

THE SOURCE

MAGAZINE OF THE PLASMA PROTEIN THERAPEUTICS INDUSTRY

SUMMER 2014

Patient Centeredness

The Important Role of the Schleussner Family in Developing Biotest into a Global Company

Ensuring the Efficacy of Therapies for Rare Disorders
'FIRST-DO NO HARM'

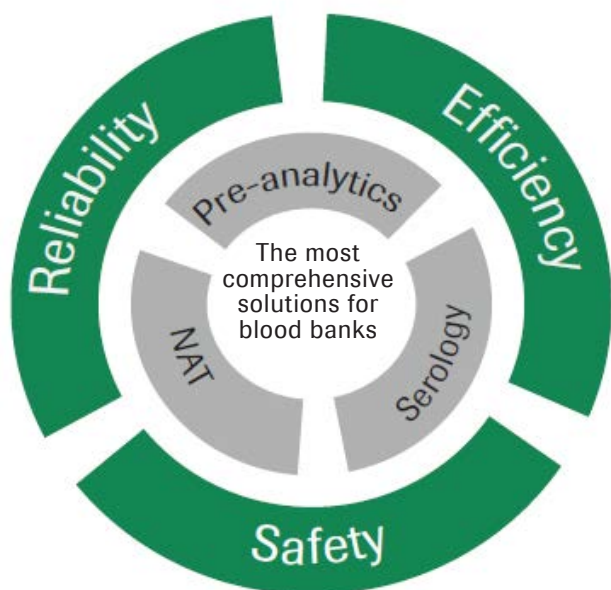
PPTA's Data Program:
A Valuable New Shortage-Preparedness Tool in Europe





Roche Blood Safety Solutions

Count on us, because patients are counting on you.



Providing Total Workflow Solutions that Raise the Standards of Performance

Safety: State-of-the-art assay sensitivity and genotype coverage allow reliable detection at the earliest stage of infection.

Reliability: With the highest reliability on the market, our ingenious technologies maintain workflow, minimize user interactions, prevent cross contamination and provide full sample traceability.

Efficiency: High assay specificity coupled with innovative multi-dye technology reduce the need for retesting, while short turn-around times, automation and uninterrupted workflow generate time savings and free staff for other tasks.

For more information, contact your local Roche Diagnostics representative.

COBAS and LIFE NEEDS ANSWERS are trademarks of Roche.
©2014 Roche Molecular Systems, Inc. All rights reserved.
www.roche.com

*The serology product range is not available for blood screening settings in Angola, Argentina, Bahamas, Bangladesh, Canada, Guyana, Iraq, Korea D.R., Latvia, Lesotho, Lithuania, Malaysia, Philippines, South Korea, Uganda, and the United States. For all other countries, please contact your local Roche representative to check availability.



GLOBAL BOARD OF DIRECTORS

Baxter BioScience | Ronald Lloyd
Biotest Pharmaceuticals | Gregor Schulz
CSL Behring | Karen Etchberger
Grifols USA | David Bell
Kedrion SpA | Paolo Marcucci, Chair
General Counsel | Paul Rosenthal, Esq.

PPTA STAFF

President & CEO | Jan M. Bult
Sr. Vice President, North America | Julie Birkofer
Vice President, Source | Joshua Penrod
Vice President, Global Access | Prof. Albert Farrugia
Vice President, Global Regulatory Policy | Mary Gustafson
Executive Director, Europe | Bruno Santoni
Vice President, Legal Affairs | John Delacourt

THE SOURCE STAFF

Editor | Michelle Krecz
Managing Editor | Rachel Liebe

Requests for permission to reprint should be directed to the editor at thesource@pptaglobal.org.

THE SOURCE is available as a PDF file at www.pptaglobal.org.

In the interest of encouraging broad and open discussion of issues relating to plasma protein therapies, collection and fractionation, the Source magazine may contain statements of opinion on such issues. These statements are those of the author and do not necessarily reflect the opinion of PPTA or its members. © Plasma Protein Therapeutics Association 2014

DESIGN AND PRODUCTION

B. Creative Group | www.agencybcg.com

THE SOURCE is published quarterly by PPTA.
 147 Old Solomons Island Road, Suite 100
 Annapolis, MD 21401

PHONE: +1.202.789.3100
EMAIL: thesource@pptaglobal.org



SUMMER 2014 Contents

3 IN MY VIEW

-
- 4 The Important Role of the Schleussner Family in Developing Biotest into a Global Company
 - 6 Ensuring the Efficacy of Therapies for Rare Disorders 'FIRST-DO NO HARM'
 - 9 "Life is short, play hard!" Interview with Stefani Bush, Immune Deficiency Foundation Patient Advocate
 - 12 PPTA's Data Program: A Valuable New Shortage-Preparedness Tool in Europe
 - 13 Online Tool Provides FDA Perspectives on Rare Diseases
 - 14 Haemonetics Corporation Leadership in Plasma Management
 - 17 Interview with Congressman Lance
 - 19 FDA Meetings and Reports Inform Upcoming Patient-Focused Activities for PPTA Stakeholders
 - 20 Affordable Care Act Impact on Patient Access to Plasma Protein Therapies
 - 22 U.S.-EU Trade Agreement Prospects: Will Opportunities for the Plasma Industry Materialize?
 - 24 Pathogen Safety: An Update
 - 25 IPOPI Global Study on PID Patients Needs and Outlooks
-

26 INSIDE PPTA

- 26 Vienna hosts the 20th Annual International Plasma Protein Congress
 - 29 Association to hold 2nd Annual International Plasma Awareness Week
 - 29 The European Plasma Collectors Committee Welcomes New Chairman Dr. Stephan Walsemann
-

30 MEET THE PPTA STAFF

Mary Gustafson

31 GLOSSARY

32 UPCOMING EVENTS

FEATURED COVER PHOTO IS OF A PRIMARY IMMUNE DEFICIENCY PATIENT.

More product options

Knowledgeable account managers

True Blue customer service

24-hour on-call access

Distribution centers across the nation

99.7% shipping accuracy*

Same-day emergency orders

Redefining the PACKAGE DEAL.

At ASD Healthcare, we redefined the package deal when we founded our company 20 years ago. We made a commitment to provide customers with more than specialty products. We made it our policy to deliver peace of mind. That's why when customers order from us, they know they'll find a wider range of product choices, the best delivery options and our superior True Blue customer service. That's our definition of a package deal. It's an assurance we will continue to put into every package we deliver to every customer, every day.



Call ASD Healthcare 800.746.6273 or visit us at www.asdhealthcare.com.

ASD Healthcare—making your patients and your purpose our priority for 20 years.



* ASD Healthcare's accuracy rate based on 5,000 packages delivered daily



In My View

BY JAN M. BULT, PRESIDENT AND CEO

This industry is grateful to the many donors who donate their valuable plasma to help so many patients in the world whose lives depend on the (often) lifesaving therapies that our members manufacture from the precious plasma that is donated. Today I want to write about the patients whose lives are many times saved because of the use of albumin and the medical experts who are involved in their treatment.

There has been growing recognition for the use of albumin in very ill patients who many times are staying in the intensive care unit. Unfortunately, I had the personal experience of my brother who stayed in the intensive care unit for 3 months and I could witness firsthand what enormous efforts are made to help these patients. My understanding and appreciation for the hard work of the medical experts and nursing staff has grown enormously.

Not all hospitals are using albumin in patients with sepsis. There are many reasons that I won't discuss. The irony of the situation was that my brother had done so much to discuss the benefits of albumin in a critical care setting and now he was the one that needed it the most and was unable to ask for it. Fortunately, I was able, with the help of Professor Albert Farrugia, to assemble important information that I could present to the medical staff. It felt like the old days when I was a medical sales representative.

We are used to dealing with many patient representatives who are very able to express their opinion and have an influence on their treatment. Over and over again it is realized how important it is to listen to the primary users. Patients in a critical care setting don't have the ability to speak up and there is no patient organization for albumin users.

The communication with intubated patients is an enormous challenge. Patients are nervous, often in pain, and very frustrated because they cannot make it known what they want to say. With the help of a lettercard, iPad, eye movements and arm signals, one might be able to understand what the patient is trying to communicate. I remember that it took me half an hour before I understood that my brother needed his glasses so he could see.

I also learned that you should not ask more than one question at the time. Then, with simple yes or no questions you might be able to get to the right answer. That takes time, patience and perseverance. In those situations, you cannot really discuss the benefits of albumin versus saline in a sepsis treatment protocol. Fortunately, my brother had authorized me to speak on his behalf and I am glad I was able to do that.

I have always had an enormous respect for donors and patients, as well as the many persons working in the collection and manufacturing industry. This personal experience showed me firsthand what an enormous important role physicians and nurses play in the wellbeing of patients.

From the bottom of my heart, THANK YOU for your hard work! ●

Jan M. Bult, President & CEO

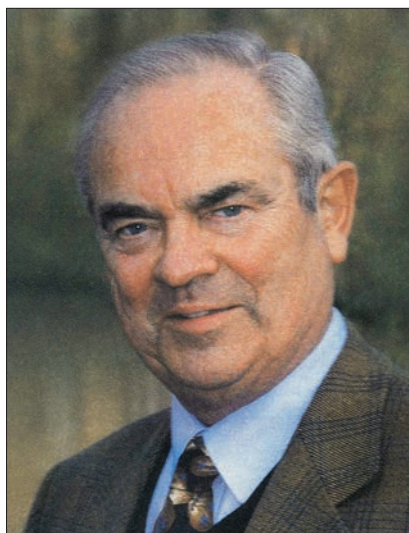


Biotest
Headquarters,
Dreieich,
Germany

The Important Role of the Schleussner Family

in Developing Biotest into a Global Company

BY JAN M. BULT



Dr. Hans Schleussner

Many people, when they hear the name Biotest, remember the name Schleussner. In 1946, the company was founded by Carl-Adolf Schleussner and his son Hans Schleussner as Biotest Seruminstitut GmbH in Frankfurt. The work of Karl Landsteiner had been very important, as we all know, and directed the research department. The first activities of the company were in Blood Group Serology with a first product being a test serum for anti-D.

