Fig 23.: This figure indicates the inline products portfolio for CSL Behring

CSL Behring Worldwide Locations

CSL Behring is planning to open ~40 new plasma collection centers in FY-2020

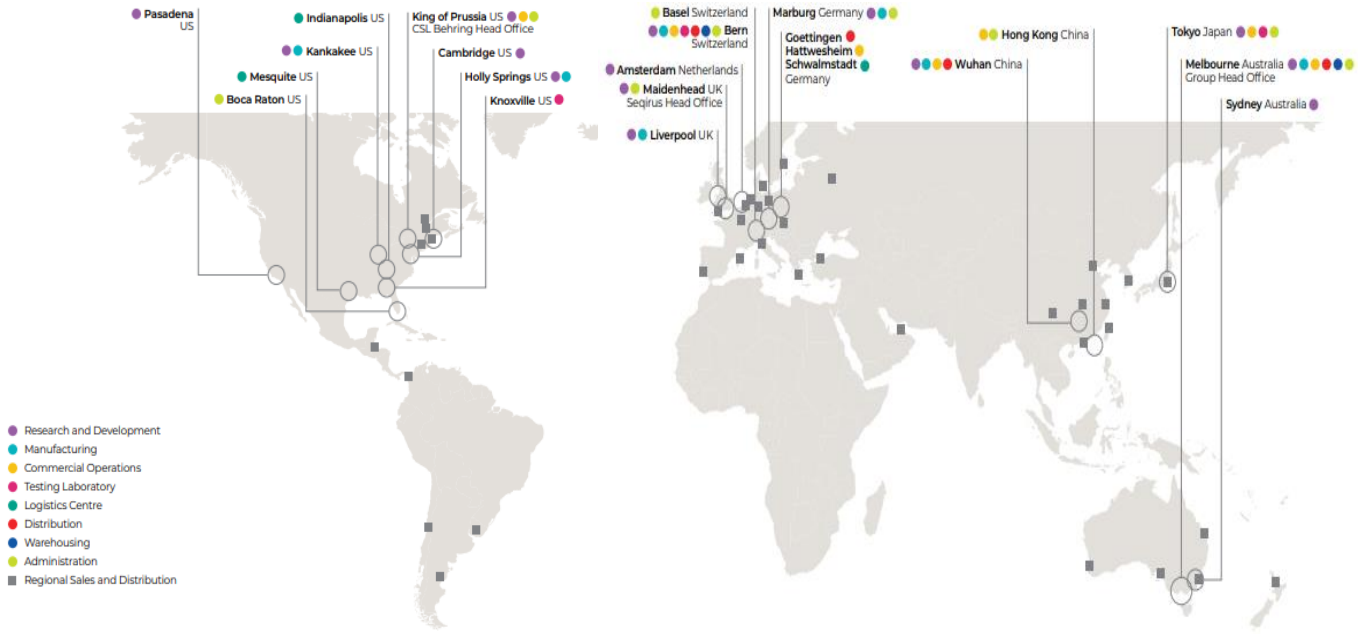


Fig 24.: This figure indicates global presence of CSL Behring's plasma collection centres

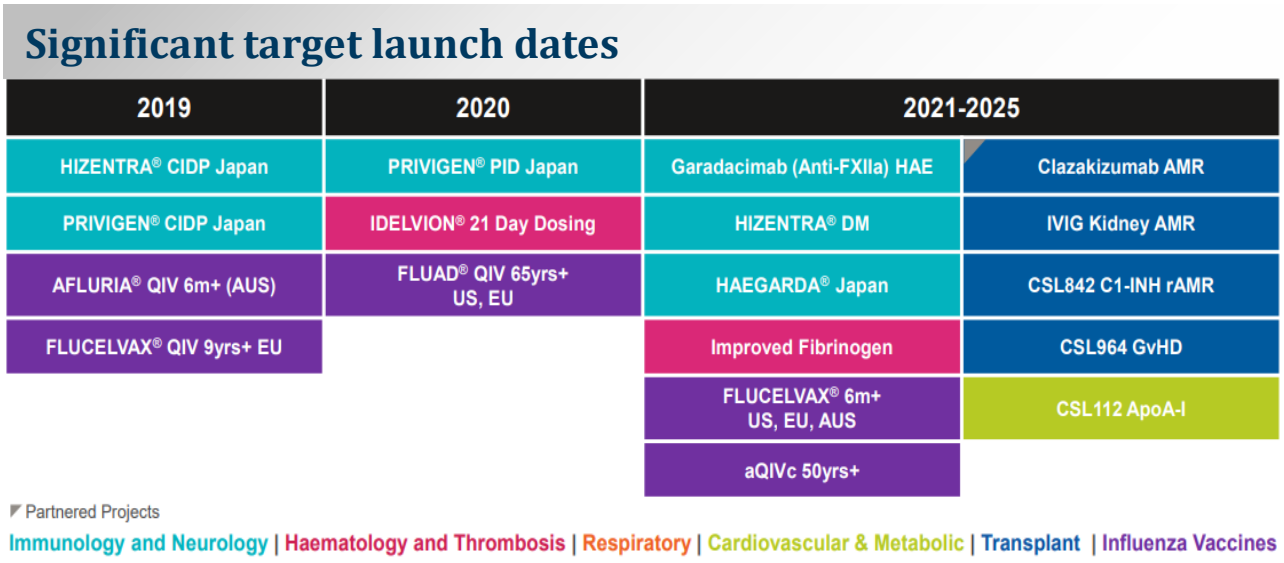


Fig 25.: This figure indicates upcoming launch dates for significant products

Plasma Sourcing

- CSL Behring opened 30 new plasma collection centers in US
- Total plasma collection centers – 221 in the US, 8 in Germany, 3 in Hungary and 5 in China
- Planning to open ~40 new centers in FY20
- Liquid saline & sodium citrate facility purchased in South Carolina US to support plasma collection
- A substantial 5,000m2 expansion of the Bio21 Institute in Parkville, Australia, incorporating CSL's Global Hub for Research and Translational Medicine was officially opened in December 2018
- CSL continues the base fractionation capacity expansion projects across their facilities in Broadmeadows, Kankakee and Marburg to meet the future global demand for their products by expanding production capacity and supporting end to-end manufacturing of plasma-derived therapies
- In order to meet the high demand for immunoglobulin products, CSL Behring is expanding its production capacity in Bern by investing CHF 300 million in the project which has created around 50 new jobs in the city of Bern

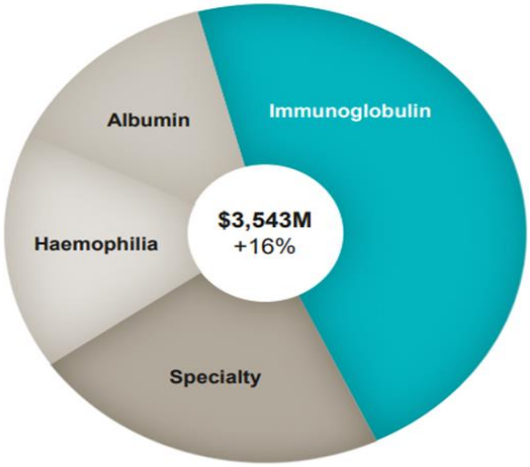


Fig 26.: This figure indicates CSL Behring's business share according to main plasma proteins.

