

2018

ANNUAL REPORT





Saving and Improving Lives

The Plasma Protein Therapeutics Association (PPTA)

represents the private sector manufacturers of plasma-derived and recombinant analog therapies — collectively known as plasma protein therapies—and the collectors of source plasma used for fractionation. Many people worldwide use these therapies to treat a variety of diseases and serious medical conditions. PPTA member companies produce approximately 80 percent of the plasma protein therapies in the United States and 60 percent of those manufactured in Europe. PPTA's experienced team of dedicated professionals continually strives to provide value to its membership and make contributions toward improving and saving lives.

Globally, PPTA works to:

- Advocate for access to and affordability of therapies for patients;
- Engage in constructive dialogue with regulatory agencies;
- Collaborate with patient advocacy organizations; and
- Administer standards and programs that help ensure the quality and safety of plasma collection and manufacturing and protect donors and patients. Standards and programs include:
 - International Quality Plasma Program (IQPP)
 - Quality Standards of Excellence, Assurance & Leadership (QSEAL)
 - National Donor Deferral Registry (NDDR)
 - Patient Notification System (PNS)
 - North American Data Program
 - European Data Program



Mission

PPTA's mission is to promote the availability of and access to safe and effective plasma protein therapeutics for all patients in the world. We will strive to achieve our mission by:

- Fostering the collection of high-quality plasma from healthy donors;
- Establishing standards for the manufacturing of lifesaving plasma protein therapies at the highest levels of safety and quality;
- Breaking down artificial barriers on trade and compensated donors that limit patient access to therapy;
- Supporting government reimbursement practices that reflect the unique nature of plasma protein therapies;
- Educating all stakeholders about the value of the therapies; and
- Adhering to the PPTA Code of Ethics.

Contents

| | |
|----|-----------------------------|
| 2 | LETTER FROM THE PRESIDENT |
| 3 | ACCESS TO CARE |
| 7 | COMMUNICATION & ADVOCACY |
| 11 | FREE TRADE |
| 14 | PLASMA |
| 16 | REGULATORY & QUALITY POLICY |
| 19 | SUPPORTING ORGANIZATIONS |
| 20 | PPTA STAFF |



Letter From the President

Having joined PPTA in January 2019 as President and CEO, I am at once impressed and heartened by the accomplishments of all those who worked together last year to advance our industry and to ensure access to lifesaving plasma protein therapies. Management credit is shared by many in the Association, but the last 23 years of growth and success are due, in large part, to the leadership of Jan M. Bult, who retired at the end of 2018. Jan leaves behind a respected, well-run, and highly successful organization. I am humbled to follow in his wake, and I speak for many when I express my sincerest gratitude for the enterprise that Jan built.

In examining the year in review and all that PPTA accomplished, you will see the fidelity to the Association's mission to promote the availability of and access to safe and effective plasma protein therapeutics for all patients in the world. This is demonstrated through the devotion of staff, our members, and our stakeholders whose collective efforts are manifest in the successes shared herein.

PPTA is a partner worldwide to patients, policymakers, payers, and health care providers in working toward a shared goal of increasing both source plasma and access to the lifesaving therapies made possible by the generosity of plasma donors and companies dedicated to innovation toward new therapies. PPTA provides deep expertise, a strong voice for advocacy, and sophisticated data management. Our organization serves as a convener for our partner stakeholders to assemble in pursuit of the best possible solutions for individuals living with serious, rare, and chronic diseases.

I pledge that PPTA will continue advocating for those we serve through educating and informing audiences about the value of the therapies provided by PPTA member companies and the vital importance of committed source plasma donors.

I look forward to sharing continued success in the years to come. ●



Amy Efantis, *President & CEO*

Access to Care

STRATEGIC GOAL: Ensure access to care through advocacy, education, and appropriate reimbursement policy.

EUROPE

POLICY OUTREACH IN GERMANY

PPTA staff continued its advocacy work in Germany regarding the unique nature of PPTs and met with the rapporteurs for pharmaceuticals and/or blood and blood products of the fractions of the German Bundestag and the new Head of the Department for Pharmaceuticals, Medical Devices, and Biotechnology of the Ministry of Health. The meeting included a discussion regarding a draft paper of the Health Ministers' Conference of the Federal States (Gesundheitsministerkonferenz der Länder) about lifesaving and supply-relevant drugs and about how to better consider PPTs' uniqueness.

Additionally, the new German Minister of Health, Jens Spahn (CDU), is advancing several legislative initiatives. One of these initiatives, the "Draft law for more safety in the supply of medicines" (Entwurf eines Gesetzes für mehr Sicherheit in der Arzneimittelversorgung [GSAV]) could have a major impact on the current system of care for people living with hemophilia. PPTA will continue to advocate for policies that foster access to care for hemophilia in Germany.



GERMAN HEMOPHILIA REGISTRY

PPTA initiated a meeting of the German AG Plasma (Working Group Plasma, consisting of PPT-producing companies, represented by PPTA, German Pharmaceutical Industry [BPI], and the German Association of Research-Based Pharmaceutical Companies [VFA]) with a representative of the Paul Ehrlich Institute (PEI) to discuss the new German Hemophilia Registry (DHR). The goal is to develop the existing epidemiologic registry into a disease registry with significant impact on the data to be collected in the future. The dataset (to be collected) and the technology platform will need to be updated and aligned with other hemophilia registries in Europe. The provisional planning foresees the launch of the updated registry in 2021.

MEETING WITH THE DUTCH MINISTRY OF HEALTH

A PPTA delegation met with the Dutch Ministry of Health to provide input to the proposed change to bring all immune globulin therapies into hospital pharmacies' budgets. The presentation and discussion were productive and will be considered when making a recommendation to the Minister of Health. PPTA expects other stakeholders to provide input as well, including internists, pediatricians, and neurologists, all of whom focus on the importance of having all brands available and not limiting choice.

EU STAKEHOLDER MEETING

As part of its ongoing engagement with national and international patient advocacy organizations, PPTA held a stakeholder meeting in Brussels to discuss common goals and priorities. Over the course of the day, several collective objectives and priorities arose, such as emerging challenges regarding access to care in several EU countries, the need for more plasma to manufacture into lifesaving therapies, and agreement regarding the need for meaningful data supporting the value of PPTs to support advocacy talking points. Participants identified educating policymakers about PPTs and how they are different from traditional pharmaceuticals as a top priority. The stakeholders expressed gratitude to PPTA for hosting a quality meeting with a meaningful agenda that allowed for substantive discussions.