Something that is not known by many is that the first activities of the family were in photography. About 150 years ago, Dr. Carl Schleussner prepared chemicals for photography. He also worked together with Dr. Wilhelm Conrad Röntgen and produced the first special plates to make the well known röntgen pictures.

Biotest has been very active in many areas like blood transfusion, serology, diagnostics, microbiology, air sampling and fractionation. Today, the company is very focused on fractionation and the development of monoclonal antibodies.

His son, Carl Moritz, continued with the production of the original dry plates but extended the business with the production of cinema film. In 1920, his son Carl Adolf took over the company. This is the same Carl Adolf who founded with Hans Schleussner what is now known as Biotest AG.

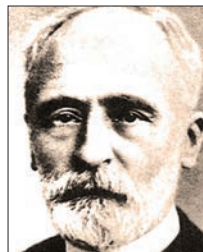
The connection with film is still there. Every year, Biotest issues a calendar that is printed on film with very special pictures. Also, the Biotest business cards are special and printed on film material!

Biotest has evolved and become a global entity with manufacturing sites in Germany and the U.S. A team of well talented people, under the leadership of Professor Gregor Schulz, is responsible for the current Biotest face in the world. Biotest has been very active in many areas like blood transfusion, serology, diagnostics, microbiology, air sampling and fractionation. Today, the company is very focused on fractionation and the development of monoclonal antibodies.

Some of you may know that I worked for Biotest from 1990 till September 1995. I do have a personal experience with Dr. Hans Schleussner that I would like to share with you. In the early 90's, I was working hard on strategic alliances and had been very busy to resolve some issues. One day, I had to be in Dreieich at the headquarters. At the end of the day when I was leaving, Dr. Hans Schleussner was at the door and asked how I was doing. I told him that it was time to go home and have dinner with my wife, something which had been difficult for a few weeks. Dr. Schleussner invited me to take my wife out for dinner and send him (and not Biotest) the invoice. He then changed his mind, opened his wallet and gave me 200 Mark for that dinner. It is this kind of thing that people never saw from Dr. Schleussner. For me he was, and still is, a great man.

He has been retired for many years and is enjoying his well-deserved family time with his wife Renate, his daughter Cathrin and son Martin. He is also a proud grandfather. •

JAN M. BULT, *President & CEO*



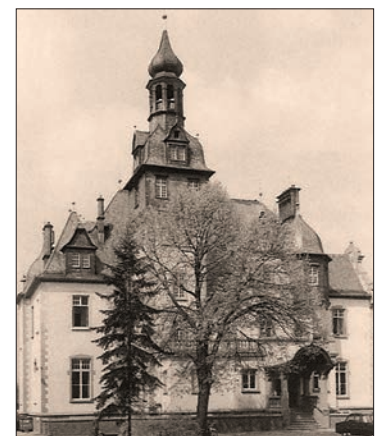
Dr. Phil. Johann
Carl Peter Ferdinand
Schleussner



Dr. Wilhelm
Conrad Röntgen



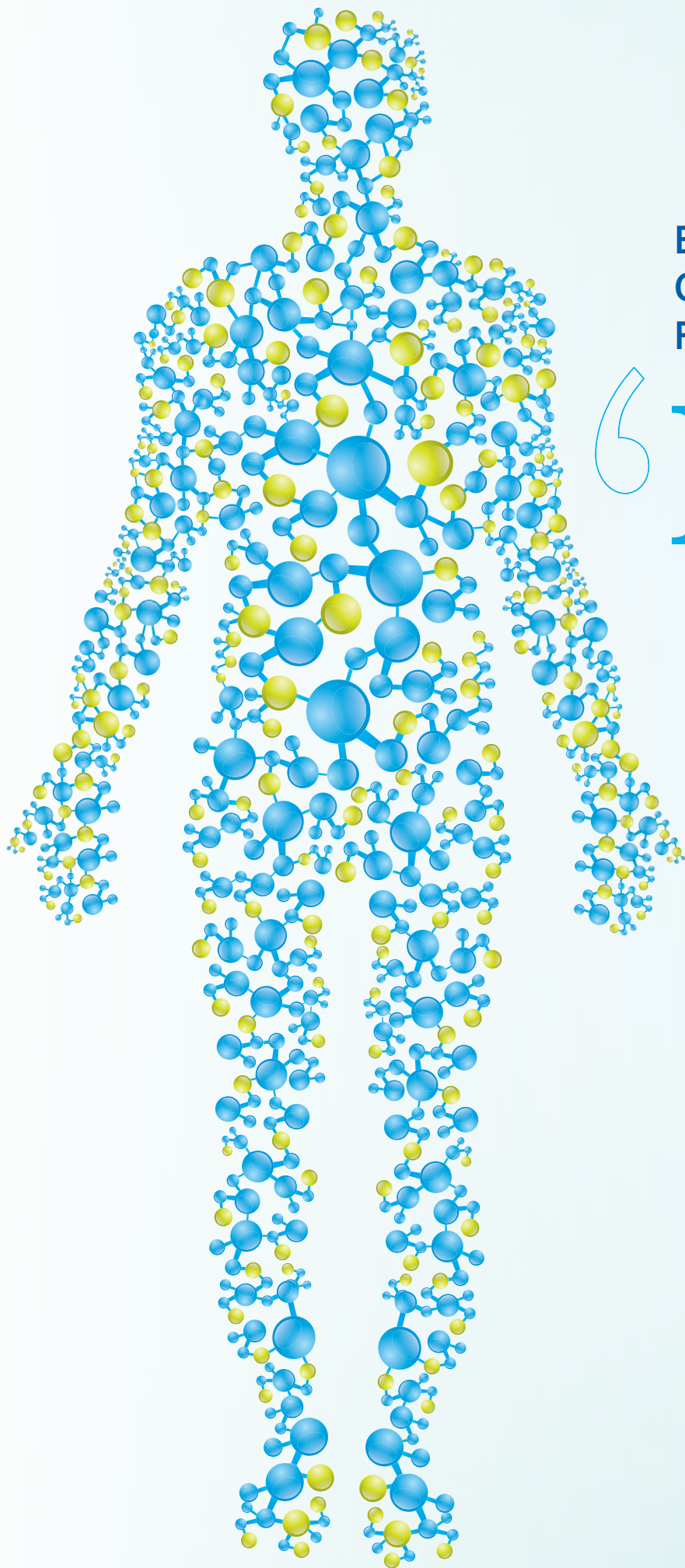
Professor Gregor Schulz



Biotest's first headquarters,
Frankfurt, Germany



The Schleussner Family. From L to R: Renate, Dr. Martin, Dr. Hans
and Dr. Cathrin.



ENSURING THE EFFICACY
OF THERAPIES
FOR RARE DISORDERS



FIRST—

-DO NO HARM⁹

BY PROFESSOR ALBERT FARRUGIA



round forty years ago, a revolution started in the practice of therapeutics. For many decades preceding this period, medical interventions, including the use of drugs such as plasma protein therapies, were mostly based on the collective or individual knowledge and experience of the providers of care, particularly medical practitioners. This was also shaped by the huge advance in the knowledge of basic services, including physiology, biochemistry, pharmacology and the then emerging science of molecular biology, which characterized the nineteenth and twentieth century.

This led to a paradigm whereby 'biology dictates therapy' and the accrued acumen of clinicians were the dominant shapers of therapeutic practice. This paradigm had obvious limitations as more accurate and objective measurements of disease management became available. Gradually, it was realized that many interventions were actually resulting in little or no improvement in disease progression.

As a result of this recognized limitation, a movement calling for Evidence Based Medicine (EBM) evolved, emanating from McMaster University of Canada and rapidly spreading in influence worldwide. This movement established objective criteria for the understanding of evidence against pre-established criteria. Powerful statistical methods were developed for quantifying the therapeutic effects of a proposed new intervention relative to established, alternative or no treatment. The previously developed mechanism of the Randomized Clinical Trial (RCT) was proposed as the highest demonstration of an alternative efficacy. In RCT's, patients are randomly allocated to the treatment under

review, or an alternative treatment, which may constitute no treatment - the placebo. This is done, in the most powerful form of RCT, in a fashion which the prescribers and the patients do not know which particular treatment arm the individual patients occupy. In this way, biases in the interpretation of results are minimized.

Unquestionably, the implementation of EBM and the use of RCT's has improved greatly therapeutic practice in many areas, particularly those involving large scale interventions in conditions with an imperfect understanding of disease pathophysiology. Additionally, the generation of systematic reviews through the combination of several RCT's in meta-analysis enabled the evidence base of several therapies to be strengthened. However, troubling features of the EBM paradigm have restricted its capacity to improve therapies for rare chronic diseases.

First of all, as a general feature, EBM has been absorbed into the cost-containment mechanisms of many payers, including governments and insurers, as a tool to minimize

health care spending. It is important to note that this was not, and still is not, an inherent feature of EBM. Despite this, the allocation of a therapy to any level of evidence other than the highest in the EBM “hierarchy” has been frequently used to deny or limit reimbursement. As an example, some of the more zealous of the systematic reviewers of the Cochrane Collaboration—a somewhat purist and extremist interpreter of EBM—have concluded that a number of therapies lack evidence and have gone beyond their brief by discouraging payment for such therapies, which reimbursement agencies, quoting the said reviews, have been very willing to do.¹

In summary, the current era of therapeutic development in plasma protein therapies is exciting and very promising for patients. However, it needs to be converged with appropriate policies and ethical principles.

Against this background, it is the uniform experience that the statistical power needed to demonstrate efficacy in RCTs is not achievable with the small patient numbers available for rare disease therapies. This has led to various ad hoc modifications to these requirements, all of them within the conventionalities of EBM, to try to get evidence for these therapies. It must be recognized that many regulatory authorities have shown commendable flexibility in their requirements for approval of these therapies because of this limitation. Recent years have seen the FDA, for example, approve therapies for rare plasma protein deficiencies such as fibrinogen deficiency and protein C deficiency using criteria which deviate significantly from conventional RCT requirements.

Despite this, RCTs continue to be demanded for approval of some therapies and this is resulting in situations where patient outcomes are being compromised. As outlined above, RCTs are credible tools in diseases with large populations and an incomplete pathophysiological understanding. With the rare congenital plasma protein deficiencies, this is not the case. The populations are small, and the mechanism—congenital deficiency of a single protein correctable by substitution—is well characterized.

As examples, it is troubling to observe recent developments in hemophilia therapies. The earliest concentrates for treating hemophilia A, including cryoprecipitate and the earliest purified plasma fraction, were introduced and established in clinical practice in the pre EBM era, in the absence of RCTs. Their effects were obvious and dramatic and have led to incredible improvements in the quality and expectancy of patient lives. It is fruitless to speculate on what the authorities’ position

would be today, and their commendable flexibility in some areas has been noted. It appears that this flexibility is not evident in some others.

As an example, the current wave of approvals for new recombinant coagulation products is invariably including approval for prophylaxis in different patient groups. In the relevant studies, we note patients are being randomized into prophylaxis and on-demand treatment arms in order to “prove” the efficacy of prophylaxis. Naturally, this is repeatedly “proved”—through demonstrating bleeding rates which are much higher in the patients on-demand. The evidence for prophylaxis, albeit not through RCTs, has existed for as long as concentrates have been available. Prophylaxis is an example of the public health axiom that “Prevention is better than cure.” Must patients be subjected systematically to harm in order to approve a company’s label claim? It is pointed out to us that these particular trials are being held in less affluent countries where the standard of hemophilia care is low and that, as a result, even the high bleeding rates of on-demand treatment represent an enhancement. We find this admission that such trials are impossible, for ethical reasons, in the rich economies to be troubling and specious. The issue of conducting clinical trials in developing countries to be bedeviled with ethical pitfalls and a scrutiny of the relevant literature indicates a need for more detail in ensuring patient protection.

We find troubling examples in other therapies as well. The justifiable accolades granted to a recent RCT for an augmentation therapy for alpha one anti-trypsin deficient (1AT) recognize that randomization of patients into a placebo (no treatment) arm definitely led to increased lung damage relative to the 2 patients fortunate enough to be allocated to the treatment. Even more troubling in this example was the subsequent decision by a major private insurer to reimburse solely this one concentrate on the basis of its “superior evidence.” While the evidence accrued from this trial is valuable, ignoring the huge body of non-RCT evidence for these therapies is deplorable, and has led to justifiable criticism from the relevant patient association. We are troubled by this example of a growing trend to merge approval and reimbursement issues, and the use of evidence to restrict access to as wide a range of therapies as possible.

In summary, the current era of therapeutic development in plasma protein therapies is exciting and very promising for patients. However, it needs to be converged with appropriate policies and ethical principles. In the era of patient centeredness, the interests of approval authorities and reimbursers need to recognize the primacy of Hippocrates primary principle “First—do no harm.” After that, they may start considering his second exhortation—“Get paid up front.” ●

PROFESSOR ALBERT FARRUGIA, *Vice President, Global Access*

¹ <http://videocast.nih.gov/vodCaptions/ccgr051513.txt>



“Life is short, play hard!”

AN INTERVIEW WITH STEFANI BUSH,
IMMUNE DEFICIENCY FOUNDATION PATIENT ADVOCATE

BY JULIE BIRKOFER

I am a mom of two beautiful children (Will, almost 11 and Sasha 8½) with Primary Immunodeficiency Disease—also known as PI (and several other medical issues). Sasha began receiving gamma globulin at 17 months and Will began receiving gamma globulin at 4½ years of age. This medication has been life changing and life-saving. I am so incredibly grateful for those who donate their time and their plasma. I feel like I can never fully convey the depth of my gratitude for the ability to have access to a treatment that has been able to keep my children thriving and living with PI.

I am so incredibly grateful for those who donate their time and their plasma. I feel like I can never fully convey the depth of my gratitude for the ability to have access to a treatment that has been able to keep my children thriving and living with PI.



Q Tell us, how did you become involved with the IDF?

When Dr. Bonilla diagnosed my son with PI, he handed me his business card at the end of the visit and wrote a website address on the back of it. It was for the Immune Deficiency Foundation. I went online that night and was so relieved to have accurate and helpful information—especially at a time in which our world had just been turned upside down. I wanted to do something to raise awareness in our area, so I reached out to Kathy Antilla at the IDF. . . and the rest is history!

Q What compelled you to get involved in advocacy through the IDF and become so integral to the passage of the IVIG Medicare Access Act?

When I heard of individuals having issues with access to the same life-saving medication that we had the blessing of acquiring with ease, it compelled me to want to speak up and fight for them to have the same quality of and access to care that we did. Everyone deserves it. No one should be denied a medication—especially because of an unintended loophole. I felt it was my responsibility to be the voice of those who were unable to speak for themselves or were physically unable to get out there and advocate because of their own health issues.

Q What has your experience been as an IDF volunteer?

It has been life-changing. When I started volunteering for IDF, I had NO idea the immense amount of joy and growth that would occur. The staff has always been kind, helpful, genuine and focused on helping every single person they possibly can with their organization. It's been 7 years since I started on this journey with IDF and I am so proud to be a volunteer for IDF. No matter where the future takes me, IDF will always have a special place in my heart.

Q How did you connect with former Senator John Kerry (D-MA)?

When IDF reached out to me and asked if I would contact Senator Kerry, I was hesitant, not because I didn't want to reach out to him, but because I didn't know the first thing about the legislative process. With further encouragement, I took the leap of faith and reached out. I am so glad I did. Senator Kerry's Chief of Staff came out within 3 days of my initial contact (during an ice storm no less!) He came to my house and met my family, the Fox family and the Spinale family. He heard our stories, our struggles and watched each of our families set up and administer their infusions. We had cake and coffee and just talked. By the end of the week, we were notified that the Senator would be attending our next blood drive and making an announcement. It was from that initial meeting, from us just being real, sharing what our story was and taking that leap of faith that a long and wonderful relationship with Senator Kerry and all of his staffers began.

© What do you think was pivotal in engaging the former Senator?

I think the pivotal moment was when Senator Kerry arrived at our blood drive. He walked through the door and my son, Will, ran up to him to give him a hug. Senator Kerry scooped him up in his arms and their eyes met. The Senator turned to his Chief of Staff and said, “We have to help these families.” And he did . . . he and his staff tirelessly kept up the fight for the Medicare IVIG Access Act.

It’s been 7 years since I started on this journey with IDF and I am so proud to be a volunteer for IDF.

© As an advocate, what challenges lie ahead for you and your community?

There are so many challenges ahead and so much work to be done. If I had to pick one thing as the “top of the ticket” for me, I’d say it would have to be the growth of “co-insurance” requirements that are becoming widespread and impacting countless individuals. The problem lies in the fact that insurance companies are beginning to institute hefty and often outrageous co-insurance requirements for patients that receive specialty drugs. To me, it’s almost like the insurance companies are punishing those who are the sickest with this newest endeavor. Because of this, people with real and serious health issues (not just PI) are unable to afford the often too costly co-insurance amounts and therefore end up going without their life-saving medications. While insurance companies might be trying to save money by doing this, I feel that, in the end, this will only result in costing more money for the affected individual and the insurance company, as lack of compliance (due to financial reasons), will then lead to more serious health complications and then larger medical costs. ●

JULIE BIRKOFER, *Senior Vice President, North America*

IVIG Access Act

Pursuant to the Medicare IVIG Access Act of 2012 (P.L. 112-242), Centers for Medicare and Medicaid Services (CMS) is implementing the Medicare IVIG Demonstration to evaluate the benefits of providing payment and items for services required for the in-home administration of IVIG for the treatment of primary immune deficiency disease (PIDD).

Since the enactment of the law on January 10, 2013, CMS has engaged with stakeholders through an Open Door Forum Call on November 22, 2013 that provided suppliers, patient advocates, providers and other interested parties the opportunity to submit input into the design and implementation of the demonstration.

Continuing the Agency’s implementation of the Demonstration, on March 7, 2014, CMS published for public comment a draft application for participation. Once finalized, each beneficiary who wishes to participate will be required to complete the application.

CMS is statutorily obligated to limit participation in the Demonstration to 4,000 beneficiaries. The Agency intends to use beneficiaries’ applications to prioritize eligibility for those individuals who demonstrate the greatest need for access in the home.

The Demonstration is expected to initiate in fall of 2014. ●

The Challenge of Co-Insurance

Specialty drugs can be covered under a health plan’s medical or pharmaceutical benefit.

Traditionally, plasma protein therapies were covered under the medical benefit, but in the last four years many health plans moved these therapies to the pharmaceutical benefit. Expensive drugs in the pharmaceutical benefit may be placed in a specialty tier with cost-sharing. Instead of a flat fee co-payment, individuals can be required to pay co-insurance, a percent of the total drug cost. The co-insurance can range from 20-50 percent, which can be several thousand dollars for rare, chronic condition treatments.

Although the ACA set out-of-pocket spending limits for some health plans, individuals on plasma protein therapies would pay the maximum with their first order of the year. ●



PPTA's Data Program:

A Valuable New Shortage-Preparedness Tool in Europe

BY JOHN DELACOURT

On April 1, 2014, PPTA completed the roll-out of its European Data Program. This constitutes a major shortage-preparedness milestone for the industry. Aggregate data on all major categories of plasma protein therapies distributed in Europe,¹ reported pursuant to strict standard operating procedures and competition law safeguards, is now available on the Association's website, www.pptaglobal.org.

The PPTA Data Program initiative was driven by the industry's long term recognition of shortage-preparedness as an important public health priority, as well as by European regulators' renewed interest in drug shortage policy in recent years. Most notably, in November 2012, the European Medicines Agency (EMA) published an influential Reflection Paper on the subject.² The Reflection Paper was followed by an EMA Drug Shortages Workshop, in which PPTA actively participated, in October 2013.³

At the EMA Workshop, PPTA proposed to implement a program similar to its existing North American Data Program, which has been in operation for more than a decade, with appropriate modifications to reflect differences in the European marketplace, ranging from clinical practice to regulatory framework. PPTA explained that the program would be valuable to all industry stakeholders, and would confer benefits in multiple areas, including:

COMMUNICATION

Effective shortage preparedness requires participation by all stakeholders. One of the strengths of PPTA's web-based data reporting model is that it communicates critical shortage-related information to everyone, not just to regulators. As a result, regulators are not forced to shoulder the burden of identifying, and responding to, a potential shortage alone. This broad spectrum approach to communication recognizes that, due to limitations of budget and legal authority, regulators are often not in a position to effectively, and quickly, disseminate shortage information on their own.

