THE SOURCE

MAGAZINE OF THE PLASMA PROTEIN THERAPEUTICS INDUSTRY

FALL 2013

Donating Plasma . Saving Lives

INTERNATIONAL PLASMA AWARENESS WEEK

OCTOBER 13-20, 2013

Expanding Horizons

PPTA Launches Global Awareness Event

Trade Negotiations Hold Promise for Industry

Look at Latin America

PPTA

Plasma Protein Therapeutics Association

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IQPP
INTERNATIONAL QUALITY PLASMA PROGRAM

QSEAL
QUALITY STANDARDS OF EXCELLENCE, ASSURANCE & LEADERSHIP

INSIDE

FALL 2013

THE MAGAZINE FOR THE PLASMA PROTEIN THERAPEUTICS INDUSTRY

In My View

BY JAN M. BULT, PRESIDENT AND CEO

EVERY TIME I VISIT A PLASMA COLLECTION CENTER, I am impressed by the many committed individuals who take time out of their day to donate lifesaving plasma for the benefit of patients who may be complete strangers and may live in regions of the world far away. It impresses me how professionally the staff works with so many people from different walks of life who donate frequently through plasmapheresis. I have visited centers in many parts of the United States, Germany, Austria and the Czech Republic. Everyone who donates their vitally important plasma has patiently completed the lengthy screening process to become a qualified donor. The standards used by these centers were developed by PPTA and exceed regulatory requirements.

It is therefore with great pleasure, I announce International Plasma Awareness Week (IPAW), a creation of the PPTA Source Division to recognize the essential contributions that plasma donors make to the manufacture of so many lifesaving therapies for so many patients in the world.

Recently, I was invited to participate in an International Society for Blood Transfusion (ISBT) panel discussion about the "old theme" of donor compensation. As we all know, plasma that is used for the manufacture of plasma protein therapies can come from two sources:—source plasma collected through plasmapheresis and recovered plasma collected through whole blood donations. Individuals who donate plasma in our centers are compensated for their time and inconvenience, whereas those who donate whole blood in blood donation facilities are normally not compensated. We are at the point now that it is widely understood that we need both sources to supply enough plasma for the growing needs of patients in the world. When you look at the collection data, it is noteworthy that plasma sourced from plasmapheresis centers is increasing, whereas the volume of recovered plasma from whole blood is more or less stable. Therefore, it is vitally important that we recognize and promote the importance of plasma collection and voluntary compensated donors.

Contrary to the needs of the plasma protein therapies community, the World Health Organization (WHO) regularly organizes and endorses meetings focusing on its holy grail of self-sufficiency and voluntary non-remunerated donation. This concept applied to whole blood is usually adequate to meet local needs for blood components within countries, but is inadequate to fulfill the expanding need for plasma-derived therapies. To meet the needs of these patients with recovered plasma, it would require more collections from whole blood resulting in unethical waste of blood components. Therefore, the collection of source plasma makes sense. Any suggestion that the clinical need for plasma protein therapies in the world can be met via recovered plasma is surreal.

I don't understand why the WHO myopically focuses on self-sufficiency and blood donors while refusing to acknowledge the global need for plasma donors. I assume the reason is that these donors receive a modest compensation for their time and inconvenience. It is time that the WHO realizes that many patients in the world can only be treated with therapies that are on the WHO's List of Essential Medicines because we have so many plasma donors who are willing to help their fellow citizens!

I certainly recognize Plasma Donors and invite you to do the same.

Patient Centeredness in Health Research: The Challenge in Rare Diseases

BY J. RUSSELL TEAGARDEN

Patient Centeredness and the Illness Experience

The term "patient-centered" is invoked frequently these days in all realms of health care. Anyone outside of health care could reasonably wonder why the term is necessary; isn't patient centeredness the very essence of health care? If only.

The ways in which science is advancing and health care delivery is becoming so complex are enough to draw attention away from the effects patients experience directly from their health problems. Medical researchers focus on how to understand and reverse disease processes while public and private institutions focus on how to organize and pay for health care services and products. Left underappreciated amidst all these activities are the consequences health problems actually cause people, or what we could call the "illness experience". Patient centeredness has become the organizing concept driving efforts to direct our attention to illness experiences and motivate responses to them. I'd like to examine patient centeredness in health research and the particular challenges that rare diseases pose to it.

The illness experience is the personal dimension of disease, or as Merilee Karr[1] puts it: "The illness equals the disease plus the person." Illness experiences—in contrast to short-term sickness—tend to be chronic, even lifelong, becoming a constant source of limitations and apprehensions. "The undercurrent of chronic illness," Arthur Kleinman[2] writes, "is like the volcano: it does not go away. It menaces. It erupts. It is out of control. One damned thing follows another." Patient centeredness aims primarily at managing illness experiences.

Patient centeredness in health research is thus concerned with effects on patients, whether caused by a disease, its treatments, its impositions, or its impacts on activities of daily living. Research that is patient centered develops lines of inquiry about what happens to patients themselves rather than what happens with blood pressure, heart rate, blood counts and other measures of disease processes. A key outcome in the patient-centeredness research is information that patients can use to make choices and act on their preferences. Patient-centered health research starts and ends with patients' experiences of illness and the information they need to manage these experiences.

Countering Opposing Forces

Compelling as the concept of research aimed at patients' direct illness experiences of rare diseases may seem, in reality it remains uncommon. Attention and resources tend to be allocated to activities perceived as ensuring the most good for the most people. Rare is not most. Also, health research is usually directed towards scientific discoveries and clinical trials related to disease processes, not to illness experiences. Further, current research methods and incentive structures do not align well with the interests of rare disease patients and their particular needs. These are but some of the forces working against more extensive uptake of patient centeredness in health research for rare diseases. Yet these forces can be countered, and interest in both patient centeredness and rare diseases is growing fast.

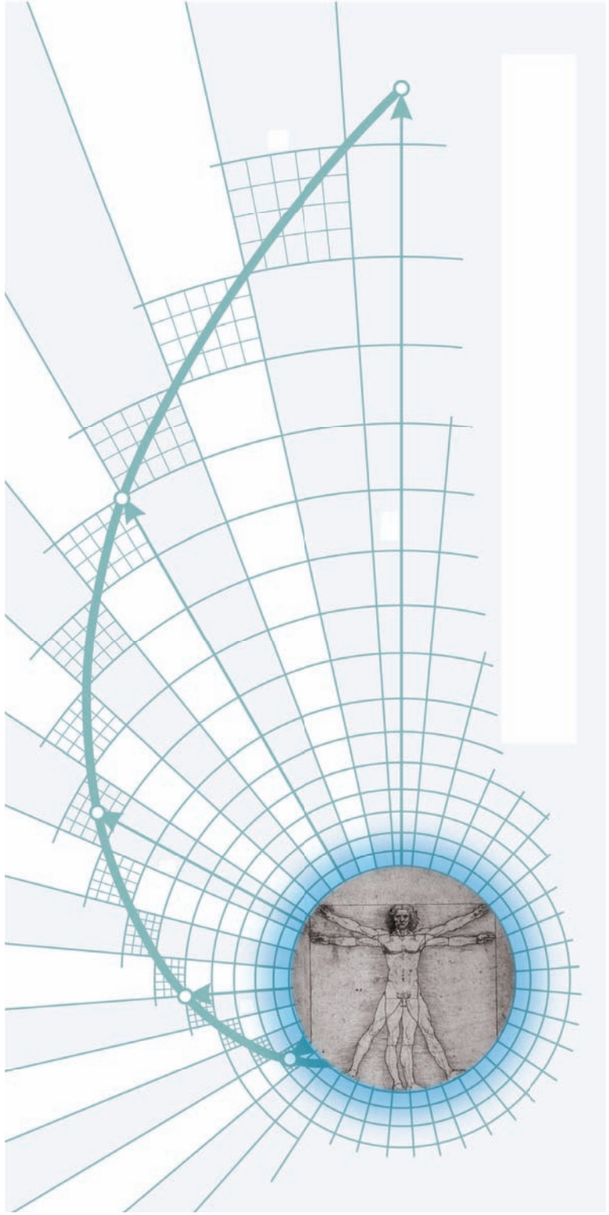
Rare disease communities are always working against the impulse that drives researchers, health care providers and government institutions to do the most good for the most people. Members of rare disease communities hear the question, "Why expend ever-so-scarce resources on patient-centered research in rare diseases when the same resources can be used to benefit much larger populations?" Why indeed? Advocates for rare disease communities argue that the most good cannot be achieved by neglecting the needs of people who, through bad luck alone, wind up with a rare disease. Is that the good we want, they ask? They also argue that it is wrong on general principles to pay attention to certain groups only because they contribute more towards the most good. And they argue for fairness, since people with rare diseases come upon their predicaments so unfairly. Many rare disease illness experiences produce extreme suffering and misery. People with rare diseases, therefore, should be given fair opportunities for research support without regard to how much the findings are likely to contribute to the greatest good as measured by straightforward calculations of benefits.