PLASMA-DERIVED MEDICINAL PRODUCTS

PPTA's UK Task Force remains engaged with UK authorities and met with representatives of the Department of Health and the Commercial Medicines Unit of the National Health Service to discuss PPTA's concerns about the potential impact of the proposed changes in the statutory scheme on plasma-derived medicinal products and their future supply in the UK.

IPOPI FORUM IN EU PARLIAMENT

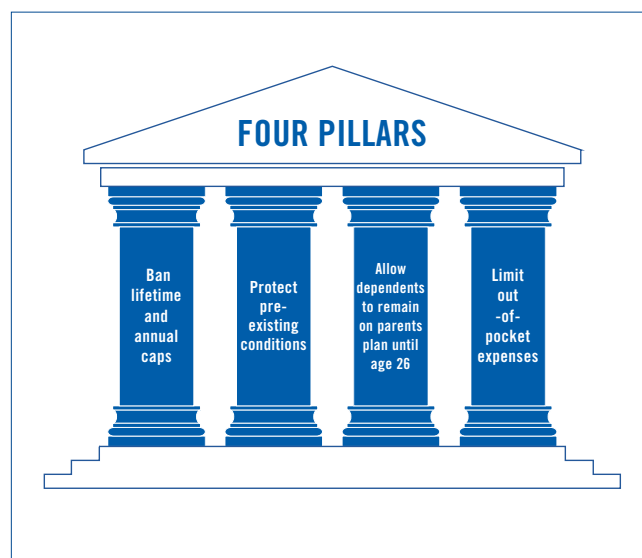
PPTA staff attended IPOPI's 12th PID Forum, "Rare Disease priorities in the European Parliament 2019–2024: The voice of PID patients," which took place in the European Parliament (EP) in Brussels. The Forum was hosted by Portuguese Member of the European Parliament (MEP) José Faria, with five more MEPs in attendance, and focused on IPOPI's vision on rare

disease and PID priorities for the next EP legislation period. The presentations addressed a wide variety of topics, including a forward-looking plan on improving care over the next five years, and newborn screening for severe forms of PID. However, the primary focus was on the patient perspective on improving access to lifesaving therapies.

NORTH AMERICA

STAKEHOLDER MEETING

PPTA hosted two stakeholder meetings in Washington, D.C. with the major patient organizations, which were well attended. Attendees discussed their organizations' priorities, including the protection of the four pillars of patient access, uncertainty surrounding the status of the Affordable Care Act, and access to orphan drugs. During the June meeting, PPTA shared information regarding the North America division's three social media channels and updates on the global "How Is Your Day?" campaign. Further, Richard Manning, Ph.D., of Bates White Economic Consulting shared insights regarding the development of the Bates White paper, "Key Economic and Value Considerations in the U.S. Market for Plasma Protein Therapies."



NATIONAL HEMOPHILIA FOUNDATION'S WASHINGTON DAYS

PPTA attended the State Advocacy Training portion of the National Hemophilia Foundation's (NHF's) Washington Days. Following the Hill Day activities, advocates from across the country shared best practices for local advocacy approaches, with a focus on the hemophilia population served by Medicaid. NHF's priorities at the state level include access to care and opposing fail first policies.

HEMOPHILIA FEDERATION OF AMERICA'S ANNUAL SYMPOSIUM

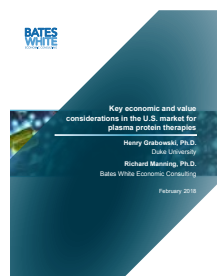
PPTA staff attended the Hemophilia Federation of America's Annual Symposium in Cleveland, Ohio, and gave a presentation focused on federal issues. Staff attended sessions on advocacy and research, exhibited the Patient Notification System, presented the "How Is Your Day?" initiative, and interacted with and learned from advocates in the hemophilia community.

IDF ADVOCACY WORKSHOP

PPTA joined the Immune Deficiency Foundation (IDF) Advocacy Workshop in Annapolis, Maryland, along with patient and family advocates from the Mid-Atlantic region who gathered to hear from IDF & state legislators on the upcoming priorities for 2019. Participants learned how to conduct an advocacy meeting and worked on crafting their "elevator" (brief, concise, typically two-minute) speech. This event helped strengthen the patient voice to advocate on behalf of access to plasma protein therapies.

GBS|CIDP FOUNDATION INTERNATIONAL BIENNIAL SYMPOSIUM

PPTA staff attended the 15th Biennial Symposium celebrating 30 years of the GBS|CIDP Foundation International in San Diego, California. The Patient Notification System (PNS) and "How Is Your Day?" (HIYD) were on display at the PPTA exhibit booth and were of high interest to attendees. Staff promoted the PNS and HIYD, answered questions related to the manufacturing and safety of IgG products, and attended various scientific presentations and patient-oriented discussions.



WHITE PAPER FROM BATES WHITE ECONOMIC CONSULTING

Bates White Economic Consulting published a white paper, entitled "Key Economic and Value Considerations in the U.S. Market for Plasma Protein Therapies." The report highlights the value and unique characteristics of the PPT market. Staff shared the paper's

insights with stakeholders, industry representatives, and key decision-makers and anticipates further utilizing the paper's conclusions in 2019 and beyond.

PPTA'S ANNUAL FLY-IN

On Thursday, May 17, PPTA held its annual Congressional Fly-In. The Association brought together member companies, individuals with rare diseases, and patient advocacy organization representatives. The Fly-In provides an opportunity to inform Congress about the unique nature of plasma protein therapies and the rare diseases they treat, the value of therapies, and the importance of policies that preserve access. Congressman G.K. Butterfield (D-NC), who serves on the Energy and Commerce Committee and is the co-Chair of the Congressional Rare Disease Caucus, provided opening remarks, and the Chair of the North America Board of Directors presented him with a leadership award. The Fly-In's 30 participants visited more than 50 offices. New in 2018, PPTA created a dedicated app that included information about schedules, maps of Capitol Hill, and interactive ways for participants to stay connected throughout the day by sharing photos and comments about their experiences.

