THE SOURCE

MAGAZINE OF THE PLASMA PROTEIN THERAPEUTICS INDUSTRY

FALL 2012

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INSIDE

FALL 2012

THE MAGAZINE FOR THE PLASMA PROTEIN THERAPEUTICS INDUSTRY

In My View

by Jan M. Bult, President and CEO

LEVEL PLAYING FIELD (*again*)

It was four years ago, in the summer edition of The Source that I wrote for the first time a column with this title. I challenged the situation in The Netherlands where (in my view) the national fractionator (Sanquin) had benefits that were not available to other private sector manufacturers. Sanquin was responsible for the blood collection in The Netherlands (public function) and the manufacture of finished products (private function). I suggested that Sanquin's acquisition price of plasma for fractionation was (too) low because of a high cost allocation to cellular components of blood collection, something that only a hybrid organization can do.

Sanquin did send us a response that we published in our 2008 fall edition. I repeated my request for transparency and fairness in business practices in The Netherlands. Soon after that, the Minister of Health requested an independent investigation in 2009.

In the spring edition of 2010 I reported that the Minister of Health informed the members of Parliament about the results of an international benchmark survey. In this report it was indeed confirmed that prices for blood components were relatively high and that the price for plasma for fractionation was lower than in the investigated countries. The Minister demanded an immediate 12% increase to Sanquin's acquisition price for the plasma for fractionation. He also indicated the need for another study.

That additional study was done by a company called ConQuaestor. This report was published in the summer of 2011 and recently, the Minister of Health gave her comments in a letter to the members of Parliament.

I quote (translated) from her letter: "The internal supply of plasma is exactly on the crossing line of the public and private part of Sanquin. The amount that the private part pays to the public part (this is the so-called internal acquisition price of plasma) is the key point whether Sanquin from a competitive viewpoint is acting correctly with the hybrid character of the organization and governmental involvement."

Later on the Minister states: "I am of the opinion that a calculation based on market price, instead of market value, leads to a better controllable and thus more transparent internal acquisition price. I would like to concur with the conclusion of ConQuestor and take Euro 85, - as the starting point for the internal acquisition price for plasma."

I commend the Minister of Health for initiating these investigations that result in more transparency and an increased level playing field. I am personally of the opinion that it would be much better to completely separate private and public activities, but this outcome is a step in the right direction.

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Binnenhof in The Hague, the House of Representatives of the Netherlands.

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Pharmacovigilance:

A Global View

by Mary Clare Kimber, Ilka von Hoegen, Ph.D. and Mary Gustafson

PHARMACOVIGILANCE is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems [and aims] to:

- improve patient care and safety in relation to the use of medicines and all medical and paramedical interventions,
- improve public health and safety in relation to the use of medicines,
- contribute to the assessment of benefit, harm, effectiveness and risk of medicines, encouraging their safe, rational and more effective (including cost-effective) use ... .[1]

Lifecycle Approach to Patient Safety

PPTA members are committed to ensuring the safety of the medically needed, life-sustaining plasma protein therapies (PPTs) that they manufacture. Patients who suffer from rare and often genetic, chronic, and life-threatening diseases rely on the vigilance of manufacturers. Manufacturers work with policymakers, providers, academics, and other stakeholders throughout the world.

Pharmacovigilance is a vital part of modern healthcare. Legislators have been arming regulators such as the European Medicines Agency (EMA) in the European Union (EU) and the Food and Drug Administration (FDA) in the U.S. with legal tools that allow for continuous monitoring of medicinal products throughout their lifecycle, for events or new information that could have a serious impact on the safety of therapies and public health. For EU legislators, "[p]harmacovigilance rules are necessary for the protection of public health in order to prevent, detect and assess adverse reactions ..., as the full safety profile of medicinal products can only be known after they have been placed on the market."[2] FDA has described a safe product as "one that has acceptable risks, given the magnitude of the benefit expected in a specific population and within the context of alternatives available."[3]

Transparency Rises with Sharing

Adverse event documentation and reporting are not new. There has also been significant investment in the technology and infrastructure within healthcare systems to systematically collect patient data from real world settings. While licensed U.S. manufacturers are required by regulation to report to FDA "adverse experiences,"[4] reporting by non-manufacturers such as providers and consumers to either FDA or to manufacturers is voluntary. FDA enters direct and manufacturer reports into the Adverse Event Reporting System (AERS).[5]

However, newer legislation has sought to improve surveillance and make regulators more accountable and transparent by sharing information early. Section 921 of the Food and Drug Administration Amendments Act of 2007 (FDAAA), for example, requires the Secretary of Health and Human Services (and, thus, FDA) to "conduct regular, bi-weekly screening of the AERS database and post a quarterly report on the AERS website of any new safety information or potential signal of a serious risk identified by AERS ... ."[6] These so-called "921 postings" are available online as part of Med Watch: The FDA

[1] World Health Organization, The Importance of Pharmacovigilance: Safety Monitoring of medicinal products (2002) at 7-8 (emphasis added), available at http://apps.who.int/medicinedocs/pdf/s4893e/s4893e.pdf.

[2] Official Journal of the European Union (OJ) L 348, 31.12.2010, p. 74.

[3] FDA, The Sentinel Initiative: National Strategy for Monitoring Medical Product Safety (May 2008) at 5, available at http://www.fda.gov/downloads/Safety/FDAsSentinelInitiative/UCM124701.pdf.

[4] 21 CFR 600.80(c) (biologics); 21 CFR 314.80(c) (drugs).

[5] http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Surveillance/AdverseDrugEffects/default.htm.

[6] FDAAA Sec. 921(codified as amended in Federal Food, Drug and Cosmetic Act 505(k), 21 USC 355).

[7] http://www.fda.gov/Safety/MedWatch/default.htm.

Safety Information and Adverse Event Reporting Program.[7] This recent increase in availability of pharmacovigilance information for consumers helps make FDA more transparent.

EMA, together with EU Member States and the European Commission, is introducing pharmacovigilance legislation, passed in December 2010 and effective since July 2012, that represents the biggest change to the legal framework since the establishment of EMA in 1995. The new legislation, Regulation (EU) 1235/2010 and Directive 2010/84/EU, centralizes pharmacovigilance for the EU, rather than by Member States, and creates a Pharmacovigilance Risk Assessment Committee (PRAC) to perform most of EMA's pharmacovigilance work, such as advising the Committee for Medicinal Products for Human Use (CHMP) and other former responsibilities of the Pharmacovigilance Working Party.

Launched and run by EMA since December 2001, EudraVigilance is a system for industry and Member States to report suspected cases of adverse reactions to a medicine.[8] Under the new pharmacovigilance legislation, marketing authorization holders, following a successful audit, now submit reports of suspected cases of adverse reactions to a medicine only into EudraVigilance whereas, previously, reports went via an individual national competent authority (NCA).

