Takeda's legacy and commitment to plasma-based therapeutics

Takeda is a global leader in serving patients with rare and hard-to-treat diseases. Our legacy in this area includes a more than 60-year history in plasma fractionation and manufacturing—with a steadfast commitment to providing life-changing plasma-based therapeutics.[1,2]

A source of plasma-based therapeutics for more than 60 years[1,2]

1954	1968	1982	1986	2003	2007	2008
Albumin	**Factor VIII**	**Activated Prothrombin Complex**	**Immune Globulin**	**Alpha$_1$-Antitrypsin**	**Protein C**	**C-1 Esterase**

Ongoing commitment to innovation

Our heritage in plasma technology extends back to the first commercially available human plasma in the 1950s with the development of therapeutic human albumin.[1,2] Takeda also has been a reliable source of immune globulin (IG) therapies for more than 30 years.[1,2]

We're committed to building upon our legacy as we work to expand treatment options for rare diseases. As a global leader in rare diseases, Takeda is focused on driving continuous innovation and personalized care through our portfolio of plasma projects.

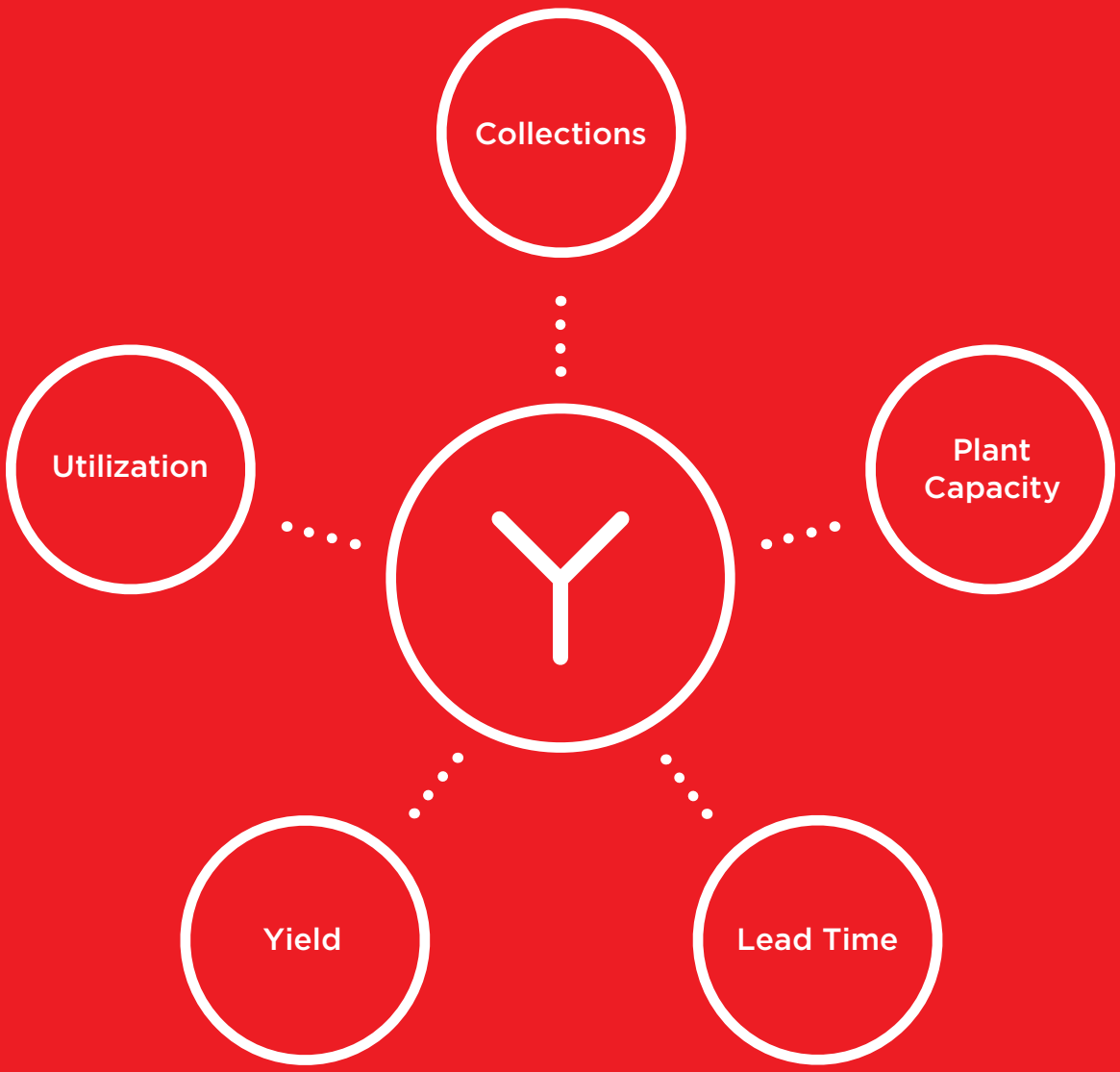
Takeda's rigorous approach to help ensure continued supply

Takeda has the experience and the expertise to confidently manage the end-to-end challenges of developing complex, plasma-based therapeutics—from securing donations to delivering treatment.