TRUMP ADMINISTRATION & DRUG PRICING

The Trump administration spent significant time in 2018 focusing on ways to lower drug costs, and PPTA responded by submitting comments advocating that any changes not affect access to plasma protein therapies. First, the Department of Health & Human Services published a Request For Information (RFI) on the administration's "Blueprint to Lower Drug Prices." The broad questions contained in the RFI dealt with areas in which PPTA has been previously involved, such as moving reimbursement for physician-administered drugs from Medicare Part B (physician office coverage) to Medicare Part D (prescription drug coverage), which is primarily a retail-based system using managed care interventions. PPTA's comments oppose such a change, objecting to the inclusion of plasma protein therapies in a flawed Competitive Acquisition Program. Patient access to PPTs in the appropriate setting remains a high priority for PPTA.

Later in the year, the Office of the Assistant Secretary for Planning and Evaluation released an analysis, "Comparison of U.S. and International Price for Top Medicare Part B Drugs by Total Expenditures." Simultaneously, the U.S. Department of Health and Human Services (HHS) released an advance notice of proposed rulemaking (CMS-5528-ANPRM) for an International Pricing Index Model for Medicare Part B Drugs. The three key parts of the proposal include reduction of Medicare reimbursement for Part B drugs to better align with prices outside the United States, implementation of a CAP-like private-sector vendor program to negotiate prices of drugs with manufacturers, and the transition of the provider add-on payment from an Average Sales Price (ASP)-based percentage to a set payment amount.

The proposal is for a five-year demonstration model that would apply to 50 percent of Medicare Part B spending in the United States starting in 2020. The reduced Medicare reimbursement would likely result in lower negotiated prices between private-sector vendors and manufacturers, thereby reducing the

calculated Average Sales Prices. The lowered ASP could then extend beyond the confines of Medicare and affect Medicaid best price, rebates, AMP, and 340b ceiling prices.

PPTA expressed concern that individuals' access to lifesaving plasma protein therapies could be negatively impacted by these experiments and that innovation of new therapies could suffer. While the HHS believes it has authority to implement the demonstration, congressional oversight would certainly be asserted. PPTA worked with its Federal and State Affairs Steering Committees, stakeholders, and industry coalitions to submit comments regarding the ANPRM and will continue advocating with Congress and HHS to protect access to plasma protein therapies.

COMMENTS

CANADA

PPTA submitted letters to Canadian Blood Services (CBS) and the Provincial and Territorial Blood Liaison Committee supporting Alpha-1 Canada's appeal to add Alpha-1 Proteinase Inhibitors to CBS's list of plasma protein therapies. This change would allow all Canadians with alpha-1 antitrypsin deficiency to access augmentation therapy. Currently, access to treatment is on a province-by-province basis, with only some Canadian provinces providing access.

CALIFORNIA ASSEMBLY BILL 613

On Sept. 27, 2018, California Gov. Brown signed Assembly Bill 613 (Nazarian), which was supported by PPTA. This law creates a two-year pilot and went into effect at the beginning of 2019. The measure allows properly trained individuals to perform the total protein test in plasma donation centers using a digital refractometer. Previously, the California law required a licensed individual, typically a registered nurse, to perform the test. The governor vetoed a similar bill in 2015 at the recommendation of the California Department of Public Health (DPH) so the governor's approval represented a major victory for PPTA, its members, and the patient advocacy organizations that worked together for two years to pass this legislation. PPTA and its members had numerous meetings and conference calls with DPH to craft a bill it would not oppose. Advocacy with the governor's office included social media efforts and letters of support from advocacy organizations such as the American Plasma Users Coalition, the California Chronic Care Coalition, the Hemophilia Council of California, and the Immune Deficiency Foundation.

CALIFORNIA'S REIMBURSEMENT METHODOLOGY FOR SPECIALTY PHARMACIES

The State Patient Access Coalition (SPAC), a coalition of blood clotting factor manufacturers and specialty pharmacies managed by PPTA, met with members and staff of the California Legislature to discuss California Medicaid's

proposed reimbursement reduction for blood clotting factors. The reduction would decrease the non-ingredient cost portion of the reimbursement formula by more than 70 percent. SPAC suggested in meetings and in a delivered letter that a reduction of this amount would negatively affect patient access to medically appropriate therapy and should have legislative oversight. Following SPAC's advocacy for legislative oversight of the proposed reimbursement methodology, the California Legislature put a stop to the implementation and passed a budget with language requiring Medi-Cal to provide certain information before a new methodology may be implemented.

FLORIDA'S PROPOSED BLOOD CLOTTING FACTOR REIMBURSEMENT METHODOLOGY

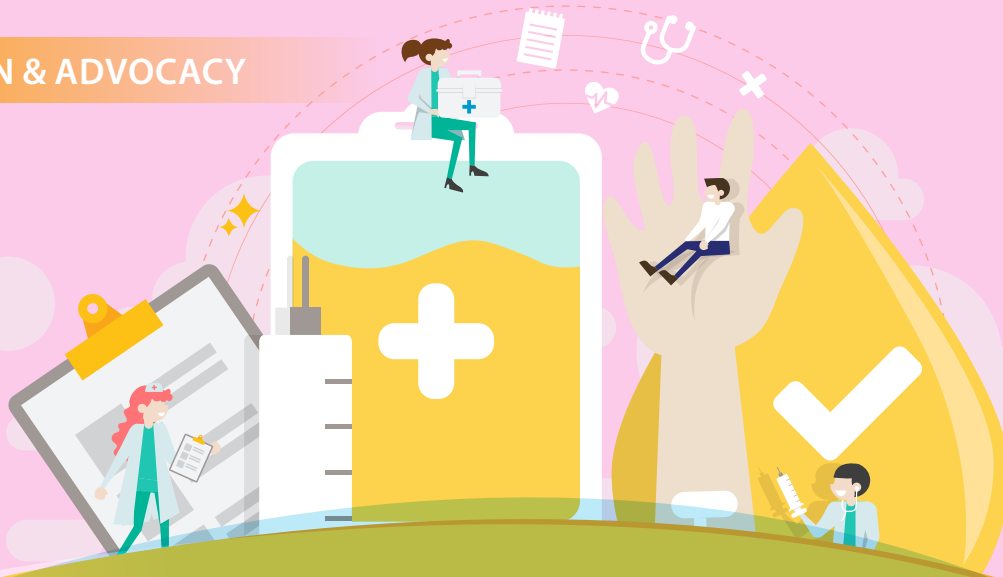
In 2018, Florida Medicaid proposed to reimburse for blood clotting factor using a methodology based on Average Manufacturer Price (AMP). PPTA was concerned that this methodology could inadvertently reveal the manufacturer's AMP when they reimburse specialty pharmacies. Federal law requires states to keep AMP confidential, so any disclosure may violate federal law.