The CHMP analyzes EudraVigilance data every two weeks to one month and may recommend regulatory action by EMA after evaluating the reports. To boost transparency, last May EMA began publishing these data for the public via a new public website, European database of suspected adverse drug reaction reports.[9]

Similarly, the updated EU Regulatory Network Incident Management Plan adopts a more "global" (EU-level) approach to management of "crisis" situations by including medical products authorized through not only national procedures but also mutual recognition and decentralized licensing routes.[10] The updated Plan applies to events or new information including pharmacovigilance issues (e.g. an urgent safety hazard), as well as both safety and quality concerns (e.g. problems of viral contamination with biological products).[11] The Plan also notes Memoranda of Understanding signed by EMA and each NCA on sharing of EudraVigilance data and other safety and pharmacovigilance-related documents.[12]

Regulators from around the world have joined FDA and EMA to become more transparent through increased sharing of pharmacovigilance information with consumers. For over 20 years, Health Canada (HC)'s Canadian Adverse Reaction Newsletter (CARN) has provided patients, providers, industry, and other stakeholders with information on "serious or unexpected side effects or adverse reactions suspected of being associated with drugs ...."[13] CARN points to potential safety signals detected by review of reports submitted to the Canada Vigilance Program before comprehensive benefit-risk evaluations and regulatory decisions are undertaken. The Expert Advisory Committee on the Vigilance of Health Products (EAC-VHP) will discuss possible areas of improvement with regards to the openness and transparency of the Canada Vigilance Program during the EAC-VHP's October 25-26 meeting in Ottawa, Ontario.[14]

Just this year, Brazil's National Health Surveillance Agency (Anvisa) published its first Pharmacovigilance Newsletter, which presented Brazil's pharmacovigilance history, examples of drugs withdrawn from the market due to adverse events, and definitions of basic concepts. The Newsletter will publish quarterly overviews of adverse event notifications in the National Health Surveillance Reporting System (Notivisa) (2008-2011) and the latest notes on drug safety.[15]

Surveillance Increases

Legislators around the world have sought not only to improve surveillance but also to increase its scope. In response largely to FDAAA Sec. 905, in May 2008 FDA launched the *Sentinel Initiative*. FDA's goal is to create a national, integrated, electronic *Sentinel System* that augments its current capability to monitor product safety by enabling access to multiple, existing, distributed data systems quickly and securely for relevant, de-identified data (so-called "active surveillance").

FDAAA points to both Federal (e.g. Medicare program, Department of Veterans Affairs) and private (e.g. pharmaceutical purchases, health insurance claims) data sources for *Sentinel*.[16] The legislation set goals of 25 and 100 million patients in the system by July 1, 2010 and 2012, respectively.[17] FDA's pilot *Mini-Sentinel* exceeded 100 million patients ahead of schedule (December 2011) and, as of July 2012, has secure access to data on approximately 126 million patients nationwide from 17 partners.[18]

Patients Benefit from Increased Transparency and Surveillance

As PPTs are used around the world, so too must effective pharmacovigilance policy be worldwide. PPTA recognizes U.S. level and EU level efforts of decision-makers to harmonize pharmacovigilance policy, the success of which is a prerequisite to international harmonization. For FDA, *Sentinel* joins AERS, academia, U.S. and ex-U.S. post market experience, and other tools in its post-approval safety "tool box." EMA, for its part,

not only works with FDA on signal-detection activities but also informs the World Health Organization (WHO) of any measures taken regarding centrally authorized medicines that may bear on public health outside of the EU.

Other efforts to harmonize international pharmacovigilance policy also are underway. Relevant International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) Guidelines (implemented by FDA, EMA, and the Japanese Ministry of Health, Labour and Welfare) include E2D (Post-approval Safety Data Management: Definitions and Standards for Expedited Reporting)[19] and E2E (Pharmacovigilance Planning).[20]

Two International Standards Development Organizations, the Health Level Seven International (HL7) and the International Organization for Standardization (ISO), also develop pharmacovigilance policy independently as well as collaboratively. The two Organizations, for example, recently published ISO/HL7 27953 Health informatics – Individual case safety reports (ICSRs) in pharmacovigilance.[21]

New recommendations Sharpen U.S. Regulators' Focus

An August 22, the New England Journal of Medicine article has recommended "the appointment of an independent ethics advisory board [that] would strengthen the decision making of the FDA as it confronts emerging ethical challenges — both those arising from required postmarketing trials and those stemming from powerful new drug surveillance systems, such as the FDA's Sentinel Initiative."[22] The authors also co-chaired an Institute of Medicine (IOM) committee formed, at FDA's request, to evaluate the Ethical and Scientific Issues in Studying the Safety of Approved Drugs post-FDAAA.[23] The May 1/ IOM report recommended that:

> *FDA require and maintain a comprehensive benefit and risk assessment and management plan (BRAMP) to track [a] medicine's benefits and harms during its entire life cycle. The BRAMP should be a living document that is publicly available and easy to understand. Working with relevant stakeholders, including drug manufacturers, the FDA should review and update the BRAMP document at both prespecified times and whenever it reevaluates the drug's benefit-risk profile.*[24]

The evolution of the pharmacovigilance laws around the world is serving to increase the surveillance of medicines and treatments, including PPTs, and to create more transparency for patients and others. PPTA continues to engage regulators from FDA, as it moves beyond *Mini-Sentinel* and into full implementation of FDAAA; and from EMA, as it works to finalize modules and otherwise complete its implementation the EU's new pharmacovigilance legislation.

While EMA's most recent efforts focus largely on applicants and holders of marketing authorizations, and FDA's on non-manufacturer data sources, both methods increase transparency and are means to the end of patient safety. This common goal should inspire a continued willingness by international regulators to engage each other and to seek actively ways to harmonize pharmacovigilance policy for medicines, such as life-saving PPTs.

Mary Gustafson, *Vice President, Global Regulatory Policy*
Ilka von Hoegen, Ph,D., *Senior Director, Quality and Safety*
Mary Clare Kimber, *Manager, Regulatory Policy*

[8] http://eudravigilance.ema.europa.eu/highres.htm.

[9] http://www.adrreports.eu/index.html.

[10] Crisis Management Plan Regarding Centrally Authorised Products for Human Use (Doc. Ref. CPMP/388/97) at 1, available at http://www.ema.europa.eu/docs/en_GB/document_library/Other/2012/07/WC500130379.pdf.

[11] Id. at 3.

[12] Id. at 2.

[13] http://www.hc-sc.gc.ca/dhp-mps/medeff/bulletin/index-eng.php.

[14] http://www.hc-sc.gc.ca/dhp-mps/medeff/advise-consult/eacvhp-ccevps/index-eng.php.

[15] http://www.anvisa.gov.br.

[16] FDAAA Sec. 905(a)(3)(B)(ii).

[17] FDAAA Sec. 905(a)(3)(C)(i)(III).

[18] http://blogs.fda.gov/fdavoice/index.php/tag/mini-sentinel/.

[19] http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E2D/Step4/E2D_Guideline.pdf.

[20] http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E2E/Step4/E2E_Guideline.pdf.

[21] 1:2011 (Part 1: Framework for adverse event reporting); 2:2011 (Part 2: Human pharmaceutical reporting requirements for ICSR).

[22] Mello MM, Goodman SN, Faden RR. Ethical Considerations in Studying Drug Safety — The Institute of Medicine Report. Nejm.org. August 22, 2012 (10.1056/NEJMhle1207160), available at http://www.nejm.org/doi/full/10.1056/NEJMhle1207160.

[23] National Research Council. Ethical and Scientific Issues in Studying the Safety of Approved Drugs . Washington, DC: The National Academies Press, 2012 [hereinafter IOM Report], available at http://www.iom.edu/Reports/2012/Ethical-and-Scientific-Issues-in-Studying-the-Safety-of-Approved-Drugs.aspx.

[24] Report Brief, IOM Report at 2, available at http://www.iom.edu/~/media/Files/Report%20Files/2012/Ethical-Issues-Drug-Safety/ethicalapproveddrugs_rb.pdf.

Juan Garcia Burgos

Dr. Juan Garcia Burgos is a welcome voice for patients and other stakeholders at the European Medicines Agency.

Tell us about your background.

I worked as an urologist surgeon at the Gregorio Maranon hospital in Madrid. I joined the European Medicines Agency (EMA) in 2002 as Product Team Leader and have been responsible for the Secretariat of the Efficacy Working Party within the Safety and Efficacy Sector. I assumed new responsibilities in 2005 by joining the Medical Information Sector where I am currently Section Head for Public Information and Stakeholder Networking. I am directly involved in interaction with patients, consumers and healthcare professionals' organizations.

Please describe what consequences the implementation of the EMA Roadmap 2015 will have for plasma protein therapies (PPTs).

The Road Map to 2015 is quite an ambitious and comprehensive document which highlights a number of activities. It identifies drivers for progress and change in the coming years for the EMA in three main areas: addressing public health needs, facilitating access to medicines and optimizing safe and rational use of medicines. Most of these apply to all medicinal products and are not really

The Road Map to 2015 is quite an ambitious and comprehensive document which highlights a number of activities. It identifies drivers for progress and change in the coming years for the EMA in three main areas: addressing public health needs, facilitating access to medicines and optimizing safe and rational use of medicines.