2. Grifols Biosciences

Grifols holds 2nd position in plasma market with ~27% market share

Grifols Biosciences division (plasma-derived medicine production) leads 78% of their total revenue:

Company Overview

Since 1909, pioneer in the field of the plasma science and is one of the largest plasma companies with a growing network of donation centers worldwide

Grifols main research areas are Transfusion Medicine, Immunology, Pulmonology, Hepatology, Hematology, Neuroscience, Critical Care

The Bioscience Division is a leading producer of plasma-derived medicines for the treatment of rare, chronic and sometimes life-threatening conditions

Grifols enters a strategic alliance with Shanghai RAAS to boost growth of its plasma-derived products and diagnostic solutions in China. Under the agreement, Grifols controls a 26.2% stake in Shanghai RAAS (economic and voting rights) in exchange for a non-majority share (45% economic and 40% voting rights) in Grifols Diagnostic Solutions (GDS)

Pipeline Product Portfolio

Clinical Development: Albutein - Acute-on-chronic liver failure, Liver Cirrhosis; Alphanate- Hemophilia A; Immunoglobin- Myasthenia Gravis; IV Fibrinogen; Thrombate- Cardiopulmonary bypass; VistaSeal for Pediatrics

Registration/Post-Launch: Albumin in bags, Plastem, SC Immunoglobin

Leadership Team

Joel Abelson

President, Bio-Science division

Carsten Schroeder

President, Diagnostics Commercial Division

Rob Jagt

President, Hospital Commercial Division

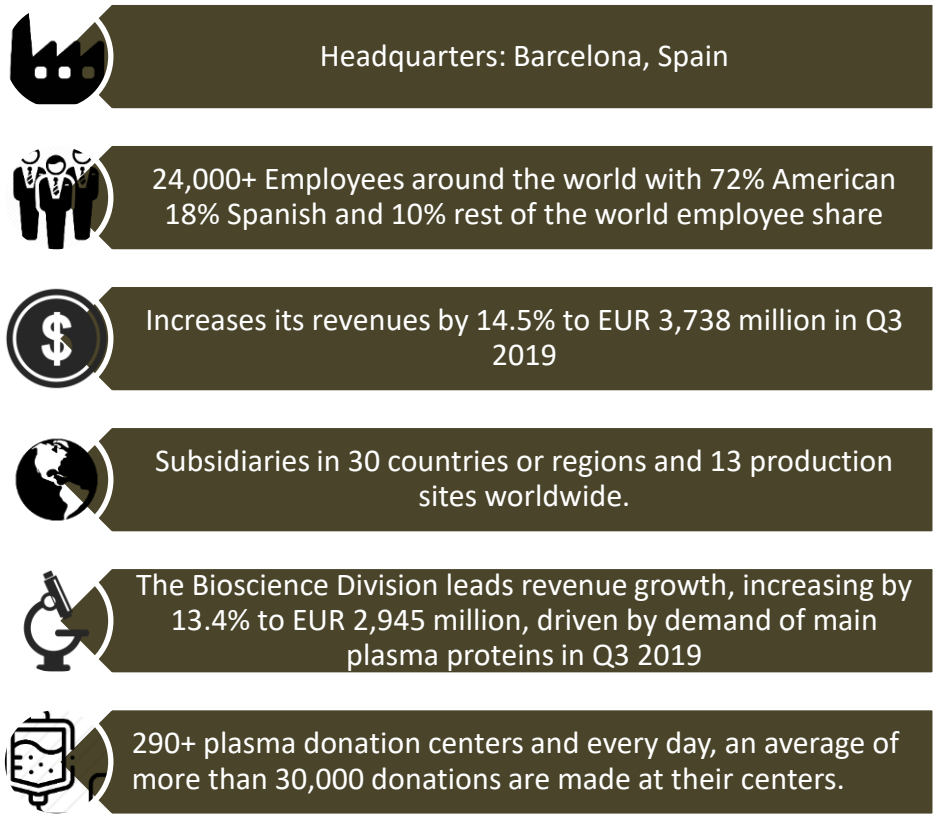


Fig 27.: This figure indicates the summary of Grifols' company profile.

Inline Products Portfolio

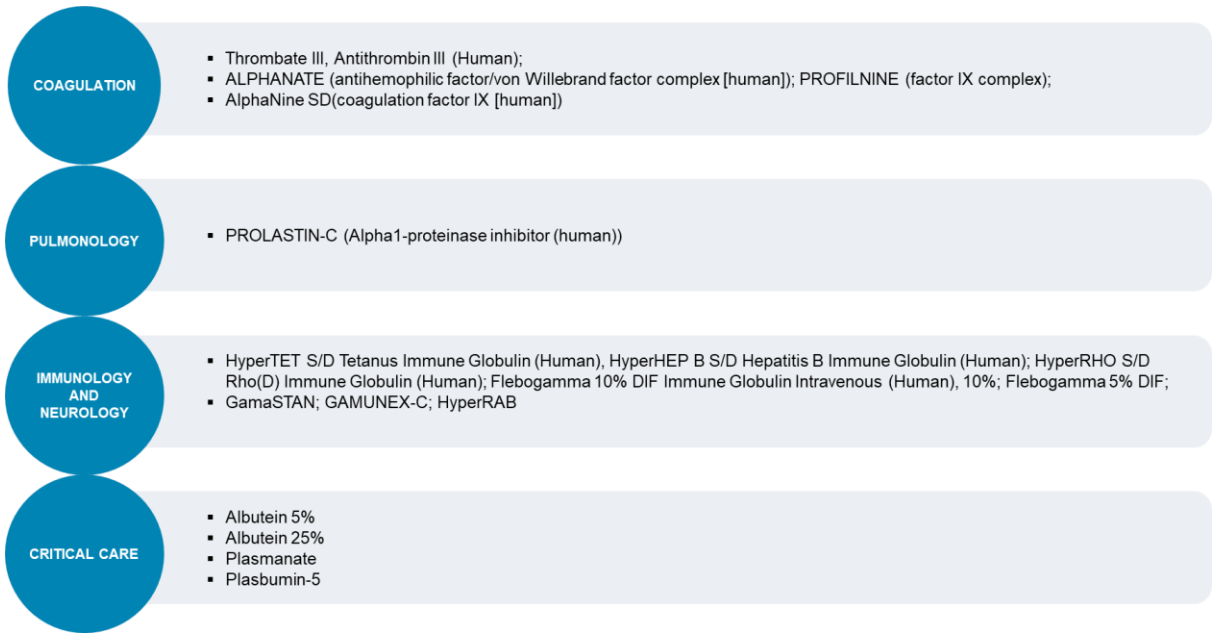


Fig 28.: This figure indicates inline products portfolio for Grifols

Fig 29.: This figure indicates the manufacturing units of Grifols'

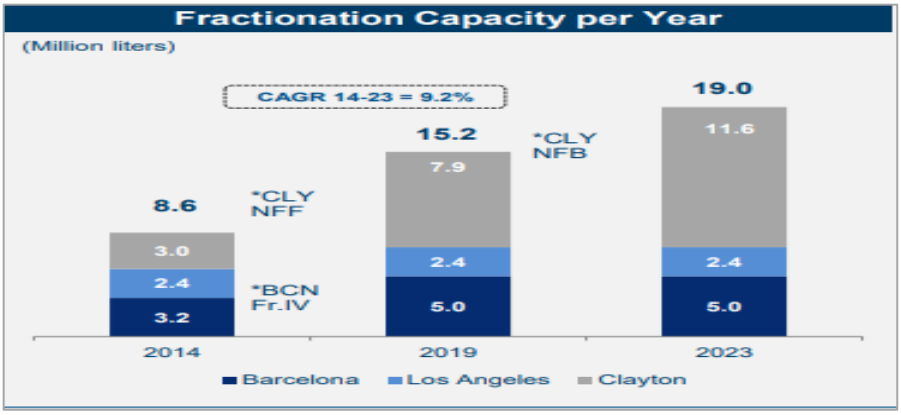


Fig 30.: This figure indicates increase in fractionation capacity of Grifols' plants

Fig 31.: This figure indicates Grifols' plasma donor centres worldwide.