PPTA wrote a letter to remind Florida Medicaid that AMP is confidential and voiced concerns that the proposal could result in its disclosure. PPTA shared that no states use AMP as a Medicaid pharmacy reimbursement benchmark and suggested the state use a different benchmark. In addition, PPTA staff and representatives from blood clotting factor manufacturers met with Florida Medicaid in Tallahassee, held a conference call with blood clotting factor manufacturers and the Florida Medicaid director, and spoke with representatives from the Centers for Medicare and Medicaid Services (CMS) about the concerns at the Annual Meeting of the Southern Association of Medicaid Pharmacy Directors. After our discussion with CMS, CMS informed Florida Medicaid that they shared our concerns about keeping the AMP confidential.

Florida Medicaid later informed PPTA that it would delay the implementation of the new contract for comprehensive hemophilia management based on the Average Manufacturer Price (AMP) of blood clotting factors until it can develop a reimbursement model that will keep the AMP confidential as required by federal law. After concluding it could not develop a model that would keep AMP confidential, Florida Medicaid withdrew the proposal.

GEORGIA HOUSE BILL 747

In early 2018, PPTA submitted a letter of support for Georgia House Bill 747, which would allow unrestricted access to therapies for Medicaid beneficiaries with hemophilia and prohibit policies like prior authorization and step therapy. The bill was sponsored by the chair of the House Health & Human Services Committee, and PPTA testified in support of the bill at the Capitol in Atlanta. ●



Communication & Advocacy

STRATEGIC GOAL: Be the trusted resource for plasma protein therapies.

PPTA EVENTS

PPTA LAUNCHES “HOW IS YOUR DAY?”

**HOW IS
YOUR DAY?**

MAKING THE DIFFERENCE WITH PLASMA PROTEINS.

PPTA officially introduced its first global education and awareness campaign at the International Plasma Protein Congress in Budapest, Hungary, in March. “How Is Your Day?” (HIYD) differentiates plasma protein therapies from traditional pharmaceuticals, raises awareness of the value these therapies provide for people living with rare, life-threatening, chronic, and genetic diseases, and recognizes the essential role of source plasma donors. The campaign launched with a video presentation featuring plasma donors and patients who rely on therapies derived from those donations, as well as with a panel presentation, and an interactive booth display.



Since its launch, HIYD has been featured at PPTA's Plasma Protein Forum in Washington, D.C., as well as several patient advocacy organization meetings throughout the United States and in Europe. PPTA also participated in a radio interview tour to promote the HIYD campaign across the United States. The interviews were heard on more than 500 radio stations by a potential listening audience of more than 10 million people. PPTA made all online content available in English, German, French, Italian, Spanish, and Portuguese in recognition of the global reach of the campaign. Looking ahead, PPTA will continue utilizing the HIYD campaign to build awareness of the unique nature of these therapies and their value with members of the public, patient advocacy organizations, caregivers, and policymakers around the world.

PPTA encourages patients, doctors, donors, and anyone interested in the "How Is Your Day?" initiative to visit www.HowIsYourDay.org to learn more and to follow the global conversation on Facebook and Twitter at @HIYDglobal.


PPTA ATTENDS WFH WORLD CONGRESS

PPTA attended the World Federation of Hemophilia (WFH) 2018 World Congress in Glasgow, Scotland. Attended by approximately 5,000 patients, caregivers, medical professionals, and representatives from industry,

WFH was an opportunity for all attendees to learn from each other and build greater awareness of the need for global access to hemophilia treatments. PPTA organized a booth in the exhibit hall and used the space to inform and educate attendees about IQPP and QSEAL, our internationally recognized standards programs, as well as to continue building awareness of the "How Is Your Day?" initiative. Attendees were glad to know PPTA is managing a global campaign to inform the public, decision-makers, and policymakers about the unique nature of plasma protein therapies and the rare diseases they treat. Several individuals with hemophilia, as well as medical professionals and caregivers, volunteered to give their own personal testimonials about how important access to PPTs is in treating bleeding disorders.

PPTA ATTENDS ESID 2018

PPTA staff joined physicians, nurses, patients, and advocates in Lisbon for the 18th Biennial Meeting of the European Society for Immunodeficiencies (ESID). Staff participated in educational sessions focused on treatment options for people living with primary immune diseases and offered attendees opportunities to learn about the "How Is Your Day?" campaign. Notably, patients and advocates from Portugal, the meeting's host country, were excited to learn about and support HIYD.



PPTA encourages patients, doctors, donors, and everyone interested in the "How Is Your Day?" initiative to visit www.HowIsYourDay.org to learn more and to follow the global conversation on Facebook and Twitter at @HIYDglobal.

"HOW IS YOUR DAY?" REPORTED IN *POLITICO*

POLITICO

The "How Is Your Day?" campaign launch was profiled in *Politico Magazine*: "Over in Budapest, producers of plasma protein therapies including

immunoglobulin launched a campaign Tuesday to differentiate their products from traditional medicines and raise awareness of the value they provide for people living with rare, chronic, and genetic diseases. Because plasma protein therapies replace missing or deficient proteins, they can allow people to lead healthy and productive lives, the Plasma Protein Therapeutics Association said."

"HOW IS YOUR DAY?" ARTICLE PUBLISHED ON PMLIVE

PMLive published an article focused on the "How Is Your Day?" global campaign, showing how plasma protein therapies improve lives. The article noted the importance of these therapies for people living with rare diseases and the role of source plasma donors in ensuring the availability of the starting material for these lifesaving biologics. "How Is Your Day?" brings together people around the world who are interested in plasma protein therapies, aiming to inform and educate policymakers and the public of their unique, lifesaving value.

RDLA ANNUAL LEGISLATIVE CONFERENCE

PPTA participated in Rare Disease Legislative Advocates (RDLA) Annual Legislative Conference as a part of February's Rare Disease Week on Capitol Hill. In addition to interacting with rare disease advocates from around the country, PPTA discussed the recently published white paper from Bates White Economic Consulting, "Key Economic and Value Considerations in the U.S. Market for Plasma Protein Therapies." Staff had an opportunity to share insights from the paper with stakeholders, representatives from industry, and congressional and government staff.