Many rare diseases progress rapidly to severe impairment, suffering, or death. Rare disease patients are in a hurry for cures, effective treatments, or meaningful improvements in functioning. The pace of science is wholly insufficient to address the urgency of rare diseases. Only the unusual research article doesn't end with "more research is needed," whereas the rare disease community wants to see "problem solved" or "disease cured." But most research organizations operate under Normal Science, which consists mostly of solving remaining puzzles and working out minor questions according to a well defined set of theories, principles, questions, study designs and interpretations (a "paradigm"). Under Normal Science, novelty is discouraged, even punished. By contrast, scientists interested in Novel Science find funding and career advancement more difficult. Rare disease communities know how to generate basic science and clinical trials. They find, and sometimes fund, researchers who are interested in novel approaches to problems in rare diseases. They need to do the same to generate patient-centeredness in health research as well.

Patient-centered research in rare diseases will require advances in research methods. The methods developed for large populations are hard for many researchers to give up; they find comfort in

"The undercurrent of chronic illness,is like the volcano: it does not go away. It menaces. It erupts. It is out of control. One damned thing follows another."

SHUTTERSTOCK / BONOTOM STUDIO



Patient centeredness in health research is thus concerned with effects on patients, whether caused by a disease, its treatments, its impositions, or its impacts on activities of daily living.

big numbers and familiar methods. Further, the data they amass is most often appropriate to address disease processes but not illness experiences. If we are to see more patient centeredness in health research, rare disease communities and researchers need to identify the data that best represent patients' illness experiences and develop methods to test the effects of curative and palliative approaches. Using the right approach, rare disease patients can convey to health care providers and payers what is valuable with regard to their illness experiences.

Moving Toward Centeredness

Bioscience focuses on diseases, people experience illnesses. Understanding the causes of rare diseases and discovering treatments for them are critically important, to be sure. But efforts to find treatments do not always address illness experiences, and in some cases, may make them worse. Only with patient-centered approaches to health research can we improve illness experiences and generate the information patients need to make good choices among the available options.

Rare disease communities face challenges in getting patient-centered research that targets their needs. But they have encountered similar challenges before in getting scientific research directed at rare diseases. They have to win over those who, in attempting the most good for the most people, disregard the needs of rare disease patients, and have to push researchers to expand their scope to encompass the experience of illness. To achieve these ends, they must bring attention to the incentives and protections researchers require before they will embrace novelty in research concepts, methods and data elements.

Rare disease communities will not be on their own as they generate more patient-centered research. Currently in development are national research network structures, methods and programs focused entirely on patient-centered health research through the federally funded Patient Centered Outcomes Research Institute (PCORI). PCORI has mandates to include rare diseases in its portfolio. In addition, a general appreciation for the importance of patient-centered health research is permeating all segments of US health care and will carry through to rare diseases. Where once centrifugal forces seemed to be countering efforts to bring patient centeredness to research in rare diseases, today the forces generated by rare disease advocates, researchers and industry are raising awareness and redirecting attention back toward the center: the person who lives the experience of a rare disease.

J. Russell Teagarden, *Senior Vice President, Medical & Scientific Affairs, National Organization for Rare Disorders*

[1]Karr, M. D. (2000). The moment of death. In *The healing arts: An Oxford illustrated anthology*, R.S. Downie (Ed.). Oxford: Oxford University Press.

[2]Kleinman, A. (1988). *The illness narratives: Suffering, healing & the human condition*. New York, NY: Basic Books.

Hemophilia in Latin America

BY CESAR GARRIDO

AFTER NORTH AMERICA AND EUROPE, Latin America has the greatest opportunity to achieve a 100% diagnosis rate, greatly increase the use of medications, and offer appropriate treatments. With a population of 600M, Latin America currently has 40,000 people with hemophilia (PWH) and other bleeding disorders according to the World Federation of Hemophilia (WFH).

Latin America increased its diagnosis rate by nearly 53% in 2007 and growing consumption of clotting factor concentrates (CFC) in the region rose by 222%. However, in the last six years, progress has only increased by a little more than a 35%, which keeps the region still below other developed regions of the world.

Latin America has experienced a major economic resurgence over the past 18 years. WFH and others have trained professionals in hematology, orthopedics, laboratory, nursing, psychology, physiotherapy and psychiatry. This has contributed to a comprehensive care infrastructure in public hospitals that is much greater than what existed in the 1980's.

Families of PWH are also educated and organized as members of the WFH and have support and advice at all times based on the organization's experiences and lessons learned. This is more than what was available in the 1990's and provides reasons to be optimistic.

Care providers have been progressing in the field of research and implementing better therapies using procedures that help create better patient care. From the 1980's until 2006, PWH's families, patient organizations, health professionals, the WFH and the pharmaceutical industries have agreed that PWH should receive CFC to provide the most effective and safest treatment possible.

In 2007, we started to notice the results of the WFH's efforts in organizing worldwide care for patients, families and medical professionals trained in hemophilia. Lobbying governments and health authorities helped to ensure access to appropriate drugs. WHF has also encouraged research and the establishment of appropriate practice guidelines within countries and worked in partnership with the pharmaceutical industry. Industry has focused on achieving greater safety with their products and has shown solidarity and respect for the hemophilia community. At that time, industry experts started talking more frequently at international conferences, symposia, publications and media on the use of CFC that were becoming increasingly available.

Additionally, developing countries deepened their efforts to adhere to better practices such as improving therapies, health systems and quality of life for patients and research for that population. Today, problems such as chronic joint disease, combating the presence of inhibitors and reducing bleeding episodes are being solved resulting in an improved quality of life for PWH.

I believe in 2008 there was a noticeable separation between the caregivers' and advocacy groups' perspectives. It is clear that CFCs and their recombinants are available and have not represented a safety threat to this community in the last 20 years. Advocacy groups need to progress to utilizing new tools in persuading the different health authorities to improve PWH care. Examples of new tools are increasing the purchases of concentrates, creating more medication options available and using better human resources to provide comprehensive care.

To influence the health authorities, advocacy groups must use statistical information to talk about the cost-benefit, cost-effectiveness and managing data that demonstrates an improvement in the quality of life for patients as a result of a comprehensive care.

The leaders of patient groups in their advocacy work are tasked with utilizing their knowledge to address priority areas such as:

- Optimizing diagnostic records with early and accurate information
- Promoting prevention and early treatment to be more appropriate and cost effective
- Providing timely, comprehensive and multidisciplinary treatment
- Developing a national strategic plan and action for addressing hemophilia and other bleeding disorders

Ten hemophilia organizations from eight countries in Latin America have been working with me to design a new route to focus on these four priorities. This group already had two meetings at the *"Latin American Summit of Experts on Hemophilia and other Bleeding Disorders"* held in Bogota, Colombia in 2012.

I am convinced that there is potential in Latin America and if we work as a single block, using stakeholders and implementing new strategies, we will increase the numbers in diagnosis and consumption which have shown a correlation in this region.

CESAR A. GARRIDO, *Project Manager, Asociación Venezolana para La Hemofilia*

VSTOCK

Primary Immune Deficiency in Latin America

BY ROBERTA PENA

LATIN AMERICA (LATAM) is a vast region of over 21 million square km formed by 20 countries with nearly 600M inhabitants. This developing region is characterized by the difficult social and economic context caused by extremely different environments.

I would like to paint a picture of what it is like living with primary immune deficiency (PID) in LATAM. One of the most important issues patients face in the first place is the lack of proper **DIAGNOSIS.** In LATAM it is very difficult to reach an appropriate, early diagnosis in the areas of pediatric and general practice. This leads patients to face three different situations:

Proper/Early Diagnosis means that care and treatment will start early and the patient will avoid days of hospitalization, unnecessary operations, medication, medical studies and emotional impact. In the case of adults, it will prevent them from missing work and in the case of children being absent from school. This means things have been well done.

Late Diagnosis means that treatment is started late and the patient has suffered from recurring infections and/or organ damage which could be reversible or irreversible. Both situations have an impact on health condition as well as on terms of cost effectiveness.

Lack of Diagnosis means that patients will not receive the necessary care and treatment which leads to a higher morbidity and death rate.

Secondly PID patients are confronted to difficulties pertaining to treatment **ACCESSIBILITY**. In the LATAM region it is difficult to reach access to adequate quality care and an appropriate treatment level due to the high costs of treatment and the relatively low incidence of the condition. There are a few patients who have access to everything but these are exceptions. However, there are a large number of PID patients who, despite receiving a proper diagnosis, have significant difficulties to access optimal treatment, care and medication. All patients in LATAM face bureaucracy and barriers to treatment accessibility. These include:

- Paperwork
- Lack of knowledge of PID among health authorities
- Legislation about PID is non-existent partly intentionally
- Ignorance about the area or no priority in health policy
- Exclusion from health care and coverage in general
- A lack of choice of plasma protein therapies

Not only patients, but also their families are affected when we refer to accessibility, because in many cases they suffer discrimination, handicaps and uprooting, as well as, geographical and economic barriers for those living far from the big cities.