There are five Grifols-owned state-of-the-art facilities, three in the US (Austin and San Marcos, Texas, and Memphis, Tennessee) , one in Germany (Berlin) and another one in Spain (Barcelona)

Four manufacturing plants:

A plasma fractionation plant in the US (North Carolina), expected to be operational by 2021

A purification plant for intravenous immunoglobulin in the US

Another plant for alpha 1-antitrypsin in Spain

Purification plant for albumin at the Grifols facilities in Dublin (Ireland) with capacity to produce between 130 and 150 million grams/year of albumin

Grifols expands in Latin America with start of production at new plant in Brazil with a capacity of more than 10 million blood collection bags annually, the more than 5,500-square-meter facility in Campo Largo, Brazil, will serve the Latin American region

Currently, global plasma collection network of 295 centers on two continents, 252 in U.S. and 43 in Europe; Will expand to approximately 370 by 2024.

At present, Grifols has a fractionation capacity of 15.2 million liters of plasma per year

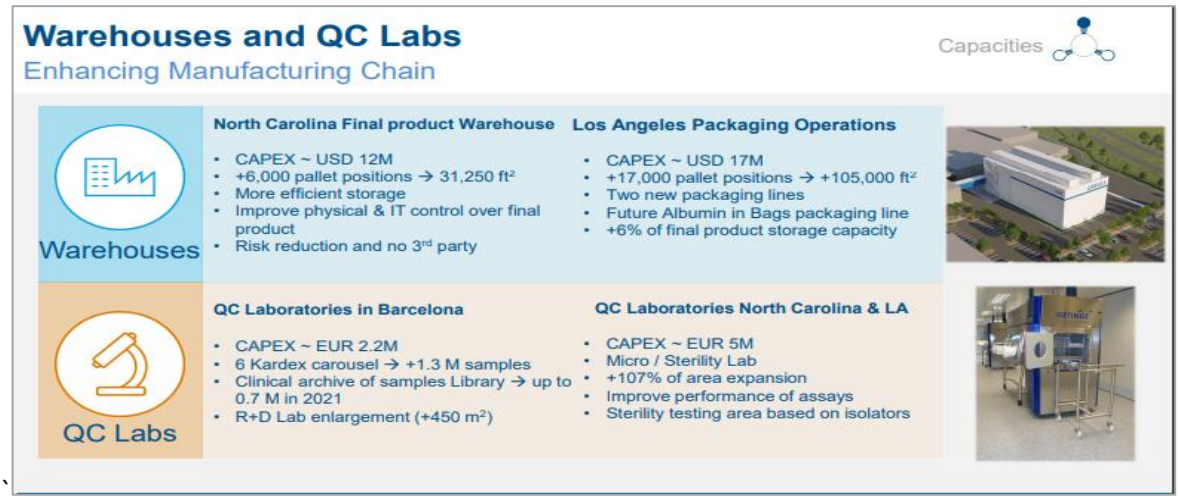


Fig 32.: This figure indicates manufacturing capabilities for Grifols'

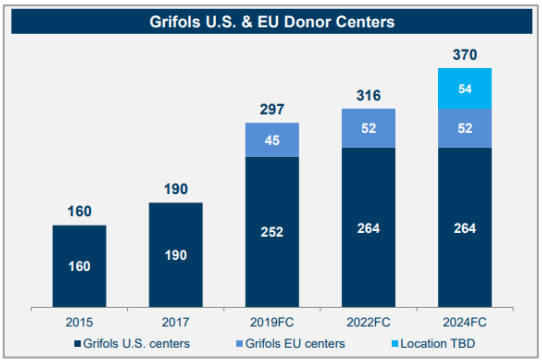


Fig 33.: This figure indicates increase in number of donor centres for Grifols'

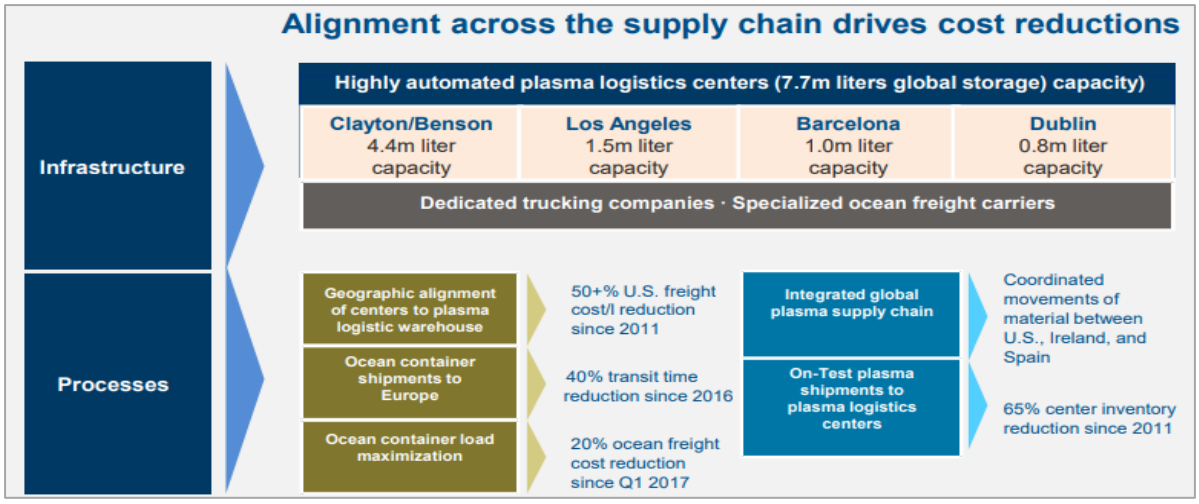


Fig 34.: This figure indicates the infrastructure and process capabilities

Grifols U.S. centers and warehouses currently operate with centralized release, enabling efficiencies in inventory management

Construction of the world's first purification, dosing and sterile filling plant of immunoglobulins in flexible bags. The plant will have an annual production capacity of 6 million equivalent liters of plasma and is expected to be operational in 2022

Plasma obtained have increased significantly, Grifols Plasma Volume Performance in Liters driven by improved processes, extension of hours, facility expansions, and acquisitions

Process efficiencies allow continuous incremental capacities: 3% fractionation capacity increase over 2018

Grifols increased its capacity to 45,000 average daily donations and total volume of plasma obtained for fractionation to nearly 15.2 million liters

3. Octapharma

Octapharma holds 3rd position with market share of ~14% in plasma industry

OCTAPHARMA, the largest privately owned and independent plasma fractionator in the world

