

# Working Together to Save Lives



*BioLife Plasma Services*

## Who we are

BioLife Plasma Services is an industry leader in the collection of high quality plasma that is processed into life-saving plasmabased therapies.<sup>1,2</sup>

BioLife operates and maintains more than 120 state-of-the-art plasma collection facilities throughout the United States.<sup>3</sup>

BioLife is committed to safety. In order to provide high quality service and a high level of safety to our donors, as well as the patients who receive life-saving plasma-based therapeutics, the company is licensed by and/or complies with requirements from the Plasma Protein Therapeutics Association (PPTA), Food and Drug Administration (FDA), Occupational Safety and Health Administration (OSHA), Environmental Protection Agency (EPA), Department of Transportation (DOT), Centers for Medicare and Medicaid Services (CMS), Federal Aviation Administration (FAA) and other state and local regulations.

Each BioLife center is a vital part of its community. The donors not only contribute the source of these life-saving therapeutics, but also contribute to the commercial vitality of their immediate neighborhoods.

BioLife Plasma Services is part of Takeda (TSE:4502/NYSE:TAK). Takeda is a global, values-based, R&D-driven biopharmaceutical leader committed to bringing Better Health and a Brighter Future to patients by translating science into highly-innovative medicines. The company is focusing on developing highly innovative medicines that contribute to making a difference in people's lives by advancing the frontier of new treatment options and leveraging our enhanced collaborative R&D engine and capabilities to create a robust, modality-diverse pipeline. Our employees are committed to improving quality of life for patients and to working with partners in health care in approximately 80 countries and regions.<sup>4</sup>

## Plasma facts

### Plasma makes up approximately 55 percent of whole blood.<sup>5</sup>

- Plasma is the pale yellow liquid portion of the blood that can be easily replaced by the body.
- Plasma functions as an aid in the circulation of red and white blood cells and platelets.
- Source Plasma is collected through a process called plasmapheresis.
- Across the industry, over 57 million liters of plasma are used worldwide to produce life-saving medicines that treat millions of people every year.<sup>6</sup>



**Plasma can only be obtained from healthy donors. It cannot be reproduced in a lab or other artificial environment. Plasma donors help save lives.**



**Donating plasma is a low risk procedure with minimal or almost no side effects.<sup>7</sup>**

### Plasma Processing

Plasma is processed into a wide variety of life-saving therapeutics, including blood clotting proteins to treat hemophilia, immune support therapies, blood volume replacements and surgical sealants that benefit thousands of people every day.<sup>1,2</sup>



## Donating plasma

### What is plasma?

Plasma consists primarily of water and proteins that help the body control bleeding and infection. It also makes possible natural chemical communication among different parts of the body by carrying minerals, hormones, vitamins and antibodies. Important plasma proteins include coagulation factors and globulins, as well as albumin.

Plasma used in plasma-based therapies is obtained through two different donation processes; recovered and source plasma. Recovered plasma is obtained from whole blood donations. In the United States, approximately 280 milliliters of plasma are obtained per a single whole blood donation.<sup>8</sup>

Source plasma is collected through the use of an automated plasmapheresis process. During plasmapheresis, the plasma component of whole blood is collected through the use of an automated machine, returning the cellular blood components, such as red blood cells and platelets, back to the donor. Approximately 600-800 milliliters of plasma can be safely obtained during each donation.<sup>8</sup>

### How is donating plasma different from donating whole blood?

#### Whole blood donation

Whole blood is collected manually into a container approved for the collection of human blood. During a whole blood donation, all components of the blood are collected. Because all of the blood's components are collected, whole blood donors are only allowed to donate once every eight weeks in order to replenish the body's blood supply.<sup>9</sup>

#### Plasma donation

Plasma is collected through a process called plasmapheresis. When donating plasma, whole blood is withdrawn from the body. The whole blood is then separated into plasma and the other whole blood elements using a sterile system. The plasma is retained and other whole blood elements – red blood cells, white blood cells and platelets – are returned to the donor during the plasmapheresis process. But because the cellular components are returned, a donor can donate as often as twice in a seven-day period, with at least one day between donations.<sup>7</sup>

