



**INDUSTRY
VOLUNTARY
STANDARDS**
The Value of the IQPP
and QSEAL Designation

“The hemophilia community is vigilant in its mission to help safeguard the nation’s blood supply. The standards programs add another layer of safety to the production of therapies for our community and, while we must not be complacent, provide valuable safety measures that bring a greater sense of confidence to patients.”

— Val Bias
CEO, National Hemophilia Foundation

“Our community feels confident that the immune globulin products we use and that often mean the difference between life and death are as safe as possible in large part because of the standards the industry has implemented.”

— Estelle Benson
Founder, GBS/CIDP Foundation International

“Jeffrey Modell Foundation is committed to raising the level of understanding about primary immune deficiencies across the world through physician education and public awareness campaigns. We know the critical importance of early diagnosis and effective treatment, and believe that the voluntary industry standards in place enhance the safety of immune globulin therapies vitally needed by our community.”

— Vicki Modell
Co-Founder, Jeffrey Modell Foundation

“Any additional measures to regulatory requirements in place aimed at enhancing the safety and quality of plasma-derived therapies is a real added value.”

— Johan Prévot
Executive Director Designate
International Patient Organisation
for Primary Immunodeficiencies

“My brother, my sister and I are among thousands of patients with alpha-1 antitrypsin deficiency whose health has been protected for years with a plasma-based product. We and more than 100,000 rare disease patients are grateful for the PPTA’s quality standards and standards of excellence that add value and give us confidence in the safety of our life- and health-preserving plasma therapies.”

— John Walsh
President and CEO, Alpha-1 Foundation

“The safety and supply of treatment products is a key concern for the global bleeding disorders community. The WFH works in close cooperation with government agencies, industry, clinicians, and patient groups to achieve both the quality and desired quantity of these essential medications. The voluntary industry standards are an important complement to the regulatory structure to attain the highest possible safety and quality of these life-saving therapies.”

— Mark Skinner
President, World Federation of Hemophilia

PPTA is a trade association representing a unique sector of the biologics and biotechnology industry. PPTA member companies manufacture high-impact, high-value plasma protein therapies that make a difference for patients throughout the world who often depend daily on these life-saving therapies. PPTA and its members put patients first and work in tandem with stakeholders to ensure that patients who infuse or inject these complex biologics know they are of the highest possible safety and quality. The Association works globally with consumer groups, policymakers, and other key stakeholders on critical issues of patient access to care. PPTA also administers global standards programs including the International Quality Plasma Program (IQPP) and Quality Standards of Excellence, Assurance and Leadership (QSEAL), and in the U.S., the National Donor Deferral Registry (NDDR), and the Patient Notification System (PNS).

Introduction

The genesis of the Plasma Protein Therapeutics Association’s (PPTA) standards programs, comprising IQPP and QSEAL, was the plasma collection industry’s desire to demonstrate an active commitment to the safety and quality of source plasma and finished plasma protein therapies. In addition to rigorous government regulation, the industry has established additional voluntary standards to help ensure a safe supply of source plasma and the therapies it yields. An initiative to strengthen the continued safety and quality of life-saving plasma protein therapies worldwide for nearly a decade, QSEAL certification represents steadfast industry commitment to producing safe plasma-derived therapies worldwide.

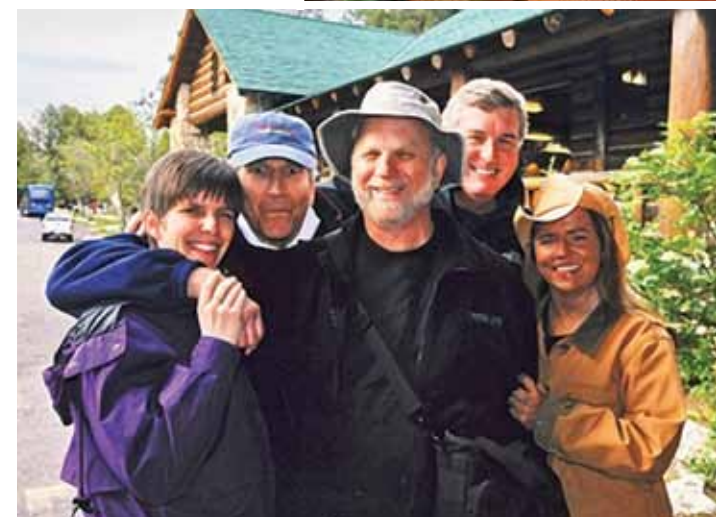
IQPP certification affirms that a plasma collection center is exceeding what is required by government regulation by providing a high-quality business operation and advancing the safety and quality of committed donors and donated plasma.

Nearly 400 licensed plasma collection centers in North America and over 30 centers (still growing) in Europe are now members of the program and engaged in advancing voluntary standards that ensure the starting material for the manufacture of life-saving plasma protein therapies is of the highest quality and safety.

The IQPP-certified plasma collectors and the QSEAL-certified manufacturers work cooperatively to enhance patients’ quality of life.

Public and National Benefit

The reach and influence of the IQPP and QSEAL standards are substantial. Participation by a company in PPTA’s voluntary standards program signifies a commitment to excellence in an open environment characterized by due process and neutral, third-party audits. PPTA’s standards program sets benchmarks for quality and performance that help to protect the public interest. They foster excellence and go beyond regulatory requirements to demonstrate a commitment to quality and safety in the manufacturing of plasma protein therapies.



Government Acknowledgement

The plasma protein therapeutics industry’s enduring commitment to standards also has garnered recognition from regulatory authorities. In 2002, the European Medicines Agency’s (EMA) Committee for Proprietary Medicinal Products (CPMP) published a position statement that discussed the safety and quality of plasma collected from both compensated and non-compensated sources. The statement noted, “For plasmapheresis donors...there are additional voluntary standards to ensure that plasma originates from a low-risk donor population. These include qualified donor programs and inventory hold of donations.” (See EMEA/CPMP/BWP/181/02/Final)

Hallmarks of the International Quality Plasma Program (IQPP) and Quality Standards of Excellence, Assurance and Leadership (QSEAL) Process

- ▶ Available to any company worldwide that can meet the criteria

- ▶ Focus on plasma safety and quality, donor safety and education
- ▶ Continuous process of optimizing standards, checklists, policy documents and other related materials
- ▶ Transparent process allows consideration of diverse industry and stakeholder viewpoints
- ▶ Standards work in concert with other industry regulations to provide a solid foundation for issues of critical importance to the stakeholder community
- ▶ Supports or establishes stakeholder confidence
- ▶ Gives industry common language by which to assess issues surrounding safety and quality



Mark of Quality

Quality ensured by sound regulatory structures and industry practice is a key facet of value for industry, patients, regulators and the public at large and is a symbol of the industry’s commitment to continual improvement and enhancement.

If conformance to standards is the

benchmark for quality, PPTA’s IQPP and QSEAL provide confidence in an established process that includes openness, public notification, coordination, consideration of views, agreement and appeals.

It is important that, over the years that PPTA’s voluntary standards programs have existed, they have been developed and implemented with wide testaments to their credibility, consistency and acceptance.

PPTA in North America

147 Old Solomons Island Road
Suite 100
Annapolis, MD 21401
Phone +1.202.789.3100
Fax +1.410.263.2298
UNITED STATES

PPTA in Europe

Boulevard Brand Whitlock 114/b4
1200 Brussels
Phone +32.2.705.5811
Fax +32.2.705.5820
BELGIUM

PPTA in Asia

Yebisu Garden Palace Tower 18F
4-20-3 Ebisu, Shibuya-ku
Tokyo 150-6018
Phone +81.3.5789.5925
Fax +81.3.5789.5757
JAPAN



PPTA Voluntary Standards

The International Quality Plasma Program (IQPP) was developed in the early 1990s and demonstrated the commitment of PPTA's source members to collect high-quality, safe starting material (source plasma) to produce plasma-derived therapies. The process of updating and optimization of these standards has been ongoing and continues today. Source plasma is used to produce dozens of life-saving therapies. People who use therapies manufactured from human plasma rely on the generosity of committed plasma donors. To ensure state-of-the-art quality and safety of source plasma, companies commit to adhering to the following IQPP standards:

Community-Based Donor

This standard allows only donors who permanently reside within the defined donor recruitment area of the plasma center to donate at that center. The standard helps to maintain a steady and reliable donor population and demonstrates that these individuals are committed to saving and improving lives, through safe, regular donations.

Cross Donation Management Standard

Sometimes, a donor may attempt to donate more often than is permitted. While this is very rare, it is necessary to take measures to protect the health of the donor and minimize this risk. This standard assesses donors and centers to ensure that donations occur within allowable and safe intervals.

Donor Education Standard

It is important that donations are collected from a low-risk donor population. This standard requires new donors to engage in an educational program and follow-up assessment regarding infectious diseases and risky behaviors. The educational

program also encourages donors to lead a healthy lifestyle. Those potential donors who acknowledge being involved in defined high-risk behaviors are deferred from donating.

Personnel Education and Training

This standard ensures that the facility has knowledgeable, experienced and well-trained staff and requires an in-depth initial training program as well as ongoing education. This training ensures that the center staff is up-to-date on the most recent regulatory requirements and latest innovative procedures.

Professional Plasma Collection Facility Standard

It is imperative that all plasma centers maintain a high level of professionalism and quality regarding their cleanliness, safety and appearance. This standard ensures that IQPP-certified plasma centers uphold that level of professionalism and quality.

Quality Assurance

IQPP-certified plasma centers comply with Good Manufacturing Practices (GMP). IQPP requires that there be a staff member who is responsible for evaluating customer and/or donor complaints, and that those complaints be dealt with and investigated as quickly as possible. Lot Release procedures must adhere to GMP rules. IQPP-certified plasma centers must have a system in place to both release shipments of plasma and stop them if necessary.

Qualified Donor

Potential source plasma donors must pass two separate medical screenings and testing for HIV and hepatitis B virus (HBV) and hepatitis C virus (HCV) on two different occasions. Only after those satisfactory screenings and negative test results does that person become a Qualified Donor. If a donor does not return within six months, that person loses his/her Qualified Donor status and must qualify again. This standard means that plasma from a one-time-only donor (even when all test results are negative) cannot be used to produce a therapy. The standard results in committed donors and eliminates the risk that so-called "test-seekers" are accepted.

Use of the National Donor Deferral Registry* (NDDR)

Any individual who tests reactive for HIV, HBV or HCV must be entered into the National Donor Deferral Registry (NDDR), a national database, used by all IQPP-certified centers in the U.S. All individuals presenting themselves at any center for the first time are checked against the NDDR. Those who have previously been deferred for reactive test results at any participating facility can quickly be identified and rejected utilizing this computerized database. This standard ensures that donors deferred for reactive test results do not donate in other facilities.

Viral Marker

It is important that donations are collected from a low-risk donor population. Each center is obliged to track and report its viral marker rates for HIV, HBV and HCV in the donor population. The center's rates are compared to the industry average. Alert Levels are set to take into account the number of annual donations. If a center exceeds the limit for any of these viruses or the aggregate, the center has to implement corrective actions that will bring the center's rates into compliance with the standard. If a center exceeds the limit again, the certification will be lost.

QSEAL Certified Companies



QSEAL certification demonstrates a company's willingness to do more than fulfill the regulatory requirements for manufacturing plasma protein therapies. Certification is based on an independent evaluation and recognizes adherence to the industry's voluntary standards. The QSEAL standards enhance existing government regulations and underscore the industry's commitment to produce the highest quality therapies possible. PPTA began awarding QSEAL certifications to manufacturers of plasma protein therapies in 2001.

Qualified Donor

Potential source plasma donors must pass two separate medical screenings and be tested for HIV, HBV and HCV on two different occasions. Only after those satisfactory screenings and negative test results does that person become a Qualified Donor. If a donor does not return within six

months, that person loses his/her Qualified Donor status and must qualify again. This standard means that plasma from a one-time-only donor (even when all test results are nonreactive) cannot be used to produce a therapy. The standard results in committed donors and eliminates the risk that so-called "test-seekers" are accepted.

Viral Marker

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Inventory Hold

The inventory hold standard requires that each plasma donation be held in inventory for a minimum of 60 days prior to being used in the production of plasma protein therapies. This robust standard allows for the identification, retrieval, and destruction of any plasma donation as a result of post-donation information. Regardless of the type of information, the Inventory Hold Standard offers a strong, important measure of quality control to the production of plasma protein therapies.

Nucleic Acid Amplification Technology (NAT) Screening

The use of Nucleic Acid Amplification Technology (NAT) screening uses state-of-the-art technology to allow for the earliest possible detection of transmissible disease. NAT screening compliments regulatory requirements for serology testing (an antibody test). NAT testing, which can detect viral

infection in the very early stage before antibodies are detectable, is done at the donation or pool level and is an additional safety measure for final therapies. The current standard includes HIV, HBV, HCV and Parvovirus B19.

Intermediates Standard

The intermediates standard is another layer of QSEAL that further ensures the consistency, quality and traceability of intermediate products being incorporated into final therapies by manufacturers. An intermediate is a plasma-derived starting material that must undergo further manufacturing steps before it becomes a final therapeutic product. The exchange of intermediates allows manufacturers to focus on the production of specific therapies. As an additional quality control measure, a "chain of custody" must exist between the supplier and the purchaser of any intermediate subject to QSEAL.



*NDDR is only available in the U. S.