Company Overview

They develop and manufacture medicines for patients in three therapeutic areas: haematology, immunotherapy, and critical care

Octapharma is a family owned global healthcare company since being established in 1983

Octapharma Plasma GmbH has 13 donation centres in Germany and helps to ensure an independent supply of plasma in Germany and the rest of Europe

Octapharma's clinical R&D sites are in Vienna, Austria; Lachen, Switzerland; and Hoboken, New Jersey, USA who are responsible for all their product trials and for the life-cycle management support of all their marketed medicines

Product Portfolio

Clinical Development:

Currently, they run over 15 ongoing interventional clinical studies

Presented an update on the clinical development plan and pre-clinical data with SubQ-8, a novel subcutaneous recombinant factor VIII (FVIII) in development, at the 27th International Society on Thrombosis and Hemostasis (ISTH) Congress in Melbourne, Australia, ISTH 2019

Leadership Team

Wolfgang Marguerre

Chairman and CEO, Octapharma Group

Frederic Marguerre

President Octapharma Plasma Inc. USA

Flemming Nielsen

President Octapharma USA Inc.

octapharma

Fig 35.: This figure indicates the summary of Octapharma's company profile.

Inline Products Portfolio of Octapharma

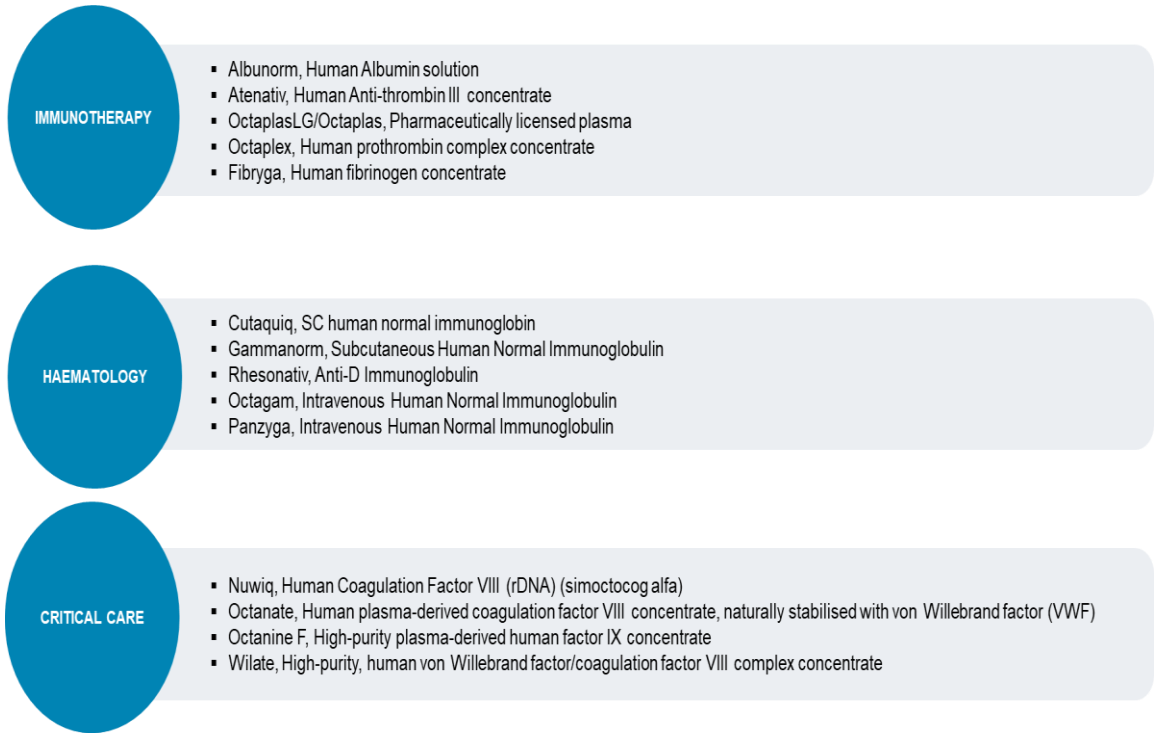


Fig 36.: This figure indicates inline products portfolio of Octapharma

Octapharma – Manufacturing Sites

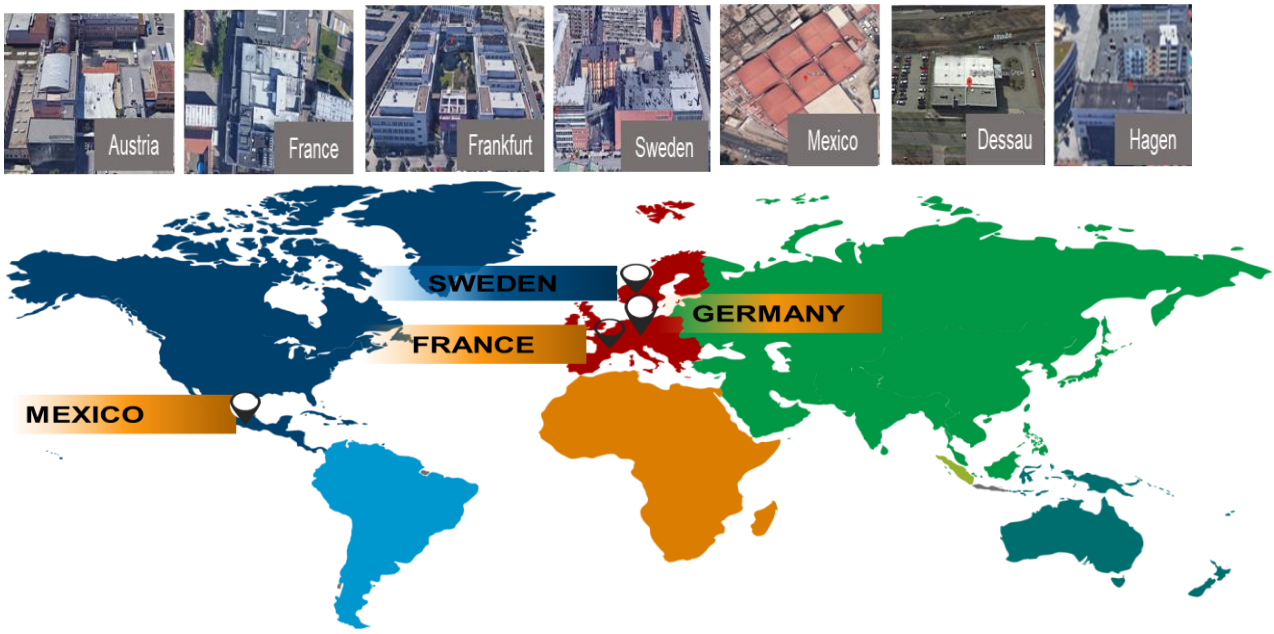


Fig 37.: This figure indicates the worldwide Octapharma manufacturing sites

<u>Plasma is central to Octapharma's business, with 80% of their supplies coming from company-owned donation centers</u>

Plasma fractionation process

A donation session takes 45-90 mins and 300-880 ml of plasma is taken for each donation with 61% of source plasma donors are male

Thawing is the first step to separate plasma in which the plasma is deep-frozen at -25° to -30°C. The cool rooms are warmed slowly up to -5°C to thaw the plasma. The plasma remains in the cool room for about 16 hours, then it is driven to pooling

