THE SOURCE

MAGAZINE OF THE PLASMA PROTEIN THERAPEUTICS INDUSTRY

SUMMER 2018

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The World Needs More Plasma

Immunoglobulin Therapies in an Era of Precision Medicine: One Size Does Not Fit All!

BRICS Countries: Challenges to Plasma Protein Therapy Access

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THE SOURCE is published quarterly by **PPTA**.
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SUMMER 2018

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In My View

BY JAN M. BULT, PRESIDENT & CEO, PPTA

OPEN LETTER TO DR. PETER FLANAGAN

I recently I saw an oration delivered by Dr. Peter Flanagan, the medical director of the New Zealand Blood Service, when he received the prestigious Ruth Sanger Award.

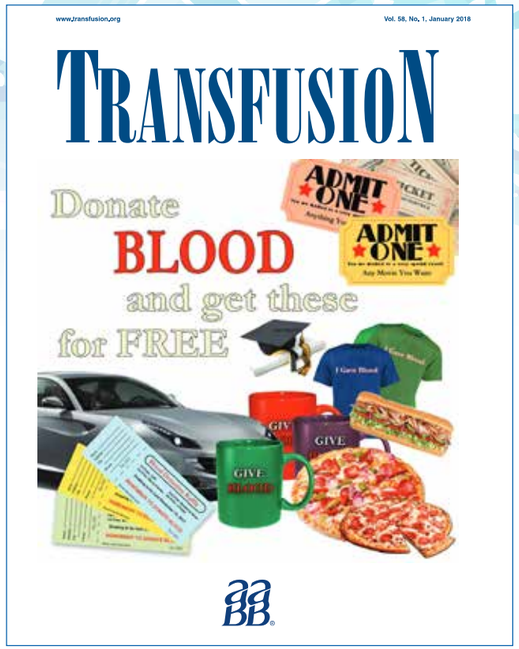
Dr. Flanagan, a transfusion expert, has done a lot of good work for the international transfusion community for which he should be commended. He has had several important positions, among them president of the Australian and New Zealand Society of Blood Transfusion and of the International Society of Blood Transfusion (ISBT). Currently, Dr. Flanagan is the chair of the ISBT Standing Committee on Ethics and vice president, Asia, of the International Plasma Fractionation Association.

During his speech, he stated that there is no difference in safety between products made from voluntary unpaid donors or compensated donors. He also commended PPTA for, in his words, "its tremendous efforts in the last 20 years to improve the reputation of the commercial plasma industry with standard programs like the International Quality Plasma Program (IQPP)." Unfortunately, he also made a few unnecessary inflammatory remarks to which I take great exception. First, he called our Association "the lobby club of the commercial industry." Is that necessary Dr. Flanagan? We don't make derogatory comments about the groups that you belong to.

He then made it worse by saying the "commercial industry continues to prey on the disadvantaged of the society resulting in a level of exploitation." Shame on you Dr. Flanagan. That is below the belt. You know that it takes a long time to earn respect but that it is easy to lose it. You are on your way to lose the respect that I had for you.

You may say it does not bother you that I lose my respect for you, what is more important is that you show your true face to the many patients whose lives depend on the plasma protein therapies manufactured by our sector. You know very well that the majority of the patients in the world depend on these therapies. There is absolutely no way all of these patients can be treated with plasma therapies made from your preferred source, voluntary unpaid donations. Why are you fighting windmills like Don Quixote? Why can't you embrace the good work our industry is doing without these unnecessary remarks? Yes, I know you said that all therapies are safe, but still you found it necessary to attack us. We do not deserve that.

There is absolutely no way all of these patients can be treated with plasma therapies made from your preferred source, voluntary unpaid donations.



There is no need to criticize the industry and/or the donors because they get a compensation for their time and inconvenience. It is, by the way, interesting to see compensation options for voluntary unpaid donors illustrated on the cover of *Transfusion* magazine.

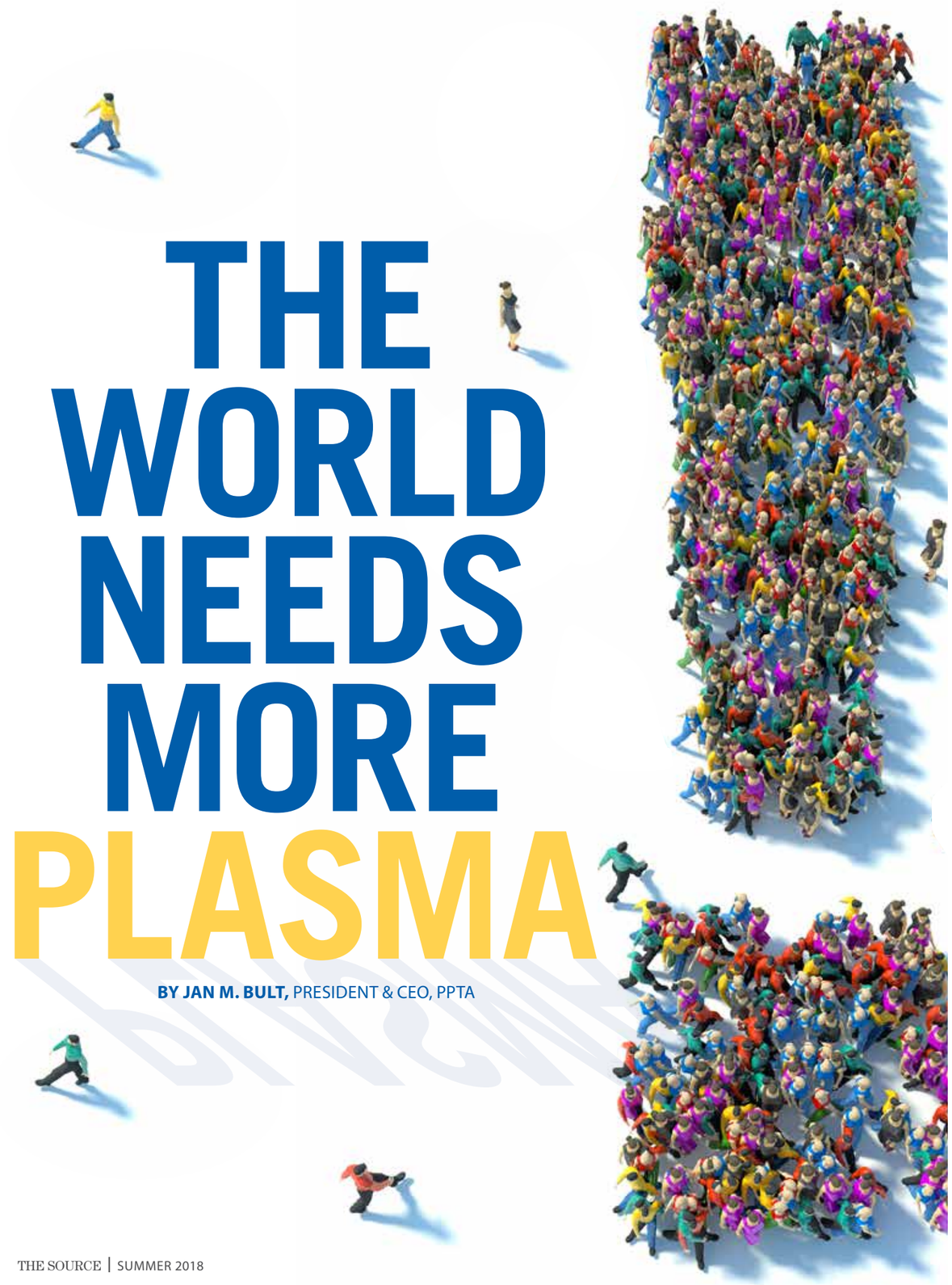
Think about the many patients with primary immune deficiency who rely on immune globulins (IG). Think about the patients with Guillain-Barré syndrome who are without problems in the morning and end up in the ICU in the evening due to a collapse of the peripheral nervous system. Not being able to talk is already scary enough. Having to worry about the availability of IG treatment makes it worse. Or what about the patients with hereditary angioedema (HAE) who, when they have an attack, are afraid of being unable to breathe when the edema blocks their airways? Not only do they have to deal with many ER physicians who do not recognize that HAE is the causal factor, but they may also endure a wrong treatment for an allergic reaction. These patients now have a chance to avoid the attacks with the C1 esterase inhibitor made both by public and private sector manufacturers. I could continue to talk about many other patients, including those Rhesus negative women who need anti-D immunoglobulin to prevent hemolytic disease of the newborn. There is no need to criticize the industry and/or the donors because they get a compensation for their time and inconvenience. It is, by the way, interesting to see compensation options for voluntary unpaid donors illustrated on the cover of *Transfusion* magazine.

It is so easy to take a cheap shot at each other, but it is my view that it can be done much more professionally. Dr. Flanagan, we have debated each other in public, and that is OK. We don't have to agree with each other, but we can still respect each other.

I am offering you an olive branch instead of a prickly cactus. It's time to take an honest look at the clinical need. It's time for you to put patients first and stop your baseless attacks. I am willing to sit down with you, accept your personal apology, and discuss how the two systems can coexist.

I will wait patiently. •

Jan M. Bult, *PPTA President & CEO*



THE WORLD NEEDS MORE PLASMA

BY JAN M. BULT, PRESIDENT & CEO, PPTA

There is nothing wrong with taking care of your own needs first and then helping your family, friends, and neighbors. That is what a good citizen does. It should be the same when it comes to the collection of plasma for the manufacturing of plasma protein therapies.

Our Association brings together manufacturers that operate about 20 manufacturing facilities in different parts of the world, as well more than 750 plasma collection centers around the globe.

PPTA's mission is to promote the **availability** of and access to **safe and effective** plasma protein therapies for all patients in the world. However, this is an enormous challenge. If we really want to focus on all patients in the world, then *all regions in the world need to collect more plasma*.

Whether we look at albumin, immunoglobulins (IG), or Factor VIII, there are indications, as reported by the Marketing Research Bureau (MRB), that clinical consumption will increase continuously over the next five years. MRB has calculated that more than 90 million liters of plasma will be needed to meet clinical need for IG in just 2025 alone.

The clinical use of IG varies from less than 10 grams to around 200 grams per 1,000 inhabitants and is used for a variety of indications, ranging from neurological indications to primary immune deficiencies. One can only imagine how much more IG (and plasma as starting material) is needed when awareness and early diagnosis of conditions that require IG treatments reach the levels we see in regions of world with higher consumption.