Mary Gustafson, Ilka von Hoegen and Juan Garcia Burgos, IPPC 2012.

special for PPT, but of course, there are priority and key activities in each area which have a major impact on PPT.

In the first area, the Road Map foresees activities which are expected to help bridge gaps in medicines development, which is of particular relevance for PPT in the case of rare diseases, where significant investments are foreseen.

In the second area, important activities refer to early and continuous dialogue with all parties during drug development which is of particular importance in the case of scientific advice and protocol assistance for orphan drugs, which is also of relevance for PPT. Preparation of guidelines and streamlining the guideline preparation process with more involvement from stakeholders on prioritisation of guidelines is also an important aspect. Additionally it is foreseen to engage and interact further with health technology assessment (HTA) bodies. We hope to help bridge the gaps between scientific and cost-assessment processes.

How can an overarching consideration of HTAs influence the decision making process on national level?

Sometimes it is not national. It is regional within the same country. I think that our role is very limited here. We don't have the capacity to address these differences. What we have to ensure is that the outcome of our clinical evaluation can be used by everybody to make the best decisions.

The third area which is very important relates to patient safety, where the implementation of the new pharmacovigilance legislation is a key milestone. There are a number of provisions that have a significant impact on PPT. Among others the Committee for Pharmacovigilance and Risk Assessment (PRAC) will evaluate and will give recommendations on the safety of all medicines authorized in the EU, not only centrally authorized, but also non-centrally authorized. This means that there will be a central point for safety evaluation, with more consistent and clear processes, which will result in benefit for the patients. Other provisions will for example improve the process for Risk Management Plans, with specific considerations for PPT.

The new legislation is as well a great opportunity to continue our work to improve transparency and communication. It will open the work in medicine regulation to patients and healthcare professionals, who are more and more involved in the work of the Agency. This is our model for the future when thinking of stakeholder engagement and I believe it is very much in line with what PPTA is doing.

U.S. EGG DONOR CASE CHALLENGES ETHICS-DRIVEN CAP ON DONOR COMPENSATION AS ANTITRUST VIOLATION

BY JOHN DELACOURT

IN APRIL 2011, LINDSAY KAMAKAHI FILED A LAWSUIT, on behalf of herself and all other U.S. women donating eggs for use in fertility treatments, alleging a nation-wide conspiracy to limit donor compensation.

Specifically, Ms. Kamakahi asserted that a reproductive health advocacy group had conspired with leading fertility clinics to cap the amount paid to any individual donor at $10,000. The case – *Kamakahi v. American Society for Reproductive Medicine et al.* – continues to wind its way through the courts. Even at this stage, however, it warrants careful consideration, as there are many strong parallels to the ongoing debate regarding compensated vs. uncompensated plasma donation.

The Egg Donation Process

As with source plasma, it is often necessary to provide human egg donors with compensation for the simple reason that the donation process is time-consuming, requires the off-putting disclosure of personal health information, and may involve physical discomfort. As with source plasma, the process begins with donor screening. The donor must provide a detailed medical and psychological history, which includes answering questions about the use of cigarettes, alcohol, and illegal drugs. A physical examination, including a pelvic exam, is also required, and includes screening for both inherited diseases and sexually transmitted infections. Candidates who successfully complete the screening process undergo a three-week course of hormone injections to stimulate egg production. During this three-week regimen, the donor must make frequent doctor visits, not only to receive the injections but to receive related blood tests and ultrasound examinations for the purpose of tracking egg development. Finally, the eggs are removed from the donor's ovaries via a surgical procedure called transvaginal ovarian aspiration. It may take several days of restricted activity to recover and routine side effects include mood swings, fluid retention, and enlarged ovaries, and the possibility of even more serious adverse reactions.

The Compensation Guidelines

The American Society for Reproductive Medicine (ASRM), while not objecting to donor compensation, in principle, nevertheless felt that it would be appropriate to explore the potential ethical implications of such compensation. ASRM's Ethics Committee was tasked with investigating the issue and, in 2000, issued a report establishing a maximum donor compensation guideline. The Ethics Committee subsequently revisited the issue and, in 2007, issued a follow-up report that remains ASRM's most current position statement on donor compensation. The 2007 report retains the maximum compensation guideline, which specifically states that "Total payments to donors in excess of $5,000 require justification and sums above $10,000 are not appropriate."[1]

Some of the Ethics Committee's justifications will sound familiar to veterans of the compensated vs. uncompensated plasma donation debate. One set of concerns relates to the donors themselves, with the report noting that a desire to address dire financial circumstances might cause some women to discount the "physical and emotional risks" of egg donation.[2] An equally important set of concerns relates to the recipients of the donation (*i.e.*, the infertile couple). As the report notes, they also face a health and safety risk, as "High payments could lead some prospective donors to conceal medical information relevant to their own health of that of their biologic offspring."[3]

Another set of concerns is more novel and unique to the egg donations. The first is an economic fairness concern that excessively high compensation might make the services of egg donors "available only to the very wealthy."[4] While there is some initial appeal to the egalitarian impulse underlying this justification, one wonders why it is solely applicable to donor compensation. Presumably, limiting compensation to fertility clinics would have an even more dramatic impact on access to care, but ASRM has made no such recommendation and it is unlikely that the Society's provider members would

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[1] ASRM Ethics Committee Report, *Financial Compensation of Oocyte Donors*, reprinted in 88 Fertility & Sterility 305, 305 (Aug. 2007) ("Ethics Committee Report").
[2] *Id*. at 306.
[3] *Id*.
[4] *Id*.

The American Society for Reproductive Medicine (ASRM), while not objecting to donor compensation, in principle, nevertheless felt that it would be appropriate to explore the potential ethical implications of such compensation.

support it. A second initially appealing, but similarly flawed, justification is that high payments "could be used to promote the birth of persons with traits deemed socially desirable, which is a form of positive eugenics."[5] While it would be hard to find a supporter of "positive eugenics," it is not clear that couples seeking to create designer babies could not do so at the existing, capped compensation level.

The Donors' Lawsuit

The plaintiffs in the *Kamakahi* case attempt to bridge the gap between ethical guidance and conspiracy by characterizing the ASRM guidelines as an agreement in restraint of trade. Their complaint notes at the outset that, in the U.S., there is no federal law restricting the compensation paid to egg donors. Consequently, with the exception of two outlier states,[6] the only limitation on donor compensation is the ASRM guidelines. As the complaint further notes, these guidelines are not merely aspirational "best practices," but have the force of a widely-accepted industry standard. As a condition of membership in the Society for Assisted Reproductive Technology (SART), an affiliate of ASRM, practitioners must agree to abide by the standards promulgated by ASRM's Ethics Committee, and 85% of U.S. fertility clinics are SART members.

The legal pleadings make for interesting reading despite the fact that, to a large extent, they talk past one another. ASRM's briefs quote extensively from the 2007 Ethics Committee report and insist repeatedly that ethical guidance prepared by medical professionals, for the protection of egg donors and infertile couples, cannot constitute an antitrust violation. In response, the plaintiffs assert that courts

[5] *Id.*

[6] In Indiana, donor compensation is limited to $3,000 per cycle. Ind. Code Ann, § 35-46-5-3(b)(1). In Louisiana, donor compensation is prohibited outright. La. Rev. Stat. Ann. § 9:122.