The most important steps in the production of octaplasLG are the pooling and the virus inactivation

There are three poolings done per day i.e. approximately 5,250kg of plasma are processed, which equates to 6,000–18,000 single donations

After pooling, mass capture, cryoprecipitation, chromatography, centrifugation and precipitation take place to get the desired product

Octapharma Capacity Analysis

Annually, Octapharma processes greater than 6 m liters of plasma

Plasma is central to Octapharma's business, with 80% of their supplies coming from company-owned donation centers

18 pallets correspond to around 13,000 litres of plasma is transported by sea from USA to Germany

In Stockholm, they pool 600–1,500 individual plasma donations in an 800-litre stainless steel vessel and produce an average of 3,600 bags of octaplasLG, which is 780kg of plasma and takes 24hrs for the whole process

Vienna is the central plasma warehouse in Europe and receives 70% of the total plasma used by Octapharma

The plasma pool size in Vienna IS 3190kg. Nine plasma pools are produced every week

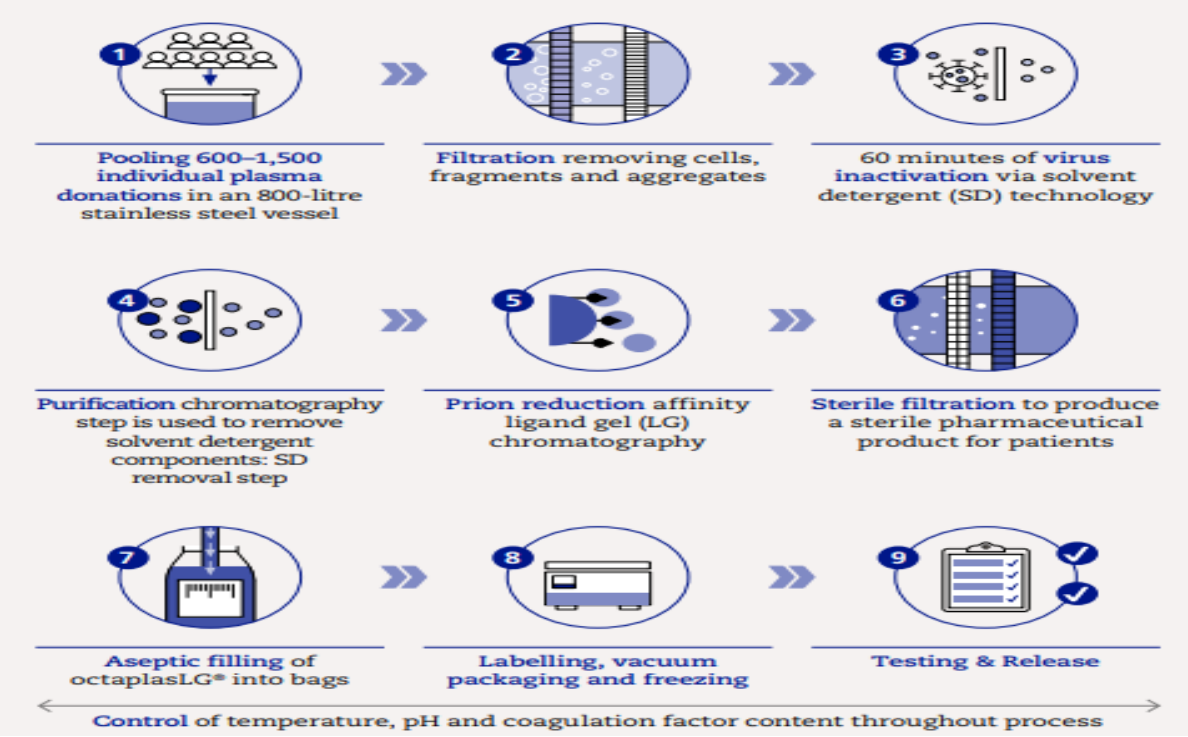


Fig 38.: This figure indicates Octapharma's manufacturing process from donation to recipient

Around 4,200 Octapharma Plasma, Inc.(OPI) employees navigate more than 20,000 donors across the USA every day

Plasma Transportation process

The donor provides plasma via an apheresis machine and is frozen and stored below -25 °C in a plastic bottle. It is recorded in a Donation Management System

Collected samples are sent for pathogen testing in different labs, including Octapharma Plasma Inc.'s Charlotte, N.C. (USA) laboratory

Plasma bottles of suitable donations are packed in cartons and stacked on pallets and transported by truck to a central warehouse in Kentucky (USA)

After a documentation check, the plasma pallets are loaded into a container and sent by truck to a port on the East coast, Norfolk, Virginia, USA

Approximately 6-9 Containers are transported every week from USA to Bremerhaven port in Germany by sea (journey time - 13 days)

The containers are transferred to a truck bound for the Vienna or Stockholm Octapharma sites

After customs clearance at Vienna (Austria), the truck arrives at the Octapharma Vienna plant or the external warehouse where the pallets of plasma are labelled, registered and moved to the main freezer warehouse in 25 mins by 4 or 5 staff

Around 60% of received plasma is transferred every week in temperature monitored trucks to other fractionation sites, such as Lingolsheim (France) and Springe (Germany)

In production, the plasma bottles are cut open and put into the thawing tank

Key Points from Leadership and Team

Jonathan and his team in North Carolina, USA, are responsible for the site selection process for new centers and Bill Griner, who runs the Operations and Marketing team plays a vital role

Around 4,200 Octapharma Plasma, Inc.(OPI) employees navigate more than 20,000 donors across the USA every day whereas 540 employees navigate more than 1,800 donors a day in Germany