Plasma can be obtained in two ways: as a by-product from whole blood collection called recovered plasma or via plasmapheresis with the sole objective of collecting plasma for manufacturing (source plasma). The annual collection of recovered plasma in the United States is stable at best and shows a decline year after year. On the contrary, the collection of source plasma increases year after year and reached more than 41 million donations in 2017. These U.S. collections are taking place in more than 650 collection centers spread all over the country, with at least one new center opening per week. The United States supplies the majority of plasma for manufacturing in the world.

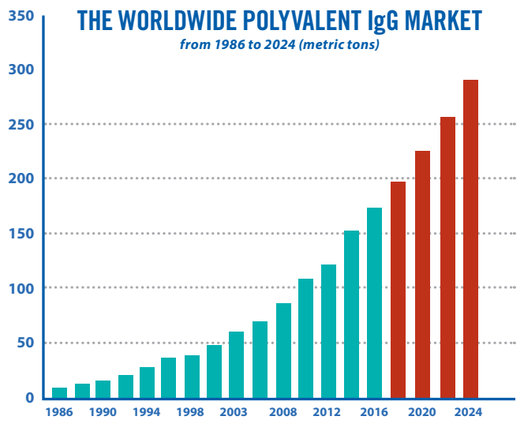
In Europe, our industry is only allowed to collect plasma in four countries: Austria, Germany, Hungary, and the Czech Republic. Thinking forward, one could ask four basic questions:

1. Can the world continue to rely on the United States for the primary supply of source material for plasma protein therapies?
2. What is Europe's responsibility to provide sufficient raw material for therapies used by its citizens?
3. What are the responsibilities of other regions to provide sufficient raw material?
4. Should we move from national through regional to global thinking?

These questions are relevant because when we look at the global picture, we see that the importance of source plasma is even more critical. Recovered plasma is on the decline and is not the starting material for a growing need. The region where recovered plasma is available the most is Europe. Within Europe, it is Germany that provides most of the recovered plasma (about 1 million liters in 2015), while at the same time, most of the source plasma is also coming from Germany (almost 2 million liters in 2015). It shows that Germany is taking its own responsibility seriously but also that the two systems can coexist.

It is important to know that to meet the growing clinical need for plasma protein therapies, all suitable starting material (source and recovered plasma) needs to be used! My qualifying statement is that if the need to collect more plasma stems from an increased use of plasma protein therapies, then the focus should be on the collection of plasma, not the collection of blood. Although recovered plasma is very valuable as a starting material and should be used when the quality criteria are met, blood collection for the purpose of producing recovered plasma should not be encouraged.

Last but not least, paid and unpaid systems should be able to coexist.

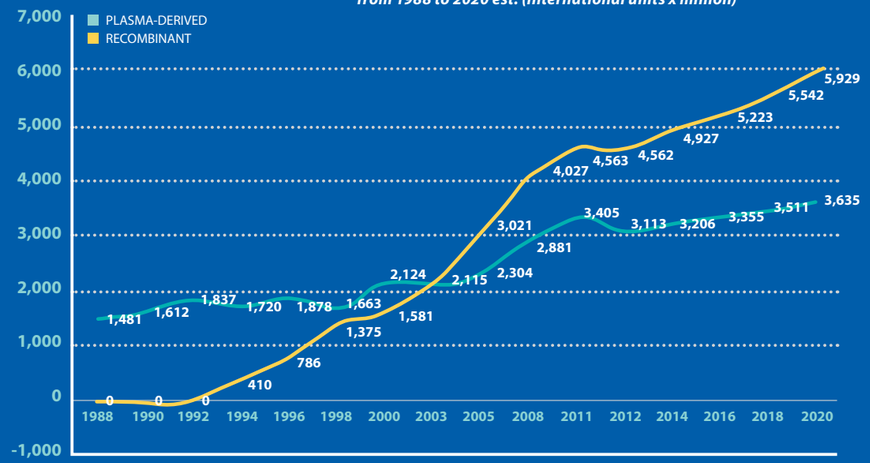


In 2024, based on a 3.9 grams of IgG per liter average yield, 290 tons of immune globulin will be produced from circa 75 million liters of plasma.

Source: Marketing Research Bureau

THE WORLDWIDE FACTOR VIII MARKET

from 1988 to 2020 est. (international units x million)



Source: Marketing Research Bureau

We continue to see a growing clinical need for plasma protein therapies because of improved awareness and early diagnosis. While the hemophilia community has options for therapeutic intervention, such as plasma-derived therapies, recombinant therapies, and gene-therapy, such options are not (yet) available for most of the other users of plasma protein therapies. They rely solely on therapies that use human plasma as starting material. For that reason, I focus a lot on the need for plasma worldwide. Many steps can and should be taken, such as:

- Open up more centers outside the United States
- Let both public and private centers collect plasma
- Allow compensation for donations in countries with well-established regulatory systems
- Respect all donors
- Increase efficiency in collection practices
- Reduce the time to discuss definitions
- Keep the patient's need in mind and be honest
- Increase plasmapheresis as the primary method to collect plasma for manufacturing
- Increase quality and use of recovered plasma
- Stop discarding recovered plasma for political reasons
- Achieve global sufficiency

Let me emphasize a few points here. We respect all donors—blood donors and plasma donors. Why is there only a World Blood Donor Day? Why cannot this be changed to World Donor Day? If you read the description then it is easy to see that this recognition can be universal.

The theme of this year's World Blood Donor Day is "Blood Connects Us All." It focuses on **thanking** blood **donors** and highlights the dimension of **"sharing"** and **"connection" between** blood **donors and patients.** In addition, the slogan is "Share life, give blood," to draw attention to the **roles that** voluntary **donation systems play in encouraging people to care for one another and promote community cohesion.**

The campaign aims to highlight **stories of people whose lives have been saved through** blood **donation,** to **motivate regular** blood **donors** to continue giving blood, and **motivate people in good health** who have never given blood **to begin doing so,** particular young people.

Do you see how easy it would be to recognize ALL donors?

The last point I want to make is about global sufficiency. The first thing we need is understanding. We need people to understand what the difference is between blood and plasma. We need them to understand the difference between plasma protein therapies and traditional pharmaceuticals.

Many countries look at what the need is in their country, which is totally understandable. What they need to do next is see how they can help their neighbor countries and then how they can help regions.

So many patients in the world in need of these plasma protein therapies, and only a few countries with enough starting material and manufacturing capabilities. We need to shift to global thinking and see what we can do to provide therapies to the world and not just to a confined territory. •

Immunoglobulin Therapies in an Era of Precision Medicine: ONESIZE Does Not Fit All!

BY DR. LARISA CERVENAKOVA, MEDICAL DIRECTOR, PPTA
BRENNA RAINES, SENIOR MANAGER, GLOBAL HEALTH POLICY, PPTA

Immunoglobulin (IG) therapies are manufactured from the plasma of healthy donors and are used as a replacement therapy for individuals with certain types of primary immunodeficiencies (PI), as well as for autoimmune and inflammatory diseases. The majority of these therapies are liquid and can be administered into a vein (intravenous or IV), under the skin (subcutaneous or SC), or, infrequently, into a muscle (intramuscular or IM). Some payers would like these lifesaving therapies to be easily interchangeable or equivalent due to budgetary pressures. However, the decision of which IG therapy a person receives should be made by expert physicians, taking into consideration product characteristics and individual safety, tolerability, medical conditions, and comorbidities. The lifelong health outcomes, impact on quality of life, and societal benefits should be considered as well. Considering basic patient rights in an era of precision medicine, individuals should have access to the right therapy, for the right indication, administered at the right dose, by the right route, at the right time, and in the right place. Proponents of IG interchangeability should take a cautious approach as the effective use of therapies for PI depends on the unique interplay between the IG product and patient characteristics.

NON-INTERCHANGEABILITY RELATED TO IG THERAPY CHARACTERISTICS

IG therapies are made mainly from source plasma collected from donors, but some are made from recovered plasma. Plasma donations are pooled together and a highly complex manufacturing process isolates the immune globulin (Ig) proteins, predominantly the IgG class, to make IG therapies. The manufacturing typically employs at least three dedicated steps to obtain highly purified, biologically functional, safe, and pathogen-free products.

Manufacturing processes are highly controlled, but the differences in the composition of the final product are significant from manufacturer to manufacturer. IG characteristics vary regarding the composition of IgG subclasses; the residual amounts of other Ig classes and other proteins (albumin, coagulation factors, etc.); the type of substances used to stabilize the therapies; trace amounts of solvents and detergents; salt concentration; acidity (pH); and osmolality/osmolarity. Each characteristic and combination thereof may affect the tolerability and may serve as a contraindication in vulnerable patient groups.

NON-INTERCHANGEABILITY RELATED TO PATIENT CHARACTERISTICS

The IG therapies in individuals with PI provide protection from infections. Differences among products and a person's individual characteristics play a significant role in IG pharmacokinetics, which is measured as a half-life survival of the product in blood. In some individuals, the half-life of IG is approximately three to four weeks. In others with certain types of PI, the half-life can be shorter or longer depending on age, gender, metabolism, comorbidities, individual genetics, route of administration, and dose.

IG treatment should be individualized with respect to the dose, frequency, route of administration, rate of infusion, and site of care. Current guidelines recommend doses of 400-800 mg/kg every 3-4 weeks for IVIG, and 100-200 mg/kg/week for SCIG.[1,2] Less frequent treatment and lower doses are neither recommended nor substantiated by clinical data. Individualized dosing offers optimal protection from infections; studies have shown that higher doses of IG inversely correlate with the occurrence of bacterial infections. Some individuals have better tolerance and fewer adverse reactions when infusing smaller doses more frequently, while others do better with larger doses less frequently.

The route of IG administration must be based on patient characteristics. In some individuals, poor venous access requires the use of SCIG instead of IVIG; others require intravenous administration under medical professional supervision instead of subcutaneous self-infusion at home. The decision about the route of administration is an important component of IG treatment that can only be made by physicians. Tolerability and adverse events (AEs) are significant factors to consider when selecting the route of infusion.

Similarly, the rate of infusion contributes significantly to the tolerability of IG therapy, and systemic mild adverse reactions related to it may resolve with adjustment. To avoid adverse reactions, a slower rate is recommended for the first-time treated patient or a patient whose therapy was changed. Good tolerability of a certain rate while infusing one product does not guarantee the same tolerability of another.

The decision regarding the site of care should be made by physicians considering clinical characteristics of the patient, patient suitability, and, most important, patient safety. Infusions may be delivered in a hospital, hospital outpatient, specialty treatment center, physician offices, or home-based setting. Home therapy may be best suited for some individuals as the hospital setting comes with the risk of exposure to infections, while the hospital may be ideal for others who require monitoring for AEs. Personal satisfaction with the treatment may result in better adherence, which has been shown to improve quality of life and increase positive health outcomes.