Accurately predicting utilization for plasma-based therapeutics, and meeting that demand, can be a complicated process for manufacturers.[3,4] At Takeda, we conduct rigorous analyses and manage multiple challenges that can impact IG supply, including collections, plant capacity, lead time, yield, and utilization of all plasma products.[3,4]

Approximately 625 to 800 mL of plasma can be safely obtained during each donation.[5]

Factors Impacting IG Supply



Factors Impacting IG Supply

Collections

The amount of plasma that can be collected for fractionation is dependent on the number of centers and donors.[3,4]

Takeda operates more than 100 state-of-the-art BIOLIFE plasma donation centers in the United States to help meet the growing demand for plasma-based therapeutics.[2]

In 2018, Takeda collected an estimated 7.4 million liters of plasma in the United States.[2]

Plant Capacity

Manufacturing plasma-based products involves a series of complex steps—including fractionation, purification, stabilization, and viral inactivation and removal—to ensure the quality and safety of the finished product.[6,7]

Lead Time

Production of IG and other plasma-based therapeutics takes significantly longer than traditional pharmaceuticals or biologics, primarily due to donor screening and complex production procedures.[3,4,8]

As part of the industry's voluntary international standards program, all plasma donations are held in inventory for 60 days before entering the manufacturing process.[7]

Yield

During fractionation, plasma is pooled from multiple donors, purified, and processed to extract plasma proteins that have a demonstrated medical use.[3,7]

IG is the most widely used plasma component.[9]

Utilization

Increasing demand for plasma-based therapeutics, such as IG, can also impact the supply of other products. Manufacturers typically balance manufacturing costs by increasing the production of all plasma-based therapeutics to help ensure an adequate supply of the product currently in greatest demand.[4]

Amount of IG needed for each patient varies depending on medical use and required dose.[3,5,7,8]

PLASMA-BASED MANUFACTURING STEPS

Plasma donation and screening

Qualified donors must pass 2 screenings within a 6-month period before their plasma donation can be accepted.[3,8]

Fractionation

Plasma yields several products for various conditions, spreading the manufacturing effort across the various products.[3,7]

Purification, stabilization, and viral inactivation and removal

Purification, stabilization, and viral inactivation and removal are critical steps to help ensure product quality and safety.[6]

Final Product

Traditional pharmaceutical manufacturing[10]

Days to weeks

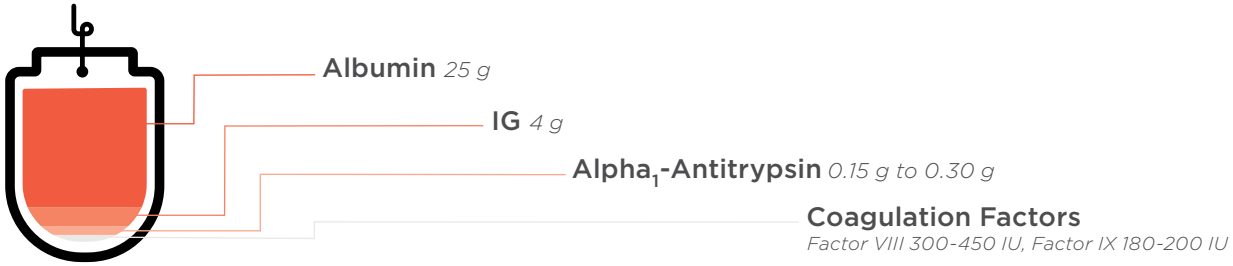
Biologics manufacturing[11]

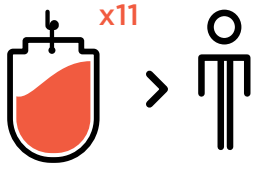
Several weeks to months

Plasma-based product manufacturing[3,8]

7-12 months from start to finish

PLASMA PROTEIN[3,7]





Primary Immunodeficiency (PI)

Unique donations required for a single month of IG treatment for PI

Approximately 140 unique donations per year would be required to yield 105 L of plasma required to treat an average hypothetical adult PI patient of 70 kg receiving a dose of 35 grams of IG per month.

Continued investment in new manufacturing capacity

To meet growing demand for plasma-based therapeutics, Takeda is focused on optimizing our global manufacturing operation.

As part of this effort, our new state-of-the-art plasma fractionation facility in Covington, GA, will expand capacity by 3 million liters of plasma each year when fully operational—an ~30% increase.[12,13]

The facility received U.S. Food and Drug Administration approval for production of one IG product in June 2018 and albumin in March 2019.[12-14]

Covington, GA—2018

Over $1 billion

investment in state-of-the-art fractionation facility[12]

Multiple Manufacturing Facilities

- Covington, GA
- Lessines, Belgium
- Los Angeles, CA
- Pisa, Italy
- Rieti, Italy
- Vienna, Austria

Committed to advancing the care of patients receiving IG

Takeda's commitment to advancing the care for people who rely on IG is highlighted by the industry's most diverse portfolio of IG product offerings, including several IV and subcutaneous therapy options.[2]

In addition to a dedicated team servicing health system customers, Takeda offers numerous programs and resources to support providers, patients, and stakeholders within each health system, including:

- Product administration education through our Clinical Educators
- Peer-to-peer clinical education to your teams about IG through Takeda's IG Stewardship Speaker Bureau
- One-on-one support from other patients and caregivers who know what it's like to live with PI through MyIgSource. Learn more at MyIgSource.com
- A comprehensive population health management toolkit Navigating Population Health Management - Primary Immunodeficiency (PI), which contains information, tools, and educational materials for health system executives, providers, and patients
- A solutions guide for utilizing your electronic medical record systems to solve a myriad of PI challenges and barriers to help your patients and organization, including: identifying challenges, providing high-level direction on how to utilize standard reporting tools, monitoring dosing and utilization protocols, improving adherence, and tracking in-network Rx fills and in-network referrals

Please contact your Takeda Account Representative for more information.

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