2018 PLASMA PROTEIN FORUM

PPTA hosted the 2018 Plasma Protein Forum, June 12–13, at the Washington Marriott in Washington, D.C. David Bell, Chair of the PPTA Global Board of Directors and Chief Innovation Officer, Grifols S.A., presented Shinji Wada, Vice President, Japanese Affairs, Grifols S.A., with the Dr. Otto Schwarz Award in recognition of his decades of dedicated service and commitment in support of the plasma protein therapeutics industry, including serving for five years as the Chair of the Source Board of Directors. Mr. Bell also presented Jan M. Bult with PPTA's Lifetime Achievement Award for his decades of service as President and CEO.

"How Is Your Day?" brings together people around the world who are interested in plasma protein therapies, aiming to inform and educate policymakers and the public of their unique, lifesaving value.

SOURCE BUSINESS FORUM

PPTA held its annual Source Business Forum in Atlanta, Georgia, on Oct. 18. The members-only event featured the following panel discussions:

- Exploring Expanded Collection Geography: Challenges and Opportunities
- Transfusion and Infusion: Meeting Patient Needs
- New Roads in Plasma Donation Ethics

Mr. Larry Moss (The Interstate Companies) was honored as the recipient of the Robert W. Reilly Leadership Award for his contributions and leadership on behalf of the Source plasma collection industry. In a simultaneously heartfelt and lighthearted speech, Mr. Moss thanked the membership for years of support, encouragement, and partnership.

IRON DEPLETION STUDY

PPTA and three member companies conducted a study of 1,254 Source plasma donors to assess whether frequent donors have an increased risk of iron depletion. Iron depletion in blood donors is well-recognized as a concern. With plasma donors donating more frequently, industry decided to assess iron status in frequent donors as part of its donor health initiative. This study was designed to examine whether frequent plasma donation reduced iron stores. Ferritin levels for four groups with different frequencies of donation were measured, and the prevalence of absent iron stores was assessed. The study provides evidence that plasma donation does not result in an increased risk of iron depletion; therefore, no additional measures need to be taken to ensure adequate iron stores in donors. The findings were published in the April 2018 issue of *Transfusion* (Volume 58, Issue 4).

SUPPLEMENT PUBLISHED IN *TRANSFUSION*

Transfusion published a Supplement (Volume 58, Issue S3) related to a workshop called "Immune Globulin Potency in the 21st Century" held in 2017, which was sponsored by the Food and Drug Administration (FDA), PPTA, the National Institute of Allergy and Infectious Disease,

Importantly, the articles provide scientifically sound evidence supporting the FDA decision to issue a recommendation "Letter to Immune Globulin (Human) Licensed Manufacturers: Option to Lower Lot Release Specification for Required Measles Antibody Potency Testing" dated Nov. 5, 2018.

and the Immune Deficiency Foundation (IDF). The supplement covers several topics, including potency testing of human immunoglobulin (IgG) products as a measure of their functionality against the measles virus. Industry investigators showed that titers of measles neutralizing antibodies in plasma donors have steadily declined since the introduction of the vaccination against measles. They also established that lowering the lot release specification for measles neutralizing antibody from 0.48x to 0.36 x CBER Standard lot 176 (16.5 percent) for IgG products would still be sufficient to protect patients on IgG against measles. Other topics discussed in the supplement include challenges the industry is facing in view of the global eradication of wild-type poliovirus through the WHO efforts. New developments in genetic engineering research offer possible

solutions to address this concern, while continuing to perform potency testing of IgG products for poliovirus neutralizing antibodies. Finally, the supplement discusses possibilities for new and more advanced potency assays that could be considered in the future. A comprehensive assessment of all aspects of the workshop was reviewed by the FDA, and IDF provided valuable comments.

Importantly, the articles provide scientifically sound evidence supporting the FDA decision to issue a recommendation "Letter to Immune Globulin (Human) Licensed Manufacturers: Option to Lower Lot Release Specification for Required Measles Antibody Potency Testing" dated Nov. 5, 2018. The articles are available in open access. Publication of this supplement was made possible by support provided by the FDA and PPTA. ●



IN MEMORIAM: SHINJI WADA

Shinji Wada, Vice President of Japanese Affairs at Grifols and Chair Emeritus of the PPTA Source Board of Directors, passed away in December 2018. He offered many years of service to the Source Board which, of course, culminated in five years of unparalleled leadership as Chair. His wisdom, intelligence, humor, and warmth were known to all. His guidance steered the industry and the Association smoothly through some very difficult issues and stormy weather. Shinji will be missed dearly by all who knew him.

Free Trade

STRATEGIC GOAL: Eliminate trade barriers and other discriminatory practices to achieve open access to plasma protein therapeutics globally.

ASIA

PPTA and member company representatives attended a series of meetings concerning plasma collection and the production of plasma protein therapies in Beijing in September with Chinese officials and regulators.

CHINESE PHARMACOPOEIA COMMISSION MEETING

PPTA and member company representatives gave presentations at a daylong meeting at the offices of the Chinese Pharmacopoeia Commission (ChP) in Beijing. The presentations covered a range of topics including donor selection, plasmavigilance, testing technologies, manufacturing, prion clearance, quality systems, and risk reduction. The meeting was attended by approximately 30 representatives from the ChP and several Chinese regulatory bodies such as the National Medicinal Products Administration (NMPA—formerly CFDA), Center for Drug Evaluation (CDE), and provincial regulators. The meeting was part of ongoing engagement in advance of the release of the newest edition of the Chinese Pharmacopoeia, expected in 2020.

CHINESE FOOD AND DRUG INSPECTORATE MEETING

The following day, PPTA members gave presentations on testing and risk reduction at the invitation of the Chinese Food and Drug Inspectorate. The meeting was attended by approximately 60 people and more than 400 inspectors in 26 cities participating via video conference. The good attendance at this meeting was particularly notable given the fact that it was held with the backdrop of recent major personnel changes due to the then-unfolding vaccine scandal in China.