IG therapies are safe treatments, but the incidence of AEs can vary. As a result of side effects, patients switch products (37 percent), delay scheduled infusions (20 percent), switch off a therapy (36 percent), or refuse a particular therapy (25 percent).[3]

A person's tolerability with respect to the incidence of an AE is the foremost factor in recognizing non-interchangeability of IG therapies that emphasizes the importance of a "personalized medicine" approach. Individuals who tolerate an initial IG therapy well should not be forced to switch to a different brand without physician oversight and approval.

CONCLUSION

Although some individuals may do well with treatment by any available brand, the individuals who for unknown reasons cannot tolerate certain products should not be ignored. These individuals should not be deprived of the right for personalized treatment because an insurance company or government agency chooses products based on cost without considering individual tolerability, suitability, or physical and psychological well-being. Economic pressure should not dictate or restrict a prescribing physician in selecting the most appropriate IG therapy for his/her patient. Payers must invest in individualized treatments that allow patients the right brand, at the right dose, at the right time, and at the right place of infusion. Medically appropriate treatment of PI will ultimately lead to spending fewer resources on the treatment of undesirable AEs, decreasing unnecessary hospital visits, increasing the productivity of a person at school or at work, and increasing quality of life and the life expectancies beyond what current statistics project for people affected with PI. The recognition of non-interchangeability of IG products is not a mere wish of treating physicians, pharmacists, patients, or patient advocacy groups, researchers, or even regulatory agencies: It is a societal obligation that any health care insurance company should not be allowed to ignore in an era of precision medicine. •

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BRICS COUNTRIES:

CHALLENGES TO PLASMA PROTEIN THERAPY ACCESS

BY JULIA FABENS, MANAGER, INTERNATIONAL AFFAIRS, PPTA
RACHEL LIEBE, ASSISTANT MANAGER, COMMUNICATIONS, PPTA

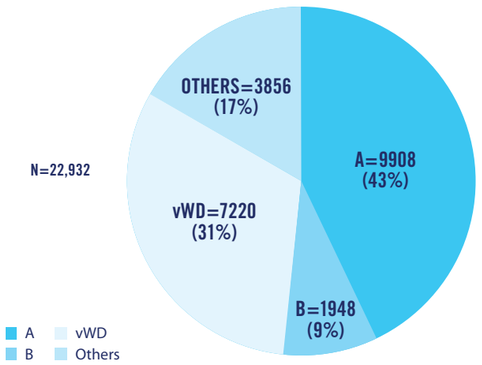
During the 2018 International Plasma Protein Congress (IPPC), held March 13–14 in Budapest, speakers provided insights into issues impacting access to plasma protein therapies in: Brazil, China, and South Africa. These three countries are part of a group of major emerging national economies, collectively known as BRICS (Brazil, Russia, India, China, and South Africa).

THE BRAZILIAN PERSPECTIVE

Dr. Silvano Wendel from the Hospital Sírio Libanês provided IPPC attendees with background information on his home country of Brazil. Brazil's population is 208 million people with a surface of 8.5 million square km. There are 5,500 municipalities, 300 of which are occupied by approximately 56 percent of the population. Sao Paolo, a municipality in the southeast region, is the most populous city with 90 million people. The plasma industry is located in the northeast part of the country. In total, there are more than 6,800 hospitals—the majority of which are private—with nearly half a million hospital beds, which is about 2.37 beds per 1,000 inhabitants. There are nearly 60 major blood transfusion services in the country with about 3.5 million donations per year, which is about 16.8 donations per thousand.

According to a 2015 report from Brazil's Ministry of Health, of nearly 23,000 patients with a bleeding disorder, approximately 43 percent had hemophilia A, 9 percent had hemophilia B, 31 percent had von Willebrand disease, and 17 percent were affected by other coagulopathies. The usage of plasma products in Brazil in 2015 was approximately 200 kg/million population for albumin, 18.8 kg/million for IVIG, nearly 68,000 IU/capita for factor VIII, and a little more than 51,000 IU/capita for factor IX. Approximately 65 percent of people with hemophilia under 18 years old are on prophylactic treatment, and 89 percent of those older than 18 are treated by prophylaxis. Dr. Wendel noted there may be an underestimation in these numbers due to several misdiagnosed cases.

"COAGULOPATHIES IN BRAZIL"
Ministry of Health (2015)



Source: http://www.hemofiliabrasil.org.br/wp-content/uploads/2014/04/Perfil-das-Coagulopatias-Hereditarias-no-Brasil-de-2015.pdf

Dr. Wendel also highlighted figures provided by the Latin American Society for Immunodeficiencies (LASID), which has seen an increase in the number of primary immunodeficiency patients entered in the LASID registry. Brazil has seen an increase in the average consumption of IVIG from 9.9 kg/million population in 2010 to 16.7 kg/million in 2013. Though several companies are available to produce IVIG in Brazil, only one company is responsible for local production—Hemobrás, located in the northeastern part of Brazil approximately 2,000 km from the major centers.

There are four levels of funding for these medical products: federal, state, municipality, and private. Albumin is never sponsored by the federal government, whereas all remaining products are mainly sponsored by the federal government. Municipalities rarely provide unless it is a dramatic situation; the money from the respective city is allocated for buying those products.

PLASMA COLLECTION IN BRAZIL

Dr. Wendel noted that in Brazil, only the public sector can collect source plasma and there is a heavy reliance on recovered plasma. Currently, Brazil collects approximately 2.6 million units of whole blood from the public sector and 1 million units of whole blood from the private sector. Of that 3.6 million, approximately 10 percent is discarded due to federal issues such as serological tests or expirations. About 15 percent is used for patients, so the availability should theoretically be approximately 75 percent of the recovered plasma, leaving about 490,000 liters of plasma left over for fractionation.

Unfortunately, Hemobrás only has a fractionation capacity of less than 250,000 liters of plasma per year, which leads to a tremendous loss of recovered plasma for the whole country. Dr. Wendel explained that Brazil collects whole blood, uses platelets and red cells, but doesn't use or fractionate plasma. He went on to add that in his hospital, the collection of plasma depends on whole blood donors per year, and nearly 90 percent of the plasma is simply discarded.

WHAT ARE THE MAJOR BOTTLENECKS IN BRAZIL?

The first major obstacle toward self-sufficiency, Dr. Wendel stated, is the collection of suitable plasma for fractionation, either source or recovered plasma. Inadequate storage of collected plasma is another issue; even if Hemobrás received the recovered plasma, there isn't the storage capacity for all the collection in Brazil. Additionally, fractionation procedures need to be updated to be more state-of-the-art. Another roadblock is the logistics of distribution: not only are the roads in poor condition, but Hemobrás is nearly 2,000 km from the majority of patients. According to Dr. Wendel, even if all patients were correctly diagnosed in the country, the current national capacity is not enough to cover all patients. Additional obstacles include:

- Lack of intellectual force and manpower backup
- Lack of specific budget, and if budget is allocated, money is not always available. There are low health expenditures per capita, even though the GDP of Brazil is the ninth highest in the world.

IN CONCLUSION

Greater capacity for source plasma collection through plasmapheresis should be developed in Brazil. Dr. Wendel shared his opinion that it is very important that Hemobrás continues to operate and to develop, but Hemobrás on its own will not be able to support the needs of the whole country. Self-sufficiency is almost impossible in the next 10 years under the current policy.

Dr. Wendel concluded that while recovered plasma is valuable as a starting material and should be used more wisely, it's insufficient to meet the Brazilian needs. He articulated his personal opinion about paid and unpaid systems, noting that both systems have to coexist in an elegant and sophisticated way; both systems should be acceptable, and they should coexist with stringent rules and mutual respect.

THE CHINESE PERSPECTIVE

Du Xiangjun, a noted independent researcher, began his presentation with a discussion of the current state of plasmapheresis in China. He noted that in the past 10 years the number of plasmapheresis centers and the volume of plasmapheresis have been steadily increasing. In 2017 in China, there were 246 plasmapheresis centers with a total collected plasma volume of 8,081 tons, a collection volume second only to the United States.

In conjunction with this increase in plasma collection is the growing acceptance of the idea that plasma donation actually saves lives and that there is nothing wrong with compensating donors. Mr. Du explained that this is accompanied by increasing respect for donors by the plasma centers and staff as expressed by, for example, decreased waiting times and reduced numbers of venipunctures. He said these improvements are reflected in the increasingly positive attitudes of donors he encounters.

PLASMA COLLECTION IN CHINA

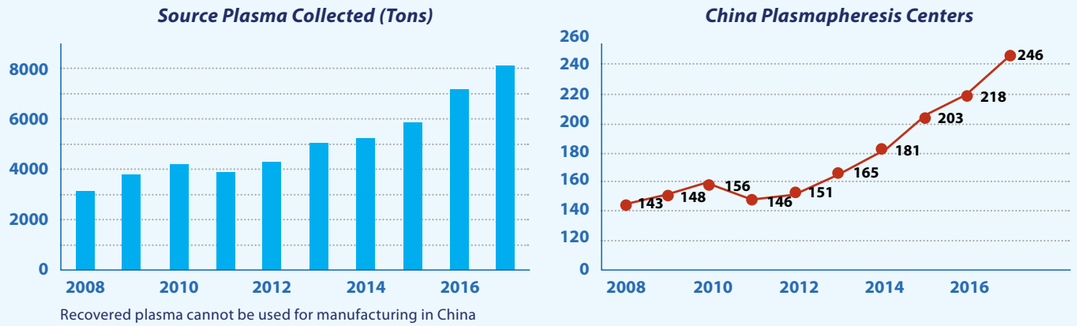
Mr. Du expressed what he believes are among the main challenges facing plasma collection in China, the first of which is the mobility of the Chinese population and regulations that prevent mobility of donation. Currently, plasma collection is not allowed in the same areas as blood collection. As blood collection centers are common in cities, this regulation has forced plasma centers to be located in more rural areas. At the same time, there are policies in place promoting the rapid urbanization of the Chinese population.

Mr. Du shared a startling statistic—the White Paper of China Blood Transfusion Services 2016 disclosed that there are 345 million people in the existing plasma collection areas, which means there are more than 1 billion people who cannot donate plasma for location reasons alone. Mr. Du tied this to "traditional" Chinese views of plasma collection—that compensated plasma collection is "selling" plasma, and as such, plasmapheresis centers are located in economically underdeveloped midwest regions. As this way of thinking becomes rightly obsolete, Mr. Du argued that regulations should change to allow plasma collection in cities, where more people have the opportunity to donate.