# Plasma therapies

The plasma collected at BioLife Plasma Services is processed into a wide variety of life-saving therapeutics that benefit thousands of people every day. Five main infusions are derived from the plasma:<sup>10</sup>

## Hemophilia therapies

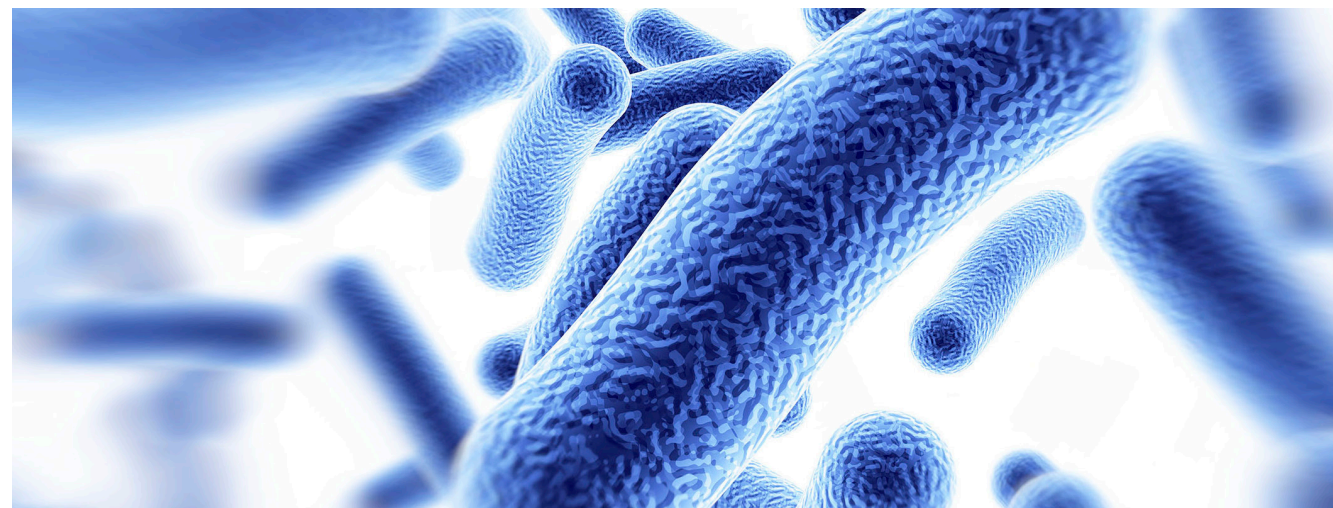
Hemophilia is a genetic bleeding disorder that prevents blood from forming an effective clot. A disorder that primarily affects males, people living with hemophilia do not have enough of, or are missing, one of the blood clotting proteins naturally found in blood. Individuals with hemophilia A (also called classic hemophilia) lack a sufficient amount of a protein called clotting factor VIII, while individuals with hemophilia B (also called Christmas disease) lack a sufficient amount of clotting factor IX.<sup>11</sup>

Plasma is processed into replacement infusions that are infused intravenously to temporarily replace a missing or nonfunctioning factor in people living with hemophilia. These plasma-based factor concentrates help individuals who suffer from hemophilia.

## Blood volume replacement

A loss of blood volume affects patients in a variety of trauma conditions. Restoration of this lost blood is often a key factor in emergency situations with a long-term favorable outcome.<sup>12</sup>

The therapeutic protein albumin, derived from plasma, is used in hospitals across the United States to treat trauma and burn victims, as well as patients suffering from shock.<sup>13</sup>



## Immune deficiency therapies

Immune deficiency disorders encompass more than 350 related disorders that affect one in every 1,200 people in the United States. These disorders occur when a part of the body's immune system is missing or does not function properly. Immunoglobulins (IG, antibodies) derived from plasma assist the patient's immune system in fighting off infection.