The Kamakahi case represents a direct challenge to one of the core justifications for bans on donor compensation: that they are necessary to prevent exploitation of the donor.

have repeatedly refused to grant competitive restraints enacted by the "learned professions" special status and, on that point, get the better of the argument. ASRM will also be hard pressed to defend the specific $5,000 and $10,000 caps set forth in the compensation guidelines. These amounts are not pegged to some generalized measure of the value of labor as in some jurisdictions – for example, in the U.K., an egg donor can be paid no more than an individual serving on jury duty (£61.28, or just under $100, per day)[7] – but rather are based on a sperm donor's extrapolated hourly rate of compensation (a calculation that must certainly be eye-opening, but is beyond the scope of this article).[8]

In addition to convincing a court that ASRM's guidelines are more about protecting margins than protecting donors, the plaintiffs primary hurdle will be demonstrating damages. Although no one disputes that the effect of the ASRM guidelines is to cap donor compensation, to an outside observer $10,000 appears to be a rather high cap. However, the Ethics Committee report itself acknowledges the existence of print and Internet advertisements offering donors $50,000 or more.[9] Furthermore, the report clearly indicates that the $5,000 and $10,000 caps were computed, at least in part, using the 2000 rate of compensation to sperm donors,[10] and the caps have not be revised upwards in the ensuing twelve years.

Implications for the Debate on Compensated Plasma Donation

It is clear from even this brief overview that there are significant differences between egg donation and plasma donation. First and foremost, eggs, unlike plasma, are not a renewable tissue, which raises at least some concerns for the egg donor that are not present in the plasma donation context. Also, the egg extraction process, which involves a surgical procedure, is far more invasive, and the compensation paid to egg donors, even at the current, capped level, is an order of magnitude higher than for plasma donation. Nevertheless, the *Kamakahi* case remains relevant to supporters of compensated plasma donation in several important ways:

- **Key Concessions** – Although ASRM's guidelines echo many of the ethical justifications employed by opponents of compensated plasma donation, they also contain some key concessions. For example, they acknowledge that the compensation donors receive is for the time, inconvenience, and discomfort associated with the donation process, not a payment for the eggs themselves. Indeed, they go further, asserting that failing to provide compensation would "arguably demean [donors'] significant contribution."[11] Even more importantly, ASRM maintains that compensated and uncompensated donation can exist side-by-side, stating that "the provision of financial or in-kind benefits does not discourage altruistic motivations."[12]
- **Growing International Divergence –** At this point, the contrast could not be starker. The *Kamakahi* lawsuit does not merely assert that capping the compensation paid to egg donors is a bad idea. If successful, it will establish that, in the U.S., such caps constitute an actionable violation of law potentially triggering millions of dollars in damages. By comparison, in much of the rest of the world, donor compensation is prohibited outright. As ASRM points out in its legal pleadings, such bans are currently the law of the land in Canada, Australia, France, the Netherlands, Belgium, Italy, and Sweden.[13] This divergence seems not only untenable in the long run, but likely to lead to unintended, undesirable consequences. Nations opposing compensated tissue donation, in the event of an increase in demand, may find themselves in the ethically contradictory position of importing needed tissues from nations that permit compensation. The divergence may also exacerbate the growing problem of "medical tourism."
- **A Promising New Source of Support –** Perhaps the most important takeaway, however, is that a growing body of judicial opinions could provide supporters of compensated plasma donation with a new source of authoritative, and highly influential, ammunition. The *Kamakahi* case represents a direct challenge to one of the core justifications for bans on donor compensation: that they are necessary to prevent exploitation of the donor. Just over a year ago, in a case involving whole blood components, the European Court of Justice flatly rejected another core justification: that compensation bans are necessary to ensure the quality and safety of donated tissues.[14] While neither case is directly applicable to plasma donation, both represent important, incremental building blocks for future health policy debates.

John Delacourt, *Senior Director, Legal Affairs*

[7] *Underpaid Ovaries: An Antitrust Suit Is Filed Against America's Fertility Clinics*, The Economist, Apr. 20, 2011.

[8] Ethics Committee Report, *supra* note 1, at 308.

[9] *Id*. at 306.

[10] *Id*. at 308.

[11] *Id*. at 307.

[12] *Id*.

[13] *Defendants' Motion to Dismiss Plaintiffs' Consolidated Amended Complaint* at 16 n.7 (Apr. 26, 2012).

[14] *See* John Delacourt, *European Court of Justice Weighs in on Donor Compensation Debate*, The Source, Summer 2011, at 16.

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Sparring symbols of U.S. political parties— Democrats (donkey) Republicans (elephant)

BY JULIE BIRKOFER

U.S. ELECTION

THE OLYMPICS HAVE ENDED, Republican Presidential candidate, Mitt Romney just announced Paul Ryan, Minnesota Republican Congressman as his pick for Vice President, gas prices have just increased about 15 cents, the national party conventions are just behind us and the final fall push to the November 6 Election Day is looming large. The election will decide if President Obama will have the distinction of being a one-term President or if he will return to fulfill his promises made in 2008 to the American people.

Presidents are often measured by the goals established in their "First 100 Days"; but equally important is what a President has identified as priorities in the last 100 days of his term. Let's take a look at the Obama scorecard:

President Obama's top five priorities in his first 100 days:

- **Middle East.** The President set deadlines for withdrawing troops from Iraq in August 2010 and closing the Guantanamo Bay military prison. (The latter deadline was ultimately abolished indefinitely.)
- **Energy.** The President also made clean energy a top priority, using $7.22 billion of the $800 billion "American Recovery and Reinvestment Act" to fund green programs administered by the Environmental Protection Agency (EPA), and earmarking $129 billion of his $3 trillion budget proposal for similar renewable energy projects.
- **Health Care.** The President focused on expanding health care coverage, supporting the reauthorization of the Children's Health Insurance Program, calling for the establishment of a reserve fund that would have enabled Congress to stabilize Medicare physician payments, including funding within the Reinvestment Act for comparative effectiveness research (this would later be transferred to the Patient-Centered Outcomes Research Institute (PCORI) under the health reform bill (Affordable Care Act – ACA), and increasing federal matching funds for Medicaid to enable states to maintain coverage for low-income families despite increased financial pressure on state budgets.
- **Economy.** Much of the President's first 100 days were spent dealing with the growing economic crisis, and it was in his first 100 days that he bailed out multiple investment banks and in additon, car manufacturers.
- **Addressing education,** the President also increased and expanded eligibility for Pell grants and called for the

elimination of the Federal Family Loan program that subsidizes private lenders and guarantees a 97% repayment rate on student loans, which lowers the cost of loans for students. The loan program has yet to be eliminated.

Notably, we are still seeing many of these issues being batted around today including the burden of student loans, the cost of Medicaid on overdrawn state budgets, and the unstable and expensive Medicare physician payment system or Part B which is where the majority of plasma protein therapies are accessed by Medicare beneficiaries and reimbursed.

A few key milestones certain to mark the last final days leading up to the election:

- **The campaign.** Winning reelection is top priority. The last 100 days represents a full court press by the Obama political machine to defeat the Republican challenger.
- **Jobs and the economy.** The economy is a key driver in this election. The unemployment rate remains high, around 8.3 %. What a difference ten years makes – in January 2001 unemployment was 4% and the unemployment rate remained below 5% for forty consecutive months.

Year Primer

- **Conventions.** Obama's September 6 Democratic National Convention Speech in Charlotte, North Carolina provided the electorate with an opportunity to evaluate the President as a candidate and decide if they want to continue to support him or make a switch. Similarly, Romney's convention speech at the Republic National Convention on August 30 in Tampa, Florida gave insight into his vision for the country.
- **Debate preparation.** There have been occasions in which a Presidential debate has helped to define a campaign. For example Kennedy/Nixon, Ford/Carter and Bush/Dukakis come to mind. Even today, people continue to talk about the first televised debate in 1960 and the contrast between Nixon's appearance, the 5 o'clock shadow contrasted with Kennedy's rested and tan appearance; Ford's bumbling of foreign policy and Dukakis' photo in the military tank. So far, three debates have been announced: Denver, Colorado (10/3/12) will focus on domestic policy, Hempstead, New York (10/16/12) will have a town-hall format and Boca Raton, Florida (10/22/12) will focus on foreign policy.

Once the debates are over, it will be decision time for the American voter. Next year, will be a time for a continuation of this Administration's priorities or it will be a time for a new direction. Only time will tell.