The second major challenge Mr. Du outlined is tied to the current practices of importing blood products, as well as current thinking around self-sufficiency impacting those practices. To illustrate this point, Mr. Du did some calculations—if China does not seek self-sufficiency, then it does not need to collect any plasma. If it does seek self-sufficiency, it could do so in three ways: self-sufficiency for albumin at 250g per thousand inhabitants would require 14,000 tons of plasma. Self-sufficiency for Factor VIII treatment at 5 IU/capita would require at least 35,000 tons, and self-sufficiency for IVIG at 200 g/thousand inhabitants (levels on par with the U.S. and Canada, among others) would require 70,000 tons, which he notes is far more than the current total amount of plasma collected worldwide. Mr. Du argues that with such substantial clinical need, to continue relying on the United States is unrealistic; China should, therefore, pursue self-sufficiency.

STEADY DEVELOPMENT OF PLASMAPHERESIS

in the past 10 years



Source: Du Xiangjun, Independent Researcher

That said, he argues that self-sufficiency has been ill-defined. Mr. Du warned that the importance of self-sufficiency must be raised to a national strategic level, and that as clinical need increases, no foreign country can credibly guarantee access for the Chinese population. He also urged Chinese manufacturers to find ways to improve quality and efficiency and to reduce plasma wastage.

CONCLUSION

Mr. Du suggested it is the responsibility of government authorities to ensure the supply of clinical use blood and plasma protein products, and not to favor blood collection over plasma, specifically as the collection zones are concerned. Authorities should recognize that recovered plasma, even if it was used in China, is not the answer because plasmapheresis is the only way that enough plasma will be collected. Standards for both domestic and imported plasma protein products should be unified to create a level playing field.

His next suggestions were for academics. Scholars discussing plasma and blood donation should have a better understanding of plasmapheresis itself and should return to the fundamental starting point of "patients first." Mr. Du would also like to see them objectively study whether crowding-out is actually occurring or would occur in China, in which the blood or plasma industry would hinder the business of the other by taking away ones donors. He said that when so many facts are presented, ignoring factual research is a violation of scientific spirit.

Mr. Du also shared an observation regarding the World Health Organization (WHO), noting that WHO should address the reality and amend its ethical position on plasmapheresis without forgetting the concept of "patient first," and it should clearly define what it means by "voluntary non-remunerated blood donation" based on facts.

To the Chinese fractionation industry, he had the following suggestions: have the courage to explore the international plasma protein market; support academic research, especially in sociology, ethics, and independent topics by welcoming researchers into collection centers; and lastly, give strong financial and resource support to the further transformation and upgrading of Chinese plasmapheresis centers.

Mr. Du closed his presentation with some words for Chinese plasma collection centers. He stressed that centers must strictly comply with national laws and regulations. He pointed out that after ownership of collection centers was transferred to fractionators in 2006, compliance with laws and regulations increased, but he said vigilance is still necessary and the health of donors should be paramount. He then urged center operators to accelerate the ongoing process of upgrading centers, and, finally, encouraged domestic collectors to give complete respect to the lifesaving donors, without whom there would be no plasma industry. He concluded with a fitting quote from the sixth Dalai Lama Cangyang Gyatso: "Nothing is important in the world except lives."

THE SOUTH AFRICAN EXPERIENCE

Ravi Reddy from the South African National Blood Service (SANBS) and International Society for Blood Transfusion (ISBT) began his presentation with background on SANBS, noting it was formed in 2001 as a merger of several smaller blood centers. Annually, SANBS collects 835,000 units of blood, 100 percent from voluntary donors, translating into about 2,800 units of blood collected daily at fixed-site centers and nearly 100 mobile blood drives. Currently, there are seven blood processing centers strategically located in major cities throughout South Africa.

In the blood transfusion process, Mr. Reddy noted, there are three key pillars: donation, technical, and blood bank.

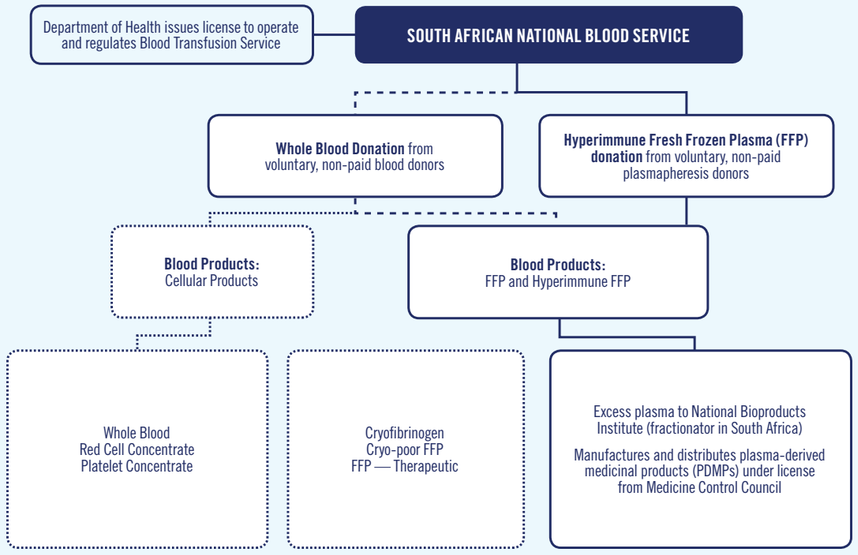
Donation: There should be a focus on regular donors; 85 percent of donors at SANBS are repeat or returning donors. SANBS focuses on recruitment of 100 percent voluntary donors. Additionally, there is strong focus on education and clinical risk, as well as evaluating and measuring the best methods to get the safest donors in the door.

Technical: Having state-of-the-art serology and nucleic acid amplification testing is important, as is implementing quality assurance schemes (internally and externally) and managing the cold chain process.

Blood bank: The plasma does not go to the patient until the donor comes back and retests negative. The excess plasma, which translates to about 170,000 liters, is supplied for fractionation.

Mr. Reddy expressed that SANBS and the National Transfusion Service in the Western province are the only licensed entities to collect whole blood, plasma, or any products (e.g., hyperimmune). Mr. Reddy provided the model for blood transfusion in South Africa (Figure 1) and noted that the Department of Health issues a license for SANBS to operate, SANBS then collects whole blood donations from voluntary, unpaid donors, and blood products are ultimately used for whole blood, red blood, and platelet concentrates. Mr. Reddy noted there are programs that send the excess plasma to the National Bioproducts Institute (NBI), which is the fractionator in South Africa. This is a non-profit company that manufactures and distributes plasma-derived medicinal products, operating under the license from the Medicine Control Council. NBI was actually a part of the Blood Transfusion Service until 2008, when the decision was made to split into two separate non-profit entities.

FIGURE 1: Model for Blood Transfusion in South Africa



The key requirements from the fractionator to the SANBS are:

- Standards and quality system. Standards equivalent to American and European standards must be in place. This includes conducting numerous audits and accreditations, as well as maintaining documentation and plasma master file.
- Epidemiology on donor selection.
- Quality-assured donation testing. For example, in a country like South Africa with a higher HIV prevalence, the epidemiology and risk associated with window period infections must be managed.
- Effective cold chain and freezing methods.
- Traceability. This allows us to look back at any donor who tested positive, and, subsequently, any patient who may have had a reaction to any product.

Mr. Reddy emphasized the value of standards by stating that the role of SANBS is to ensure that quality systems are in place for fractionation. In 2003, only 73 percent of plasma that was available actually made it to the fractionator; the other 27 percent that was available was not frozen in time because of quality issues. Currently, blood collection comes from "low-risk" donors in a country with a high disease burden which, Mr. Reddy stated, is an area of concern because this resulted in nearly 85 percent of the population being excluded, which is not sustainable. To ensure quality, SANBS has stringent donor selection and deferral criteria and has also implemented a collections management system to optimize blood collection in order to meet the growing demand. Additionally, there is a focus on clinical risk, efficiency, and education on a regular basis; currently SANBS has 14 educators who go out to clinics to provide information to donors.

To ensure all the blood collected from mobile drives and collection centers meet all the requirements of a cold chain inspector, SANBS has made significant investments in educating at clinics optimizing the processing in centers, and creating a better workflow in seven processing labs, compared to the previous 18 small labs. Mr. Reddy added that the plasma supply in South Africa has increased from 109,000 liters in 2004 to 170,000 liters in 2017.

DONATION TESTING

Testing at the donation level is the key aspect of improving the quality of plasma, according to Mr. Reddy. The WHO mandates serology testing for anti-HIV, anti-HCV, HBsAG, and syphilis. The majority of infectious donations will be detected with quality-assured testing using either the third- or fourth-generation assays. In a country like South Africa where the HIV prevalence is about 16.5 percent in the 16- to 49-year-old population, the incidence is now decreasing. But there is a significant increase in the risk of window period donations in the donor pool and potentially high viral loads introduced into plasma pools for fractionation. In October 2005, SANBS implemented Individual Donation Nucleic Acid Testing (ID-NAT), which has had a major impact in South Africa. As a result, infectious donations are detected much earlier, thus reducing the risk of transmissions.

South Africa still has steps to take before it can be fully self-sufficient, Mr. Reddy noted. All the plasma for the factor VIII, immunoglobulins, albumin, etc., is from recovered plasma. South Africa does not collect source plasma, except for hyperimmune plasma. Red cell usage, and collection of whole blood as a result, has increased slightly over the past five years—though with patient and blood management being more rigorous, there may be a slight decrease in usage. However, clinical need for plasma-derived medicinal products, particularly immunoglobulins and factor VIII, continues to increase in South Africa and neighboring countries. Currently, there is not enough recovered plasma to satisfy clinical need for all PDMPs, so some cryoprecipitate has been imported for factor VIII. Mr. Reddy added that SANBS and NBI have begun looking at a partnership for the collection of source plasma and will likely do a pilot program this year.

CONCLUSION

In closing, Mr. Reddy shared his thoughts on improving access to care in low- and middle-income countries (LMICs), noting a clear public health need for affordable essential medicines and other plasma derivatives in LMICs. Additionally, the lack of quality recovered plasma produced from blood collected in LMICs is a major impediment. The focus should be on improving the quality of recovered plasma from local donations, while simultaneously increasing the safety and efficacy of the other blood components being transfused.