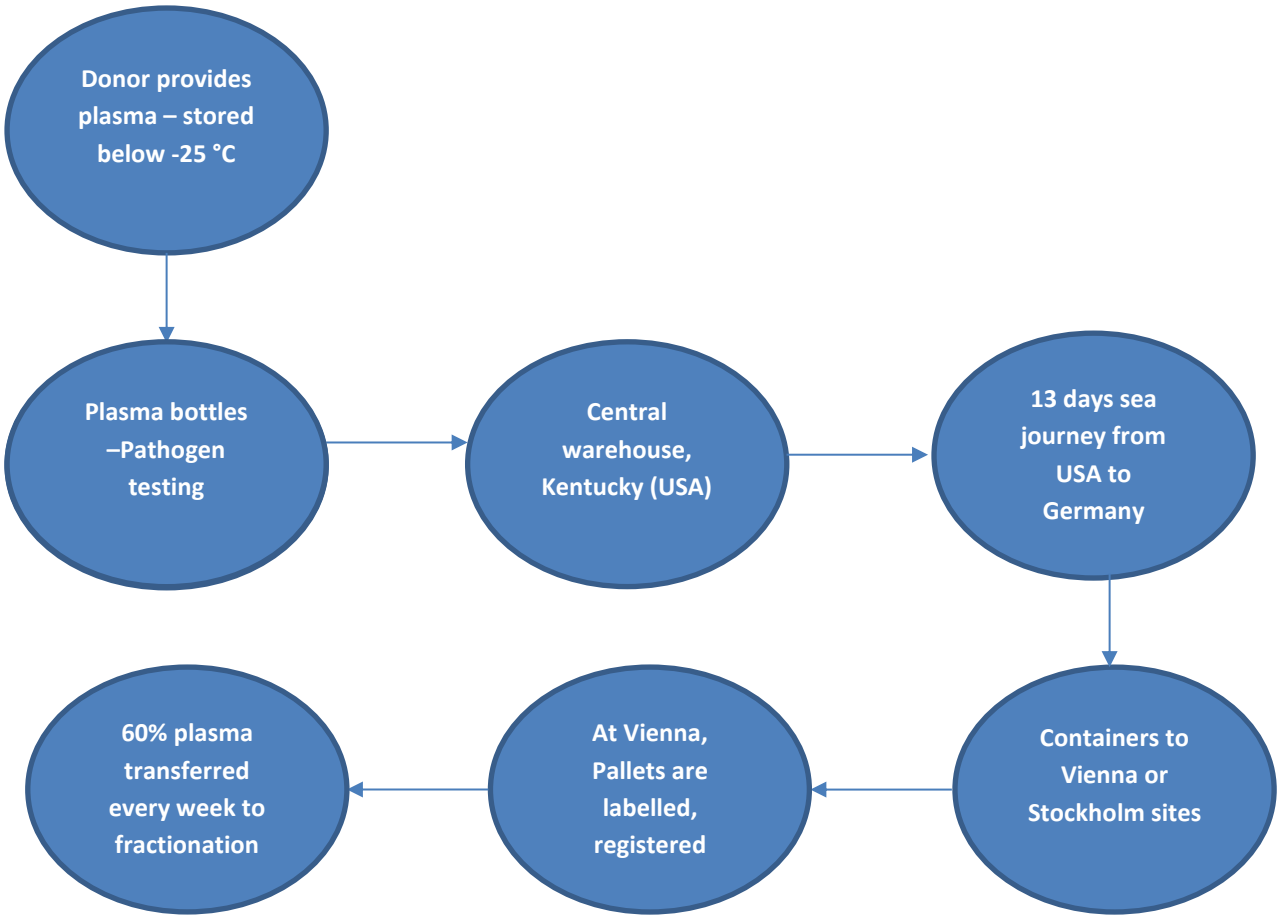


Fig 39.: This figure indicates journey of collected plasma at Octapharma

4. Takeda

Takeda, with ~13% market share holds 4th position in plasma industry

TAKEDA is a global, R&D driven biopharmaceutical leader with a presence in 80 countries and regions

Company Overview:

Takeda has a 75+ year pioneering legacy in producing plasma-derived therapies

Takeda focusses on five key business areas of GI, rare diseases, plasma-derived therapies, oncology and neuroscience

In the fiscal year ended Mar 31, 2019, revenue from plasma-derived therapy products was ¥111.7 billion

Plans to increase plasma supply and manufacturing capacity by >65% over the next five years

BioLife, part of Takeda, is their global plasma collection network and an industry leader in the collection of high-quality plasma

Product Portfolio

Clinical Development:

They have a broad and differentiated portfolio of plasma-derived products, including more than 20 therapies with no patent expiry, including a diverse offering of subcutaneous IG (SCIG) products

Leadership Team

Christophe Weber

Representative director,
President & CEO

Masato Iwasaki

Director

President, Japan

Pharma Business Unit

Andrew S. Plump

Director

President, R&D

Source : Takeda reports

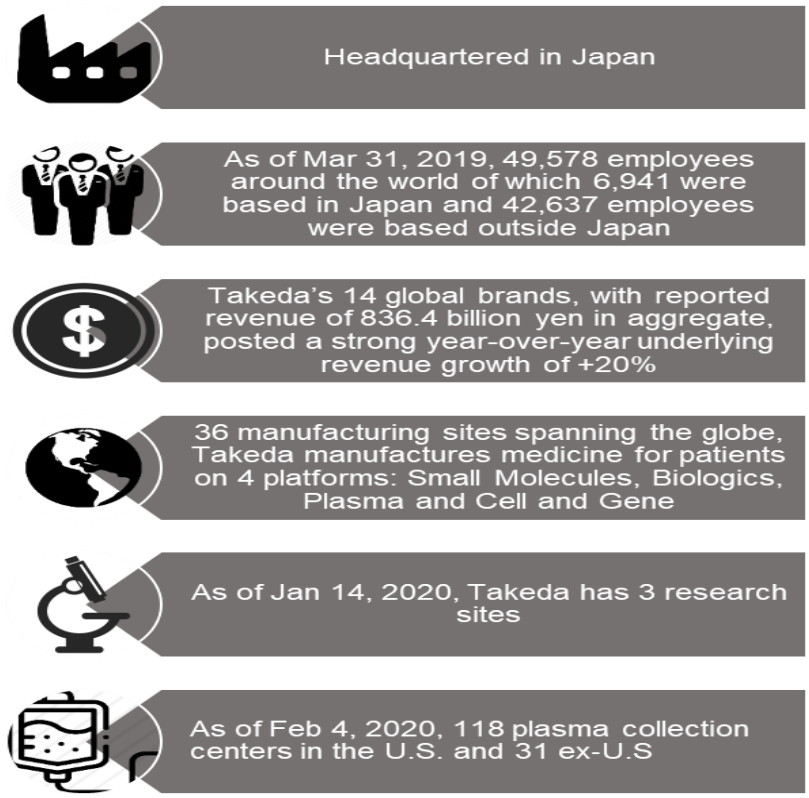


Fig 40.: This figure indicates the summary of Takeda's company profile.

Inline Products Portfolio of Takeda

Fig 41.: This figure indicates inline products portfolio of Takeda

BioLife Plasma Services operates numerous state-of-the-art plasma collection facilities throughout U.S. and Austria where plasma is tested too

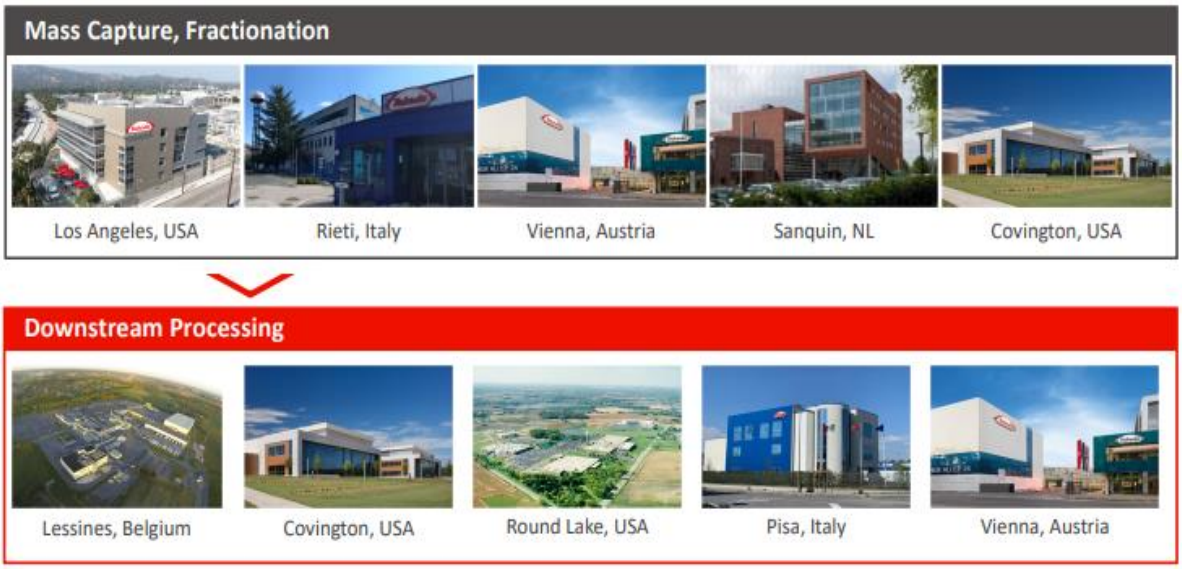


Fig 42.: This figure indicates the worldwide plasma fractionation centres and processing centres owned by Takeda