Finally, what will the last 100 days hold for the plasma protein therapeutics industry? The conventional wisdom holds that after the elections, Congress will return to Capitol Hill for what is known as a "lame-duck" session.

During this time several issues pertinent to assuring patient access to plasma protein therapies will be in play. For example, sequestration is looming. What does this mean?

- Under the Balanced Budget and Emergency Deficit Control Act of 1985 (BBEDCA), as amended by the Budget Control Act of 2011 ("BCA"), the November 23, 2011 failure and resultant dissolution of the Joint Select Committee on Deficit Reduction (Super Committee) triggered sequestration of $1.2 trillion over 9 years beginning **January 2, 2013.**
- The total cut to budgets under sequestration is $984 billion or $109.3 billion per year.
- While cuts to Medicare are capped at 2%, sequestration is projected to reduce average sales price (ASP) by approximately 2.4%, down to ASP+3.6%. ASP is the methodology used by the federal government to reimburse Medicare part B physician office setting; it is currently set in statute at ASP +6%. Medicare, always a topic of debate, will be a hot campaign issue, since Republican Vice Presidential candidate, Ryan is the author of a plan before Congress to slow Medicare's growth.
- Additionally, the National Institutes of Health (NIH) is expected to see an approximate 8% ($2.4B) reduction in 2013, with 5.5% reduction every year through 2020, effectively freezing the issuance of new grants from NIH. Likewise, Centers for Disease Control and Prevention (CDC) funding is expected to be cut by an approximate 7.3% ($444M) in 2013, and the Food and Drug Administration (FDA) will see a reduction of $191M.
- The primary concern for plasma protein therapies include: the cuts to ASP and the cuts to CDC funding. Cuts to ASP could affect patient access to all therapies, and cuts to CDC funding could affect the hemophilia blood safety surveillance/tracking project.

In addition, trillions of dollars in expiring tax provisions and spending will be up for negotiation during the lame-duck session of Congress on everything from the scope of tax cuts for the wealthy to deficit reduction and the future of social spending programs, including Medicare and Medicaid could also be considered.

Julie Birkofer, *Senior Vice President, North America*

Health Care Reform

by Kym H. Kilbourne
and Bill Speir

ON JUNE 28, THE UNITED STATES SUPREME COURT surprised almost everyone with its ruling on the Affordable Care Act (ACA) in *National Federation of Independent Business v Sebelius (NFIB)*[1]. In addition to ruling that the individual mandate was a proper exercise of Congress's taxing power, the Court ruled that states could choose not to expand Medicaid as required by the ACA. This means the portion of the ACA that was to provide health benefits to the poorest of the uninsured may not be implemented in all 50 states.

Prior to the Court's ruling, the ACA was expected to provide an estimated 32 million Americans with health benefits, 16 million of whom were adults without dependent children who were expected to become eligible for Medicaid. Now optional in the states, the ACA expanded Medicaid eligibility to include all U.S. citizens and qualified legal aliens with incomes of less than 133% of the federal poverty level ($14,856 for an individual). As a result of the Court's ruling, these 16 million individuals may not have health care coverage. The Court's ruling found the ACA's required expansion to be coercive on state governments because states faced losing all of their federal Medicaid funds if they did not expand their programs. The Court ruled that individual states can decide if they will implement the Medicaid expansion. If a state agrees to expand its Medicaid program, it will receive the enhanced federal funding and be subject to all requirements associated with the expansion as outlined in the law.

Alabama Governor, Robert Bentley summed up concerns, "We don't know that the state can afford it. We have serious concerns about the increased costs associated with expanding entitlement programs, but we need to understand the larger implications of the ruling as a whole before deciding the best course of action."

States are concerned that expansion, while drawing millions in federal dollars to the state, will cost the states millions of their own funds. Beginning in 2017, states would have to contribute 5% of the cost for benefits provided to those newly eligible, which would increase to 10% in 2020 and subsequent years. States will also incur significant administrative costs to certify, enroll and manage new recipients.

These concerns were voiced at the National Conference of State Legislatures 2012 Legislative Summit in early August. Some states like Maryland and Vermont reported they were moving full steam ahead with implementation, while a number of states such as Oklahoma and Wyoming are waiting until after the elections. Under the law, states can develop their own health insurance exchange or participate in a federal exchange, the details of which are not yet known.

The Court's decision places healthcare reform at the center of election debates. Former Massachusetts Governor, Mitt Romney, the GOP presidential nominee, has pledged to repeal the ACA upon his election as have close to 30 Republican Senatorial candidates. If the election goes as Republicans would like, Governor Romney would have the advantage of his party controlling Congress, potentially allowing for the repeal of the ACA. Yet, neither Republicans nor Democrats will get everything they want on Election Day and that means there are aspects of the law that will likely prove politically and practically difficult to repeal for either party.

Politically, the ACA already has made a tangible impact for many people, including closing the gap for 5.1 million seniors on Medicare, extending the age at which children can stay on their parents' insurance plans to 26, and expanding access to affordable preventive care, a benefit already affecting 54 million people. These benefits of the ACA will likely prove resilient through any repeal process in part because they have already been felt by significant portions of the population. Practically, there are provisions within the law that have been, or are in the process of being implemented, and that makes a wholesale repeal difficult as such action would likely leave gaps in coverage or at the very least gaps in anticipated coverage. Those provisions include the small business tax credit implemented in 2010, the pre-existing condition insurance plans also implemented in 2010, elimination of lifetime insurance caps in 2010, and elimination of annual insurance caps (phasing out between 2010 and 2014).

Aspects of the law that acutely affect the plasma protein therapeutics industry, namely the annual pharmaceutical fee

[1] No. 11-393, slip opinion (U.S. June 28, 2012), available at http://www.supremecourt.gov/opinions/11pdf/11-393c3a2.pdf.

Impacted by Court Decision

and the structure of the orphan drug exclusion as it has been implemented, remain an ongoing concern for many manufacturers of orphan therapies, including PPTA members. The industry has advocated expanding the orphan exclusion from the annual tax to include all therapies solely indicated to treat one or more rare disease, not just those that took the Orphan Drug Act tax credit as is the case in the current law. PPTA and its members have advocated for legislation introduced in the House and the Senate that would modify the orphan drug exclusion from the annual fee, While there is significant understanding in some Congressional offices of how the existing policy is disproportionately harmful to our industry Congress has been wary to make many changes to the politically charged ACA. PPTA will continue to strongly support bipartisan legislation that modifies the orphan drug exclusion from the annual pharmaceutical fee imposed under the ACA. The goal is to have this legislation included as part of a larger legislative package that is considered during the lame-duck session, the period when Congress meets between the November election and mid-January when the President and new Congress are sworn into office. It is the last opportunity to advocate for legislation introduced in the current Congress, and the election outcome will shape the debate during this session. Both Congress and advocates will push to have their priorities included in any moving piece of legislation under consideration between the election and installation of the new Congress.

Regardless of federal politics and the ACA's prospects, much is riding on state-based health exchanges and state legislatures' reactions to the Court's decision; thereby imposing the character of the healthcare within individual states on the nation.

Kym H. Kilbourne,
Director, Federal Affairs
Bill Speir,
Director, State Affairs

Rare Diseases and U.S. Health Policy

BY KYM H. KILBOURNE

SINCE THE ORPHAN DRUG ACT (ODA) BECAME LAW IN 1983, nearly 400 drugs have been approved for the treatment of rare diseases and over 2,500 drugs have been orphan drug designated.

Without question, the ODA has proven a powerful tool in the development and marketing of innovative rare disease medicines; however, there remain more than 7,000 untreated rare diseases which affect nearly 30 million Americans. Eighty-five percent to 90% of these are considered serious or life threatening. While the number of diseases that remain orphaned is daunting, recent trends in research and development, legislative and regulatory actions, and patient advocacy and rare disease registry networks are reducing the number of untreated rare diseases and improving treatment options for individuals living with rare diseases.