PARENTERAL DRUG INDUSTRY CONGRESS

On the final two days of meetings, PPTA co-organized and participated in the Plasma Protein Industry Summit at the Parenteral Drug Industry Congress for the second year in a row. This year, the Congress featured PPTA member companies and leadership, Chinese and U.S. regulators, and

Chinese fractionators. The audience of around 220 people was largely made up of representatives of Chinese industry, with the addition of some regulators and representatives of foreign companies.

CANADA

RECONSIDER BANS OR PROPOSALS AGAINST COMPENSATED PLASMA DONATION

In early 2018, a group of 26 ethicists and economists, including two Nobel Prize winners—Alvin E. Roth and Vernon Smith—published a letter urging Canadian provincial governments to reconsider bans or proposals to ban compensated plasma donation. The letter was addressed to the Health Canada Expert Panel on Immune Globulin Product Supply and Related Impacts in Canada, which PPTA followed closely. It refutes the common arguments against compensated plasma donation, further noting that it would, in fact, be unethical not to compensate donors. The letter was developed by Georgetown University ethicist Peter Jaworski, who spoke at the 2017 PPTA Business Forum. Professor Jaworski is a native of Ontario. The letter can be read at www.donationethics.com.

CANADIAN OUTREACH

PPTA staff met with a Canadian senator and a representative of Health Canada in Ottawa to discuss Bill S-252, which would ban compensated plasma donation in Canada. PPTA provided facts about the safety and ethicality of compensated donation and discussed how crucial compensation is to collecting sufficient plasma to meet patient needs. The bill has been referred to the Senate Committee on Social Affairs, Science, and Technology for further study. ●







Plasma

STRATEGIC GOAL: Ensure the availability of safe, high-quality plasma for fractionation.

MEETING WITH MEMBERS OF GERMAN HEALTH COMMITTEE

Members of the Health Committee of the German Parliament visited plasma collection centers in Würzburg (Bavaria, Germany) and Lübeck (Schleswig-Holstein, Germany) during the summer of 2018. During the meetings, participants addressed the global need for more plasma and the need for more plasma collection in Europe to meet the increasing patient needs. The meeting was also an opportunity to discuss potential measures to increase public awareness of plasma donation in Germany and other opportunities to recognize the specificities of our sector. A member of the German patient advocacy organization dsai (Deutsche Selbsthilfe für angeborene Immundefekte) attended the meeting in Würzburg and reported about her life as a PID patient and issues patients face regarding access to specialized care.

MEETING WITH EDQM

A PPTA delegation met with the European Directorate for the Quality of Medicines (EDQM) in June in Strasbourg. During the meeting, the Association introduced the "How Is Your Day" campaign and focused on the data from the pilot study on donor vigilance with 7.5 million donations. The presentation was very well-received, and the EDQM



stressed the importance of publishing the data so it can be considered when preparing the 2020 EDQM. The delegation stressed the importance of a transparent consultation with all stakeholders included.

INTERNATIONAL PLASMA AWARENESS WEEK

The sixth annual International Plasma Awareness Week (IPAW) was held October 8–12 and was marked by the introduction of a new animated video about plasma donation; updated infographics and social media images; and events in Berlin, Vienna, and Washington, D.C. The “How Is Your Day?” social media channels highlighted and thanked source plasma donors each day, and the North America social channels posted notes of appreciation for the 46 state proclamations we received celebrating and acknowledging Plasma Awareness Week in the United States.

PPTA hosted an event on Capitol Hill to educate policymakers and their staff members about the importance of plasma donation. This event was also an opportunity to demonstrate appreciation for the commitment shown by source plasma donors. PPTA staff educated attendees about the plasma donation process and how donations are used to make lifesaving plasma protein therapies for people living with rare, genetic, and chronic diseases.

Representative Doris Matsui (D-CA) recognized IPAW by entering testimony into the Congressional Record in the United States. The content leveraged the sentiment of the “How Is Your Day?” initiative and noted the importance of plasma donation in the lives of individuals who rely on plasma protein therapies.

In conjunction with the Austrian Interest Group Plasma (IG Plasma) and the Austrian Pharmig (Association of the Pharmaceutical Industry of Austria), PPTA organized a press conference in Vienna to recognize plasma donation, plasma protein therapies, and the patients who rely on these lifesaving therapies. The panel discussion included a representative of the PID patient organization, one leading PID physician, as well as representatives from the private plasma collectors and plasma-derived medicinal products manufacturers. Further, PPTA hosted a roundtable in Berlin during IPAW to discuss the importance of source plasma donation with German legislators. Policymakers, staff members, officials of the German Ministry of Health, and patient representatives were invited to discuss the plasma collection and fractionation industry in Germany and steps taken to raise awareness about plasma donation in the general population, including a discussion about the “How Is Your Day?” campaign and advertising for blood and plasma donation by the Federal Center for Health Education (Bundeszentrale für gesundheitliche Aufklärung [BzgA]).

STANDARDS AND PROGRAMS



IQPP STANDARDS PROGRAM

PPTA launched a new mobile app for implementing the IQPP audit checklist. Use of the app allows for more transparency in the audit process and allows staff to review and respond to IQPP audit reports more efficiently. It will also facilitate the use of metrics to evaluate the standards program.

PPTA has developed a training tool focusing on standards relating to donor health and safety. It is intended to help plasma center staff communicate with donors about the requirements in the IQPP standards.



QSEAL STANDARDS PROGRAM

Plasma protein therapeutics manufacturing facilities in six countries hold certification for compliance with the QSEAL standards, a mark recognizing their commitment to excellence, leadership, and quality.

We are proud to welcome one new facility, which achieved first-time QSEAL certification:

- Takeda, Social Circle, United States

These facilities successfully completed audits in 2017 for renewal of their certifications:

- CSL, Marburg, Germany
- CSL, Bern, Switzerland
- Grifols, Clayton, United States
- Kedrion, Melville, United States
- Shire, Vienna, Austria. •

2018 IN NUMBERS

| | |
|-----|--|
| 753 | Plasma centers hold IQPP certification |
| 6 | Countries have centers with IQPP certification |
| 23 | Companies hold corporate certification |
| 327 | Audits were conducted |
| 425 | Centers have been certified for five years or longer |
| 321 | Centers have been certified for 10 years or longer |
| 155 | Centers have been certified for 20 years or longer |
| 92 | Centers have been certified for 25 years or longer |
| 105 | Centers received initial certifications in 2018. |
| 234 | Centers received recertification audits in 2018 |

Regulatory & Quality Policy

STRATEGIC GOAL: Advocate for regulatory and quality policies that reflect the special nature of plasma protein therapies and promote a harmonized approach.