Mr. Reddy added that transfer of technologies to LMICs blood establishments to improve plasma quality is feasible at several levels but doing so will require some initial financial support for infrastructure improvements. Local production of higher quality plasma can improve the cost-effectiveness of the local blood establishment and ensure its sustainability. It is also important to further develop relationships with established plasma fractionators if contract fractionation is feasible. Supporting the local production of quality plasma collected locally from volunteer blood donors is a pragmatic way to improve the supply of lifesaving medicines in LMICs. •

HOW BRICS STACK UP AGAINST OTHER COUNTRIES

COUNTRY	2016 POPULATION, MILLIONS[1]	2016 LIFE EXPECTANCY AT BIRTH, TOTAL (YEARS)[2]	2016 INFANT MORTALITY RATE, PER 1,000 LIVE BIRTHS[2]
Brazil	206.101	76	14
China	1,382.710	76	9
Germany	82.732	81	3
Japan	126.901	84	2
South Africa	55.909	63	34
US	323.298	79	6

COUNTRY	2016 GDP PER CAPITA, CURRENT PRICES USD[1]	2015 CURRENT HEALTH EXPENDITURE PER CAPITA, PURCHASING POWER PARITY (PPP)[2]	2016 GROSS NATIONAL INCOME PER CAPITA, PPP[2]
Brazil	8,726.90	1,392	14,810
China	8,113.26	762	15,470
Germany	41,902.28	5,357	49,690
Japan	38,917.29	4,405	43,630
South Africa	5,260.90	1,086	12,830
US	57,436.41	9,536	58,700

1. International Monetary Fund. http://www.imf.org/external/index.htm.
2. The World Bank. http://www.worldbank.org/.

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- **Strengthen donor relationships** by simplifying and accelerating data collection, reducing wait times and accelerating donor flow through the center.

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Clawback Tax Policies:

COUNTERPRODUCTIVE IMPACTS ON PATIENT ACCESS TO PLASMA-DERIVED MEDICINAL PRODUCTS IN THE EUROPEAN UNION

BY KARL PETROVSKY, DIRECTOR, HEALTH POLICY EUROPE, PPTA

INTRODUCTION

In the past decade, the growth of public spending on pharmaceuticals has led to the introduction of various cost containment policies in European Union (EU) countries, particularly in the wake of the economic crisis. This led to a wide range of different mechanisms that aim to control the extent of public spending. Some of these mechanisms, operated through taxation policies, are known as payback or clawback tax policies.

Nominally, payback or clawback tax policies require manufacturers to pay back a share of their revenue to the public payer; this share is captured as a discount to the revenue—if a pre-specified budget ceiling for public pharmaceutical expenditures is exceeded.

The "one size fits all" application of these mechanisms on plasma-derived medicinal products (PDMPs) has serious consequences on patient access to care with these products. PPTA monitors these mechanisms to ensure they do not negatively impact patient access to care. It is also important to consider what needs to be done to prevent such unwanted dynamics to avoid patient access issues.

OVERVIEW

PDMPs are specific, essential, often lifesaving medicinal products with no therapeutic alternative that treat rare, congenital, and life-threatening disorders, such as hemophilia or immmunodeficiencies. It typically takes seven to 12 months to produce a PDMP—from the moment where source plasma is collected from the donor until the administration of the final product to the patient. The complex and long manufacturing process, the unique biologic starting material for the therapies, and the non-interchangeability of treatments are only a few of the ways PDMPs are differentiated from traditional pharmaceuticals.

This specificity has been recognized by several EU Member States that have established distinct application mechanisms of the clawback taxation to PDMPs. As a matter of fact, several EU countries have implemented specific mechanisms for plasma-derived medicinal products to prevent a lack of coverage for patient needs, such as:

- **Belgium** has exempted plasma-derived medicinal products from the pharmaceutical companies' contribution (a mechanism working similar to the clawback tax) since 2008.
- **Poland** also exempts PDMPs from the application of a clawback tax.
- **Portugal** applies a different tax rate to PDMPs. The Contribution of the Pharmaceutical Industry (CPI) applies a rate of 2.5 percent to PDMPs, compared to the 15 percent rate applied to other medicines.
- **In Germany**, the tax, called a mandatory rebate, is limited to a maximum of 7 percent for all pharmaceuticals, while antihemophilic clotting factors are completely exempted from it.
- **Romania** decided to suspend the application of the clawback tax to PDMPs for a period of two years, effective January 1, 2018; this clawback tax has been in place since 2009.

Moreover, those EU countries that applied the clawback tax throughout a longer time span and that have recently ceased are also facing serious problems with patient access to PDMPs. This is the consequence of a downward trend lasting several years (in some cases almost a decade) caused by the application of the clawback tax on top of, and in conjunction with, other serious reimbursement constraints, such as tender mechanisms and pricing laws focused on cost control. PPTA has made the relevant authorities aware of these risks and called for timely action. Patient organizations have also advocated about the risks and the burden of clawback policies on patient access to PDMPs.

Political decisions that are intended to bring relief from those constraints (e.g., to suspend the application of the clawback tax to PDMPs) do not and cannot be expected to have immediate effects on improved access to PDMPs. The reason lies in the specifics of the PDMP sector, namely the complex manufacturing requirements for these therapies and the need for a predictable and adequate reimbursement framework. These elements trigger the existence of a very complex allocation process within companies which starts well in advance of every calendar year. Once an amount of PDMPs is allocated to a specific country, this implies contractual obligations for the company, and it implies that an already allocated amount of therapies cannot simply be re-allocated overnight to another country "in need" of PDMPs.

CONCLUSION

What matters most is that public policies which recognize the unique nature of PDMPs are identified and applied in a timely manner, thus ensuring unimpeded patient access to these therapies. •

"How Is Your Day?" Launches at IPPC

HOW IS YOUR DAY?

MAKING THE DIFFERENCE WITH PLASMA PROTEINS.

BY MAT GULICK, DIRECTOR, GLOBAL COMMUNICATIONS, PPTA

PPTA officially launched the "How Is Your Day?" (HIYD) initiative in March in conjunction with the International Plasma Protein Congress (IPPC), held this year in Budapest. HIYD was envisioned by the PPTA Global Board of Directors as an outlet to publicly discuss plasma protein therapies (PPTs) in a way that differentiates them from traditional pharmaceuticals and helps others better understand the value of PPTs. The initiative also provides those living with rare diseases, as well as their families, loved ones, and communities, a forum to share their story and raise awareness.

Jan M. Bult, PPTA's President & CEO, officially announced the launch of the campaign during a special panel presentation at IPPC. The panel, titled "Global Awareness for Plasma Proteins," also included presentations from Alain Weill, World Federation of Hemophilia (WFH), and Johan Prevot, International Patient Organization for Primary Immunodeficiencies (IPOPI), who discussed global awareness of hemophilia and primary immunodeficiency (PI) diseases, respectively. Mr. Bult followed these two presentations by offering HIYD as an opportunity to build greater awareness of rare diseases, such as hemophilia and PI, and as a platform to inform global audiences about the role PPTs play in treating these individuals.

The campaign's launch included a series of patient and donor testimonials, as well as other materials displayed throughout the conference. Additionally, Mr. Bult's presentation included a video featuring patients and plasma donors, explaining what access to these therapies means to them and why they choose to donate their plasma. Several people from the video and marketing posters joined us to share their stories with IPPC attendees.

Janika lives in Sweden and has been diagnosed with common variable immunodeficiency (CVID). Access to PPTs allows her to pursue a career and continue playing basketball on a local community league. Frank, who lives in Belgium, has Alpha-1 Antitrypsin Deficiency and relies on PPTs to keep his lung capacity as high as possible so he can continue running his business. Finally, Alex has severe hemophilia A, and access to his therapy has given him the chance to become a world-champion cyclist. Each of these individuals attended IPPC and shared their stories.

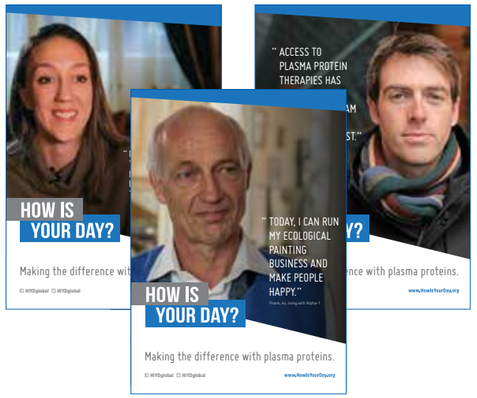
As part of the HIYD launch, a booth featured two stationary bikes and IPPC attendees were invited to cycle as fast as they could for one kilometer; Alex was then invited to show everyone how quickly a champion could cover the same distance! More than 120 people took their turn on the bikes throughout IPPC, and each of them took home a branded HIYD bike jersey to wear on future rides.

PPTA is grateful for the extraordinary support as we prepared to launch "How Is Your Day?"—the feedback we received from stakeholders and member companies made the campaign's messaging, imagery, and goals more widely understood, ultimately setting us up for a successful campaign over the next year.

So what are our plans for HIYD? We will continue introducing the initiative via stakeholder meetings throughout North America and Europe this year, as well as at industry meetings, first in Washington, D.C., in June at the Plasma Protein Forum, and then subsequently in Asia. As a global initiative, PPTA understands the need for our work to resonate and reflect the needs of individuals around the world whose conditions require regular access to plasma protein therapies. We also recognize the integral need for source plasma donors and will celebrate the men and women who generously donate their plasma; without committed and healthy donors, a majority of the plasma protein therapies relied on by people with rare disease would not be available. HIYD will also be integrated into International Plasma Awareness Week later this year (Oct. 8-12).

Policymakers and payers, whether they are insurers or governments, need to recognize the value that PPTs bring to smaller, more fragile patient populations and how different PPTs are from traditional pharmaceuticals. The goal is to make payers and policymakers aware of the unique, lifesaving nature of PPTs and avoid unilateral reimbursement mechanisms when making decisions to control costs and utilization.

The initiative is just in its infancy, however with support from stakeholders and other partners, we hope HIYD will have a positive global impact on improving patient access to PPTs. ●



JOIN THE CONVERSATION

Our social media channels on Facebook and Twitter provide the "How Is Your Day?" initiative a voice to people around the world, offering direct communication to those we are informing about the campaign, its goals, and the importance of PPTs.

Many of the posts on social media link back to our dedicated website, where we offer links to videos, helpful infographics, and posters available for download. If you have not yet visited the website, we encourage you to do so at **www.HowIsYourDay.org**, and we would love to have you join our conversation on Facebook and Twitter—**@HIYDglobal**—and help share our messages.