The Orphan Drug Act

To stimulate product development, the ODA established incentives for the investigation and marketing of products indicated to treat a population of 200,000 or less. These include tax credits for half of the qualified costs of clinical development, marketing application user fee exemption, government grants for qualifying research and development costs, and a seven year period of marketing exclusivity that prevents FDA approval for the "same" drug treating the "same" orphan disease or condition. These incentives have been instrumental in increasing rare disease research and development. In the first 15 years after the ODA was enacted, the pharmaceutical and life science industries increased the number of new molecular entities indicated for rare diseases by more than 500 percent. With 77 new orphan products added to the market since 1998, the Act continues to be a powerful force for research and development.

In addition to attracting the development of wholly new products, the ODA has also encouraged research and development of rare disease indications for existing commonly indicated drugs. Today, of the all orphan drugs on the market, 37% are drugs that were initially brought to market under a common indication and because of ODA incentives have had their indications expanded to include one or more orphan indications. In sum, the addition of rare disease indications to already commonly indicated medicines underlines the capacity of the ODA to continue to direct significant investigative resources to the rare disease space. ***continued on page 20***

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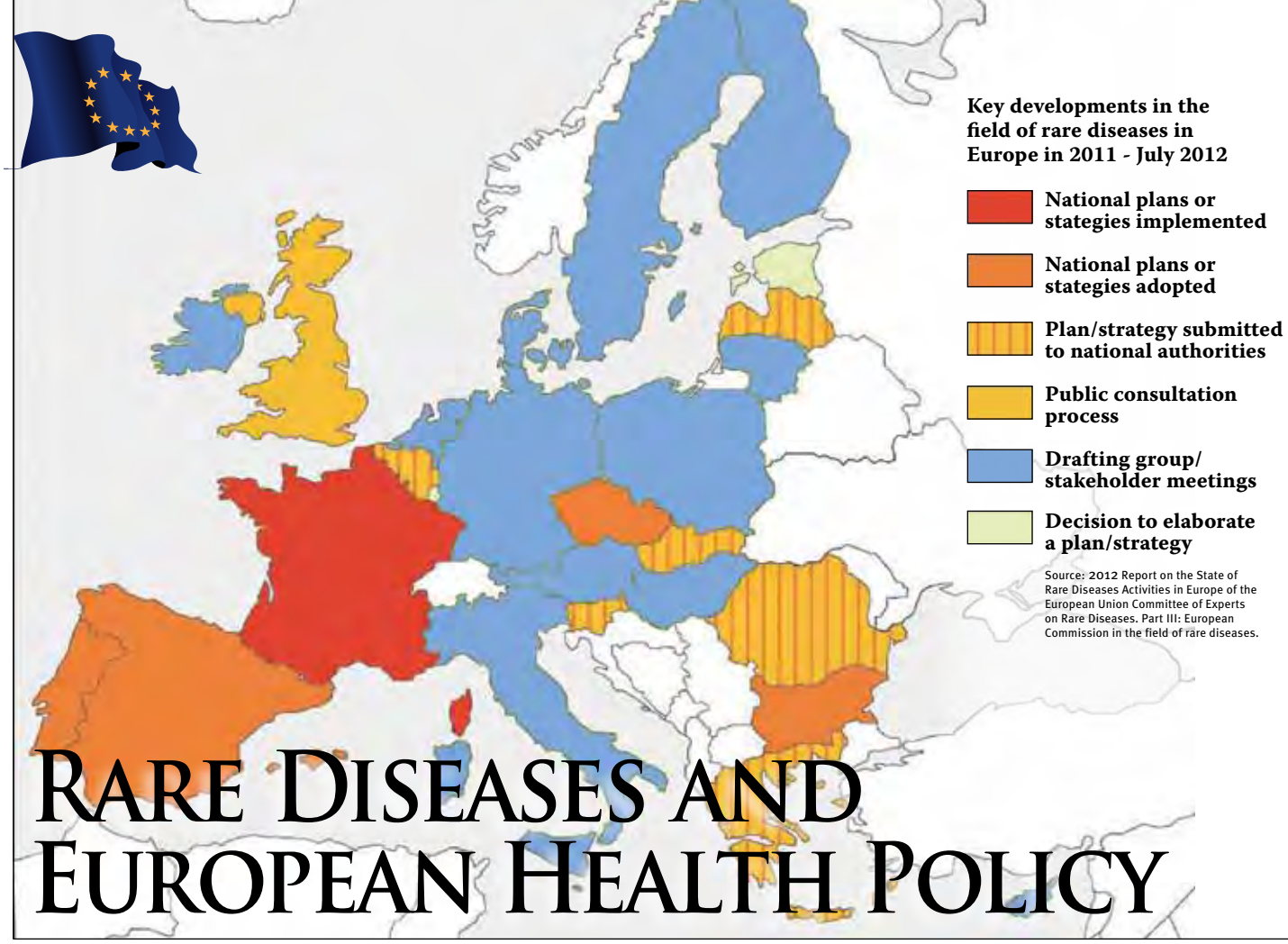

Rare Diseases and European Health Policy

BY LAURA SAVINI

IN THE PAST 10 YEARS, EUROPE HAS SEEN THE RISE OF VARIOUS LEGISLATIVE and health policy initiatives promoting the research, diagnosis and treatment of rare diseases. A concise overview of the major legislative and policy actions that have influenced the rare disease community in Europe follows:

Orphan Drugs in Europe

The first significant step in promoting research into rare diseases and development of medicinal products treating these conditions was the adoption of the regulation (EC) No 141/2000[1] that establishes the criteria for orphan medicinal product designation in Europe. This regulation defines that an "orphan medicinal product needs to be intended for the diagnosis, prevention and treatment of a life-threatening or chronically debilitating condition affecting no more than 5 in 10,000 people in the European Union"[2]. Today, this equals a population of approximately 253,000 people in the 27 Member States. Furthermore, pharmaceutical companies need to prove that "the marketing of this medicinal product would not generate sufficient return to justify the necessary investment and that there is no other satisfactory method of diagnosis, prevention or treatment that has been authorized in the European Union or that the new product would bring a significant benefit for the patients compared to the existing products."[3]

If a pharmaceutical product fulfils these conditions it earns several advantages such as a ten years market exclusivity, easier access to protocol assistance and a fee reduction for all types of centralized activities such as marketing authorization, inspections, variations and protocol assistance. Furthermore, sponsors of such medicinal products may be eligible for grants for research from the European Union and Member States.

It is currently estimated that between 27 and 36 million people in the European Union are affected by rare diseases, which represents between 6% and 8% of the population.

In 2010, the European Medicine *continued on page 20*

[1] Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products.
[2] Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products.
[3] Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products

US HEALTH POLICY

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Scientific Advances

Historically, efforts to develop treatments for rare diseases have been undermined by the limited knowledge of the causes of many and the shortcomings of technology needed to investigate potential treatment targets. Building on the human genome mapping and significant advances in biostatistics and biotechnology, the time required to determine whether a treatment will have a meaningful effect has significantly shortened.

One example of these advances is the Therapeutics for Rare and Neglected Diseases (TRND) program, a National Institutes of Health (NIH) initiative. TRND funds translational research for novel therapeutics to cross the gap from the basic investigative stage to human testing. By capitalizing on recent technology advances, TRND and like-minded programs and research and development efforts are successfully realizing cost-effective investigation methods. As a result, the global orphan drug market is expected to expand at a nearly 6% rate in the coming years, and the U.S. portion of that is anticipated to grow to $65.9 billion by 2014. The global share of biological orphan drugs, which account for 64.3 percent of all orphans, is on pace to reach $76.2 billion by 2014.[1]

Registries provide insight and awareness

The use of disease registries as effective tools for understanding diseases and treatment options continues to expand. This is especially important because of the large gaps in understanding and data associated with rare diseases. These gaps exist because rarity limits the ability of researchers to study certain diseases under varying conditions and in varying populations. Accordingly, registries have the capacity to capture and correlate data over a greater population to reveal events such as infections and malignancies that are only occasionally associated with a disease. Registries can also provide a clearer timeline of serious events associated with a disease and treatment regimen, which is especially important for rare diseases because of their genetic and life-threatening nature. The increase in rare disease registries provides policymakers with a better understanding of the burdens faced by patients, their families, communities, and providers. Additionally, registries are facilitating the efficient direction of resources to improve existing treatments and provide greater access to innovative therapies.