PREVENTION

Although PPTA's data program cannot prevent shortages on its own—it has little ability to impact problems with manufacturing practices or the distribution channel, for example—it is a critical component of the plasma protein industry's prevention strategy. Because the program is in place, EMA now has an industry-wide perspective on product supply. This is in sharp contrast to the state of play prior to the program's implementation. Then, if EMA learned of a problem affecting one company, it was required to make frantic phone calls to all other market participants to determine if there was an industry-wide problem (i.e., a true shortage). Now, EMA receives much more comprehensive periodic snapshots of the product distribution situation.

PATIENTS

The shortage-related information provided by the PPTA program is equally important to patients. Monitoring the data on PPTA's website enables them to observe trends in product supply over time, and empowers them to make important decisions regarding their own health. The shortage of recombinant Factor VIII in 2000 provides a specific, real world example. At that time, because of the PPTA data, many hemophilia patients were able to make better informed decisions about the timing of elective surgery.

Now that the initial roll-out is complete, PPTA will continue to engage in stakeholder outreach to answer questions and receive feedback. An initial target of these efforts will be national level European regulatory authorities, whose role in shortage prevention and mitigation is at least as important as EMA's. Indeed, PPTA staff have already met with the Austrian Agency for Health & Food Safety (AGES) and both the Ministry of Health and the Paul-Ehrlich-Institut (PEI) in Germany. In keeping with the Association's focus on "patient centeredness," European patient advocacy groups will be an initial focus of these outreach efforts as well. ●

JOHN DELACOURT, *Vice President, Legal Affairs*

¹ The product categories currently included in the program are: albumin ≤ 5%, albumin 20%–25%, intravenous immune globulin, subcutaneous and intra-muscular immune globulin, plasma-derived factor VIII, recombinant factor VIII, and plasma-derived factor IX.

² European Medicines Agency, Reflection Paper on Medicinal Product Supply Shortages Caused by Manufacturing/Good Manufacturing Practice Compliance Problems (Nov. 22, 2012), available at http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/11/WC500135113.pdf.

³ European Medicines Agency, Workshop on Product Shortages due to Manufacturing and Quality Problems: Developing a Proactive Approach to Prevention (Oct. 14, 2013). Proceedings and related documents available at http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/events/2013/10/event_detail_000796.jsp&mid=WC0b01ac058004d5c3.



Online Tool Provides FDA Perspectives on Rare Diseases

On Rare Diseases Day, February 28, 2014, the U.S. Food and Drug Administration's Office of Orphan Product Development (OOPD), launched an online tool that provides educational resources for patients, advocacy groups, research investigators and orphan product developers. The webpage provides recorded educational topics about OOPD and rare disease issues. Also in conjunction with Rare Diseases Day, OOPD Director Gayatri R. Rao, M.D., J.D., posted a blog, "Rare Diseases in Children Pose Unique Challenges," that highlights the tool.

THE TOOL IS AVAILABLE HERE:

<http://www.fda.gov/ForIndustry/DevelopingProductsforRareDiseasesConditions/ucm385535.htm>

THE BLOG IS AVAILABLE HERE:

<http://blogs.fda.gov/fdavoices/index.php/2014/02/rare-diseases-in-children-pose-unique-challenges/>



Haemonetics Corporation

LEADERSHIP IN PLASMA MANAGEMENT

BY ANDRÉ BUECHNER

Haemonetics has proudly served the global plasma community for more than 40 years. The hallmark of the organization's success is a long-standing commitment to donor safety, understanding its customers' collection processes, reliably delivering quality products, designing equipment that is easy to use, and providing comprehensive service support and training programs.

The company's story began in 1971 when Jack Latham founded Haemonetics by manufacturing and selling one perfectly designed component for a new blood collection device: a centrifuge disposable called the "Latham Bowl" that could automate the separation of blood. He built the company's values on the belief that blood was a medical drug that needed to be respected and missteps in that regard could cause considerable harm to patients. At the core of these values was his commitment to protecting patients' safety.

The Latham Bowl technology merged expert engineering with the ground-breaking scientific discoveries of Dr. Edwin Cohn, a protein chemist and Harvard Medical School professor, who in the 1930s, pioneered techniques for fractionating blood to isolate the serum albumin protein from plasma, a discovery that led to a revolution in the blood community.

Haemonetics is committed to donor safety and comfort and device reliability.



Mr. Latham knew the dangers patients could experience with whole blood transfusions, understood the potential for transfused fractionated blood products to help minimize those risks, and trusted his device would make this possible on a large scale for the benefit of patients globally. With that drive, he laid the foundation of what would become Haemonetics Corporation.

FROM MEDICAL DEVICES TO BLOOD MANAGEMENT SOLUTIONS

As industry needs changed, Haemonetics evolved from a medical device company focused on blood processing systems to its current position as *THE* Global Leader in Blood Management Solutions. Haemonetics is strongly committed to streamlining the efficiency of the blood management continuum and improving blood management practices for commercial plasma centers, blood centers, and hospitals around the world.

Since its inception, Haemonetics has experienced steady growth through disciplined execution of a strategy focused on delivering the value of its blood management solutions to customers.

COMMITMENT TO THE PLASMA INDUSTRY

Today, Haemonetics helps plasma fractionators and collectors around the world meet the ever-increasing need for plasma-derived bio-pharmaceuticals with a comprehensive suite of products and services that covers the entire plasma management continuum. The organization offers full-service collection solutions to the global plasma community—from an automated supply chain management system, to

a comprehensive suite of software products, to device and disposables innovations—that are designed to support multiple facets of its customers' operations. This comprehensive suite of solutions is a direct result of Haemonetics' ongoing commitment and investments in the plasma industry throughout its history.

But the success of Haemonetics is about more than innovation and investments, it's about trust as described by Peter Allen, President of Global Plasma, Haemonetics... "Our customers trust us to deliver solutions that address the things that matter most to them: donor recruitment and retention, operational efficiency, economics (cost per liter), and plasma demand met with quality product. Everything we do starts with listening to our customers so we understand what is most important to them. We recognize that every customer-facing interaction is an opportunity to learn what we need to do to improve our company, services, products, and strategies."

Haemonetics is committed to meeting the future needs of its plasma customers by investing in next generation technologies that will deliver the solutions that matter most to them.

LOOKING FORWARD... LOOKING BACK

More than 40 years after Jack Latham founded Haemonetics, the organization now offers the industry's most complete portfolio of devices, software, and services to the plasma, blood center, and hospital markets around the world. Mr. Latham's legacy and vision of creating a company dedicated to improving patient care continues to burn brightly. ●

ANDRÉ BUECHNER,
Director, Global Marketing, Haemonetics Corporation

Collect with confidence and optimize operational efficiencies

At Haemonetics, we understand the pressures you face—from costs to increasing regulations to managing your supply chain. Our comprehensive portfolio of products and services is designed to support multiple facets of your operations, helping you achieve efficiencies and manage costs.



Solutions for the global plasma industry

An ongoing commitment
to **donor safety** and satisfaction

Dedicated customer support,
training, and process improvements

A **reliable supply chain**
helps ensure business continuity

Our **supply chain management model**
streamlines ordering and fulfillment

To learn more about our full range of products, programs and services,
contact your Haemonetics Account Manager or visit www.haemonetics.com



Interview with Congressman Lance

BY EVERETT CROSLAND

Q As the Republican Co-Chair of the Congressional Rare Disease Caucus, alongside your Democratic counterpart, Congressman Joe Crowley, you've led your colleagues in Congress informing legislation and policymaking to improve the lives of the 30 million Americans living with one or more of the 7,000 identified rare diseases. Can you please describe why you have chosen improving innovation and access for rare disease patients as a top priority?

As a member on the Health Subcommittee of the House Energy and Commerce Committee, I have an extraordinary opportunity to inform health policy. I have long been inspired by the experiences of patients to leverage my position on the Committee to support patients living with rare diseases and advance the innovations of the pharmaceutical industry. I am particularly moved by the story of John Crowley who, after receiving the news that his children, Megan and Patrick, had been diagnosed with Pompe's disease, set out to and eventually successfully accelerated the development of an effective drug for the treatment of this rare genetic disorder, saving the lives of his and many other children. It is stories like John's and the many others that I hear every day from patients living with rare diseases that invigorate our message and help inform our leadership.

MODERN would modernize our Nation's drug and diagnostics evaluation and regulatory network by encouraging the discovery and development of new treatments for the many diseases that currently have few or no options.

Q The Modernizing Our Drug and Diagnostics Evaluation and Regulatory Network (MODDERN) Cures Act (H.R. 3091), of which you are the lead sponsor, has been lauded by patients and patient advocates as having the potential to unlock significant innovation potential, and “greatly improve the lives of people living with chronic diseases and disabilities.” Can you please describe how the bill improves the state of biomedical innovation and accelerates effective treatments to patients?

MODDERN would modernize our Nation’s drug and diagnostics evaluation and regulatory network by encouraging the discovery and development of new treatments for the many diseases that currently have few or no options. The Act would also create a system that rewards efficiency and effectiveness to the benefit of all people with chronic diseases.

In an era of increasingly scarce resources for health research, it is critical to ensure that outdated barriers in the regulatory system are removed and limited dollars are spent most effectively to meet the needs of patients. The status quo is not yielding treatments needed to address the growing epidemic of chronic disease. That is why it is vital that we update the regulatory system by removing the barriers to invention and provide greater predictability in the search for therapies for unmet medical needs.

Importantly, the bill also would promote the production of co-developed diagnostics and therapeutics and encourage the development of drugs abandoned in the development process by creating a new category of drugs known as dormant therapies. The bill defines dormant therapies as compounds with insufficient patent protection that offer the promise to treat conditions with unmet medical needs. Updating patent reforms would help open the pipeline for new innovations and therapies and would help patients with degenerative conditions and autoimmune diseases, as well as cancer.