ALEX DOWSETT
World-champion cyclist with hemophilia A

Interview with Alex Dowsett

BY MAT GULICK, DIRECTOR, GLOBAL COMMUNICATIONS, PPTA

Q Thank you, Alex, for joining PPTA in Budapest as we launched the "How Is Your Day?" initiative. What does it mean to you to have been part of the campaign's launch?
I think that all of this is a really nice message.

The meeting was a great opportunity for the community to come together and meet others, to share our stories, and to raise awareness of how plasma proteins are really life-changing; and I don't use this word lightly.

I'm incredibly grateful to so many people. To people, some whom I've never met. "How is Your Day?" is a way to share these positive experiences.

Q How do you imagine your life would have been different had you not been diagnosed with hemophilia at an early age and had access to plasma protein therapies?
If I didn't have hemophilia, I probably wouldn't be racing a bike.

I'm one of the lucky ones because of where I was born, when I was born, and the treatement that was available to us.

The doctors also advised my parents that, in addition to the treatment, I should be fit and healthy. I started swimming and was in good shape. So when I started cycling, I was fast straightaway.

Q What is your hope for the "How Is Your Day?" campaign and its global impact?
It's about being able to have the same opportunities as anyone else. That's what the treatments, the knowledge, and healthy lifestyle give you: the opportunity to lead a normal life—just like anyone else.

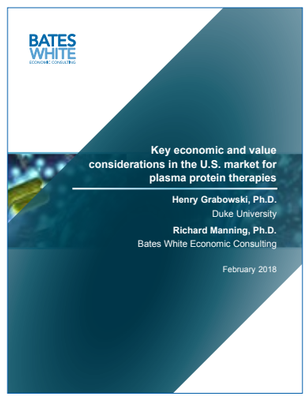
Taking my condition as an example, if you look at a hemophiliac without treatment and someone like me who has treatment, the difference is massive.

If my story can help change the menalities in many countries—to governments, to parents to every level...that would be massive. •

New Economic Paper on the Value of Plasma Protein Therapies

BY BRENNA RAINES, SENIOR MANAGER, GLOBAL HEALTH POLICY, PPTA

Patients and their families, physicians, industry, and other stakeholders have long recognized the unmatched health benefits provided by plasma protein therapies.



However, since the highly publicized stories of price spikes in off-patent and generic drugs and the subsequent Senate investigation, many critics of industry allege that prices are set irrespective of costs or value. In response, many elected officials, including some members of the Trump administration, are developing proposals to reduce spending for consumers and payers. Some proposals include sweeping, "one size fits all" approaches that could result in the unintended consequence of negatively impacting patient access to plasma protein therapies. PPTA's North America Board of Directors recognized that the Association's advocacy about the value of plasma protein therapies and differentiating them from other pharmaceuticals is more important now than ever, and it solicited a firm to independently study the unique nature of the plasma protein industry.

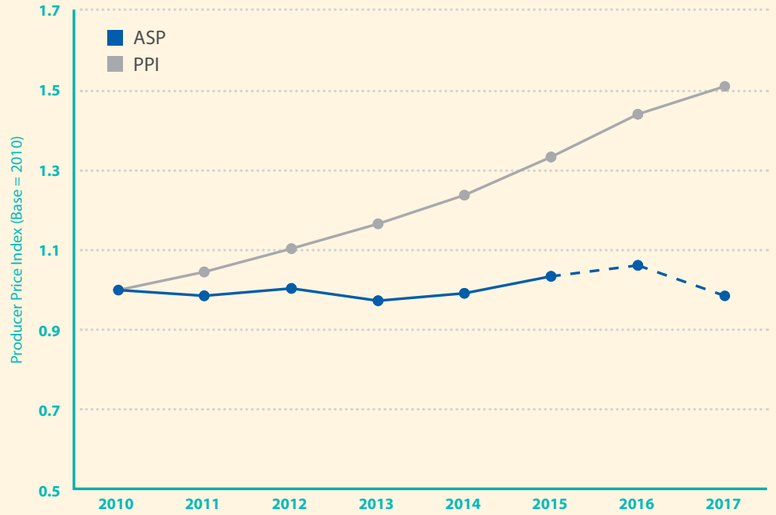
In February, Bates White Economic Consulting published the paper, "Key economic and value considerations in the U.S. market for plasma protein therapies." The Bates White paper outlines the value, complex manufacturing, and economic and policy considerations of plasma protein therapies. The findings are timely as the Association's concerns mirror those of the authors, "It would be easy for the importance of this sector to be passed over and for policy solutions to be enacted that inadvertently impair the ability of the plasma products sector to meet the vital needs of current patients and to address needs that will arise in the future."

This and other findings from the paper have been incorporated into PPTA's advocacy materials, and stakeholders should feel free to use relevant messages in their efforts as well. The full report is available at https://www.bateswhite.com/insight-196.html.

FIGURE 1:

Indexed Average Sales Prices (ASP) for IVG products compared with the Producer Price Index (PPI) for pharmaceutical preparations, 2010–2017

This figure shows the trend in prices for IVIG products from 2010 to 2017 (the dashed line indicates a projection based on 2015 utilization). Over this eight-year period, average IVIG prices essentially remained the same, while the PPI grew just over 50 percent. (p. 18)



Source: Centers for Medicare and Medicaid Services; U.S. Bureau of Labor Statistics

Q & A WITH DR. RICHARD MANNING & DR. HENRY GRABOWSKI

We sat down with authors Richard Manning & Henry Grabowski to ask about their backgrounds, thoughts on the current environment, and future research.

Q Tell me about how you were first introduced to the plasma protein industry, and what got you interested in the space?

I first became involved in work on plasma therapies through consulting on a public policy project for a plasma protein manufacturer, remarked Dr. Manning. After that project, other opportunities arose that led me to seek collaboration with Dr. Grabowski, who is one of the premier experts in the economics of the life sciences industry. We enjoy collaborating on this work because of the unique economics of the plasma

"Arguably the most important attributes of PPTs are the benefits they provide to the patients who use them. **PPTs extend life expectancy, increase quality of life, and decrease complications related to conditions.** Without these treatments, many patients would either not be able to survive or would have a substantially diminished quality of life and productivity." (p. 2)

products industry and because so few economists are familiar with the challenges it faces, particularly in the public policy environment. One consequence of being such a unique industry is that it makes it more likely for policymakers to make decisions for the overall pharmaceutical industry that could impact the plasma protein industry and the patients they serve in unforeseen and unintended ways.

Q In your opinion, how are plasma protein manufacturers unique?

The primary differences between plasma manufacturers and traditional pharmaceutical and biologics manufacturers have much to do with where these products come from. Products derived from human blood plasma face challenges that other manufacturers in the life sciences space do not face, such as obtaining source plasma for manufacturing products; dealing with a wide range of regulatory conditions in the United States and abroad covering the collection, storage, and purification of plasma; and the manufacture of plasma-derived medicinal products. As such, size and structure of the costs facing these companies can be very different from those of traditional biopharmaceutical companies.

Q What challenges do you think plasma protein manufacturers will face in the near future?

Certainly, it seems that navigating any changes that are made in the U.S. payment environment will be important. Concern about drug prices may lead to policy decisions that increase the difficulty of maintaining an adequate supply of plasma-derived medicines. If such policy decisions do not account for the key differences the industry faces, they could pose significant challenges not only for the industry but also for the patients who depend on its products.

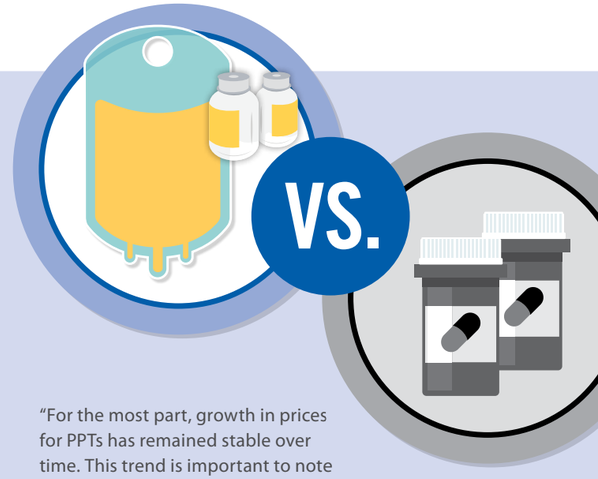
"It is important that policymakers understand the unique contributions of and challenges facing [the plasma protein therapeutics industry]. As policy proposals move forward, it is important to avoid a **"one size fits all" approach that will ultimately result in higher health care costs and adversely affect patient health."** (p. 3)

"When considering access to care, it is important to bear in mind that patients with rare, genetic conditions who are treated with PPTs typically exhibit different responses to therapy. Due to differences in patients and **because of the complex nature of the products, different PPTs are not interchangeable** from a medical perspective. They should not be treated as such by regulatory and payer policies." (p. 24)

Another key challenge is the ability to continue identifying valuable new uses of plasma-derived medicines. We understand there are some very interesting potential applications of plasma-derived therapies. Being able to fund the R&D necessary to bring new treatments to market is a key challenge that the industry faces.

Q What do you think are the most effective arguments plasma protein manufacturers can make to appeal to policymakers with limited budgets?

Perhaps the most important thing for policymakers to understand is the high value delivered by plasma-derived medicines to the patients who depend on them. Second, policymakers need to understand the complexity of the challenges the manufacturers face. Several solutions under discussion, such as reimbursement limitations and access restrictions, are likely to have severe impacts on patients. The most appropriate policy solutions to perceived problems would be to assure that the FDA and other regulatory agencies foster a healthy competitive environment that encourages innovation in payment systems and product development, thereby helping assure access to products that patients need.

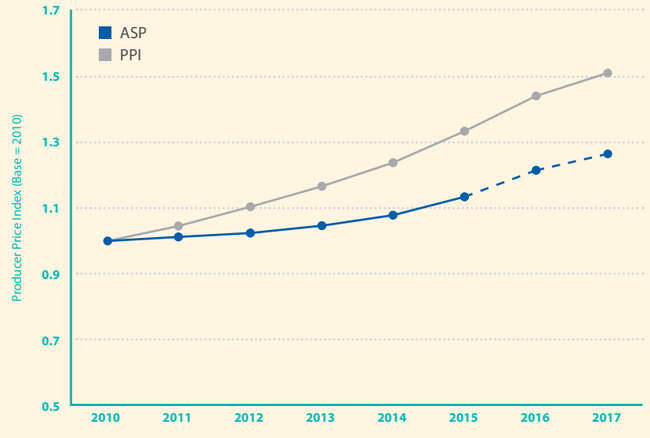


"For the most part, growth in prices for PPTs has remained stable over time. This trend is important to note in an environment where there is greater attention to pharmaceutical prices and costs. The data demonstrate that despite economic constraints such as a finite supply of starting material, **PPT prices have generally risen at lower rates than have prescription medicines since 2010." (p. 22)**

FIGURE 2:

Indexed Average Sales Prices (ASP) for alpha-1 proteinase inhibition products compared with the Producer Price Index (PPI) for pharmaceutical preparations, 2010–2017

Alpha-1 proteinase inhibitor prices demonstrate a similar trend to IVIG products in that price growth for these products has remained lower than the inflationary trend for prescription drug production costs (the dashed line indicates a projection based on 2015 utilization). On average, the alpha-1 ASP-based rates have risen less than 20 percent when compared to their base years, showing substantially less growth than PPI. (p. 19)



Source: Centers for Medicare and Medicaid Services; U.S. Bureau of Labor Statistics

Q What future research do you think is needed in this field?

The unique challenges faced by the industry in collecting plasma from donors and the regulatory issues faced along the supply chain are very interesting and important. One question that we did not directly address here, but that has occupied our attention on other projects, is the status of compensation for plasma donors. Many countries abroad do not permit compensation but offer other incentives such as time off work. We see compensation as a beneficial, and even necessary, element of plasma collection. We think there is room for much greater additional research into the determinants of safe and reliable plasma supply and into the processes established in various countries to increase the available supply of plasma for manufacturing. •

"PPT manufacturers also contribute more than 1 billion dollars annually to the U.S. economy through their donor compensation programs. [Plasma] donors receive a nominal amount to compensate them for the time needed for the donation process. When considered in aggregate, donor compensation is a helpful inflow of funds in local communities throughout the country and also engenders multiplier effects that would add substantially to the direct effect of such payments." (p. 8)

"As policymakers suggest proposals to address high drug expenditures, they should take into consideration how these policies would affect the individuals who rely on these lifesaving therapies, given the unique nature of plasma protein therapies. These lifesaving therapies cannot simply be substituted one for another. Therefore, **patient access to medically appropriate therapy should remain a priority in the changing U.S. health care environment."** (p. 31)

DR. HENRY GRABOWSKI

DR. RICHARD MANNING

Henry Grabowski is professor emeritus in the Economics Department at Duke University. Having earned his Ph.D. at Princeton University, Dr. Grabowski specializes in the investigation of economics in the pharmaceutical industry, government regulation of business, and the economics of innovation. His specific interests within these fields include intellectual property and generic competition issues, the effects of government policy actions, and the costs and returns to pharmaceutical research and development (R&D). He has been publishing research papers on the economics of the health care and life sciences for more than four decades. Dr. Grabowski has served as an advisor and consultant to various organizations, offering his ideas and insights gained through extensive investigations to the National Academy of Sciences, the Institute of Medicine, the Office of Technology Assessment, the Federal Trade Commission, and the General Accounting Office. He also has testified to different congressional committees on policy and economic issues pertaining to competition and regulation of the pharmaceutical industry.

Richard Manning is a partner in the Life Sciences Practice at Bates White, an economics consulting firm in Washington, D.C. Dr. Manning earned his Ph.D. in economics at the University of Chicago and was an assistant professor at Brigham Young University and a visiting assistant professor at the University of Chicago Graduate School of Business. His teaching and publications have focused on price theory, the economic analysis of law, industrial organization, and the economics of government regulation. He has extensive experience providing data-driven insights and expert services in life sciences and other industries to clients in law firms, corporations, and public policy organizations. Prior to joining Bates White, Dr. Manning worked as an executive at both Pfizer and Merck and as a consultant at PricewaterhouseCoopers.

MRS. JOSE DRABWELL AND ROTTERDAM MAYOR MR. AHMED ABOUTALEB

IPOPI President Recognized for Dedication to Improving Lives of Others

BY MAT GULICK, DIRECTOR, GLOBAL COMMUNICATIONS, PPTA

Mrs. Jose Drabwell, President of the International Patient Organisation for Primary Immunodeficiencies (IPOPI), was appointed on April 25 as an Officer of the Order of Orange-Nassau in recognition of her years of outstanding contribution to the global primary immunodeficiency community. The royal award, presented in the Netherlands by Mr. Ahmed Aboutaleb, mayor of Rotterdam, is given only to the most deserving individuals who have shown personal commitment, vision, and skills in the betterment of society.

In presenting the award, Mayor Aboutaleb remarked, "We don't come across people like yourself who dedicate themselves primarily for the good of others." He went on to say he was "delighted" to be the person who gave Mrs. Drabwell the award as a recognition from her native country.

As an individual living with a primary immunodeficiency herself, Mrs. Drabwell understands the importance of early diagnosis and access to appropriate care for all those who rely on plasma protein therapies to treat their illnesses. This personal awareness and knowledge of rare diseases and the importance of their plasma-derived therapies has made her decade-long tenure as the president of IPOPI one marked by growth and success, largely due to her devotion and relentless drive to bring care to all individuals with primary immunodeficiencies.

"Jose is a true advocate and is very deserving of her appointment as an Officer of the Order of Orange-Nassau. Her dedication and vision are an inspiration," said Jan M. Bult, President & CEO of the Plasma Protein Therapeutics Association. I am proud of Jose and all she has done to help people living with primary immunodeficiencies around the world. We look forward to many more years of being inspired by her work. Personally, I am thrilled that she received this from the country where Jose and I were born." •

THE ORDER OF ORANGE-NASSAU

The Order of Orange-Nassau is a Dutch order of chivalry founded on April 4, 1892, by the Queen Regent Emma. The Order of Orange-Nassau has two divisions, civil and military, and six grades: Knight Grand Cross, Grand Officer, Commander, Officer, Knight, and Member. The order is a chivalric order open to "everyone who has earned special merits for society." These are people who deserve appreciation and recognition from society for the special way in which they have carried out their activities.[1]

References:
1. "De Orde van Oranje-Nassau/Onderscheidingen ." Lintjes.nl.

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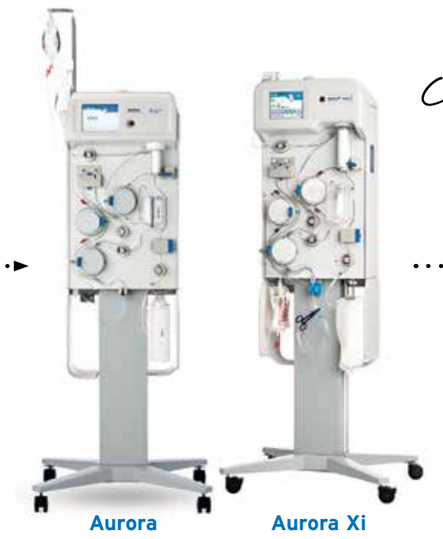

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Inside PPTA

NEWS FROM AROUND THE GLOBE

MEET THE PPTA STAFF

Sara Stefanelli

COMMUNICATIONS ASSISTANT

Q How long have you been with the Association?

I started with PPTA in January 2017.

Q What do you focus on in your role as Communications Assistant?

As part of the Communications team and being based in PPTA Brussels office, my role is to help build and raise awareness of the plasma protein therapeutics industry, especially highlighting the European perspective, the specific issues, and peculiarities of the various European countries in relation to the industry. I work closely with colleagues from the different departments to produce communications materials that convey concerted messages and provide support for joint efforts to underline the uniqueness of plasma protein therapeutics and the importance of access for patients to these lifesaving treatments.

Q Tell us about your background.

Last year I moved from Rome to Brussels to join PPTA. Prior to that, I worked in communications and external relations. I was responsible for media relations, external relations with embassies, and political and cultural organizations in Italy for institutional events, often in cooperation with the Vatican. Working on different projects with diverse partners allowed me to experience a variety of contexts and the multiple aspects of communications, also in relation to special protocol requirements. Leaving Rome for Brussels and getting involved in this industry was an incredibly stimulating challenge. I am proud of having the opportunity to help develop materials and messages to support PPTA's efforts to ensure better access to care to plasma protein therapeutics worldwide.

Q What is most rewarding about working in this industry?

I have been working in communications for about eight years. However, before joining PPTA, I had never experienced the feeling of being able to make a difference for someone with my work. Despite my short time with PPTA, I've already seen the impact the Association and its communications efforts can have on the lives of those who rely on plasma protein therapies. In particular, through our new "How Is Your Day?" global initiative, I feel how incredibly rewarding it is to be part of a team that works to raise awareness of the life-changing difference that plasma protein therapeutics can make to thousands of people worldwide, people who are able to lead normal lives thanks to their treatments.

Q What characteristic do you most admire in others?

I most admire honesty and generosity in others.

Q Who has been an inspiration to you in your life?

My best memories are those with my grandfather. He was the most gentle and generous person I have ever known, and he taught me to always look at the bright side of things, even when they seem too hard to stand or to deal with. Though he became very ill when he was only in his thirties and, despite having had to cope with his poor health throughout his entire life, he never gave up and always said that difficulties helped him become stronger. •

Inside PPTA: Health Policy in Action

INTERNATIONAL AFFAIRS

The International Affairs department is continuing to round out PPTA's global initiatives with ongoing projects in China and Canada. We are busy preparing for two events in Beijing during the week of September 3 —a training session for Chinese Food and Drug Administration GMP inspectors and the second Plasma Protein Industry Summit at the Parenteral Drug Industry Congress. The Summit, which will feature PPTA members and staff as well as leading experts and Chinese and U.S. regulatory officials, will focus on areas of possible cooperation, with discussions on how Chinese industry and PPTA might be able to find common ground on some existing differences. PPTA is also closely following the ongoing changes in the Chinese health regulatory structures.

In Canada, Source and International Affairs staff members are working together to fend off continued attempts to ban compensated plasma collection by private companies in British Columbia and Nova Scotia. These bans leave open the possibility of Canadian Blood Services (CBS) compensating its donors. Also in Canada, PPTA International Affairs staff worked with the PPTA Global Health Policy Committee to send letters to CBS and the Provincial and Territorial Blood Liaison Committee supporting Alpha-1 Canada's appeal to get alpha-1 proteinase inhibitor included on CBS's list of plasma protein therapies. This would allow all Canadian patients to access augmentation therapy. Currently, access to treatment is on a province-by-province basis, with only some provinces providing access.

EUROPE

In the multifaceted context of the health policy issues in Europe, PPTA has recently been involved in the public consultation for the reform of the so-called "Pharma Incentives Package" by the European Commission. This includes the EU Orphan Medicinal Product (OMP) Regulation 2000/141/EC, whose review will significantly impact the plasma industry. In December 2017, the commission published an evaluation and fitness check road map to define the review procedure. Any feedback from the various stakeholders was due by early January 2018, and given the special significance of the issue, PPTA participated actively in the consultation and provided input.

Another current major issue at the European level is the Health Technology Assessment (HTA) regulation, whose scope is to implement a mandatory use of common HTA tools and procedures, as well as of the results of the joint clinical assessments by the member states. PPTA has engaged in the activities of the Industry Association Stakeholder Pool, led by the European Federation of Pharmaceutical Industries and Associations, to provide comments and aims to be involved in the upcoming discussion.

NORTH AMERICA

On May 17, PPTA hosted its annual Capitol Hill Day on which the Association brings together producers of plasma protein therapies, patients with rare diseases, and patient group representatives. The fly-in provides this community an opportunity to inform Congress about the unique nature of plasma protein therapies and the chronic diseases they treat and to discuss policies that preserve access to safe and effective treatments. If you are interested in information about the 2019 congressional Fly-In, please reach out to Cthomas@pptaglobal.org.

There's more to come in the fall issue, which will cover the 2018 midterm elections, provide an update on the efforts of the Trump administration, and outline advocacy plans for 2019.

In the meantime, we encourage all readers of The Source to monitor our legislative activity and to engage with our Facebook and Twitter handles (@PlasmaProteins). Follow our updates and share with your networks so we can, as a collective network, boost awareness of the unique nature of plasma protein therapies and share information about the value they provide to patients, families, and communities. •

PPTA INTERVIEW

Caroline Kruse

EXECUTIVE DIRECTOR, PDSA

BY KIMBERLY SEROTA, ASSISTANT MANAGER, GOVERNMENT RELATIONS, PPTA

2018 marks the 20th anniversary of the Platelet Disorder Support Association (PDSA), an organization that enhances the lives of people with immune thrombocytopenic purpura (ITP) and other platelet disorders through education, advocacy, research, and support. PPTA sat down with Executive Director Caroline Kruse to discuss PDSA's past and future. Caroline worked in journalism for more than 20 years and hosted a radio show, "Family Matters," for 14 years. After being diagnosed with ITP, Caroline found a new passion and was able to use her expertise to educate and support members of the PDSA community. In 2011, Caroline was diagnosed with CVID and credits her Ig replacement therapy for keeping her healthy and able to do the work that she loves at PDSA.

Q Tell me about how you got involved with PDSA.

My hematologist introduced me to another ITP patient he treated and suggested we start a support group. I found PDSA online and attended my first national patient conference where I met the group's founder, Joan Young. Joan was an ITP patient with an IT background. With limited information about ITP, she started PDSA as an online discussion group. Thirteen years ago, she asked me to be on the PDSA Board of Directors, where I served for two years before becoming the organization's first director of public relations. In 2008, Joan retired, and the Board asked me to be the new executive director.

Q What is one thing you would like the public to know about PDSA and living with ITP?

Patients with ITP face a complex set of challenges. ITP is a heterogeneous disease associated with significant morbidity not limited to bleeding. Due to variability in its underlying pathobiology and natural history, management of the disease can be unpredictable despite the availability of several therapies with different mechanisms of action. Once diagnosed, ITP patients experience a range of physical and emotional challenges as they seek to monitor their platelet counts, balance treatment side effects, and manage the fear and frequent reality of relapse. Patients often cycle on and off of treatments for years. Stories of physicians who over-treat or incorrectly treat ITP patients due to their minimal knowledge about this rare disease are too common.

Q PDSA is celebrating its 20th anniversary this year. What has been its greatest achievement to date?

PDSA's greatest achievement in the first 20 years has been empowering ITP patients and families. ITP patients and parents of children with ITP often feel very isolated and alone. PDSA's educational and support services provide a place where patients and families can empathize, share knowledge, and simply talk about the ITP experience—often learning from other patients.

Even as we evolve and grow, we remain committed to the original values on which PDSA was founded: Informed patients are in a better position to understand their disease, have more meaningful dialogue with their doctors, and potentially have an improved opportunity to heal.

We've accomplished this by raising awareness of ITP on an international scale. Although ITP is considered a rare disease, it's more common than many people think, making the opportunity to connect much easier. Patients just need to seek out that initial connection to other patients. In 2016, PDSA established the ITP International Alliance, an intercontinental partnership of ITP patient support organizations committed to education, awareness, and establishing a global voice for ITP patients. Through the creation of the website www.globalitp.org and Global ITP Awareness Week, we made great strides in raising awareness for ITP around the world. We currently have 28 alliance members and have translated 16 of our educational booklets into other languages to assist and support groups in countries where they don't have the same resources as PDSA.

PDSA celebrated our eighth official ITP Awareness Month last September by educating our patient community and the general public about lifesaving plasma therapy and the importance of plasma donation. Immunoglobulin therapy is one of the most common treatments for ITP as it blocks antibodies that destroy platelets; some patients use IVIG as a regular ongoing treatment for their ITP, while others use it as a safety therapy to increase their platelet count when at a critically low level or before surgery, a dental procedure, or even when they want to travel. Our educational awareness initiatives on social media during September 2017 reached 4 million people.

Q What would you like to see happen in the next 20 years?

As PDSA celebrates its 20th anniversary, our renewed focus on research this past year resulted in the launch of the ITP Natural History Study Registry (funded by the National Organization for Rare Disorders and the U.S. Food & Drug Administration [FDA]). Progress in research drives progress in identifying and understanding ways to advance the ITP treatment paradigm. The registry establishes baseline information, longitudinal disease progression, and identifies patient-reported outcomes. It characterizes and describes the ITP population as a whole, assists the ITP community with the development of recommendations for standards of care, assists researchers in studying the pathophysiology of ITP and interventional outcomes, and can support the design of clinical trials for new treatments.

We also restructured our research program through an award from the Patient-Centered Outcomes Research Institute (PCORI) so that the research we fund involves patients throughout the entire investigational process. We have also increased our advocacy and policy efforts, being involved in many patient advocacy meetings, lobbying for access to care and increased funding for government agencies such as the National Institutes of Health, Centers for Disease Control and Prevention, and the FDA. As a result of our recent accomplishments with the registry, we have begun to engage with the FDA to express the unmet medical and scientific needs of ITP patients and to ensure the patient voice is included in regulatory process.

We would also like to establish ITP Centers of Excellence to improve care and outcome. Raising awareness for ITP in the clinical sphere is crucial in better informing medical professionals, and raising public awareness for ITP is vital in empowering patients to take control of their disease. Comprehensive treatment centers for ITP and other bleeding disorders would mitigate the risk posed by non-specialists treating ITP patients, thus improving a patient's treatment options, therapy experience, and quality of life. ●

(From left to right): ITP patients from 6-56 at the Cleveland "Pump it up for Platelets" walk/run. Caroline Kruse moderating the 2017 Rare Disease Day Congressional Caucus.


San Francisco, United States

Upcoming Events

CONFERENCES & SYMPOSIUMS

June

29 – July 1 Alpha-1 Foundation 27th Annual National Education Conference
San Francisco, United States

July

13 – 15 Platelet Disorder Support Association (PDSA) 18th National Patient Conference & 20th Anniversary Celebration
Cleveland, United States

September

5 – 7 Parenteral Drug Industry Congress
Beijing, China

October

8 – 12 International Plasma Awareness Week (IPAW)

11 – 13 National Hemophilia Foundation (NHF) 70th Bleeding Disorders Conference and Annual Meeting
Orlando, Florida, United States

13 – 16 AABB Annual Meeting
Boston, United States

15 – 16 National Organization for Rare Disorders (NORD) Rare Diseases and Orphan Products Breakthrough Summit
Washington, D.C., United States

18 PPTA Business Forum
Atlanta, United States

24 – 27 18th Biennial Meeting of the European Society for Immunodeficiencies (ESID)
Lisbon, Portugal

November

1 – 3 15th Biennial GBS/CIDP (Guillain-Barré Syndrome/Chronic Inflammatory Demyelinating Polyneuropathy) Symposium
San Diego, United States

12 – 15 Third International BioProcessing Asia Conference
Langkawi, Malaysia

2019

March

19 – 20 International Plasma Protein Congress (IPPC)
Amsterdam, the Netherlands

June

18 – 19 PPTA Plasma Protein Forum
Reston, Virginia

GLOSSARY OF TERMS

AE – ADVERSE EVENT

ASP – AVERAGE SALES PRICE

BRICS – BRAZIL, RUSSIA, INDIA, CHINA, AND SOUTH AFRICA

CBS – CANADIAN BLOOD SERVICES

CPI – CONTRIBUTION OF THE PHARMACEUTICAL INDUSTRY

CVID – COMMON VARIABLE IMMUNODEFICIENCY

EU – EUROPEAN UNION

HAE – HEREDITARY ANGIOEDEMA

HIYD – "HOW IS YOUR DAY?"

ID-NAT – INDIVIDUAL DONATION NUCLEIC ACID TESTING

Ig – IMMUNE GLOBULIN

IG – IMMUNOGLOBULIN

IM – INTRAMUSCULAR

IPOPI – INTERNATIONAL PATIENT ORGANIZATION FOR PRIMARY IMMUNODEFICIENCIES

IPPC – INTERNATIONAL PLASMA PROTEIN CONGRESS

IQPP – INTERNATIONAL QUALITY PLASMA PROGRAM

ISBT – INTERNATIONAL SOCIETY OF BLOOD TRANSFUSION

ITP – IMMUNE THROMBOCYTOPENIC PURPURA

IV – INTRAVENOUS

LASID – LATIN AMERICAN SOCIETY FOR IMMUNODEFICIENCIES

LMICS – LOW- AND MIDDLE-INCOME COUNTRIES

MRB – MARKETING RESEARCH BUREAU

NBI – NATIONAL BIOPRODUCTS INSTITUTE

PDMP – PLASMA-DERIVED MEDICINAL PRODUCT

PDSA – PLATELET DISORDER SUPPORT ASSOCIATION

PI – PRIMARY IMMUNODEFICIENCIES

PPI – PRODUCER PRICE INDEX

PPT – PLASMA PROTEIN THERAPY

R&D – RESEARCH AND DEVELOPMENT

SANBS – SOUTH AFRICAN NATIONAL BLOOD SERVICE

SC – SUBCUTANEOUS

TRALI – TRANSFUSION-RELATED ACUTE LUNG INJURY

WFH – WORLD FEDERATION OF HEMOPHILIA

WHO – WORLD HEALTH ORGANIZATION

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1. Data on file.
2. DXT Relay is cleared for use with Aurora in the U.S. DXT is cleared for use with Aurora Xi in the U.S.

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