PPTA and Rare Diseases

PPTA continues to partner with patient advocacy organizations to raise awareness and inform decision makers of the unique nature of the rare diseases served by PPTs. PPTA supports the achievements of the ODA, scientific advances, and patient registries. Specifically, PPTA works to ensure that legislative and regulatory actions establish reimbursement methodologies that support access to therapies that treat rare, chronic and life-threatening diseases.

In recent months, PPTA has worked with the Food and Drug Administration (FDA), members of Congress, and representatives of the rare disease community to raise awareness that including plasma protein therapies in the annual pharmaceutical fee provision of the Affordable Care Act (ACA) has the potential to curtail innovation. Because the ACA narrowly defines "orphan drugs" as it pertains to the annual pharmaceutical fee as drugs for which the manufacturer or sponsor claimed the ODA tax credit, many plasma protein therapies are not included in the orphan drug exclusion, and as a result are exposed to the annual pharmaceutical fee despite their being solely indicated to treat one or more rare diseases. PPTA continues to work with decision makers to demonstrate that the inclusion of plasma protein therapies in the annual pharmaceutical fee places downward economic pressure on the rare disease innovation of the industry, in effect reversing the success of the ODA.

PPTA also continues to work to ensure that reimbursement methodologies are implemented in a way that fulfills the intentions of the ODA and the work carried out by researchers. Specifically, PPTA seeks to limit specialty tiering of plasma protein therapies that create burdensome cost-sharing for patients, and to expand unfettered access to all therapies in all sites of care.

Since the inception of the ODA public entities, industry, and patient organizations have come together to direct a vast migration of resources and efforts to finding cures and meaningful treatments for rare diseases. This direction has had unprecedented success, yielding hundreds of treatments and significant advancements in science and knowledge of rare diseases. With these, comes great opportunity for continued progress. Future success depends upon understanding the unique nature of rare diseases, therapies, and continued collaboration and leadership among patients, industry, and policymakers.

Kym H. Kilbourne, *Director, Federal Affairs*

[1] J Pharm Bioallied Sci. 2010 Oct-Dec; 2(4): 290–299.

EUROPEAN HEALTH POLICY

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Agency (EMA) stated that since its implementation the regulation had attracted more than 1,000 applications for orphan drug status, with application numbers rising every year. By the end of 2011, over 800 medicinal products had received the "orphan drug" designation and 65 medicinal products had received marketing authorization since the implementation of the regulation. It is estimated that approximat ely 2.5 million patients in Europe benefit from these products.

In April 2011, the European Commission and U.S. National Institutes of Health (NIH) launched the International Rare Disease Research Consortium (IRDiRC) an initiative that

brings together regulatory agencies, researchers, patient group representatives, members of the biopharmaceutical industry, and health professionals. The IRDiRC has an ambitious goal to develop 200 medicinal products or diagnostics for rare diseases by 2020. The idea behind this consortium is to bring together international efforts on research for rare diseases, to share data and information, to avoid duplication of research and maximize existing resources. The consortium is composed of government agencies from Europe, North America and Australia.

Rare Disease Policy in Europe

In 2008, the "Commission Communication on Rare Diseases: Europe's Challenge" was established as a European strategy to support Member States in the diagnosis and treatment of patients suffering from rare diseases. Its scope was to improve the visibility of rare diseases, support a coherent rare disease strategy amongst Member States and develop cooperation, coordination and regulation for rare diseases in Europe.

Following the Commission Communication on Rare Diseases, the Council of the European Union published its Recommendation in 2009. This document engages Member States to adopt before 2013 several actions including the creation and adoption of national plans to improve rare diseases visibility and to stimulate research. The recommendations encourage Member States to implement systems that can link centres of excellence and networks of professionals in different European countries. It also stresses the importance of patients' participation in rare disease policy and of providing patients with adequate access to information on rare disease activities. Another important aspect described by the document is to ensure long-term sustainability in the field of research and healthcare infra-structures. The European Commission was charged with monitoring and reporting on the status of implementation of these recommendations. This task is currently carried out by the European Union Committee of Experts on Rare Diseases (EUCERD) which produces annual reports on the activities of the European Commission, the EMA and the Member States. Since its implementation, the EUCERD has also developed sets of guidelines and recommendations on quality criteria for the development of Centres of Expertise for Rare Diseases, European Reference Networks and Expert Clinical Laboratories.

In 2011, the Council of the European Union adopted the directive on cross-border healthcare. This piece of legislation is unique insofar as it legally binds Member States to cooperate in the field of diagnosis and treatment capacity for rare diseases. Although, the directive does not allow patients to obtain a treatment in another country that is not reimbursed in their own country, it contributes to strengthen information and resource sharing among Member States by putting the European Commission in charge of supporting the continued development of reference networks between healthcare providers and centers of expertise.

Research in Europe

At the European level, research on rare diseases has been addressed as one of the priority areas under the EU Framework Programmes for Research and Technological Development (FP) since the early 1990s. Under the current program (FP7, 2007-2013) it is estimated that rare diseases have received €430 million and that over 70 projects have been funded.[4]

Another tool that is widely used to further and consolidate research in the field of rare diseases is patient registries and databases. These registries are a unique way to gather information on the diagnosis and treatment of patients suffering from rare diseases. According to Orphanet, the online portal for rare diseases and orphan drugs, there are currently just under 600 patient registries in Europe, 70% of which are national registries. Although, these are invaluable instruments to follow epidemiological data and information on patients' responses to treatment protocols, there are a series of obstacles that limit their potential, such as technical issues regarding data formatting, encoding and patient consent.

The role of patients groups

Patients groups have certainly been one of the major factors in raising the profile of rare diseases in Europe and impacting health policy. There has also been a shift in patients' attitudes from passive to very active. In general, patients identify themselves as consumers of health services and products and have become a much more critical and demanding stakeholder; and the rare disease community is no exception. There are consortia of rare diseases patients' representatives both at the EU level and at the national level and they are incredibly active in advocacy. The Plasma Users Group (PLUS) has quickly increased its visibility at the European level, demonstrated by its engagement with the Commissioner for Consumers and Health Safety, Mr. John Dalli.

Conclusion

Europe is on a positive path to providing adequate access to diagnosis and treatment to patients suffering from rare diseases; however, there are still a many patients who are not diagnosed or treated. Furthermore, even though Europe has clearly showed its commitment to rare diseases via investments in research and policy actions, it is now facing the most challenging economic times in over a century. In short, stakeholders believe that the primary challenge for rare diseases and related activities will be sustained financing for both research and treatment. The future challenge will be whether Europe can maintain its commitment to rare diseases under tight financial conditions.

Laura Savini, *National Affairs Manager, PPTA Europe*

[4] 2012 Report on the State of the Art of Rare Disease Activities in Europe of the European Union Committee of Experts on Rare Diseases. Part III: European Commission Activities in the Field of Rare Diseases.

Reaching Out to European Policymakers

BY LAURA SAVINI

FOR SEVERAL YEARS, PPTA'S HEALTH POLICY STEERING COMMITTEE (HPSC) has conducted its policymakers network outreach program, to European officials in Brussels, Belgium and Strasbourg, France.

The targets are Members of the European Parliament, European Commission officials and civil servants working in Member States' Permanent Representations. The objective is to maintain an ongoing dialogue with policy-makers who work on policies and legislation either directly or indirectly influencing PPTA members. Meetings are held one to three times a year and are valuable in increasing and maintaining PPTA's visibility.