Q In addition to the MODDERN CURES Act, please tell us about the current priorities and activities of the rare disease caucus, and where you see opportunities for Congress to improve access for rare disease patients and engender an environment of innovation where rare disease R&D is feasible?

The Rare Disease Caucus will continue to bring Congressional attention to the nearly 7,000 known rare diseases that currently have no approved therapies. We are dedicated to ensuring sufficient funding for research and orphan product development, exploring ways to incentivize companies to create new drugs, biologics and humanitarian use devices and providing an opportunity for Members of Congress, families and advocacy groups to exchange ideas and policy concerns on rare diseases.

Q In Chairman Camp’s recent tax reform proposal, he proposes eliminating the orphan drug tax credit. What is your position on the repeal of the orphan drug tax credit as considering its effectiveness in accelerating rare disease therapies to patients?

The Internal Revenue code has ballooned to a 5,600-page, 4 million-word complicated mess. It’s time to clean it up and enact a tax code that is simpler, fairer and more conducive to economic growth. In particular, we must simplify the tax code to help America’s working families and entrepreneurs, and close special-interest loopholes to help lower individuals’ rates and ensure that middle-class Americans will pay no more taxes than they do under current law. We must also level the field for companies by lowering the corporate rate so U.S. firms can compete with rivals abroad.

Q The National Institutes of Health (NIH) plays a vital role in developing the basic science underlying plasma protein therapies and other rare disease treatments. Can you please describe the policies that you believe stand to amplify NIH’s basic research capacities, while also aiding in the translation of this science into investigational targets and ultimately lifesaving treatments?

Prioritizing medical research and innovation is critical to helping patients, accelerating cures and treatments for patients living with common and rare diseases, and keeping America’s biomedical economy competitive with the rest of the world. NIH does an extraordinary job of conducting fundamental research and it is incumbent on us in Congress to ensure that our funding of the agency continues to build on its fundamental research capacities, while also improves the rate at which research is translated into treatments for patients. ●

EVERETT CROSLAND, *Director, Federal Affairs*

FDA Meetings and Reports Inform Upcoming Patient-Focused Activities for PPTA Stakeholders

BY MARY CLARE KIMBER

The U.S. Food and Drug Administration (FDA) recently announced the eighth of 16 public meetings to be held in fiscal year (FY) 2013-2015 (by September 2015) as part of the Agency's Patient-Focused Drug Development Initiative.

The June 10, 2014 meeting on manifestations of inborn errors of metabolism follows meetings that began in April 2013 on chronic fatigue syndrome and myalgic encephalomyelitis, lung cancer, human immunodeficiency virus (HIV), narcolepsy, sickle cell disease, fibromyalgia and pulmonary arterial hypertension, respectively (see Table 1). Four more meetings will be held in FY 2016-2017, for a total of 20 by September 2017.

THE VOICE OF THE PATIENT

Patient-Focused Drug Development is part of FDA's performance commitments in the fifth authorization of the Prescription Drug User Fee Act.¹ Due in large part to the efforts of PPTA stakeholders, alpha-1 antitrypsin deficiency, as well as, hemophilia A, hemophilia B, von Willebrand disease and other heritable bleeding disorders, will be the topics of two of the remaining eight meetings to be held by September 2015. PPTA stakeholders can look to a series of reports entitled "The Voice of the Patient" for insight on the upcoming meetings, possible outcomes and next steps. The reports are available here: www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm368342.htm

FUTURE OPPORTUNITIES FOR PPTA STAKEHOLDER ENGAGEMENT

FDA first nominated 39 disease areas in September 2012 as potential candidates for the focus of each of the 20 meetings. In addition to alpha-1 antitrypsin deficiency and clotting disorders, the list included thrombotic disorders (e.g., antithrombin deficiency and protein C deficiency), primary humoral immune deficiencies (e.g., common variable

immune deficiency), neurological disorders treated with immune globulins (e.g., chronic inflammatory demyelinating polyneuropathy) and hereditary angioedema. FDA will initiate a second public process to determine the final four disease areas and PPTA will continue its support of patients in their partnership with the Agency in this important initiative. ●

MARY CLARE KIMBER, Senior Manager, Regulatory Policy

TABLE 1
FDA Progress in Patient-Focused Drug Development Initiative*

	DISEASE AREAS TO BE ADDRESSED IN FY 2013-2015	FDA MEETING HELD/ SCHEDULED	THE VOICE OF THE PATIENT PUBLISHED
1	Chronic fatigue syndrome and myalgic encephalomyelitis	X	X
2	Lung cancer	X	X
3	HIV	X	X
4	Narcolepsy**	X	
5	Sickle cell disease**	X	
6	Fibromyalgia	X	
7	Pulmonary arterial hypertension	X	
8	Neurological manifestations of inborn errors of metabolism	X	
9	Alpha-1 antitrypsin deficiency***		
10	Breast cancer		
11	Chronic Chagas disease		
12	Female sexual dysfunction		
13	Hemophilia A, hemophilia B, von Willebrand disease, and other heritable bleeding disorders		
14	Idiopathic pulmonary fibrosis		
15	Irritable bowel syndrome, gastroparesis, and gastroesophageal reflux disease with persistent regurgitation symptoms on proton-pump inhibitors		
16	Parkinson's disease and Huntington's disease		

* as of May 2014 ** FDA indicated on May 21, 2014 that report "will be posted soon."²

*** 9-16 listed in alphabetical order

Sources: Federal Register Notice (April 11, 2013); <http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm347317.htm>

¹See Mary Clare Kimber, PPTA Stakeholders Drive Patient-Focused Drug Development Initiative, THE SOURCE Summer 2013, at 4.

²<http://blogs.fda.gov/fda/voice/index.php/2014/05/>

fda-voice-of-the-patient-listening-to-those-most-affected-by-their-disease-and-treatments



Affordable Care Act Impact

ON PATIENT ACCESS TO PLASMA PROTEIN THERAPIES

BY BRENN RAINES

Preventing a negative impact on access to plasma protein therapies due to the Affordable Care Act (ACA) is a priority of PPTA, manufacturers and the patients who rely on these life-saving medicines. As of January 1, 2014, the majority of the legislation's provisions are implemented, including expanded Medicaid coverage in some states, the individual mandate for health insurance and the establishment of marketplaces to purchase insurance. Although it is still too soon to realize the full impact of the ACA on patients who rely on plasma protein therapies, we can take a first look at some initial patient experiences.

OBTAINING APPROPRIATE COVERAGE

In the past, individuals with rare, chronic conditions experienced two major access issues: affording and qualifying for coverage. The ACA reduced these challenges with the elimination of life-time caps, annual benefit limits and denials based on pre-existing conditions. Some patients who rely on plasma protein therapies will be newly covered by states that elected to expand Medicaid coverage. Patients with non-grandfathered employer-sponsored plans will benefit from out-of-pocket spending limits. Others will purchase plans through a state- or federally-run insurance marketplace. Once the deadline to enroll through the marketplace passed, we reached out to patient advocacy groups to see how easy or difficult it was for users of plasma protein therapies procure adequate coverage. The lack of transparency in the enrollment process and plans offered made it difficult for patients to obtain coverage and understand their benefits.

In a state marketplace, a patient on immunoglobulin therapy was unable to see the covered benefits offered by each plan. He purchased a plan that seemed appropriate, though later found out his plan did not cover his immunoglobulin therapy. Neither the patient nor his

doctor could reach the insurance company to discuss the authorization. The therapy was finally approved, only after intervention from the state's Attorney General.

A previously uninsured hemophilia patient successfully enrolled in the federally facilitated marketplace. This patient aged out of his state's Children's Health Insurance Program, did not qualify for Medicaid, and could not afford private insurance. For the past two years he has received his hemophilia treatments through a generous manufacturer charity plan. He experienced transparency issues, as well as technical difficulties with the federal website. His enrollment required dozens of attempts and the assistance of an independent insurance agent. Although relieved to have insurance, he still does not know if his therapy is covered. Blood clotting factors are not listed on the 2014 formulary, so he assumes it is covered under the medical benefit, although the plan does not explicitly state it. He has received four months supply of blood clotting factor but the claims are still being processed by his insurer. These patient experiences demonstrate the need for transparency about how plasma protein therapies are covered before, during, and after enrollment.

Some health plans are responding to ACA implementation with strategies that are negatively affecting patient access to plasma protein therapies. In response to imposed fees, insurance companies are employing cost-saving strategies. Patient advocacy groups report examples of fail-first policies, changes in specialty pharmacies, and changing how plasma protein therapies are reimbursed.

FAIL-FIRST POLICY

In late 2013, a major health insurance company issued a new formulary policy that limits Alpha-1 Antitrypsin Deficiency (Alpha-1) patients to a single augmentation therapy. Insurers will require patients to first fail on the least expensive therapy in a class before authorizing a more expensive one. Patients can only access alternate treatments after they suffer an allergic reaction or adverse response. Currently stable patients must switch to the preferred product and risk harm before their doctor may prescribe the most medically appropriate therapy. Alpha-1 patients and patient advocacy groups urged the company to reconsider its decision, describing how plasma protein therapies are not interchangeable or clinically equivalent. However, the insurance company has defended their decision in a response letter to the Alpha-1 Foundation, claiming the covered product is the only Alpha-1 replacement therapy that demonstrates positive clinical outcomes. The insurance company only referenced the covered product's

package insert as the source for this efficacy claim. The Alpha-1 Foundation responded to the letter, informing the insurance company that the package insert does not support its claim, and no similar evidence is found in peer-reviewed literature or U.S. Food and Drug Administration (FDA) reports. The insurance company has not responded.

COVERED SPECIALTY PHARMACIES

Some health plans switched from using many small specialty pharmacies to one larger chain specialty pharmacy. Patients feel the larger pharmacies can be less experienced with the nuances of bleeding disorder treatments. For example, hemophilia patients described the smaller pharmacies as being more accessible; they were able to get deliveries of blood clotting factor early or on Sundays. Unlike other specialty drugs, blood clotting factor is often taken more frequently than prescribed when patients experience unexpected bleeds. Patients had difficulty obtaining premature refills from the larger chain pharmacies if their blood clotting factor supply depleted before their next scheduled delivery.

COST-SHARING

Another cost-saving strategy is to change how expensive medications are covered and reimbursed. Plasma protein therapies can be covered under health plan's medical or pharmacy benefit. Under the medical benefit, patients are responsible for a flat co-payment fee. Some health plans have switched coverage of plasma protein therapies to the pharmacy benefit. Under this design, very expensive plasma protein therapies are placed into a specialty tier and patients are required to pay a percentage of the medication cost rather than a flat co-pay. This percentage is called co-insurance and it requires patients to pay between 20-50 percent of the therapy's cost. The ACA limits annual out-of-pocket spending to \$6,350 per year for an individual and \$12,700 per year for a family. Individuals affected with hemophilia, immune deficiency, and Alpha-1 could pay the full cost-share with the first order of medication. States including Delaware, New York, Vermont, Maine, and Maryland passed legislation that limits high co-insurance rates for specialty tier drugs; a similar bill will be considered by Congress, H.R.460 *Patients' Access to Treatment Act*.

PPTA will continue to interact with patient groups to assess the impact of ACA on access to plasma protein therapies and advocate for access to care. ●

BRENNNA RAINES, *Manager, State Affairs*



U.S.–EU Trade Agreement Prospects:

WILL OPPORTUNITIES FOR THE PLASMA INDUSTRY MATERIALIZE?

BY PAUL ROSENTHAL

Negotiations have been underway, for about a year, on a trade deal that some are calling one of the most significant events of the new century.

The proposed agreement between the United States and the European Union (EU)—known as the Trans-Atlantic Trade and Investment Partnership, or TTIP—would create a trade zone worth nearly \$34 trillion in GDP, covering virtually every aspect of trade for every industry. Opportunities for the global plasma industry and other regulated industries are significant. With exiting tariffs relatively low, key anticipated gains are regulatory harmonization and reduced non-tariff barriers.

For plasma fractionators, collectors and patient groups, TTIP presents an opportunity to promote U.S. and European Commission (EC) regulatory compatibility in the biopharmaceutical sector by eliminating inefficiencies and expediting access to new, innovative and life-saving plasma therapies. Numerous plasma industry-related issues could be addressed through TTIP, including: mutual recognition of the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) inspection findings; harmonization of clinical trial data results and regulatory guidelines for therapeutic areas; protection of confidential commercial information from inappropriate disclosure; and the development of medicine approval and reimbursement policies using transparent, science-based procedures. TTIP may also provide a forum to address industry concerns with prohibitions on compensated donation and self-sufficiency policies.

Many of these issues have been flagged for U.S. negotiators, but progress has been slow. Despite an ambitious intent

to complete negotiations within 18 months, many gaps on granular issues like these remain. In fact, there has been no agreement on the structure of regulatory negotiations, and the proposed frameworks are at odds. The U.S. favors a horizontal approach that cuts across multiple sectors, and wants the EU to make its rulemaking process more like the notice-and-comment procedure under U.S. law. The EU, however, prefers reviewing specific regulatory issues sector-by-sector. Whatever the ultimate approach, the nut-and-bolt discussions will be tough. Many of these issues are controversial, and the level of ambition and support from high-level officials will drive the results.

Procedural and substantive obstacles aside, domestic politics may also hinder progress this year. There are mid-term elections in the U.S., and trade has been an extremely difficult and divisive issue for Democrats. The EU also has parliamentary elections, and the present EC's term ends this fall. Progress is further complicated with U.S. resources devoted to closing-out another major trade agreement, the Trans Pacific Partnership.

However, not all news is discouraging. The silver lining counter-weight is what is at stake if TTIP fails. The global economic forces that prompted the agreement have not changed. The EU economy must grow, and the U.S. needs to increase jobs. Both sides face serious competition from the BRIC countries—Brazil, Russia, India and China—incentivizing stronger economic ties. Russia's aggression in Crimea provides a geopolitical reason to bolster the Trans-Atlantic relationship, and may invigorate talks. Most importantly, TTIP presents an opportunity—perhaps the only one—for the U.S. and EU to define the high-standard rules of trade they expect of everyone else. As long as pressure from these greater dynamics continues, real opportunities exist for PPTA members and their patients to benefit from TTIP. ●

PAUL ROSENTHAL, PPTA General Counsel and Partner,
Kelly Drye & Warren, LLP



Procleix

Procleix Solutions | SETTING NEW STANDARDS IN SAFETY & OPERATIONAL EFFICIENCY

Procleix NAT Solutions

By Hologic and Grifols

Innovative solutions to increase lab efficiency

In today's evolving NAT landscape, labs need versatile and efficient screening solutions to deliver safe blood for patients. Procleix NAT Solutions offer comprehensive blood and plasma screening products to help you achieve the highest levels of safety and operational efficiency.

Grifols (formerly Novartis Diagnostics) is proud to support you with advanced automation and a range of new products in development. Learn more about the Procleix NAT solution that's right for your laboratory by contacting your representative or visit us at www.novartisdiagnostics.com.

GRIFOLS

Copyright © 2014 Grifols Diagnostic Solutions Inc. Procleix is a trademark of Grifols Diagnostic Solutions Inc. Product approval and availability varies based on jurisdiction. For a complete list, visit www.novartisdiagnostics.com/approvals.

Pathogen Safety: AN UPDATE

BY ILKA VON HOEGEN

At the recent International Plasma Protein Congress (IPPC) in Vienna, Thomas R. Kreil, Chairman of PPTA's Pathogen Safety Steering Committee (PSSC), provided an update on current issues pertaining to pathogen safety of plasma protein therapies.



Plasma protein therapies exhibit an excellent safety record for lipid-enveloped viruses such as HIV, HCV and HBV, yet newly discovered agents and/or known agents spreading through the “global village” still raise stakeholders’ concern about the safety of these therapies.

Chikungunya (CHIKV) virus (in Makonde language “that which bends up”), is a lipid-enveloped arthropod borne virus, which is transmitted to humans by mosquito bites. Infection with the virus causes fever, rash and arthralgia or arthritis affecting multiple joints. The pain in the joints can persist for several months and even years. After large epidemics in the French overseas and then India, CHIKV has recently begun to emerge on the islands of the Lesser Antilles, with many thousand confirmed cases. In view of the relatively close proximity to the U.S., e.g. Florida, and travel frequency between the Islands and the U.S. mainland, a CHIKV epidemic in the U.S. in the foreseeable future is entirely possible. While CHIKV is of potential concern for the safety of blood products for transfusion, the robust virus reduction capacity, as built into modern fractionation technologies, has already been verified for their capability to inactivate CHIKV¹. Based on the lessons learned from West Nile Virus (WNV), another arthropod borne virus of the same family, that emerged in the U.S. a decade ago, manufacturers were quick to assess this new potential threat, thus getting ahead of the curve in reassuring stakeholders that the virus does not pose a threat to the safety of plasma protein therapies.

Hepatitis E virus (HEV) is a non-enveloped virus, first described in India in 1980. Since 1980, there has been an increasing awareness of the rather wide distribution of HEV, with seroprevalence rates of up to 50 percent in certain geographies. The incidence of viremia in blood and plasma-donors was, by comparison, found to be only in the range of 1 in a few thousand. It is reassuring that direct testing of plasma protein therapies has so far produced negative results, since any investigation of the capacity of established virus reduction methods has been hampered by the exceedingly complex virology of HEV. Despite very significant efforts even using fully recombinant virus systems, data on HEV reduction remain rather scarce. Manufacturers are thus also applying the model virus concept, to understand the behavior of HEV during virus reduction.

Since the introduction of Nucleic Acid Test (NAT) for virus screening of blood and plasma, molecular diagnostics have made a quantum leap forward. Multiplex NAT, microarrays, and next generation sequencing (NGS) form part of the established tools to investigate the presence of a wide variety of viruses.

NGS is a particularly promising technology for use in virus discovery; but interpretation of findings remains challenging, as exemplified by, for example, the initially claimed association between Xenotropic murine leukemia virus-related virus and the occurrence of chronic fatigue or prostate cancer, which was later determined to be an error.

For routine testing in the manufacturing process of plasma protein therapies, the deployment of multiplex NAT has established a very effective state of the art for testing for HIV, HBV, HCV, B19V and HAV, to support the very significant safety margins afforded by the virus reduction capacity of modern manufacturing processes.

Finally, Dr. Kreil provided a comparison of the safety profile of labile blood products for transfusion versus plasma protein therapies, which highlighted their dependence on very different safety interventions. While for labile blood products, donor selection and donation testing are the only measures generally available to enhance product safety margins, the very potent virus reduction techniques universally implemented into the manufacturing processes of plasma protein therapies provide for dependable safety margins that are then complemented by donor selection and donation testing approaches. ●

ILKA VON HOEGEN, Senior Director, Quality & Safety

¹ Leydold et al., Transfusion [2012] 52: 2122



IPOPI Global Study on PID Patients Needs and Outlooks

The International Patient Organisation for Primary Immunodeficiencies (IPOPI) recently published the results of its first global study demonstrating the importance of providing access to different treatment options and modes of administration to ensure individual patient needs are best met.

The study, "Improving current immunoglobulin therapy for patients with primary immunodeficiency: quality of life and treatment views" was published in the May 2nd edition of the *Journal of Patient Preference and Adherence*.

The purpose of this study was to understand how existing PID therapies affect patient lives and to identify desired improvements to immunoglobulin treatments. "One of the objectives of IPOPI is to stimulate global efforts to improve awareness, diagnosis, treatment and quality of life of people with primary immunodeficiencies (PID)," said Jose Drabwell, Chair of IPOPI Board. "The survey highlights the importance of providing access to different treatment options and routes of administration to ensure individual patient needs are best met. Patient and physician choice of treatment is a key priority for our patients' community."

A total of 300 responded to the survey (72 percent patients with PID and 28 percent caregivers) from across 21 countries. The survey's main results found that most respondents (76 percent) were satisfied with current treatment, reflecting the benefits that Ig therapy provides to patient health and well-being. However, patients remained below physical and mental well-being norms for Health Related Quality of Life (HRQoL) determined by the questionnaire. All respondents expressed the desire for a 4-weekly infusion, the ability to administer at home, self-administration, shorter administration duration and fewer needle sticks.

"IPOPI's global survey provides a clear confirmation that immunoglobulin replacement therapy enables PID patients to lead active and productive lives and improves quality of life significantly," said Dr. Teresa Español, Immunology Unit, Vall d'Hebron University Hospital, Barcelona, Spain. "66 percent of intravenous immunoglobulin replacement therapy (IVIg) respondents and 69 percent of subcutaneous immunoglobulin (SCIg) respondents reported missing 10 or fewer work/school days due to ill health during the past six months. 35 percent of IVIg respondents and 37 percent of SCIg respondents reported zero absences, a clear improvement compared to their health status before IG therapy was commenced."

"IPOPI would like to focus on HRQoL in the future and looks forward to continue its recently started collaboration with Professor Farrugia on this important topic," said Johan Prevot, IPOPI's Executive Director. ●

This survey questionnaire was conducted online and made available through IPOPI to patients with PID and their caregivers from April 2011 to October 2011. It focused patients' current treatment, satisfaction, living with PID and patient preferences using a conjoint approach (a research technique for eliciting and quantifying preferences). The study was funded by Baxter Healthcare SA.

The article is freely accessible online: <http://www.dovepress.com/improving-current-immunoglobulin-therapy-for-patients-with-primary-imm-peer-reviewed-article-PPA>

About IPOPI: www.ipopi.org



Inside PPTA



● Vienna hosts the 20th Annual International Plasma Protein Congress

BY MICHELLE KRECZ

Rich with music and art culture, Austria also has a successful history of source plasma collection and manufacturing. So it was only fitting the 20th annual International Plasma Protein Congress (IPPC) was held in Vienna, March 11-12, 2014. Over 300 physicians, scientists, policymakers, industry leaders and patient advocacy group representatives from around the world gathered to discuss a broad range of topics pertaining to plasma protein therapeutics.

Dr. Paolo Marcucci, President and CEO of Kedrion SpA, presented the keynote address on Patient Centeredness in the plasma protein therapeutics (PPT) industry. He stressed that the health of the patient is a top priority of the PPT industry, and advocated for patient involvement on all levels. The current discussions on prohibiting compensated plasma donation and encouraging self-sufficiency were touched upon,

reiterating that these concepts are not useful, are not realistic and do not consider the impact on the patients that receive plasma protein therapies. The theme of patient centeredness was echoed throughout the two days.

Following the keynote address, there was an update concerning the EU Blood Directive Developments, specifically highlighting the gray areas of voluntary unpaid donations (VUDs) and self-sufficiency between The Blood Directive (EU Directive 2002/98) and The Pharma Code (EU Directive 2001/83). The boundaries and interactions of both Directives are not clear, and the differences between blood for transfusion and plasma for fractionation are not sufficiently understood by policymakers. Discussions following the presentations voiced concern that this could impact patient access to therapy in general.

Over 300 physicians, scientists, policymakers, industry leaders and patient advocacy group representatives from around the world gathered to discuss a broad range of topics pertaining to plasma protein therapeutics.

Professor Dr. Reinhard Schneppenheim and Professor Dr. Ulrich Budde were awarded the Association's Hilfenhaus Award for their outstanding work in the field of primary hemostasis and von Willebrand disease (vWD). Their work has resulted in a new classification for vWD with implications for diagnostic and therapeutic approaches for both children and adults with von Willebrand Syndrome (vWS).

Following sessions looked at clinical developments, specifically on immunoglobulins and hyperimmunoglobulins, as well as Orphan Drug Regulation. Hyperimmunoglobulins are proving effective in treating severe and often life-threatening conditions and are effective for prophylaxis in chronic patients. A specific production pattern has to be followed for their production. New long-acting recombinant factor technologies are under evaluation for the treatment of hemophilia. These therapies are, in principle, eligible for Orphan Drug Regulation. While Orphan Drug designation may incentivize companies to develop products where there are no existing products, this designation may lead to market exclusivity and lack of access to alternatives in the case of hemophilia. Early dialogue between payers, manufacturers, regulators and patients is encouraged.

The final session of Day 1 focused on aspects of plasma and plasma donation. Presentations on EU regulations and pathogen safety illustrated the synergy of regulatory oversight and measures to ensure a high margin of safety of plasma for fractionation and the final therapies manufactured thereof. Discussions about donor compensation highlighted the ongoing debate regarding voluntary non-remunerated donation (VUD) with altruism being touted as the number one motivation that should exist for donors. Two presentations reasoned that compensation does not affect safety nor does compensation presume that donations are non-voluntary and not based on altruistic motivation.

Professor Schneppenheim and Professor Budde Honored with Hilfenhaus Award



Jan M. Bult and Professor Dr. Ulrich Budde

Each year, PPTA recognizes outstanding contributions to the provision of plasma protein therapies with its prestigious Hilfenhaus Award. The Hilfenhaus has been awarded since 1998. It is named in honor of Dr. Joachim Hilfenhaus, a well-respected virologist who worked for Behringwerke in Marburg and was the first Chairman of the Industry Experts Working Group on viral safety.

Professor Dr. Reinhard Schneppenheim, MD, PhD, Professor of Pediatrics; and Head of Klinik und Poliklinik for Pediatric Hematology and Oncology at the University Medical Center Hamburg and Professor Dr. Ulrich Budde, Doctor of Hemostasis, Hamburg were presented with the award during the 20th annual International Plasma Protein Congress (IPPC) held in Vienna, Austria.

Prof. Schneppenheim and Prof. Budde have done outstanding work in the field of primary hemostasis and von Willebrand disease (vWD). Their lifelong dedication to vWD has resulted in creating principles of care for the diagnosis and treatment of von Willebrand syndrome (vWS). Their work has focused on the phenotypic and molecular diagnostic of VWD and the importance of characterizing the von Willebrand Factor. The laboratory of Prof. Budde is the reference laboratory in several international studies because he has established the technique to investigate this multidomain and multifunctional protein.

Their work has resulted in a new classification for vWD with implications for diagnostic and therapeutic approaches for both children and adults with vWS.

The award was presented by PPTA President and CEO, Jan M. Bult, who congratulated the experts for their outstanding work that benefits so many patients around the world.

"Vienna hosts the 20th Annual International Plasma Protein Congress" continued...



Dr. Paulo Marcucci, PPTA's Chairman of the Board, gives the keynote address.



Amanda Bok, CEO, European Haemophilia Consortium (EHC) gives the patient perspective.



Dr. Ranjeet Ajmani, CEO, PlasmaGen BioSciences Pvt Ltd, discusses plasma fractionation in India.

Day 2 opened with presentations on manufacturing, focusing on the development of two emerging markets: Latin American and India. Both regions are operating in a recovered plasma model that is hard to regulate and results in a lot of waste. In Latin America, overall plasma protein therapies usage is expected to grow as economies in the region develop and health expenditure increases. While local fractionation capacity is increasing in the major economies of this region, it's not yet sufficient to meet the clinical needs of all countries. In the case of India, one of the fastest developing economies in the world, there is a large contrast between rich and poor and availability of rare disease treatment is scarce for the majority of the population. Sometimes if the diagnosis is a rare disease and the treatment is not available, the doctor is reluctant to officially diagnose the condition. Further issues are a complex and fragmented regulatory system and the exclusion of compensated plasma in 1996. India currently operates on an import model. There are signs of change in India, however, with a five year plan to focus on public health and changes to the Drug and Cosmetics Act, including consideration of plasma and plasma products. The challenge will be to create a technically and financially sustainable model of plasma protein therapies for these developing economies.

Sessions 6 and 7 focused on regulatory and reimbursement issues. Pharmacovigilance and global harmonization were discussed, stressing the importance of communication, at all levels, to improve reporting on adverse reactions and maintaining supply chain security. The European Medicines Agency (EMA) Product Supply Shortages Initiative discussion emphasized the detrimental impact of product shortages on patients and outlined the EMA implementation plan to mitigate future shortages should they arise. The two main objectives are to provide a framework for assessment and raise awareness. Key action points are to develop international co-operation to foster sharing information, to work closely with stakeholders and to promote better and proactive risk management by Marketing Authorization Holders (MAHs). PPTA has recently launched the European Data Program, a voluntary manufacturer initiative to provide a reliable, country-by-country assessment of the availability of life-saving therapies. The reimbursement session focused on the necessary involvement of patients in the evaluation process and access of drugs and therapies. Several ideas and possibilities for including the patient's voice were proposed and discussed to achieve this objective.

According to the post event survey, the sessions and debates brought a lot of very useful information. The participants left Vienna after two full days focused on the improvement of patient access to plasma protein therapies around the world. ●

MICHELLE KRECZ, *Senior Manager, Communications*

● Association to hold 2nd Annual International Plasma Awareness Week

BY MICHELLE KRECZ

PPTA is pleased to announce the second annual International Plasma Awareness Week (IPAW) to be celebrated October 12-18, 2014. The Association and its member companies are planning activities and events designed to:

- » Raise awareness about source plasma collection
- » Celebrate and recognize the contributions of plasma donors
- » Expand knowledge about plasma protein therapies and rare diseases

Capitalizing on the success of last year, PPTA is organizing new material for promotion, as well as preparing continuing activities from last year, including press releases, events and securing state proclamations.

The event will be highlighted at the International Plasma Protein Congress (IPPC), the Plasma Protein Forum (PPF) and via Association publications, websites and communications. Member companies are actively planning events including donor appreciation celebrations at plasma collection centers, open houses and tours for patients, community leaders and the media, as well as, internal company communications and activities. Both the Source Industry Profile Committee (SIPC) and the Global Communications Steering Committee (GCSC) are responsible for planning and executing company events and promotions.

All are welcome to participate and take advantage of tool kit resources to plan events or promote the week. The online tool kit may be found at: www.pptaglobal.org/meetings-events/international-plasma-awareness-week/media-center. More resources will be added as they become available.

We are in the early stages of developing the new materials and more updates will be forthcoming. Together we are bound by a common goal—to save and improve lives. IPAW serves as a catalyst for sharing that mission and our many contributions to helping patients throughout the world. ●

MICHELLE KRECZ, *Senior Manager, Communications*



● The European Plasma Collectors Committee Welcomes New Chairman Dr. Stephan Walsemann

BY ALEXA WETZEL



The European Plasma Collectors Committee (EPCC) is pleased to announce that Dr. Stephan Walsemann, Managing Director of KEDPlasma Germany, has been appointed as its new Chairman.

Dr. Walsemann is succeeding Dr. Gerold Zerlauth, Director Plasma Sourcing Europe of Baxter AG, who retired in late 2013. The EPCC welcomed the new chairman and thanked Dr. Zerlauth for the outstanding leadership and valuable contributions over the past years.

“As a longtime member of the EPCC, I’ve seen the impressive work that’s been done by PPTA and its members,” said Walsemann. “I look forward to building upon EPCC’s successes as we continue to strengthen the role of the EPCC as a stakeholder and to promote plasma collection in the EU Member States.”

EPCC was founded in 2001 to advocate for plasma collection in Europe to foster patients’ access to plasma derived medicinal products. The role of the EPCC is to provide input to EU and national regulatory authorities and policy makers and to improve the landscape for plasma collection in Europe. At the time of its foundation, plasma collection took place predominantly in Germany and Austria. Today, EPCC members are also engaged in the collecting of plasma for further manufacturing in the Czech Republic and Hungary.

Source plasma donation is an important activity that contributes to saving lives. For many with rare diseases, plasma derived medicinal products are the only therapies available to treat these chronic conditions. Unfortunately, diagnosis and treatment is still suboptimal in many EU Member States and many patients have no or limited access to plasma protein therapies. Therefore, it is important to raise the awareness of stakeholders that more plasma for fractionation is needed to mitigate the current limitations. ●

ALEXA WETZEL, *Manager, Source Europe*

MEET THE PPTA Staff

Mary Gustafson

VICE PRESIDENT,
GLOBAL REGULATORY POLICY



Q How long have you served at PPTA?

11 years

Q What do you focus on in your role as Vice President, Global Regulatory Policy?

Plasma protein therapies and its starting material, source plasma, are highly regulated in the U.S., Europe and in other regions of the world. We are a global industry, so working with our member companies and regulators around the world to make sure regulatory policies are rational and harmonized as much as possible is the primary focus of the PPTA regulatory department.

Q Tell us about your background.

I kind of grew up in the blood business. I started working in a hospital laboratory when I was 15. I became a medical technologist after college, earned a master's degree in immunohematology and became a blood bank specialist. I worked in clinical blood banking and was the technical supervisor at the National Institutes of Health Clinical Center Blood Bank (now the Division of Transfusion Medicine). While there, I entered the Commissioned Corp of the Public Health Service (PHS). I continued my public service career at the Food and Drug Administration (FDA), advancing to the rank of Captain (O-6), PHS. While at FDA, I worked some in sterile drug compliance, but the bulk of my career was regulating, both in licensing and compliance, the blood and plasma protein industries. When I left in 2000, I was the Director, Division of Blood Applications, in the Center for Biologics Evaluation and Research (CBER). Before coming to PPTA, I worked in regulatory affairs at Nabi Biopharmaceuticals.

“We work well together and with our regulatory steering committees and other committees. Each day is challenging and fun! Our work is never boring.”

Q What is your proudest professional achievement?

It is hard to pick one thing over the course of a career. I have been blessed with wonderful career opportunities. Last year, I was given a Distinguished Alumni Award by the FDA. It was nice to be remembered fondly after being gone for over a decade and being in a position now where I am sometimes at odds with them over practices, policies and regulations.

Q What is most rewarding about working in this industry?

It is always good to know that you are working in an area that impacts people's lives in a positive way. Meeting and working for a common goal with advocates for the patients we serve is noteworthy. Also, I have had the privilege to get to know and work with many industry and regulatory people worldwide. Within our regulatory department (Ilka von Hoegen, Mary Clare Kimber and Michelle Mason), we work well together and with our regulatory steering committees and other committees. Each day is challenging and fun! Our work is never boring. ●

GLOSSARY OF TERMS

ACA	AFFORDABLE CARE ACT
AGES	AUSTRIAN AGENCY FOR HEALTH & FOOD SAFETY
CBER	CENTER FOR BIOLOGICS EVALUATION AND RESEARCH
CHIKV	CHIKUNGUNYA VIRUS
CHIP	CHILDREN'S HEALTH INSURANCE PROGRAM
CMS	CENTERS FOR MEDICARE & MEDICAID SERVICES
EBM	EVIDENCE BASED MEDICINE
EMA	EUROPEAN MEDICINES AGENCY
EPPC	EUROPEAN PLASMA COLLECTORS COMMITTEE
EU	EUROPEAN UNION
FDA	FOOD AND DRUG ADMINISTRATION
FY	FISCAL YEAR
GCSC	GLOBAL COMMUNICATIONS STEERING COMMITTEE
HAV	HEPATITIS A VIRUS
HBV	HEPATITIS B VIRUS
HCV	HEPATITIS C VIRUS
HEV	HEPATITIS E VIRUS
HIV	HUMAN IMMUNODEFICIENCY VIRUS
HRQOL	HEALTH RELATED QUALITY OF LIFE
IDF	IMMUNE DEFICIENCY FOUNDATION
IPAW	INTERNATIONAL PLASMA AWARENESS WEEK

IPOPI	INTERNATIONAL PATIENT ORGANISATION FOR PRIMARY IMMUNODEFICIENCIES
IPPC	INTERNATIONAL PLASMA PROTEIN CONGRESS
IVIG	INTRAVENOUS IMMUNOGLOBULIN
MAHS	MARKETING AUTHORIZATION HOLDERS
MODDERN	MODERNIZING OUR DRUG AND DIAGNOSTICS EVALUATION AND REGULATORY NETWORK
NGS	NEXT GENERATION SEQUENCING
NAT	NUCLEIC ACID TEST
NIH	NATIONAL INSTITUTES OF HEALTH
OOPD	OFFICE OF ORPHAN PRODUCT DEVELOPMENT
PEI	PAUL-EHRlich-INSTITUT
PHS	PUBLIC HEALTH SERVICE
PI	PRIMARY IMMUNODEFICIENCY DISEASE
PIDD	PRIMARY IMMUNE DEFICIENCY DISEASE
PPF	PLASMA PROTEIN FORUM
PSSC	PATHOGEN SAFETY STEERING COMMITTEE
RCT	RANDOMIZED CLINICAL TRIAL
SCIG	SUBCUTANEOUS IMMUNOGLOBULIN
SIPC	SOURCE INDUSTRY PROFILE COMMITTEE
VUD	VOLUNTARY UNPAID DONATIONS
VWD	VON WILLEBRAND DISEASE
VWS	VON WILLEBRAND SYNDROME
WNV	WEST NILE VIRUS



Philadelphia, Pennsylvania

Upcoming Events

CONFERENCES & SYMPOSIUMS

June

- 27 6th edition of the Anti-Thrombosis Masterclass
Vilnius, Lithuania

July

- 1-2 3rd Annual Bioplasma World Asia 2014
Singapore

- 30- 7th African Society for Blood

- Aug 2 Transfusion Congress/SATS Congress
Victoria Falls, Zimbabwe

August

- 21-24 43rd Annual Scientific Meeting of Society for Hematology and Stem Cells
Montreal, Canada

September

- 7-8 2013 East Asia Hemophilia Forum
Seoul, South Korea

- 9-12 47th Annual Congress of the German Society for Transfusion Medicine and Immunohematology
Dresden, Germany

- 10-12 47th Nordic Coagulation Meeting
Visby, Sweden

- 18-20 66th Annual Meeting of the National Hemophilia Foundation
Washington, DC

- 23-24 IPFA/BCA Global Symposium on the Future for Blood and Plasma Donations
Sacramento, California

October

- 3-5 8th Bari International Conference
Bari, Italy

- 3-5 European Haemophilia Consortium (ECH) Annual Conference
Belfast, Northern Ireland

- 12-18 **International Plasma Awareness Week (IPAW)**

- 25-28 AABB Annual Meeting
Philadelphia, Pennsylvania

- 26 **PPTA Business Forum (PPTA Members Only)**
Philadelphia, Pennsylvania

- 27-31 Haemophilia Academy 2014
Edinburgh, Scotland, United Kingdom

- 29- IPOPI/INGID/ESID Biennial Meeting

- Nov 1 *Prague, Czech Republic*

November

- 11-12 IPFA Workshop on Plasma for Fractionation, Asia Pacific
Taipei, Taiwan

- 12-14 5th Annual World Orphan Drug Congress Europe 2014
Brussels, Belgium

December

- 6-9 American Society for Hematology 56th Annual Meeting

March 2015

- 10-11 **International Plasma Protein Congress (IPPC)**
Rome, Italy



QUALTEXSM
LABORATORIES

Your Testing Service SolutionSM

QUALTEXSM
LABORATORIES

Our Mission

QualTex Laboratories is dedicated to supporting global public safety with the timely delivery of high quality testing services for patients, donors, and regulated biological products.

Services Provided

- Infectious Disease Testing
- Nucleic Acid Testing
- Immunohematology Reference Lab
- Microbiology Testing
- Specialty Testing

About QualTex

- Customer-centric culture
- Independent not-for-profit laboratory
- Innovative testing solutions
- Multiple laboratory sites
- State-of-the-art technologies
- Supports multiple industries
- 24/7/365 testing schedule
- FDA registered
- EU GMP certificate of compliance
- German Health Ministry certification
- ISO9001:2008 certified
- Active research & development



Power and productivity with touch screen simplicity.

The Aurora™ Plasmapheresis System.



- Intuitive touch screen display
- Easy, accurate data collection, remote procedure setup and paperless documentation with DXT™ Relay
- Designed to improve plasma center efficiency
- A better experience for operators plus an enhanced display for donors

VITAL RESOURCE. TRUSTED PARTNER.

www.fenwalinc.com

Fenwal, Inc.
5/2013 FENWAL, AURORA and DXT are trademarks of Fenwal, Inc.