The third and last key issue for patients is **TRANSITION.** There are great difficulties in establishing transition care programs for pediatric to adult patients.

When comparing pediatric with adult services in LATAM, we are confronted by a large gap because although most patient services work well and in an interdisciplinary manner, this is not the case for adult services where there is a lack of adult reference centers, adult immunologist and interdisciplinary cooperation, which leads to difficulties for continuing the follow-up, monitoring and treatment of adult patients.

BIGSTOCK

From all the above you may infer that the LATAM region faces many difficulties; however, I would like to point out that there are excellent immunologists in some of these countries.

The Jeffrey Modell Foundation (JMF) who, through their commitment to patients care, has also set up many JMF Centers to improve diagnosis and research for PID patients.

National patient organizations are also important advocates for patients. They:

- Raise awareness of primary immunodeficiencies
- Focus on early diagnosis and screening
- Educate health professionals and promote exchange of expertise
- Organize data collection and research
- Advocate for appropriate legislation
- Participate in meetings with health authorities
- Provide legal support to patients
- Provide emotional support to patients
- Comprehend patient´s conditions and verify an appropriate treatment and care
- Promote interaction among patients
- Ensure the supply of a wide choice of plasma for an adequate, effective optimal treatment levels

They do this by:

- Creating awareness programs and holding medical symposiums, workshops, regional meetings in hospitals, as well as, in medical and nursing schools
- Building communications and support networks; disseminating scientific information such as warning signs; promoting a better understanding of PIDs; providing guidance and advice to all professionals, patients and families related to primary immune deficiencies; offering support and advice in dealing with health insurance companies and advocate among decision makers to ensure the availability of treatments and medications
- Establishing a PID Patient Registry

The International Patient Organization for Primary Immunodeficiency (IPOPI) through its Association of National Member Organizations is dedicated to improving awareness, access to early diagnosis and optimal treatments for primary immunodeficiency (PID) patients worldwide.

IPOPI currently has 47 National Member Organizations (NMOs) around the world, eight of which are established in LATAM: Argentina, Brazil, Colombia, Chile, Mexico, Peru, Uruguay, and Venezuela.

IPOPI is actively liaising with three additional countries in the region namely, Costa Rica, Panama, Puerto Rico. IPOPI started working in the LATAM region in 2008 especially with the Latin American Society of Primary Immunodeficiency (LASID).

IPOPI has held and given financial support for two regional meetings in Colombia in 2009 and in Mexico in 2011. The next IPOPI LATAM Regional Patients Meeting will be held in October of this year in Chile. IPOPI also recently organized an awareness campaign workshop in Brazil and for the first time in Latin America. A joint stakeholder awareness campaign was agreed upon and established an action plan that centered on treatment, diagnosis and patient associations. The action plan has already started to pay off as a joint position statement was submitted to the Ministry of Health by patient groups and key opinion leaders highlighting the key priorities for the PID community in Brazil in the context of the national consultation on rare disorders. Several follow up actions are planned for the coming months.

IPOPI supports yearly World Primary Immunodeficiencies Week Campaigns both with direct support to its NMOs to ensure the national implementation of the campaign, as well as through a series of tool kits available in different languages.

World Primary Immunodeficiencies Week is our symbol which brings together, empowers and engages all global stakeholders in the Primary Immunodeficiency cause (patients, nurses, physicians, scientists, allied health professionals and industry). Each National Patient Organization works hard to organize the events for this week according to their own needs. We are very pleased that PPTA is also one of the supporters of this important campaign.

National Patient Organizations in the LATAM region have accomplished many achievements thanks to their own efforts but the work and guidance that IPOPI is offering is essential to help the LATAM PID community to continue improving and growing in the future. We always bear in mind that patients are our main focus.

ROBERTA PENA, *IPOPI Board, Regional Director for Latin America*

Regulatory Developments in Latin America

BY ILKA VON HOEGEN, PH.D.

ALTHOUGH PPTA'S WORK IS FOCUSED primarily in Europe, the United States (U.S.)and Asia, the Association does engage in activities in other countries. Involvement is largely issue driven and the Association makes its experts available for legal, scientific and regulatory concerns related to plasma protein therapies as need arises. Recently, PPTA has engaged in regulatory issues in Latin America, in both Brazil and Mexico.

Most of the major manufacturers of plasma protein therapies are located in the U.S. and the European Union (EU); and therefore, plasma collection and manufacture must be in compliance with either U.S. or EU regulatory requirements, as well as with the European Pharmacopoeia. Regulatory authorities outside these jurisdictions generally accept plasma protein therapies manufactured under the respective regulation of the importing company. However, at times, regulatory authorities in other countries may decide to implement regulations of their own in order to fulfill their mandates to protect public health in their countries. Although such decisions are made with the best intentions, the consequence may adversely affect patient access to plasma protein therapies, thereby endangering the lives and well-being of patients who rely on them.

Brazil

The Brazilian authority, Agéncia Nacional de Vigilancia Sanitária (ANVISA) recently implemented Resolution RDC No. 55, dated December 16, 2010, Section III, Production Documentation and Quality Control of Hemoderivatives, VI. These serological controls require testing of each donation of source plasma for *Treponema pallidum*, the causative agent of syphilis, and testing of finished product for HIV, Hepatitis C and Hepatitis B. Such divergent approaches from U.S. /EU manufacturing requirements would mean that manufacturers wanting to import plasma protein therapies into Brazil would need to segregate the starting material, the manufacturing process, or the testing procedures from mainstream operations. In addition to operational disruptions that might discourage the manufacture for Brazilian use, there are many valid arguments as to why testing of finished product, either by the nucleic acid amplification test (NAT) or with serological methods, is not appropriate. The strategy employed by manufacturers to ensure that the starting material, human plasma, is of the highest quality plus the dedicated manufacturing processes that include at least two virus inactivation/removal steps has proven for decades to be the most efficient approach for the production of safe and efficacious plasma protein therapies. In fact, the Brazilian approach would result in inadequate testing since available serological or NAT tests are neither intended nor validated for the purpose of finished product testing. It is also unnecessary to test for *T. pallidum* as part of the manufacturing process.

Upon review of the arguments brought forward by PPTA, with respect to syphilis and final product testing, ANVISA agreed with PPTA. However, the verdict is still out whether they will also revise their views pertaining to regulation RDC 55 of December 16, 2010 (Registration of Biological Products). Under this Regulation, ANVISA requires the submission of clinical data for renewal of an existing marketing authorization in Brazil, and in some cases, the studies that supported the approval in the original region (e.g. EU, U.S.) for the pursued indications are considered insufficient for Brazil. This would require manufacturers to perform clinical studies for Brazil for well-established products. Performing such studies would be a burden for not only the companies, but for the small patient populations of therapies for rare disorders, such as bleeding disorders, where there may not be enough patients available. In essence, manufacturers would not be able to provide therapies to Brazil. Recently, a meeting between ANVISA and the diplomatic representatives of several EU countries took place, but the outcome of these discussions is not yet determined.

Mexico

In Mexico, authorities recently introduced regulations for human plasma for fractionation, as stipulated in PROJECT PROY Standard NOM-257-SSA1-2013, Authorization of Medicines Registration, Renewal and Modifications, Section 5.7 Blood Products. PPTA participated in the consultation process with the intention of helping to establish a robust regulatory framework that does not include any provisions that would restrict importation, serves to ensure patient access to therapies and increases awareness of the safety and quality of plasma protein therapies.

Conclusion

These regulatory initiatives demonstrate that the world of plasma protein therapies is changing. As demand for therapies increases, so does the awareness of national competent authorities. It is understandable that these institutions do not want to rely entirely on EU and/or U.S. regulatory oversight.

Additionally, such as in the case of Brazil, there may be an element of nationalism in its policy making. Brazil has recently established two fractionation facilities.

However, it has to be kept in mind that manufacturing plasma protein therapies requires a very specific infrastructure that includes the procurement of suitable plasma for fractionation as the first step. Depending on a country's own plasma resources may appear noble, but the ability to provide patient access to therapies should be the primary goal.

ILKA VON HOEGEN, PH.D., *Senior Director Quality and Safety*

SHUTTERSTOCK

The Imperative for an International Awareness Event

INTERNATIONAL PLASMA AWARENESS WEEK is a joint effort of PPTA and its member companies. Some of our Source Industry Profile Committee members address the importance of this event.

GOALS

Raise global awareness about source plasma collection

Recognize the contributions of plasma donors to saving and improving lives

Increase understanding about lifesaving plasma protein therapies and rare diseases

MATTHIAS GESSNER, Ph.D., *Director Plasma Operations, Baxter BioLife Europe*

Plasma does not grow on trees; the global demand for plasma protein therapies continues to increase. Every day thousands of people around the world make a conscious and voluntary decision to donate plasma for others who depend on the lifesaving therapies manufactured from it. Despite its vital importance for so many patients, plasma donation by plasmapheresis is virtually unknown to many, which limits the potential of finding new plasma donors. International Plasma Awareness Week (IPAW) is one way to spread the word and let more people around the globe know about the importance of donating plasma.

Once informed about the value of plasma donation, the possibility for someone to become a plasma donor depends largely on the country of residence. Plasma is currently not collected in all countries worldwide, but to a very large extent in the U.S. where many persons become plasma donors. In contrast, in many countries around the world, plasma collection by plasmapheresis is not practiced at all, depriving many people of the opportunity to contribute to the global plasma supply. In Europe, for example, private sector plasmapheresis is performed mainly in three countries: Austria, the Czech Republic and Germany. Plasma collected in these countries not only serves to provide products to patients in these countries but also to other European and non-European countries, which do not have a system to collect sufficient volumes of plasma for their own needs.

Therefore, IPAW will raise awareness that many more—ideally all—countries in need of plasma therapies for their patients, ought to provide plasma for fractionation collected by plasmapheresis, to make these therapies available in sufficient quantities globally. Hopefully, IPAW will raise global awareness for this vital issue and will be successful to carry this message into the world!

DAN GAMACHE, *Director of Plasma Marketing Operations, Biotest Pharmaceuticals*

When I first joined the Industry Image Task Force (now the Source Image Profile Committee), our main goal was to help educate, market and encourage the general public to donate plasma. The notion of an

industry celebration, never mind an international one, seemed too enormous to tackle.

Flash forward a few years and we are launching the first ever global awareness week. A lot of effort and work has gone on behind the scenes to make this possible, but how exciting for our industry to see this idea bloom and come to fruition. Those fortunate enough to work in this industry are already aware of how plasma protein therapies save and improve lives, now we get to show our appreciation to those who deserve much respect and make it all possible—our plasma donors.

IPAW provides us with the opportunity to recognize and celebrate these individuals that donate the precious raw material that benefits patients worldwide. Where else can you walk into a facility and see so many devoted individuals committed to helping people who suffer from rare, life-threatening, chronic diseases and disorders? Since only a relatively small number of people are eligible to donate, the services these unique individuals provide are invaluable. Without them, we would not be able to produce the therapies required by so many. I have met some wonderful patients and they all have one thing in common—they love to personally express their gratitude for what we do, what our donors do and for giving them the opportunity to enjoy a full and fruitful life.

Just how do we thank the many thousands of donors that provide so much hope and promise to others? There is no precise answer. Some companies will choose to recognize and express this appreciation through a kind word; some may offer small tokens of appreciation while others may choose to go all out and celebrate with balloons, food, giveaways and special promotions. Whatever your choice, just make sure the message is clear and that it includes everyone—from donors to center employees and corporate staff. This is a time for our industry to be proud of what has been accomplished without losing sight of the very people who make it possible. However you choose to acknowledge and celebrate this special occasion, I do know this; it can never be enough. Just how do you truly thank individuals that help save lives every day by devoting their time and commitment to helping others?

IPAW is an opportunity we now have for one week a year. However, plasma donors world-wide deserve to be recognized and celebrated for their devotion and willingness to donate every day. So let me conclude by asking this, what do you do the other 51 weeks a year?

SCOTT NEWKIRK, *Director of Marketing, CSL Plasma*

CSL Plasma, in collaboration with PPTA and other source plasma collectors, is excited to promote IPAW throughout our facilities. As the Director of Marketing for CSL Plasma and Chairman of the PPTA Source Industry Profile Committee, I view IPAW as yet another opportunity to recognize our valued plasma donors and their role in helping to provide therapies for patients with rare and serious diseases.

Although most donors may never have the opportunity to meet a patient who receives a plasma protein therapy, CSL Plasma is using this week to promote greater understanding and appreciation among patients, employees and donors alike. In particular, during this week CSL Plasma staff will be thanking donors for their time and highlighting the impact their donations have on patients' lives. We are also holding various donor appreciation events in each of our collection centers and corporate locations.

IPAW creates a unique opportunity, one that will extend into the communities where our centers operate in both the U.S. and Germany. Events will focus on educating community and civic leaders to dispel common misperceptions about plasma donors and to highlight the economic impact, employment opportunities and other benefits a plasma center brings to the community.

CSL Plasma, which operates one of the largest plasma collection networks in the world, is committed to ensuring a continuous supply of plasma so that our parent company, CSL Behring, can continue to manufacture it's life-enhancing and lifesaving therapies.

Nothing puts IPAW in sharper perspective than the words of one whose life has been changed by a plasma protein therapy. According to Mona Nyman, a patient who is being treated for common variable immunodeficiency. Her life has taken on new meaning since she's been receiving the appropriate therapy for her condition.

"I feel like I can do so much more and only have all of the wonderful people who donate plasma to thank for that. I do regret all of the things that I cannot do now, due to the lung damage that I have, but again, I can do a whole lot more than I could several years ago, and I enjoy each day.

"I am one of 50,000 people with common variable immunodeficiency in the United States. My life is enriched because of plasma donations. I hope people will continue to donate plasma and encourage their families and friends to do so. I am alive, because of them. Thank you to all of the plasma centers, too. I am indebted to you, also. Most of all, thank you for my life."

BETH EACRET, *Vice President Plasma Operational Development, Grifols*

Grifols is one of the proud manufacturers responsible for the development, manufacturing and delivery of plasma protein therapies used in emergency medicine and to treat patients with rare diseases. With this privilege comes the opportunity to partner with organizations like PPTA, patient advocacy groups, healthcare providers, legislative bodies and the biotechnology industry to guarantee safe production practices and ensure adequate supply and access to therapies around the world.

We are thrilled to be a part of the first IPAW. Over our 70 year history, Grifols' commitment and dedication to the plasma industry, which includes our founders' development of the plasmapheresis technique in 1950, has led us to establish the world's largest plasma collection platform and highest plasma protein fractionation capacity. We are deeply invested in the industry and fully realize the importance of raising awareness about plasma donation to meet the increasing global demand for our therapies.

IPAW represents an opportunity for our industry to further educate and embrace our stakeholders. Engaged stakeholders understand the imperative to keep a steady supply of plasma moving between our plasma centers, testing labs and manufacturing floors to meet the daily needs of patients who rely upon our products.

Stakeholder engagement begins close to home

I am one of 50,000 people with common variable immunodeficiency in the United States. My life is enriched because of plasma donations. I hope people will continue to donate plasma and encourage their families and friends to do so. I am alive, because of them. Thank you to all of the plasma centers, too. I am indebted to you, also. Most of all, thank you for my life."

with committed donors, dedicated employees and satisfied patients. But it also spans well beyond to healthcare providers and legislators who advocate on the patient's behalf. It is our collective message and voice that serves people and grows our industry. International Plasma Awareness Week is paramount to this communication approach—it represents a time for our industry to come together, reinforce our message and drive our vision to reality.

Grifols is incorporating IPAW into a broader, global initiative to better connect key stakeholders with our company, employees and industry—an initiative that will permeate our entire company, including our 150 donor centers, field sales and scientific personnel, manufacturing and testing sites and corporate offices. It is our shared responsibility to create a positive perception of the donor community and to recognize that their contributions continue to ensure a steady and reliable supply of plasma to produce therapies impacting patient lives on a daily basis.

Our simple mission—when a donor sees plasma being extracted during a donation, he also envisions the smiling face of a patient on the receiving end. When an employee sees a bottle travel down the production line, she thinks of patient lives being impacted by her work. When a patient meets a donor, he sees a source of life.

Grifols thanks PPTA for its commitment to the plasma industry and we are privileged and honored to participate in IPAW.

STEPHAN WALSEMANN, M.D., *Managing Director, KEDPlasma*

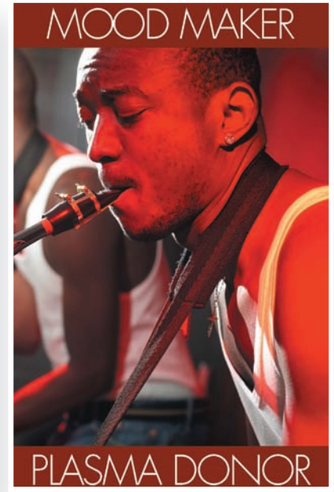
In October, IPAW will be celebrated for the first time. From a German, European and "KEDPlasma perspective", this is the first opportunity to raise awareness of our work. The need is: to remind ourselves how often we tell our relatives, friends, neighbors and acquaintances what our business is about.

During IPAW, alongside PPTA and international colleagues, we will stress the importance of plasma donors whose contributions provide the starting material for life-saving therapies. Our donors and our staff are proud of their contribution to the health of the patients suffering from rare diseases and who depend on plasma protein therapies. Mayors will be proud of having plasma centers and plasma donors, and the press will recognize and spread the knowledge of the importance of donors and their plasma.

In our plasma centers, we will celebrate and honor established donors, patient groups and local politicians. Every day of the week should be a special day for our donors and guests, because it's IPAW. The posters and banners that were developed by PPTA and a public relations campaign in advance of IPAW, shall ensure a good turnout at open houses, as well as, wide press coverage of the events. And we are looking forward to welcoming new donors, of course, not only during IPAW.

We are already looking beyond this first IPAW, which we believe will be a success and the start of a new tradition. Our mission is to draw public attention to our ethically, as well as, technically high standards that - though often not known in public - are among the highest in the health care industry, as proven by our excellent quality and safety recalls for all the years we have been working on the development of plasma protein therapies.

Let us celebrate our donors and all those working in our industry for the benefit of the patients.



RUDOLF E. MEIXNER, *CEO, Europlasma Group*

I fully support PPTA's initiative to proclaim the first IPAW in October 2013. We should not forget that the majority of healthy people, even in the countries with plasmapheresis infrastructures, are still not aware of the existence and importance of the plasma donation. So raising the awareness on a global basis is of paramount importance as blood plasma donations assure the availability of lifesaving plasma protein therapies. Together with PPTA, the Austrian IG Plasma will sponsor an event in Vienna on Oct 17. The marketing activities of all our plasma centers will focus on the messages of IPAW with the clear goal to encourage as many people as possible to become plasma donors.

MICHAEL SZKUTTA, *Head Corporate Quality Management Plasma, Octapharma*

For patients who are dependent from plasma derived medicinal products, IPAW will help them to get their deficiencies known or better known in the population. This knowledge will hopefully inspire new donors who are one important piece in the pharmaceutical industry supply chain.

To maintain an adequate supply of plasma derived medicinal products it is important for the industry to get enough plasma. IPAW will also support the global plasma supply by making the whole topic visible to a broader "audience".

The foundation philosophy of Octapharma is our patient-oriented approach. Our goal is to expand products and indications so we can optimally utilize every litre of our precious plasma raw material, with the strategic aim of increasing plasma availability and throughput and increasing our product portfolio to access the global market. The philosophy of Octapharma is that we have a responsibility for transparent and open communication with all our stakeholders. In this context, the IPAW provides a good opportunity to support the company's long-time strategic goals and philosophy.

DAVID MORAD, *President, Southern Blood Services, Inc.*

International Plasma Week is an important recognition of the uniqueness of Plasma Protein Therapies and the critical role they play in our healthcare system today. From our Anti-D donors who donate their plasma for Rho (D) Immune Globulin to our rare antibody donors who donate to insure the safety of blood transfusions, Plasma Therapies are lifesaving therapies for people on a daily basis. We celebrate our donors during this very special week.

New Trade Partnership Agreement Holds Promise for Industry

BY JOSHUA PENROD

EARLIER THIS YEAR, leaders from the European Union (EU) and the United States (U.S.) announced a program for a new trade partnership, called the "Trans-Atlantic Trade and Investment Partnership" (TTIP). In the middle of June, EU Member States authorized the European Commission to begin negotiations, which was the last step needed prior to actual commencement of the agenda.

Trade flows between the two continents are not new, neither are political and cultural exchanges nor alliances. The negotiations for TTIP will be a long and detailed process, but it promises to be the single most important strategic trade initiative for both the U.S. and EU in decades. Most importantly for plasma fractionators, collectors and patient groups, opportunities exist for the global plasma industry to help shape the agenda.

A U.S. / EU market alliance will be a true economic juggernaut. The EU's combined economic power is currently the largest in the world, in excess of $16.5 trillion (2012). The total economic footprint of the U.S. was $15.7 trillion in 2012. While recently Asia, particularly China, has been a focal point of global trade, growing political and economic factors have created a push to re-examine the trade dynamic in the North Atlantic. European policymakers stated that the conclusion of the TTIP will be the largest bilateral trade agreement in history.

Truly, the scale and coverage of the TTIP negotiations is impressive, and includes several areas that will be important to the plasma fractionation and collection industries. The general thrust of the agreement is to expand upon ongoing trade trends of the past several decades, which include minimizing tariffs and non-tariff trade barriers, increasing regulatory harmonization, expanding market access and protecting intellectual property. Other important features of the TTIP will include labor and environmental agreements, harmonized anticorruption practices, which include shared investigations, competition policies and dispute resolution.

Industry will benefit in particular through regulatory harmonization, rationalization of sanitary/ phytosanitary standards (SPS) and technical barriers to trade (TBT) restrictions and greater market access.

Regulatory Harmonization

Regulatory harmonization has been a long-term goal for the industry. One of the roadblocks to its achievement has been conceptual disagreement among stakeholders and policymakers alike regarding the level of harmonization that is necessary or even achievable. The struggle has been for FDA and EMA, as well as national authorities, to agree on mutually accepted inspections. The TTIP calls for increased "compatibility" of regulations by creating more uniform procedures for drafting and executing regulatory obligations. Experts in the medical device industry anticipate this will create a beneficial environment for single audits or inspections by authorities and, therefore, mutual recognition of requirements and standards. Development of common licensure and marketing requirements is also a possibility for greater agreement.

Rationalization of SPS and TBT Restrictions

SPS and TBT remain significant barriers to trade rules that ordinarily contemplate free exchanges of goods and services. While sometimes the SPS and TBT measures are based on measurable health or environmental impact, they are often used as pretexts for protection of a domestic industry and are not truly related to health or safety. The most common relevant occurrence for the global plasma industry takes the form of prohibitions on compensated donation and self-sufficiency polices. Major obstacles exist for agreement on SPS/TBT elimination or reduction, which include considerations of risk and impact based on agreed scientific measures. Such considerations will also be important for inclusion in any debate relating to other areas of trade, including regulatory harmonization.

Market Access

The past two decades have seen integration of markets among the EU countries. However, the EU system of governance creates much autonomy for its Member States. For example, the European Blood Directive is implemented in diverse ways among different countries. Therefore, open access to markets in certain countries has been impeded. By increasing the expectations accorded to process transparency, including decisions on allowance of products into markets, the industry could be beneficially impacted by changes in certain policies. Changes in policies relating to self-sufficiency and prohibitions on donor compensation would most directly affect the plasma industry. Through consistent policy and increased transparency for these issues, industry will be well-positioned to scientifically demonstrate the importance of compensated donation in achieving self-sufficiency.

Conclusion

Given the difficulties that the EU and U.S. have sometimes experienced in reconciling trade imbalances with Asian economies, it is perhaps not surprising that the Atlantic trade flow has garnered a second look. It is not clear what the TTIP will mean overall, or how much of a difference it will really make for the participants. Some benefits and risks are likely to be minimal at the conclusion of a long negotiating process; it may be driven largely by consensus and compromise. However, the TTIP could, at the least, have a beneficial effect on ongoing efforts to open barriers to trade with Asia, where countries could lift trade restrictions if they fear new or more competition. Whatever the results may be, the opportunity exists for the global plasma industry to play an important role in helping shape the systems that deliver high-quality medicines to patients.

JOSHUA PENROD, *Vice President, Source*

Inside the Orphan Drug Act

An Interview with Stephen C. Groft

BY MARY CLARE KIMBER

Steve Groft, Pharm.D., has served as Director of the National Institutes of Health (NIH) Office of Rare Diseases Research (ORDR) since its establishment in 1993.

During this year's celebration of the 30th anniversary of the passage of the Orphan Drug Act (ODA), the Food and Drug Administration's (FDA) Office of Orphan Products Development (OOPD) honored the NIH Office of Rare Diseases Research (ORDR) as "One of Many Rare Disease Heroes." Tell us about NIH/ORDR.
ORDR was established with the goals of stimulating and coordinating research on rare diseases. Today, ORDR supports research as part of the National Center for Advancing Translational Services (NCATS) and responds to the needs of the global rare disease community by leveraging NIH resources and fostering collaboration across the NIH Institutes and Centers, among academic and industry stakeholders and with national and international patient advocacy groups. ORDR and the National Human Genome Research Institute support the Genetic and Rare Diseases Information Center. NIH collaborates with FDA on several rare disease areas, including adaptive clinical study design, meetings regarding potential products, translational research and identification of appropriate clinical endpoints.

Tell us about some of NIH/ORDR's current programs/activities.
NIH supported approximately 9400 research projects on rare diseases and approximately 1650 research projects on orphan drugs as is reported in the Research, Condition, Disease Categorization for Rare Diseases and Orphan Drugs Fiscal Year 2011. ORDR's Rare Diseases Clinical Research Network (RDCRN) consists of 17 consortia at 225 institutions worldwide. Within the RDCRN, studies of more than 200 diseases are underway with 86 active protocols and more than 85 patient advocacy groups are participating. ORDR's Scientific Conferences Program identifies research opportunities and assists in establishing research agendas (1200 conferences). Other ORDR programs include the Clinical Center Hospital Bedside to Bench Research Program and the Middle School Curriculum Module on Rare Diseases and Scientific Inquiry. Other ORDR activities include the expansion of the NIH Undiagnosed Diseases Program, the WHO International Classification (ICD 11) as part of Orphanet, the International Rare Diseases Research Consortium (IRDIRC) and several patient registries.

Tell us about NIH/ORDR's involvement in patient registries and why they are important.
NIH has established the web-based Global Rare Diseases Patient Registry and Data Repository (GRD-PRDR). ORDR currently is developing a web-based searchable registry of biospecimen repositories. Registries benefit all stakeholders—patients and foundations, researchers and academia, government and industry. Registries provide industry, in particular, with the ability to link proprietary information to a shared patient record and to share de-identified pan-disease patient information, as well as information with patients based on a specific profile. Registries also provide industry with multi-lingual capabilities to collect international patient data.

What was the most important provision of the ODA at the time of its passage? Today?
When the ODA was signed into law by President Reagan on January 4, 1983, the protocol and study design assistance provision of the ODA in the drug development process was thought to be the most important provision for orphan drug developers. Thirty years of experience with the ODA have taught us that the seven year marketing exclusivity to the first sponsor obtaining FDA approval of a designated drug is, in fact, the most important provision; followed closely by the tax credit equal to 50% of clinical investigation expenses. Another important orphan drug incentive for manufacturers is orphan products grant funding.

Please highlight amendments to the ODA and other legislation/programs that have built on the Act since its passage.
The ODA has been amended to possibly receive a waiver from the user fees charged under the Prescription Drug User Fee Act (PDUFA), which was passed in 1992 to allow FDA to collect fees from manufacturers to fund the drug approval process. PDUFA has been reauthorized every five years since 1992. In Fiscal Year 2013, the user fee was approximately $1.9M per application. This fee would otherwise be paid to FDA. The Food and Drug Administration Modernization Act of 1997, the Food and Drug Administration Amendments Act of 2007 and the Food and Drug Administration Safety and Innovation Act of 2012 also have amended the ODA. Programs that have built on the ODA since its passage include the CDER Rare Disease Program and the EU/EMA/Committee for Orphan Medicinal Products—US/FDA/OOPD Agreement on Orphan Product Designation Request Data Elements.

PPTA has recognized this year's 30th anniversary celebration of the passage of the ODA. What should manufacturers of plasma protein therapies and the patients who rely on them celebrate most about the legislation and about the future of orphan drug development?
The future of orphan drug development is bright. Due to increased public and media interest over the last 30 years, public recognition that rare diseases represent a global public health issue is growing. At the same time, federal, national and international interest and support—including public-private partnerships—are expanding. The development of more directed research agendas are leading to interventions and diagnostics, as well as increased scientific opportunities. The number of research investigators experienced in rare disease multi-center and international clinical trials is increasing; with expanded roles of patient advocacy groups, improved patient recruitment is possible. Industry has also shown increased interest in developing orphan drugs. For manufacturers, opportunities to repurpose approved and investigational products are particularly valuable. Where there once was reluctance, there now is interest, especially with the growing availability of information from patient registries and natural history studies. NCATS has considered 57 different products for possible repurposing.

The future of orphan drug development is bright. Due to increased public and media interest over the last 30 years, public recognition that rare diseases represent a global public health issue is growing. At the same time, federal, national and international interest and support—including public-private partnerships—are expanding.

MARY CLARE KIMBER, *Manager Regulatory Policy*

European Union Considers Revisions to Blood Directive

by Laura Savini and Alberto Giummarra

More than ten years after its implementation, the "Blood Directive" may be revised. This article explores the potential impact on the plasma protein therapies industry.

IN EUROPE, the processing, storage, testing, distribution and manufacturing of plasma for fractionation is regulated by the Directive 2001/83/EC governing medicinal products for human use. However, the quality and safety for the collection and testing of plasma for fractionation is regulated by Directive 2002/98/ EC also known as the "Blood Directive", which is currently under review.

The Blood Directive, as known today, was created in 2002 and, at the time, this was a significant development. Traditionally European legislation had dealt more with matters such as the creation of a common economic area or the assurance of similar democratic rights for citizens across Europe. Healthcare had always been considered a Member State competency, so with this legislation and with Directive 2001/83, the Europaen Union (EU) had taken a step towards the regulation of healthcare matters.

A Directive is a legislative act that is prepared by the European Commission (EC), typically after consultation with national experts and stakeholders, and then presented to the European Parliament and the European Council, which may approve, amend or reject the legislation. EU directives lay down mandates that must be achieved by every Member State. National authorities have to adapt their laws to meet these mandates, but are free to decide how to do so. When intended for harmonization, Directives are used to bring different national laws into line with each other.[1] In the case of the Blood Directive, the objective is to ensure that patients across Europe have access to blood and blood components with a consistent level of safety and quality.

However, Directives give Member States certain freedoms on how to interpret particular aspects of the legislation. An example of these freedoms is demonstrated in differences among Member States involving donor compensation practices. Donor compensation may range from remunerated time off work to small financial compensation for a donor's time and inconvenience.

In 2012, PPTA was informed that the EC was starting an inquiry into the availability of blood, blood components and plasma derivatives to European patients. The intent was to provide the EC with enough information to evaluate whether the Directive would need to be revised or not. Typically European legislation is revised on average every 10 years to reflect technical, societal and economic changes in the EU. Furthermore, since 2002, 15 additional Member States have joined the EU, meaning that the revision of the Blood Directive will also need to take into account their needs.

The EC outsourced the inquiry to an external consultant and PPTA Europe has been involved throughout the process by providing responses to various questionnaires and valuable data and information for the study. In particular, the European Health Policy Steering Committee (HPSC) has played a key role in providing information for the preparation of a report to the EC. At this time, several points have been identified as important and considerations include: the differentiation between blood for transfusion and plasma for fractionation, donor compensation, self-sufficiency, freedom of choice and EU market for plasma protein therapies. A report from the consultant was received in late August. Following its publication, PPTA has planned a series of outreach meetings to key Brussels-based stakeholders to discuss the outcomes and to gather intelligence on other stakeholders' positions.

Finally, another development that may have a significant impact on the revision of the 'Blood Directive' is the legal action taken by Octapharma against the French State earlier in 2012. This case is founded on the fact that the French National Safety Agency for Medicines and Health Products (ANSM[2]) included in its labile products list blood products containing 'freshly-frozen, leukocyte-depleted, solvent/detergent-treated virus-deactivated plasma'. Octapharma is contesting this decision and referred to the fact that according to the European legislation on medicinal products[3], *labile products prepared with a method involving an industrial process are considered medicinal products* and not labile products. Based on this interpretation of the legislation, Octapharma also stated that the ANSM had no right to require additional permissions to put these products on the market. The French Conseil d'Etat (Council of State[4]) was asked for legal advice on this case and it addressed two questions to the European Court of Justice (ECJ). The first question regards whether two pieces of legislation regulating one product[5] can be both applied or whether only the legislation on medicinal products should be applied when it is stricter than the other legislation. If the Court decides that the medicinal products' legislation takes precedence, then the Blood Directive would not apply any longer to plasma prepared by an industrial method and intended for transfusion. The question would then be whether this would also be the case for plasma for fractionation. The second question regards certain provisions in the Blood Directive[6] and the EU Treaty[7], which allow Member States to maintain stricter rules regarding the quality and safety of blood and blood components. The question is whether these provisions would apply to plasma prepared with an industrial process and, if so, whether these provisions take precedence over Directive 2001/83, including its requirement for pre-market authorization of the product. If the court decides that this is not justified, then Member States would not be able to impose stricter rules than existing EU legislation, which could have an impact not only on the marketing of these products, but also for example on matters such as donor compensation.

In the case of the Blood Directive, the objective is to ensure that patients across Europe have access to blood and blood components with a consistent level of safety and quality.

The EC is following the case and it is expected that it will take it into account while revising the blood legislation. PPTA has long advocated for the EC to improve the European market for plasma protein therapies and the Association will follow closely the response of the ECJ which will conclude the matter.

Laura Savini, *National Affairs Manager and*
Alberto Giummarra, *Junior Manager, Health Policy*

1 http://ec.europa.eu/eu_law/introduction/what_directive_en.htm

2 Agence Nationale de Sécurité du Médicaments et des produits de santé. The ANSM is responsible for publishing technical requirements for labile blood preparations and hemovigilance.

3 See article 3 of Directive 2001/83 on the Community Code relating to Medicinal Products for Human Use, as amended by Directive 2004/27

4 The Conséil d'Etat is a body of the French government that provides legal advice on the preparation of legislation.

5 In this case the Blood Directive and the Community Code relating to Medicinal products for Human Use for whole blood which is prepared by a method involving an industrial process and which is intended for transfusion

6 Directive 2002/98/, article 4(2)

7 Treaty on the Functioning of the European Union, article 168.

U.S. HEREDITARY ANGIODEMA ASSOCATION JOINS PPTA STAKEHOLDER GROUP

An Interview with Janet Long, Executive Vice President

BY JULIE BIRKOFER

PPTA WORKS WITH MANY TALENTED REPRESENTATIVES from the leading patient organizations that represent individuals who use plasma protein therapies. Over the years, we have successfully collaborated on significant issues at the federal and state level that enhance patient access to these life-saving therapies. Working together has yielded positive outcomes including: mitigating reimbursement reductions, avoiding restrictions on access to plasma protein therapies and expanding access in sites of service.

Earlier this year, the U.S. Hereditary Angioedema Association (HAEA) began participating in the PPTA Stakeholder group. HAEA is a vibrant organization and we are pleased to be working with them. HAEA's tagline on their website best captures their spirit: "Research, Advocacy, Compassion, Empowerment". This conveys a powerful message that resonates with all of us.


Janet Long

Tell us about your personal experience with HAE?
First, for anyone unfamiliar with Hereditary Angioedema (HAE), it is a very rare and potentially life-threatening genetic condition that occurs in about 1 in 10,000 to 1 in 50,000 people. HAE symptoms include episodes of edema (swelling) in various body parts including the hands, feet, face and airway. Patients also often have bouts of excruciating abdominal pain, nausea and vomiting that is caused by swelling in the intestinal wall. Airway swelling is especially dangerous and can lead to death by asphyxiation.

I am often asked if I can think back to my first HAE attack. I can remember at age seven having severe stomach pain that no one could quite get a handle on, but it was eventually named "growing pains" and I learned to live with it, as I was instructed to by my doctor. During puberty, the abdominal attacks became much more debilitating and I missed days of school. At 22, I ended up in the intensive care unit (ICU) from an abdominal attack that caused internal bleeding. I was forced to change my plans for graduate study.

After marriage, I toughed it out when I had an attack. My husband rarely knew I was sick because I hid it. I did not want to be defined by my illness. I was blessed with three daughters—and as is typical for women with HAE, each pregnancy was a gamble as to whether I would feel better or worse while pregnant. Of my three girls, my middle one, inherited HAE from me.

Finally, after 40 years, and at the point of death because my frequent abdominal attacks morphed into frequent life-threatening airway swellings, a doctor connected the many dots of my medical history and provided the diagnosis I had been searching for- Hereditary Angioedema. This 40 year gap in diagnosis is what motivated me to join the HAEA—to make sure no one else had to suffer so much for so long.

Today, I am fortunate to live in a new era for HAE with four FDA-approved therapies available to me, a knowledgeable physician and an amazing patient advocacy organization—all leading toward an ever better future.

Founded in 1999, the HAEA is led and run by HAE patients. The organization's fundamental mission centers on helping patients with HAE achieve lifelong health by providing unbiased information and highly personalized patient services.

For those unfamiliar with the U.S. Hereditary Angiodema Association (HAEA), please describe the organization, its mission and your background and role with the organization.
HAEA is a growing organization of more than 4400 patients that leads a nationwide advocacy movement focused on:

- increasing HAE awareness and education
- empowering patient access to optimal therapy
- establishing a presence in the health policy legislative and regulatory environments and
- fostering clinical and translational research that includes searching for a cure

Founded in 1999, the HAEA is led and run by HAE patients. The organization's fundamental mission centers on helping patients with HAE achieve lifelong health by providing unbiased information and highly personalized patient services.

The HAEA is governed by a proactive board of directors and, since its inception, has worked closely with expert allergy/immunology physician-researchers, many of whom also serve on the HAEA Medical Advisory Board. The HAEA has been a powerful force in driving programs, activities and research that improve patients' quality of life.

As Executive Vice President, I am responsible for day-to-day operations, managing electronic communication channels, developing educational materials and organizing all patient and medical advisory board meetings for the Association. I also serve as a liaison with all HAE stakeholders.

What are the HAEA's key priorities this year?
The major priorities include the opening of the U.S. HAEA Angioedema Center at University of California, San Diego (UCSD); to provide state-of-the-art patient care, groundbreaking research, clinical trials and national and international educational opportunities for healthcare professionals. Also, we are planning a National Patient Summit; an interactive event in which patients and family members can make a difference for their future right at the meeting and work toward an international scientific HAE meeting; in collaboration with the National Institutes of Health (NIH) and the Office of Rare Diseases Research (ORDR).

Tell us about your chief public policy goals?

- To raise awareness of HAE on a federal level
- To have a voice on Capitol Hill in all legislative issues that impact the lives of HAE patients
- To participate in federal agency programs (such as the FDA's Patient-Focused Drug Development program)
- To state our case through an annual Capitol Hill Day with personal visits to Congressional leaders.

What is the greatest challenge your organization faces?
The HAE landscape continues to be a quickly evolving one, which can make staying relevant and keeping ahead of the curve a challenge. We constantly reinvent ourselves to be the very best we can be; providing the most unbiased source of angioedema information available and the most comprehensive patient services possible.

Please share any final thoughts about your work and the Association's mission.
Our mission is simple—to help patients achieve lifelong health. All of our efforts circle around this goal. Each of the HAEA staff understands deeply and fully what it means to live with HAE—we are here for our fellow patients and their families. It is not work, it is our passion.

JULIE BIRKOFER, *Senior Vice President North America*

QUALITY STANDARDS OF EXCELLENCE, ASSURANCE & LEADERSHIP

QSEAL STANDARDS REVISIONS DEMONSTRATE INDUSTRY LEADERSHIP

BY SONIA BALBONI

THIS SUMMER, the Association completed its update of the Quality Standards for Excellence in Manufacturing (QSEAL). The existing standards were revised, and two new documents were adopted. The changes introduce new requirements for manufacturers and address the changes in an increasingly diverse and global industry. Undoubtedly, the new requirements bring value to the industry; however, what lies behind them is of greater importance. The standards demonstrate a commitment from the leaders in plasma protein therapy manufacturing to stand for no less than the highest possible levels of quality and safety and to inspire others in the industry to follow.

The fact that PPTA's standards programs are voluntary and that Global Member companies choose to follow them is significant[1]. The revised documents are the most visible sign of the achievement, but the continued commitment of the QSEAL Standards Committee as a body devoted to ensuring that the standards program is robust and relevant, is even more valuable.

> "The Committee is composed of technical experts and leaders from the industry who have conferred and, as a group, agreed on what the industry can deliver, and have indicated what users can expect from industry, in responsible and state-of-the-art practices. The QSEAL standards challenge companies to live up to these expectations."
> —Karen Etchberger, CSL Behring, *Chair, QSEAL Standards Committee*

The standards stem from insight and leadership among manufacturers that industry should be the first to stand up and demand better, safer and responsible manufacturing processes. The QSEAL Standards Committee provides a forum for industry to collectively, through a transparent and established process, agree on conditions that allow manufacturers with diverse practices to produce therapies that meet equivalent levels of safety and quality. When the Global Board of Directors established the Committee, it understood that government can effectively enforce compliance and that companies ultimately benefit from stakeholders' vigilance. However, the Board also recognized that the technical and operational experts within companies, who implement practices on a daily basis, are best positioned to take notice and act effectively when an issue requires attention.

The Committee was established in 2010 with the following mission: "The Standards Program will be transparent, credible, innovative and responsive to stakeholder and industry needs."

In its first year of operation, the Committee agreed on the importance of upholding these tenets without deviation. As a first step, the Committee felt the entirety of the standards program should be reviewed and revised as needed to address changes in manufacturing practices that have occurred since the standards were originally implemented in 2000.

Participants quickly recognized that a key facet of manufacturing today is the use of plasma from multiple origins. The Committee agreed that while source plasma today predominates in the makeup of today's fractionation pools, recovered plasma plays a significant role in pool composition. With this in mind, the Committee developed the Controls on Incoming Plasma Standard, a document that recognizes the importance of placing *controls* on incoming plasma, regardless of its source. The requirements in this standard are simple but consequential: simply put, they require the manufacturer to place controls on incoming plasma, regardless of its source.

In line with developing the Controls on Incoming Plasma standard, the members renewed their commitment towards uniform acceptance criteria for recovered plasma. In short time, they reached consensus on the Recovered Plasma Specification, laying down mutually-agreed conditions for manufacturers that include plasma originating from whole blood donations. Furthermore, the members made sure that the revisions to the existing QSEAL standards (e.g., NAT Testing) included requirements that addressed recovered plasma.

The Committee also undertook a comprehensive review of the other standards and agreed on further noteworthy changes to the QSEAL program. These include lowering the Parvovirus B19 in-process requirement (from not to exceed 10^5 IU/mL to not to exceed 10^4 IU/mL in the manufacturing pool), mandating in-process Hepatitis A Virus (HAV) NAT testing and streamlining the event notification process for intermediates. Before publication, the proposed revisions underwent a two-month public comment period and were also reviewed by the Global Board of Directors.

The Committee has finished its review of the standards, but its work has only just begun. The group meets on a regular basis and continues to discuss enhancements to the standards program. Also, because processes change over time, the current requirements will be reviewed periodically to determine whether further revisions are warranted. By continuing to establish and enhance performance benchmarks, the QSEAL program will serve as one of industry's most viable tools for upholding the principles of quality and leadership in the manufacture of plasma protein products for therapeutic use.

SONIA BALBONI, *Manager, Source and Standards*

1 The following companies hold QSEAL certification: Baxter Bioscience, Biotest, CSL Behring, Grifols and Kedrion.

COMMITTEE SPOTLIGHT

BY BILL SPEIR

STATE AFFAIRS STEERING COMMITTEE

The State Affairs Steering Committee (SASC) provides a united advocacy voice for the industry with state decision-makers. The three goals of the Committee are to protect patient access to plasma protein therapies in state funded health programs including Medicaid; assist patients with their advocacy efforts; and advocate for industry interests with state regulators and decision-makers.

SASC includes very talented state affairs professionals from the member companies. The successes of the SASC efforts are a direct result of the dedication of these professionals to provide the Association with access to their talents. In recent years, results achieved by the SASC include:

Alabama

Alabama Medicaid implemented an emergency rule to limit Medicaid recipients to one brand pharmaceutical per month. It also put out a proposed rule for comment that would make the emergency rule permanent. Advocacy efforts of the SASC included phone calls and letters that pointed out the importance of providing Medicaid recipients access to their medically appropriate plasma protein therapies and that the policy was contrary to the National Hemophilia Foundation's Medical and Scientific Advisory Council (MASAC) recommendations, which would likely increase costs for other Medicaid services, and would not benefit the Medicaid recipients. Alabama Medicaid decided not to continue the one-brand limit.

California

SASC supported the efforts of the Hemophilia Council of California to pass AB 389, the Standards of Service for Providers of Blood Clotting Products for Home Use Act. This bill passed and went into effect on January 1, 2013 and established standards for the safe and timely delivery of blood clotting products.

Florida

SCID Funding. SASC was instrumental in achieving funding for Severe Combined Immunodeficiency Disease (SCID) testing in Florida. The Governor of Florida had vetoed the funding in 2011. PPTA staff met with the Florida Governor's staff to advocate for the funding and to discover what the Governor's objections were to the funding, as well as, answer any questions they may have. PPTA staff provided answers to the Governor's objections and questions. The funding was part of the 2012 budget signed by the Governor.

Blood Establishments. Florida Chapter Law 2012-37 (FL SB 364) was passed by the Florida Legislature in March of 2012 and signed by Governor Scott in April. This law requires blood establishments that collect blood or blood components in Florida to disclose information about the collection and distribution process; the volume of collections, purchases and distributions; certain financial statements and corporate ethical policies on the establishment's Internet site. A blood establishment that fails to comply with these disclosures is subject to a civil penalty. The efforts of SASC led to plasma collection centers being exempt from this law.

STATE AFFAIRS STEERING COMMITTEE

Melissa Bowie
Michael Bradley
LaTatia Colbert-Reed
Rya Faden
Vlasta Hakes
Karla White
Bill Speir, PPTA Staff Liaison

Kentucky

Kentucky Medicaid proposed a rule that appeared to require Medicaid recipients to receive their blood clotting factor from a 340B Hemophilia Treatment Center (HTC). SASC, working with patient groups, responded to the rule and requested that the proposed rule be amended to ensure Medicaid recipients' access to the provider of their choice. Based on SASC's recommendation in a letter, Kentucky Medicaid amended their proposed rule to state, "A recipient shall have freedom of choice of provider." This is a clear victory for patient access.

North Carolina

The North Carolina Senate's Appropriations Act for 2010 (SB 897) included a proviso that would require the creation of a specialty drug provider network for hemophilia, hepatitis C, and intravenous immunoglobulin (IVIG) drugs. SASC and the patient organizations, through successful advocacy efforts, were able to persuade the North Carolina General Assembly to change the language during conference.

West Virginia

SASC demonstrated to the West Virginia Office of Pharmacy Services that the West Virginia Medicaid program was inappropriately reimbursing alpha-1 proteinase inhibitors at the generic rate of (average wholesale price) AWP-30 % instead of the brand rate of AWP -15 %. West Virginia changed their reimbursement policies as a result of SASC efforts.

MEET THE PPTA

STAFF

ALBERTO GIUMMARRA

Junior Manager, Health Policy

How long have you served at PPTA?
I have been at PPTA since January 2012.

What do you focus on in your role as Junior Manager, Health Policy?
As Junior Manager, Health Policy, my main task is to represent PPTA's interests before European Union (EU) institutions. My responsibilities include: coordinating the Health Policy Steering Committee's (HPSC) activities at the EU level; organizing outreach meetings with members of the EU Parliament and representatives of national permanent representations. Currently, I am engaged in the coordination of the industry responses to the EU sectoral study on blood and blood components. In addition, I am involved in the development of the PPTA long-term strategy for the revision of the EU Blood Directive. In particular, I am responsible for developing possible future scenarios and analyzing the legal impact that the revision could have on the availability of and patient access to plasma protein therapies in Europe.

Tell us about your background.
Despite my Sicilian origins, I was born in Bari, Puglia. However, after just one year I moved back to Sicily. When I was 18 years old, I moved to Rome to study law. Following my graduation, I lived in London and in Strasbourg, where I worked for the Council of Europe. Living in each of these cities gave me the opportunity to develop fluent English and French, which I was then able to use at the College of Europe in Bruges, where I obtained my LL.M. in EU law. In Brussels, I worked for another trade association representing pharmaceutical industries in the biotechnological sector before joining PPTA.

What is your proudest professional achievement?
That has to be the success of the Patient Access Toolkit project for Europe. The Patient Access Toolkit was one of the three PPTA Europe priorities for 2012 and I remember feeling particularly stressed about the development of the project. At that time, I had been working for PPTA for three months and this was a nine-month project with a large number of documents to review and select. In parallel to this, I was preparing for the Italian Bar Exam, which I passed with flying colors last September. In the end, I was happy to see that the Patient Access Toolkit was a success and is available on the PPTA global website.

What is most rewarding about working in this industry?
Contributing to improving the quality of life of patients around the world.

GLOSSARY OF TERMS

ANVISA	Agencia Nacional de Vigiláncia Sanitaria
CFC	Clotting Factor Concentrate
FDASIA	Food and Drug Administration Safety and Innovation Act
HAE	Hereditary Angiodema
HAEA	U.S. Hereditary Angiodema Association
HPSC	Health Policy Steering Committee
IPOPI	Association of National Patient Organisations
LATAM	Latin America
NAT	Nucleic Acid Test
NCATS	National Center for Advancing Translational Services
NIH	National Institutes of Health
NMO	National Member Organization
ODA	Orphan Drug Act
ORDR	Office of Rare Diseases Research
PDUFA	Prescription Drug User Fee Act
PID	Primary Immunodeficiency Disease
PWH	Person with Hemophilia
RDCRN	Rare Diseases Clinical Research Network
SASC	State Affairs Steering Committee
TTIP	Trans-Atlantic Trade and Investment Partnership
TBT	Technical Barriers to Trade
QSEAL	Quality Standards of Excellence, Assurance and Leadership
WFH	World Federation of Hemophilia
WHO	World Health Organization

EVENTS UPCOMING CONFERENCES & SYMPOSIUMS

Patagonia, Chile

2013

September 24—27	46th Annual Meeting of the German Society for Transfusion Medicine and Immuno-Haematology *Münster, Germany*
September 26—27	World Federation of Hemophilia Global Forum on the safety and supply of treatment products for bleeding disorders *Montreal, Canada*
October 3—5	National Hemophilia Federation Annual Meeting *Anaheim, California*
October 3—5	9th Annual Conference of South Asian Association of Transfusion Medicine *Delhi, India*
October 4—6	European Haemophilia Consortium Conference *Bucharest, Romania*
October 12—15	AABB Annual Meeting *Denver, CO, USA*
October 12—13	9th Annual Symposium on Primary Immunodeficiency Diseases *Newport Beach, CA, USA*
October 13	PPTA Business Forum *Denver, Colorado*
October 13—20	International Plasma Awareness Week
October 17—19	Latin American Society for Immunodeficiencies (LASID) 3rd Meeting *Santiago, Chile*
October 20—23	Haematology Society of Australia and New Zealand 2013 *Broadbeach, Australia*
October 26—27	NACLIS VI International Conference for Primary Immune Deficiency Disease *Kuala Lumpur, Malaysia*
November 7-8	1st International Primary Immunodeficiencies Congress *Estoril, Portugal*
December 1—4	24th Regional Congress of the ISBT *Kuala Lumpur, Malaysia*
December 7—10	American Society of Haematology Annual Meeting *New Orleans, Louisiana*

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