ASIA

CHINESE PHARMACOPOEIA

In anticipation of a 2020 version of the Chinese Pharmacopoeia, which is updated on a five-year cycle, certain revisions to the 2015 version have been released for public comment. PPTA provided comments on the Quasi Revised Contents of Plasma Products (Volume 3) in the 2015 Edition of Chinese Pharmacopoeia. PPTA's comments focused on the allowable content of IgA in IG products. PPTA specifically mentioned the risk of discrepancies in results based on the different test kits and equipment used.

PPTA also responded to the China Center for Drug Evaluation's request for public comments concerning the proposed Administrative Measures on the Information Disclosure of Drug Review and Approval. PPTA's comments focused on manufacturer proprietary information disclosure and appeal rights.



EUROPE

PLUS MEETING

In January, PPTA staff attended the Platform of Plasma Protein Users (PLUS) meeting in Dublin, which gathered patient advocacy organizations and stakeholders involved in the access to plasma protein therapies. After the first session on emerging viruses and safety measures related to plasma protein therapies, the meeting focused on how to ensure access to these therapies, considering global clinical use trends and access to care limitations in several countries. The participants discussed various strategies to encourage blood and plasma donations in Europe. Topics such as the risk of crowding out of donors, the coexistence of private and public sectors, compensation systems, and frequency of donations were also discussed. Participants agreed to maintain an open dialogue among stakeholders, and efforts should be continued to reach a better consensus on key issues.

EUROPEAN ALPHA-1 AWARENESS DAY

PPTA attended the "European Alpha-1 Awareness Day: European health made national," organized by the Alpha-1 Foundation, which took place at the European Parliament in Brussels. It was the very first Alpha-1 event of its kind in the EU Parliament and was hosted by MEP Marek Plura/Poland and MEP José Faria/Portugal. The objective of the event was to promote the European Alpha-1 Recommendations, "Time to get better," to improve diagnosis and treatment by bringing them to the national level. To this end, Alpha-1 national organizations from Poland, Spain, Italy, the Netherlands, Belgium, Romania, and the UK presented and discussed Alpha-1 issues in their countries. The meeting was attended by other EU policymakers, treaters, and industry.

MEETING WITH EU COMMISSION ON EU BLOOD DIRECTIVE

PPTA had a successful meeting with the EU Commission DG SANTE B4 Blood Unit in Brussels, demonstrating PPTA's acceptance as a trusted partner. The objective of the meeting was to have a follow-up exchange of views on the need to revise the Blood Directive after a previous meeting in 2017. The Commission presented the status of the Evaluation of the Blood Directive, while PPTA offered a thoughtful proposal to improve the Blood Directive in the event that it is opened for reconsideration. PPTA's presentation was very well-received by those in attendance. The "How Is Your Day" campaign was introduced with a video featuring testimonials from patients and plasma donors; the Commission gave positive feedback and suggested it might consider formally acknowledging it.

EU COMMISSION STAKEHOLDER EVENT AT BLOOD NATIONAL COMPETENT AUTHORITIES MEETING IN BRUSSELS

EU Commission DG SANTE B4 Unit invited PPTA and the European Plasma Alliance (EPA) to this stakeholder meeting in Brussels with the 28 National Competent Authorities on Blood. Two main issues were addressed by DG SANTE B4:

- The impact of critical medical devices on blood and plasma supply (risk and strategies).
- The importance of microbial reduction steps in blood preparation for transfusion.

UK — FINALIZED NEW STATUTORY REIMBURSEMENT SCHEME

The Department of Health and Social Care published the finalized regulations of the statutory scheme to control the costs of branded health service medicines, which came into force in January 2019. The final regulation implements a new payment scheme that is somewhat less than what was initially proposed. The payment percentage will increase from 7.8% in 2018 to 9.9% in 2019, and then to 14.7% in 2020, 20.5% in 2021 and "any subsequent calendar year." The government's response to the public consultation includes detailed comments related to Plasma-Derived Medicinal Products, acknowledging the specificities of our sector.

NORTH AMERICA

MEASLES TITER

PPTA worked with the U.S. Food and Drug Administration (FDA) Center for Biologics Evaluation and Research (CBER) to ensure the industry proposal to lower lot release specification for measles virus neutralizing antibody levels in potency testing of IgG products meets FDA requirements and provides protection from measles infection to patients with primary immunodeficiencies. The FDA published the "Letter to Immune Globulin (Human) Licensed Manufacturers: Option to Lower Lot Release Specification for Required Measles Antibody Potency Testing," dated Nov. 5, 2018, informing manufacturers that under 21CFR 640.104(b)(2), the CBER sets the minimum specification for measles neutralizing antibody levels in Immune Globulin products as 0.36 x CBER Standard lot 176 (16.5 percent). The letter also recommends labeling the Prescribing Information that contains dosing recommendations for patients with Primary Humoral Immunodeficiency who have been exposed, or are likely to be exposed to measles.

COMMENTS ON FURTHER TESTING OF DONATIONS GUIDANCE

PPTA submitted comments to the FDA draft guidance on the further testing of donations that are reactive on a licensed donor screening test for antibodies to hepatitis C virus (anti-HCV), as required under 21 CFR 610.40(e). FDA's guidance suggested that if NAT is nonreactive for HCV, further testing is necessary using a second, different licensed donor screening test for anti-HCV. PPTA's comments suggested the second test was unnecessary to meet the goals of donor health shared by PPTA and the FDA and requested an exemption from the guidance. PPTA asked the FDA to include an alternative algorithm choice of using FDA-cleared moderate or high-complexity serology assays (anti-HCV or NAT) to provide additional information concerning the reactive donor's HCV infection status in addition to assays licensed for donor screening.

DRAFT GUIDANCE FOR INDUSTRY

PPTA commented on the draft guidance for industry "Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management: International Council for Harmonisation Draft Guidance." The purpose of the proposed guideline is to provide a framework to facilitate the management of post-approval of Chemistry, Manufacturing and Controls (CMC) changes in a more predictable and efficient manner. It is also intended to demonstrate how increased product and process knowledge can contribute to a reduction in the number of regulatory submissions. Effective implementation of the tools and enablers described in this guideline should enhance the industry's ability to manage many CMC changes effectively under the firm's Pharmaceutical Quality System with less need for extensive regulatory oversight prior to implementation.