Plasma Sourcing

Takeda has more than 140 plasma collection centers

They increased plasma volumes by approx. 20% in 2018

As of Feb 2020, they increased European plasma collection centers to 31

They also leverage third party plasma supply through long-term contracts. Currently they have 5 US suppliers and 50 EU suppliers

Takeda participates in contract agreements with government

They acquired additional 10 plasma collection centers since Shire acquisition close- 1 in US, 2 in Austria and 7 in Hungary

BioLife Plasma Services operates numerous state-of-the-art plasma collection facilities throughout the United States and Austria where plasma is tested too

Plasma Manufacturing Capabilities

In Japan, Takeda has domestic manufacturing capabilities through their subsidiary Nihon Pharma with a fractionation capacity of 400 KL

They have 8 strategic manufacturing locations at Belgium, Italy, Austria, Japan, Georgia, Illinois, California and 4 external manufacturing partners at Netherlands, Israel, California, Indiana (Baxter)

Over the next 5 years, Takeda plans to increase their manufacturing capacity by 65% within its existing network

With respect to diagnosis, Takeda has partnered with large hospital systems in US to leverage electronic medical records

Takeda co-chairs the Global Commission to end the diagnostic Odyssey for children with rare diseases

They have more than 40 trained staff dedicated to virology department to maintain safety standards and has 3 screening labs

Their Plasma Derived Therapies leadership team has 19 members

By 2023, Takeda plans to allocate 70% of resources to improve in-line products and product efficiencies

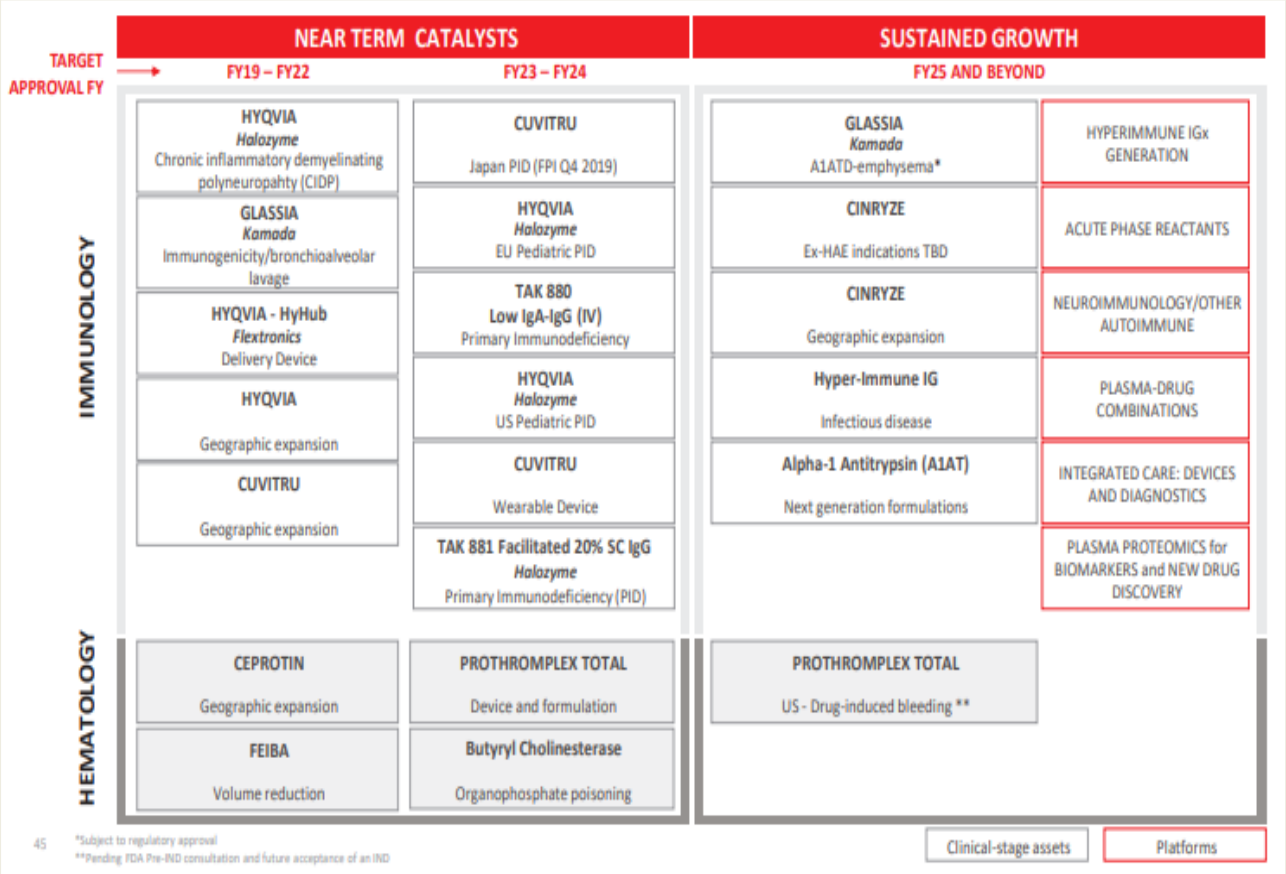


Fig 43.: This figure indicates Takeda's future growth plans venturing and allocating more funds to plasma products

Fig 44.: This figure indicates estimated percentages of spend allocated to PDT for FY 2023

By 2023, Takeda plans to allocate 70% of resources to improve in-line products and product efficiencies by

Device-driven solutions for management, diagnosis, and long-term follow up

By expanding indications, global expansion of products and new formulations

The rest 30% is planned to be allocated for new targeted therapies in diverse therapeutic areas

2.13Major Mergers and Acquisitions of plasma industry

Major Mergers & Acquisitions of Plasma Industry

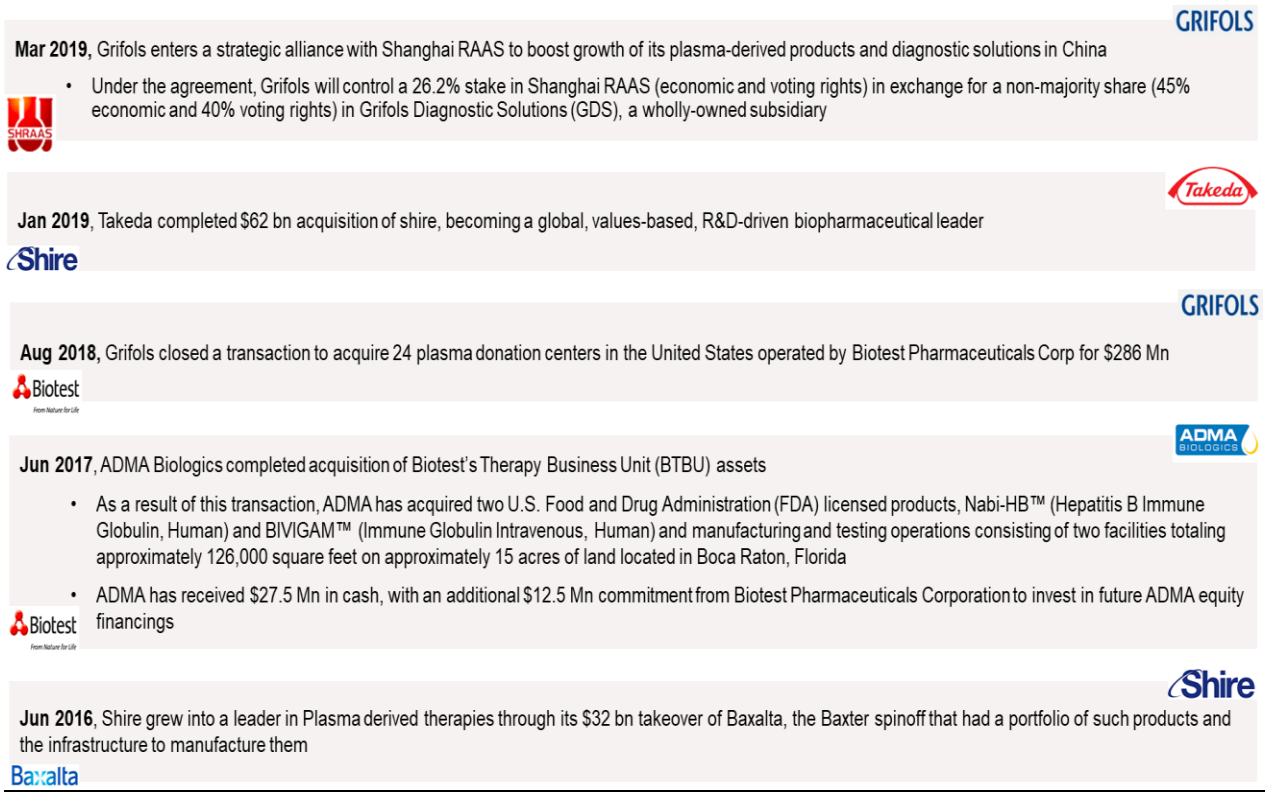


Fig 45.: This figure indicates major mergers & acquisitions of Plasma Industry

2.14 Effect of COVID-19 on plasma industry

Blood draining spell by Corona:

Blood collection centers around China have reported sharp drops in donations, with one even issuing a “red alert” as stocks dwindle

With quarantine measures to prevent the coronavirus spread limiting large gatherings, donation centers are struggling to match regular levels of giving by students, military members, employees at state-owned companies and walk-in contributions

Some collection centers promoted donations as a way of supporting the fight against the pandemic

The same situation is in US. Dozens of blood drives have been canceled, and regular donors are no-shows, industry officials said, especially in states like Washington and California where the virus is spreading more broadly within communities and health officials are urging residents to avoid public gatherings to reduce risk

Worried citizens have two key concerns about the blood supply, officials said: whether potential donors are at greater risk of contracting COVID-19 infections by taking part in blood drives or at donation centers and whether donors infected with coronavirus risk contaminating the blood supply

The American Red Cross said that as of 19 March 2020, more than 5,000 of its blood drives were canceled across the US over coronavirus concerns – resulting in approximately 170,000 fewer donations

However, Red-cross officials are trying to emphasize that there is no data or evidence that COVID-19 can be transmitted by blood transfusion, and there have been no reported cases of transmissions for any respiratory virus, including this coronavirus, worldwide

Plasma to treat COVID-19 disease

Doctors in Shanghai are using infusions of blood plasma from people who have recovered from the coronavirus to treat those still battling the infection, reporting some encouraging preliminary results, said Lu Hongzhou, professor and co-director of the Shanghai Public Health Clinical Centre

Mar 27, 2020, Chinese researchers reported that convalescent plasma appeared to help Covid-19 patients on ventilation, but the study involved only five patient

Mar 24, 2020, The FDA allowed use of investigational convalescent plasma under single-patient emergency Investigational New Drug Applications (INDs), since no known cure exists, and a vaccine is more than 1 year away from becoming available

This does not include the use of COVID-19 convalescent plasma for the prevention of infection, according to a statement issued by the FDA

FDA asked the Red Cross to help identify COVID-19 recovered donors and manage distribution of the plasma to hospitals treating patients in need

Convalescent Plasma to treat COVID-19

octapharma

- **Apr 17, 2020,** Octapharma USA is supporting a new investigator initiated clinical trial led by George Sakoulas, M.D. of Sharp Memorial Hospital in San Diego, California focused on treating the most critical COVID-19 patients, those experiencing respiratory failure who become ventilator dependent

CSL Behring

- **Apr 8, 2020,** CSL Behring and SAB Biotherapeutics (SAB) announced partnership for the rapid development of SAB-185, generated from SAB's proprietary DiversitAb™ platform producing large volumes of human polyclonal antibodies targeted specifically to SARS-CoV-2, the virus that causes COVID-19
- CSL Behring have donated their proprietary adjuvant technology, MF59®, to the **University of Queensland (AUS)** 's pre-clinical development program of COVID-19 vaccine

- **Apr 6, 2020, Biotest, BPL, LFB, and Octapharma have** joined the CoVIg-19 plasma alliance formed by **CSL Behring and Takeda** to develop anti-SARS-CoV-2 polyclonal hyperimmune globulin **(H-IG)** medicine with the potential to treat individuals with serious complications from COVID-19

emergent

- **Apr 2, 2020,** Emergent BioSolutions partners with U.S. Government for the development of two Plasma-Derived Therapy, one based on horse-derived plasma and other human-derived plasma for COVID-19

GRIFOLS

- **Mar 25, 2020,** Grifols announced its formal collaboration with Biomedical Advanced Research Development Authority (BARDA), FDA and other Federal public health agencies **to collect plasma from convalescent COVID-19 patients, process this into a H-IG** in Clayton, North Carolina and support preclinical and clinical studies to determine if anti-SARS-CoV-2 **H-IG** therapy can successfully be used to treat COVID-19 disease
- **Grifols is providing viral inactivation technology to ensure inactivated plasma units for COVID-19 treatment** use for which it will be building a new facility in the Clayton site
- In Spain, the **Grifols is collaborating with certain hospitals in the design of diverse clinical studies on the use of intravenous immunoglobulin and alpha-1 antitrypsin**, with the goal of proving their efficacy in the treatment of COVID-19
- In addition, **Grifols has accelerated the development and validation of an automated TMA (transcription-mediated amplification) based diagnostic test to detect SARS-CoV-2** with each unit able to run more than 1,000 samples per day, and is expected to be ready by early May

2.15 CONCLUSION

At the end, Plasma industry is fast moving towards a whole therapeutic expertise and is going to positively affect both the pharma industry and the recipients. The government should now focus on helping these firms lower the cost to end user as most of these therapies cost around thousands of dollars a year. Blood supply shortage, the crisis at hand must be mitigated first to keep the business viable. Incentivising the process might help some may say but a forthcoming expense of testing so many samples would increase the end product cost, one may argue. The ball would again fall in the industries court to see how in the coming years they can modify the current practices to make the process more efficient and more cost effective.

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