The EU, as illustrated below, requires interacting with three distinct entities:

- The European Commission that initiates and sometimes implements legislation
- The European Parliament which represents the interests of the European people
- The Council of the European Union which represents the interests of the European Member States

Both the European Parliament and Council review, amend and adopt legislative proposals. PPTA had engaged with members of the European Commission's Directorate General for Health, Safety and Consumers, DG SANCO., HPSC members have also met with approximately 50 Members of the European Parliament (MEP), either members of the Parliamentary Committee for Environment, Public Health and Food Safety (ENVI) or MEPs with interests in health-related matters. Finally, PPTA members are pursuing advocacy activities with the Council of the European Union by meeting health attachés of Permanent Representations (representing the interests of Member States in the work of the EU Council) and through the work of national working groups who meet with Member States governments' officials. PPTA maintains national working groups in Belgium, France, Germany, the Netherlands and the United Kingdom.

This year's advocacy has focused on: educating relevant policy-makers on the industry and its complexities, carrying out the members' positions on upcoming legislative proposals such as the legislative proposal on pharmacovigilance, the legislative proposal on information to patients, and the legislative proposal on the revision of the Transparency Directive. PPTA members have also discussed issues relating to the EU Health for Growth and Horizon 2020 programs.

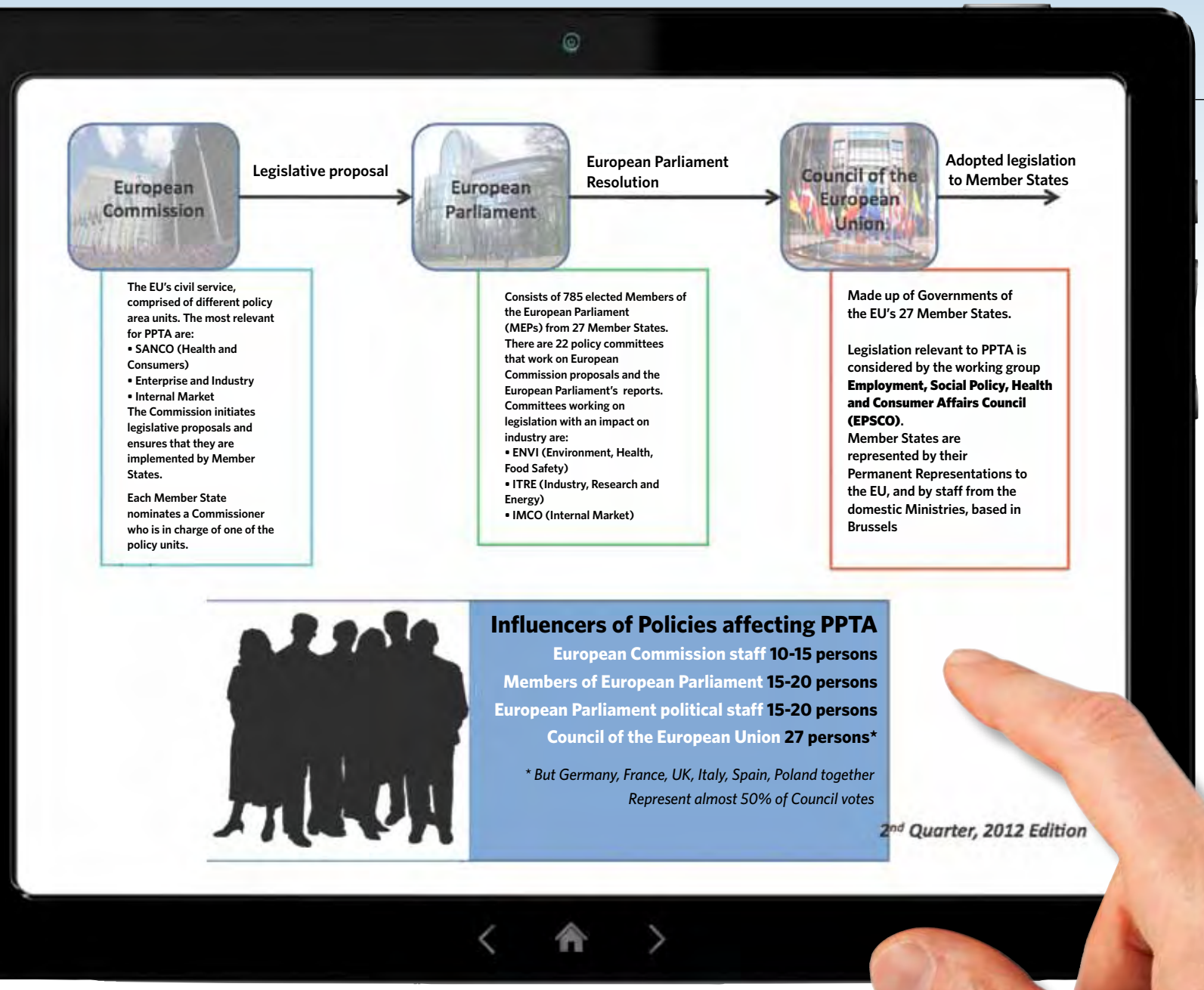
These outreach meetings have proven beneficial. Through contacts made by the HPSC members, PPTA was informed in a timely manner on European Commission's decision to launch a study into the availability of blood, blood components and plasma derivatives to European patients. Subsequently, PPTA members were able to reach out to members of the European Parliament which led to several offers from MEPs to host lunch debates on the study in the upcoming year. Furthermore, HPSC members met with the European Commission Unit officials in charge of this study to educate them on the challenges faced by the industry in Europe. Participants were informed that the study might potentially lead to a modification of Directive 2002/98, also known as the "Blood Directive" setting the standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components in Europe.

In addition, in 2010, MEP, Jorgo Chatzimarkakis championed a set of expert recommendations for better management of primary immunodeficiency (see Source Fall 2010). This document has since been adapted to the German patients' needs and supported by German politicians (see Source Spring 2012). PPTA was informed that these recommendations are widely used by patients for advocacy work in both Europe and Latin America.

Finally, in 2008 when the European Commission launched its Communication on Rare Diseaes (see page 20), MEPs Miroslav Mikolasic and Jorgo Chatzimarkakis chaired two parliamentary lunches centered around rare diseases and, in particular, plasma-related disorders (see Source Spring 2009). Both lunches resulted in a call for action on rare diseases calling for Member States to develop Rare Disease Plans and to facilitate access to diagnosis and treatment for individuals suffering from rare diseases (see Source Fall 2009). The document, still active, is signed by 20 MEPs active in the field of health policy and policies affecting regulations of substances from human origin.

LAURA SAVINI, *National Affairs Manager, PPTA Europe*

THINKSTOCK. BONOTOM STUDIO



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EVENTS

UPCOMING
CONFERENCES & SYMPOSIUMS

2012

September 19 – 23	1st Central and Eastern European Conference on Sepsis *Budapest, Hungary*
October 3-6	15th Biennial Meeting of the European Society for Immunodeficiencies (ESID) - Joint meeting with International Patient Organisation of Primary Immunodeficiencies (IPOPI) and The International Nursing Group for Immunodeficiencies (INGID) *Florence, Italy*
October 6-9	AABB Annual Meeting *Boston, Massachusetts*
October 6-9	Source Business Forum (PPTA members only) *Boston, Massachusetts*
October 6-9	22nd International Congress on Thrombosis *Nice, France*
October 13-17	The European Society of Intensive Care Medicine Annual Congress *Lisbon, Portugal*
October 13-17	Anesthesiology 2012 *Washington, D.C.*
October 25-26	3rd Pan-European Conference on Haemoglobinopathies and Rare Anaemias *Limassol, Cyprus*
October 26-28	European Haemophilia Consortium Conference, 25th Jubilee *Prague, Czech Republic*
November 8-10	National Hemophilia Foundation, 64th Annual Meeting *Orlando, Florida, United States*
November 17	2nd International Fluid Academy Day *Antwerp, