

# Plasma:

## A Finite Resource with Infinite Value

Understanding the plasma donation and manufacturing processes to develop lifesaving therapies such as immune globulin can provide a greater appreciation for the products and the donors who make them possible.



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**PLASMA HAS BEEN** a valuable resource and lifesaving therapy since it was first used on the battlefields during World War II. Through science and technology, the use of plasma products has expanded to treat many diseases. Today, millions of people rely on a safe and continuous supply of plasma to manufacture products that have a positive impact on their lives.

The demand for plasma products continues to grow. The immune globulin (IG) market, specifically, has increased an average of 8 percent per year. With this increase in demand for plasma products comes an increase in the demand for the plasma donations needed to maintain the supply. In 2016, more than 38 million individual plasma donations were collected at the hundreds of plasma donation centers across the U.S.

While most primary immunodeficiency disease (PI) patients treated with IG therapy are aware this lifesaving therapy is derived from plasma donations, it's likely many are unaware of the strict guidelines in place for donations and manufacturing. Those who have experienced a manufacturer

product shortage can relate to the anxiety and uncertainty associated with the possibility of not receiving a scheduled infusion. Therefore, understanding plasma donation and the IG manufacturing process may increase appreciation for these products and the donors they may never meet.

### What Is Plasma?

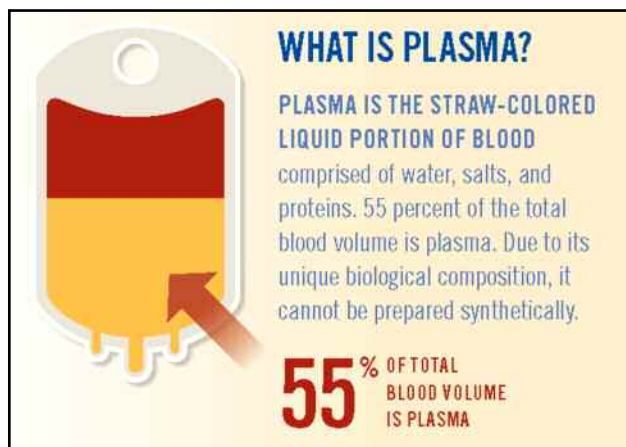
Plasma is the starting material for all plasma-derived products (Figure 1). More than 50 percent of blood is composed of plasma, a straw-colored fluid that contains water, salts and proteins. Proteins contain antibodies, known as immunoglobulins, that play an essential role in helping the immune system to fight infection. If a person has missing or defective antibodies, they are more susceptible to infections and a variety of other chronic medical conditions. These antibodies can't be manufactured in a lab. Instead, qualified plasma donors are needed to continually replenish the supply so new and existing patients will not experience a disruption in therapy.

## The Qualified Plasma Donor

The plasma donation process begins with healthy, compensated volunteers who must meet strict physical and medical requirements. Potential donors must live within a defined recruitment area, provide proof of residence and a valid photo ID. Prospective donors are checked to determine whether they have been entered into the National Donor Deferral Registry (NDDR) before being allowed to donate. The NDDR, one of many safety measures in place to protect both donors and recipients, is a database of donors who have been permanently deferred from donating plasma. Individuals can be deferred from donating plasma for a variety of reasons, including feeling unwell such as with cold or flu symptoms, having an immune or sexually transmitted disease or are pregnant, and the deferment can be either temporary or permanent.

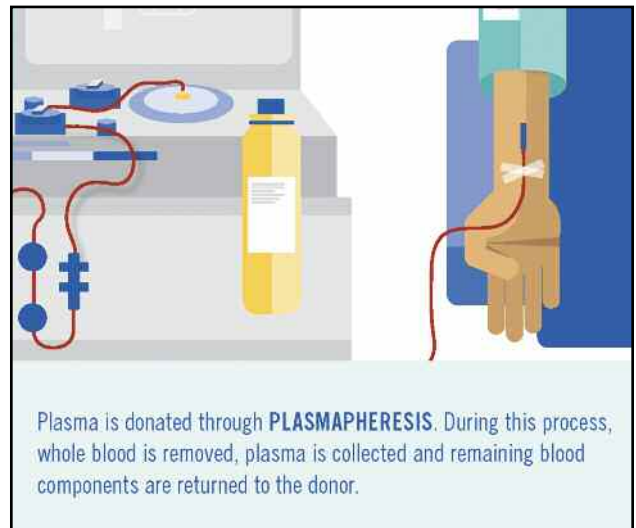
Donor screening begins with a medical history and physical examination. The extensive donor history questionnaire examines the medical and surgical history of donors, as well as any risk factors that may exclude them from donating. This includes a thorough sexual history and exposure to any person infected with HIV. Information regarding current or past drug use, recent tattoos and body piercings must also be provided. Donors are educated about the risks and hazards of donation, as well as about HIV/AIDS and activities that may put them at risk. Keeping donors healthy and informed is a key function of donor facilities, and donors are encouraged to lead a healthy lifestyle and must receive a yearly physical exam. The donor questionnaire can be viewed at [www.ppta-global.org/images/dhq/2016/1\\_Full\\_Length\\_DHQ\\_V2.0\\_July\\_2016.pdf](http://www.ppta-global.org/images/dhq/2016/1_Full_Length_DHQ_V2.0_July_2016.pdf).

Figure 1.



Source: Plasma Protein Therapeutics Association

Figure 2.



Source: Plasma Protein Therapeutics Association

Following the medical screening, a fingerstick test is completed to evaluate protein and hemoglobin levels. If these levels meet the requirements, donors can begin the collection process known as plasmapheresis (Figure 2).

## The Plasma Collection Process

Plasmapheresis is the process of separating plasma from other components in the blood. To accomplish this, whole blood is passed through a series of filters that collect the plasma, after which the red blood cells and platelets are returned to the donor. The initial collection process may take up to several hours, with subsequent sessions lasting approximately 45 minutes each. An individual's body replenishes its plasma supply within 24 hours to 48 hours.

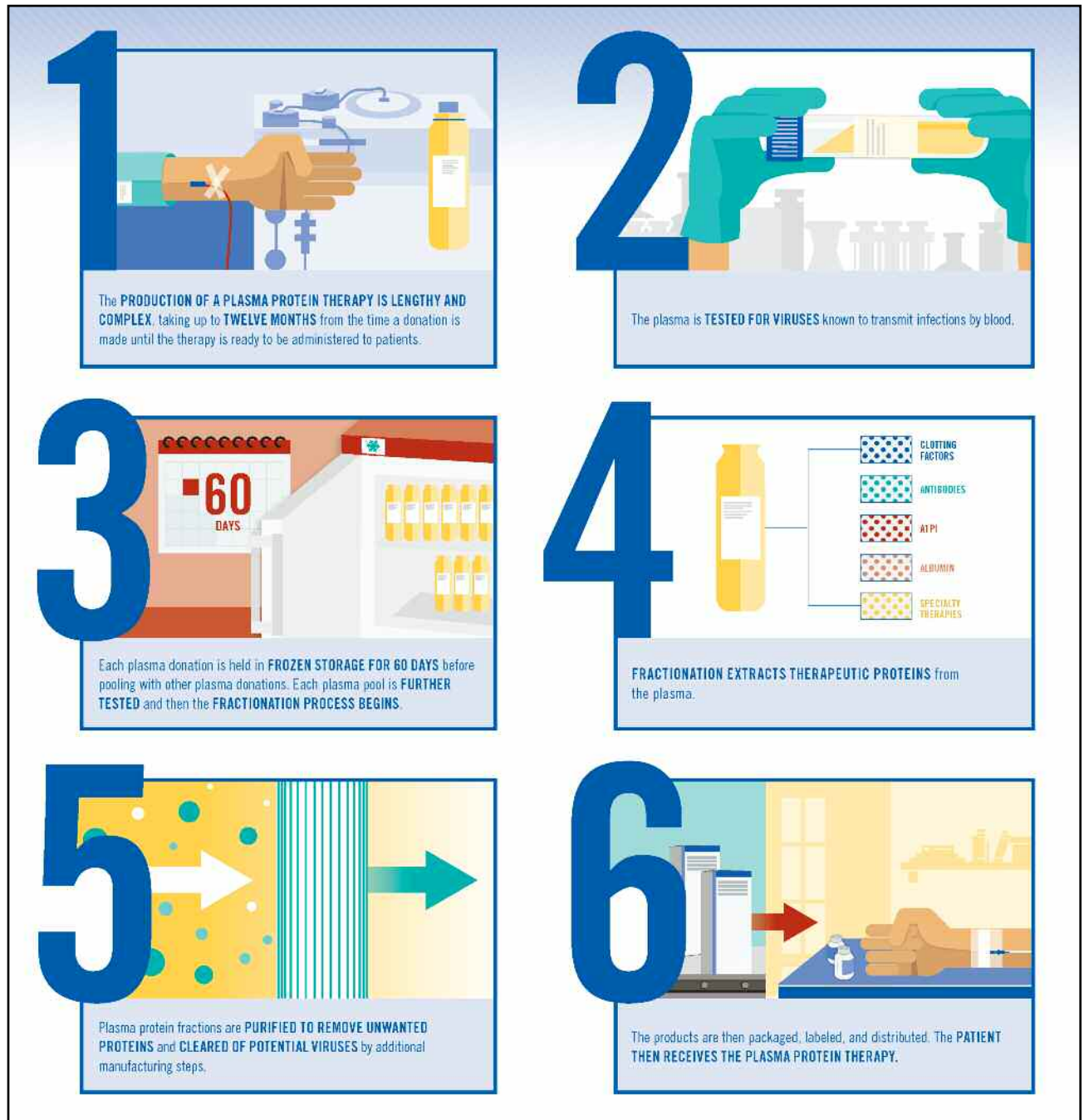
Each unit of plasma is given a unique identification number so it can be tracked throughout the process. All initial donations are placed in storage until the donor returns to provide a second donation within a period of 60 days. One-time donations will not proceed to the manufacturing stage. Instead, that plasma is discarded if the donor does not return. The second and subsequent donations allow for an additional health screening and sample testing, and they demonstrate a level of commitment on the part of the donor. Plasma can be donated up to two times per week with at least 24 hours between donations.

Ensuring the safety and quality of plasma products takes time. On average, it takes seven months to 12 months to manufacture plasma-derived products from the time of

donation to the finished product. Multiple voluntary and mandated processes are in place to monitor products and donation centers for safety and quality issues. The U.S. Food and Drug Administration (FDA) must approve plasma

before it can be used to manufacture products and routinely inspects plasma donation facilities. In addition, the Plasma Protein Therapeutics Association establishes internationally accepted standards and conducts separate facility inspections.

Figure 3.



Source: Plasma Protein Therapeutics Association

All plasma donations are held for a period of 60 days after collection. During this period, samples are tested at several stages for viruses such as HIV, hepatitis B, hepatitis C and others. The testing methods can detect levels of viruses at an early stage, even before a person has developed symptoms. Over the years, this technology has greatly improved the quality and safety of the plasma supply.

## Manufacturing Plasma Products

When plasma is approved for manufacture, the individual units are frozen for transport to a facility where they are pooled (mixed) with thousands of other individual units. Pooling of plasma allows for patients to receive a wide variety of antibodies with each infusion. Once the batches are pooled, they are tested again for viruses.

Plasma proteins are used to treat a variety of illnesses from bleeding disorders to immune deficiencies and autoimmune disorders. Plasma proteins are separated during the fractionation process, which uses various methods such as temperature, pH and alcohol concentrations. Today's technology allows for little waste in the fractionation process.

Once separated, plasma proteins go through a series of steps to filter and inactivate any pathogens that may remain (Figure 3). FDA requires a minimum of two viral removal steps during manufacturing. A multitude of product safety and quality assessments are also conducted along the way. After a final filtration process, the product is bottled and ready to ship.

## The End Result: A Healthier Patient

Plasma products are unlike many pharmaceuticals that can be produced in large quantities and in a short amount of time. Those products start with raw materials rather than with human plasma.

Donor screening and testing and the many quality and safety steps built into the manufacturing process have resulted in plasma products such as IG that are safe and effective for treating many diseases and that have improved not only patients' quality of life, but their life expectancy. For example, the 10-year survival rate of a person with common variable immunodeficiency, the most prevalent form of PI, has increased from 37 percent in 1971 to 90 percent in 2008.

Plasma products would not be possible without people who regularly commit their time and energy to give this gift

## How Can PI Patients Get Involved?

PI patients can get involved in the PI community through a variety of programs established by the Immune Deficiency Foundation (IDF; [www.primaryimmune.org](http://www.primaryimmune.org)):

*IDF Plasma Center Partners Program.* In this program, patients are matched with local participating plasma donation centers, where patients can get a better understanding of the donation process, how the centers function and what safety measures are in place for both patients and donors. Patients are able to speak to other donors and center employees to see firsthand how important their jobs are.

*Share Your Story.* Patients with PI often feel alone and isolated, so IDF encourages patients to make videos that can be uploaded and viewed by other patients who may be experiencing something similar in their lives.

*IDF PI Connect.* PI Connect allows patients to become a part of research by confidentially sharing their information and experiences as a patient with an immune deficiency. The information will help to advance research in the field and allow patients to see how their experience with PI compares to those of others.

*IDF Outreach Initiative.* Patients can become IDF liaisons or Get Connected leaders to learn about new research and developments in the PI community.

*IDF Advocacy Center.* Through this program, patients can help advocate for legislation such as government policy changes, access to products and assistance with copayments, to name a few.

of life. Without a doubt, plasma is a finite resource. To ensure plasma availability for the future, patients should encourage the people close to them to consider donating. Truly, it all starts with people. ■

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### Sources

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