THE ANSWER STUDY

On May 31, *The Lancet* journal published the long-awaited data from the "ANSWER Study" on its website under the title "Long-term albumin administration in decompensated cirrhosis (ANSWER): an open-label randomized trial." Professor Mauro Bernardi, M.D., a senior author on the study representing the "ANSWER Study" investigators, presented interim data of the trial at various meetings, including ISICEM 2017 (supported by PPTA) and IPPC 2018. The four-year study was funded by the Italian Medicine Agency and included participants from 33 academic and non-academic Italian hospitals. The study design can be found at EudraCT, number 2008-000625-19, and ClinicalTrials.gov, number NCT01288794. More than 400 patients were randomly assigned and included in the modified intention-to-treat analysis. Patients were divided into two groups: one received standard medical treatment, and the other received standard treatment plus human albumin (40g twice a week for two weeks and then 40g weekly for up to 18 months). The authors concluded that "in the trial, long-term human albumin administration prolongs overall survival (18-month mortality) and might act as a disease-modifying treatment in patients with decompensated cirrhosis."

NEW YORK

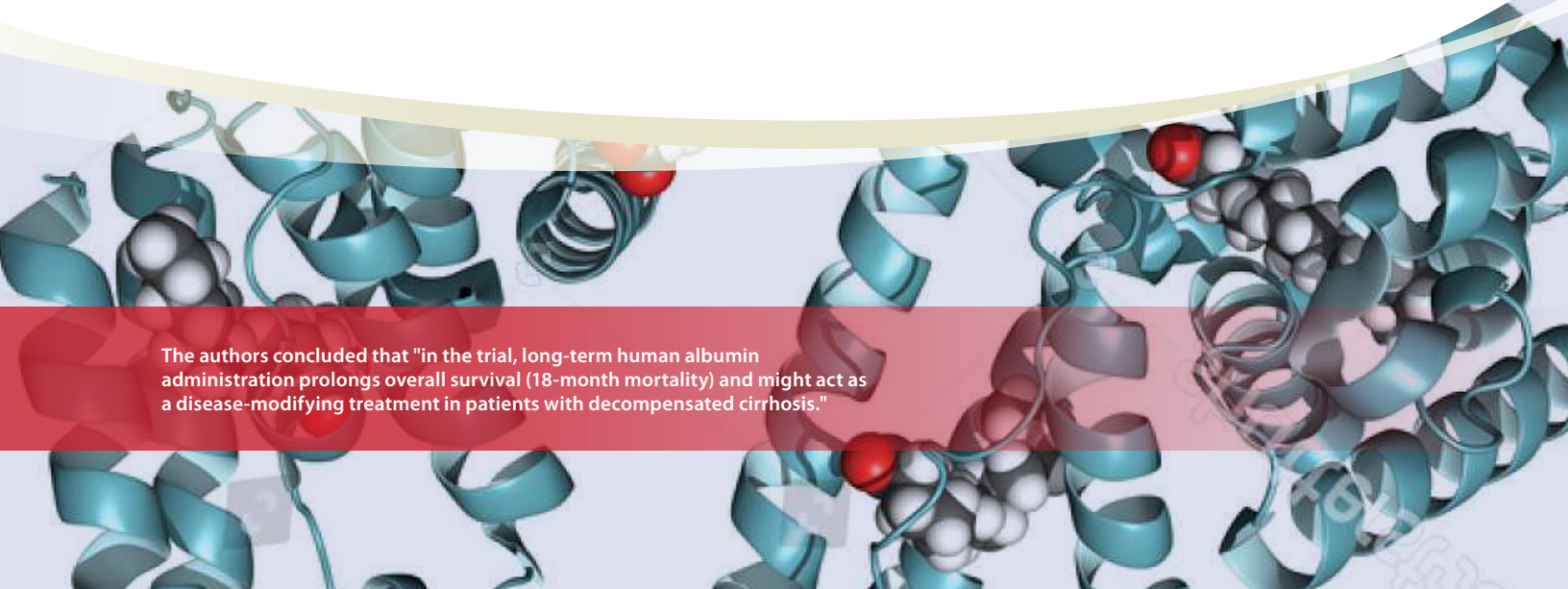
PPTA staff and members met with the New York Department of Health, the New York State Education Department, and legislative staff. The purpose of the agency meetings was to discuss the Association's objective to improve the regulatory environment for plasma donation in the state. Attendees discussed how improvements may require changes to the scope of practice laws. The agencies' staff were helpful in identifying areas that would require statutory and/or regulatory changes. The legislative meetings were held with the staff who would advise members on the Association's goals when legislation is filed.

WASHINGTON STATE: NECESSARY SUPERVISION

PPTA received word from the Washington State Department of Health (DOH) on its interpretation of the amount of supervision necessary at a plasma donation center. There is confusion in the Revised Code of Washington as to the need to have a health care practitioner on-site during the performance of plasmapheresis and total protein tests. PPTA spoke to DOH about our concerns that some members are being told by DOH auditors that there must be a health care practitioner on-site. DOH informed PPTA that it does not think a health care practitioner must be on-site for plasmapheresis or the performance of total protein tests. The department did stress, however, that a health care practitioner must be immediately available, if necessary, during plasmapheresis.

FDA ANNUAL LIAISON MEETING

PPTA and the FDA held their annual liaison meeting in Bethesda, Maryland on Nov. 2, 2018. PPTA and its members shared their current concerns and priorities. Presentations included: 2019 priorities; the collection of convalescent plasma from ex-U.S. sources; challenges of using tests licensed for donor screening; donor health update; whether a change in male hemoglobin is necessary for a Source plasma collection program; and a China update. ●



The authors concluded that "in the trial, long-term human albumin administration prolongs overall survival (18-month mortality) and might act as a disease-modifying treatment in patients with decompensated cirrhosis."

Supporting Organizations

PPTA would like to thank these patient organizations for their support.



PPTA Staff

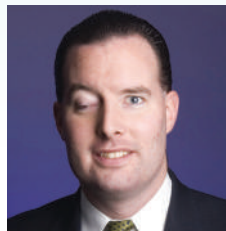
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