Immunoglobulin is a therapeutic derived from plasma for use in primary immune deficiencies, such as B-cell Chronic Lymphocytic Leukemia and Idiopathic Thrombocytopenic Purpura.<sup>16</sup>

## Alpha-1 Antitrypsin deficiency treatments

People with alpha-1 antitrypsin (AAT) deficiency are born with a lack or low levels of a blood protein called AAT. This protein helps protect lung tissue from damage from enzymes that are released by white blood cells. This condition may cause serious lung disease, resulting in emphysema.<sup>17</sup>

Chronic augmentation infusions derived from plasma are used to treat patients with congenital deficiency of AAT with clinically evident emphysema.

## Therapies for hereditary angioedema (HAE)

Hereditary angioedema (HAE) is a rare genetic disorder that results in recurring attacks of edema (swelling) in various parts of the body, including the abdomen, face, feet, genitals, hands and throat. The swelling can be debilitating and painful. Attacks that obstruct the airways can cause asphyxiation and are potentially life-threatening. HAE affects an estimated 1 in 10,000 to 1 in 50,000 people worldwide. It is often under-recognized, under-diagnosed and under-treated.<sup>18</sup> Plasma derived C1-inhibitors are one of the primary treatment options.<sup>19</sup>

## Plasma collection process

Source plasma is collected through an automated process called plasmapheresis. The procedure requires the use of an automated device and disposable sterile single-use kit in which the donor's blood is collected and processed to separate the plasma from the other blood components.

A needle is placed in the donor's vein and blood is pumped into a specialized device that separates the plasma from the cellular components of the blood, such as red and white blood cells and platelets. While the plasma is collected, the other blood components are pumped into a reservoir. Once the reservoir is full, the red and white blood cells and platelets are returned to the donor's body. Throughout the process, the system automatically alternates between collection and reinfusion until the predetermined amount of plasma is obtained. Once the donation is complete, the disposable equipment is discarded and replaced with new materials for the next donation.

On each donor's initial visit, and at least annually, the donor undergoes a physical examination and their medical history is recorded. During each subsequent visit, a staff member checks the donor's vital signs and donors answer questions about their medical history. In addition, the donor's hematocrit (the percentage of blood volume occupied by red blood cells) and plasma protein levels are checked. Once the plasma is collected, samples from each donation are sent to a BioLife laboratory and tested for indicators of viral infections including hepatitis and human immunodeficiency virus (HIV). Additionally, periodic tests, including syphilis, are performed on each donor to help ensure donor health and acceptability for the plasmapheresis process.

For new donors, the entire plasma donation process, including a physical examination, donor screening and the plasmapheresis process, usually takes about two hours. Repeat donors can expect to spend approximately one hour in the center, with the average plasmapheresis process taking around 45 minutes.<sup>7</sup>

## Plasma safety

Safety is a critical element of plasma collection. While the risks associated with plasma cannot be totally eliminated, BioLife Plasma Services is committed to the highest standards of safety and employ numerous measures to ensure the safety of its donors and its products. Takeda's world-renowned Global Pathogen Safety group assures product safety of life-saving therapies manufactured from plasma, relying on three key process steps:<sup>20</sup>

### From donor to patient...

#### 1. Donor selection and screening<sup>20</sup>

Before a donor is accepted into the BioLife Plasma Services donor program, he or she must pass a physical examination and survey of their medical history. A donor must return to provide a second donation within six months of the first donation before the plasma from that donor may be considered for use. If the applicant donor successfully completes a secondary round of screening interviews and laboratory tests, the donor becomes a "qualified donor" and his or her plasma may be considered for use. These steps help ensure the safety of the donor and protect the recipients of the therapies processed from their plasma. The donor screening process is required every time an individual returns to donate plasma and is intended to identify a variety of infectious diseases, including human immunodeficiency virus (HIV) and hepatitis. All BioLife plasmapheresis centers voluntarily comply with the quality and safety standards defined by the International Quality Plasma Program (iQPP) of the Plasma Protein Therapeutics Association (PPTA), a global organization dedicated to important issues relating to the quality, safety and efficacy of plasma therapeutics.

BioLife Plasma Services is also licensed by the Food and Drug Administration (FDA) and the Centers for Medicare and Medicaid Services (CMS). In addition, each facility is expected to comply with the regulations set forth by the Occupational Safety and Health Administration (OSHA), Environmental Protection Agency (EPA), Department of Transportation (DOT), Federal Aviation Administration (FAA) and other state and local regulatory organizations.

#### National donor deferral registry<sup>20</sup>

The National Donor Deferral Registry (NDDR) is a computerized safety network that allows plasma collection facilities to check all applicant donors against a list of permanently deferred donors in the United States. BioLife and Takeda accept plasma for processing only after verification that the applicant donor is not in the NDDR. Should BioLife Plasma Services identify a donor as ineligible for further donations after a laboratory sample testing for viral markers, the NDDR is notified and the donor is listed as a deferred donor.

## Plasma safety *(continued)*

### The plasma fractionation process

After the plasma is collected, it is frozen, tested and shipped to a fractionation facility where it is processed into life-saving therapeutics and distributed. Cryoprecipitation, filtration and solvent/detergent treatments isolate and purify the plasma proteins.

### 2. Plasma screening and inventory hold<sup>20</sup>

Once the plasma is collected, samples from each donation are sent to a BioLife Plasma Services laboratory. The plasma is screened for viruses such as hepatitis and HIV using two uniquely different testing methodologies, including PCR (polymerase chain reaction) technology, one of the most sensitive tests available for detecting viruses. With PCR testing, it is not necessary to wait until the body has produced antibodies in order to detect the presence of a virus. Instead, the technique reduces the time from initial infection to laboratory detection. PCR testing can therefore increase the safety margin significantly by earlier detection of a virus that might enter the process. Other periodic tests, including syphilis, are performed on each donor to help ensure donor health and acceptability for the plasmapheresis process.

Plasma donations from qualified donors are held for 60 days (inventory hold) prior to further processing. This measure allows for the retrieval, prior to processing, of plasma units from previously qualified donors who are later found to have unacceptable results. The primary goal of plasma screening and inventory hold is to ensure quality controlled plasma for further processing into therapeutics.

### 3. Virus inactivation and removal<sup>20</sup>

Using the latest technologies to screen plasma is a highly effective way to reduce the risk of viral transmission. However, any screening procedure has a detection limit and can only test for known viruses. Moreover, unknown and/or emerging pathogens may also be present in the plasma. These potential contaminants can be reduced and sometimes eliminated by a process of virus inactivation and removal. Virus inactivation steps are treatments that are able to inactivate virus infectivity through steps such as solvent/detergent treatment, heating or chromatography. Takeda manufacturing processes utilize one or more virus inactivation processes to help improve the safety profile of the finished product.

## Facility information



BioLife Plasma Services operates numerous plasma collection centers throughout the United States and Europe. The following data represents the per center statistics of our newer US-based facilities:<sup>3</sup>

Average square feet	12,000-15,000
Number of donor beds	36 - 72
Number of employees	50 - 70
Donations per week	Up to 4,000

### Economic impact on the community:<sup>3</sup>

Initial Capital investment (building, land)	\$3-6 million
Donor compensation (annual per center)	\$2-3 million

### Demographics of our plasma donors<sup>3</sup>

BioLife plasma donors mirror the demographics of the different communities in which its centers are located. The majority of donors come from within a seven-mile radius of the center. In general, the gender ratio is fairly equal. In regards to occupation, BioLife centers attract a wide mix of individuals: blue and white collar workers, stay-at-home parents, professionals and individuals in the military... people from all walks of life. Donors have varying reasons for giving, including the self-fulfillment of knowing they are helping others and the opportunity to receive extra money, as well as the social aspects of donating. Many BioLife donors come in to donate twice a week and see their time spent donating as a chance to socialize with friends.

<sup>20</sup>Products made from human plasma may contain infectious agents, such as viruses, that can cause disease. The risk that such products will transmit an infection agent has been reduced by screening plasma donors for prior exposure to certain viruses, by testing for the presence of certain current virus infections, and by inactivating and removing certain viruses.

## Patient testimonials<sup>3</sup>



**Mitchel,**  
recipient of a  
plasma-based  
therapeutic

“As a baby I would develop large bruises on my body just from being picked up out of my crib or my dad playing with me. My parents suspected something was wrong since this hadn't happened to my older brother or sister when they were babies. After several visits to the doctor, at the age of six months I was diagnosed with having Hemophilia - a genetic bleeding disorder that prevents my blood from clotting. Any little trauma to my body would cause me to bleed internally.

Upon being diagnosed with Hemophilia A, I began receiving Factor VIII replacement therapy. Thanks to Factor VIII replacement treatment, my life is basically like any other 18 year-old. I run track and high jump, play basketball with my friends and rough-house with my older brother. I have this great life and can enjoy normal activities because of people who generously donate plasma each week and who work at BioLife Plasma Services. Thank you for giving me a normal life!”



**Isaac,**  
recipient of IGIV,  
a plasma-based  
therapeutic

“I was born on September 13, 1991. I was really small as a baby. The doctor put me in a specialbed. In fact, I was so small that I had to wear socks from my sister's doll. My head was as big as my mom's fist.

Since I was a little kid I've liked playing basketball. I've had a ball in my hands ever since I can remember. But what I really liked to do was lay on the couch because I was always sick, and nobody could find out why.

Finally, after five and a half years of suffering we found a certain doctor who I still see today. His name is Dr. Shapiro. He told my parents and me that I had Common Variable Immune Deficiency Disease or CVID. It's one of over 120 primary immune deficiency diseases.

In my case the treatment for CVID is IGIV infusions every 14 days. IGIV is made from plasma. Without this drug I would be sick all the time. My life is much better now that I receive infusions. I'm able to do whatever I want to do. I am able to eat all types of foods. I can be outside playing sports as much as I want. My dream for the future is to start my own business or have a good paying job. I want to go to college, but no matter what happens to me in the future I'll be happy with whatever I do. I'll be fine however I end up in the future as long as I can continue receiving my infusions.

Thank you to everyone who donates plasma and works at plasma collection centers. You have helped to change my life and the lives of others.”



**Wayne,**  
recipient of a  
plasma-based  
therapeutic

“As a self-employed consultant in New Orleans, Wayne has enjoyed the freedom to truly appreciate where he lives. Wayne is also an avid traveler, and it was a mild hiking excursion in Aruba several years ago that eventually led him to be diagnosed with alpha-1 antitrypsin deficiency (AATD).

Although he had been treated for asthma for a number of years, Wayne was surprised at the breathing difficulties that came over him while walking up a hill on the island. “I actually had to stop and catch my breath,” he recalls. “I saw that a lot of the people passing me on the trail were elderly and wondered why I has having so much trouble.” When he returned from his trip, Wayne was referred to a pulmonologist. “He put me on a heavy dose of medication,” Wayne explains. “When my breathing didn't improve, he recommended testing for something I had never heard of before, AATD.”

“I met with him and learned much more about this deficiency of a protein that protects the lungs,” he said. “I also learned that any current damage to my lungs could not be reversed, but that through what is called ‘augmentation therapy’ I could receive a weekly infusion that would replace the protein that my body isn't producing naturally.”

Wayne says he is inspired to tell anyone diagnosed with AATD that there is help and hope. “It has become a routine part of my life. I continue to do all the things I've done before. I say thank goodness that my doctor tested me for AATD that day.”



**Evin,**  
recipient of IGIV,  
a plasma-based  
therapeutic

“I had spent 12 years in and out of hospitals and missed most of elementary school due to a disorder called Immune Thrombocytopenic Purpura (ITP), which attacks the platelets of the blood and destroys them. My life was completely at the whim of my illnesses. Then came IGIV treatment. My fevers abated, my infections became less frequent and most amazingly, I began to grow.

The ability to carry on a healthy, happy life and being one of many who receive products made from donated plasma is not a coincidence. There is not a simple way to express my gratitude to the staff of BioLife Plasma Services and to all the caring donors who give of themselves to keep me alive. Thank you from the bottom of my heart.”

## Frequently asked questions

### **Q** Who is eligible to donate plasma?

**A** To donate plasma, an individual must be at least 18 years of age, weigh at least 110 pounds and pass all other required donor eligibility criteria.

### **Q** Is it safe to donate plasma?

**A** Yes. Donating plasma is a low risk procedure with minimal or almost no side effects. Before a donor is accepted into the BioLife Plasma Services donor program, he or she must pass a physical examination and a survey of their medical history performed by a member of BioLife's professional medical staff. During each subsequent visit, a staff member checks the donor's vital signs and the donor answers questions about their medical history. In addition, the donor's hematocrit (the percentage of blood volume occupied by red blood cells) and plasma protein levels are checked. These steps help ensure the safety of the donor and protect the recipients of the therapies processed from their plasma. Each donation procedure uses sterile and disposable collection materials. Once the donation is complete, the disposable equipment is discarded and replaced with new materials for the next donation.

### **Q** How often can I donate plasma?

**A** The body replaces the plasma removed during the donation process quickly; therefore, healthy individuals can donate as often as twice in a seven day period, with at least one day between donations.<sup>7</sup>

### **Q** How long does it take to donate?

**A** On a donor's first visit, the whole process, including a physical examination, medical screening and the plasma donation, usually takes about two hours. Repeat donors generally spend approximately an hour and a half in the center, with the average plasmapheresis process taking around 45 minutes.

### **Q** Do you test the plasma every time?

**A** Yes. Once the plasma is collected, samples from each donation are sent to a BioLife Plasma Services laboratory and tested for indicators of viral infections including hepatitis and human immunodeficiency virus (HIV). Additionally, periodic tests, including syphilis, are performed on each donor to help ensure donor health and acceptability for the plasmapheresis process.

### **Q** Why do I need to donate more than once?

**A** Before a donor is accepted into the BioLife Plasma Services donor program, he or she must pass a physical examination and survey their medical history. A donor must return to provide a second donation within six months of the first donation before the plasma from the donor may be considered for use. If the applicant donor successfully completes a secondary round of screening interviews and laboratory tests, the donor becomes a "qualified donor" and his or her plasma may be considered for us. These steps help ensure safety of the donor and protect the recipients of the therapies processed from their plasma.

### **Q** How does a plasma center affect the community blood supply?

**A** It can often enhance a community's whole blood donations if BioLife comes to a new location since the general awareness of the need for blood and plasma donations is increased through BioLife's marketing efforts.

### **Q** Why do plasma donors receive money for donating?

**A** Plasma donors spend up to two hours, as often as twice a week, in our centers to help save someone's life or improve the quality of it. In addition, plasma donors must undergo physical examinations at least annually and a medical history questioning every time they come in to donate. All of these measures help to guarantee a healthy donor population. We merely offer compensation to our donors for their commitment to the program.

### **Q** How do I get started?

**A** Visit our website to find your local center and make an appointment today.

### **Q** Do you test the plasma every time?

**A** Yes. Once the plasma is collected, samples from each donation are sent to a BioLife Plasma Services laboratory and tested for indicators of viral infections including hepatitis and human immunodeficiency virus (HIV). Additionally, periodic tests, including syphilis, are performed on each donor to help ensure donor health and acceptability for the plasmapheresis process.



## Additional resources

For more information about plasma and the life-saving therapies it provides, please visit the following websites:

**Biolife Plasma Services**

[www.biolifeplasma.com](http://www.biolifeplasma.com)

**PPTA: Plasma Protein Therapeutics Association**

[www.pptaglobal.org](http://www.pptaglobal.org)

[www.donatingplasma.org](http://www.donatingplasma.org)

**National Heart, Lung, and Blood Institute (NHLBI)**

[www.nhlbi.org](http://www.nhlbi.org)

**American Society of Hematology**

[www.hematology.org](http://www.hematology.org)

**Takeda**

[www.Takeda.com](http://www.Takeda.com)

**National Hemophilia Foundation**

[www.hemophilia.org](http://www.hemophilia.org)

**World Federation of Hemophilia**

[www.wfh.org](http://www.wfh.org)

**Immune Deficiency Foundation**

[www.primaryimmune.org](http://www.primaryimmune.org)

**Immune Disease**

[www.immunedisease.com](http://www.immunedisease.com)

**Albumin Therapy**

[www.albumintherapy.com](http://www.albumintherapy.com)

**Hemophilia Federation of America**

[www.hemophiliafed.org](http://www.hemophiliafed.org)

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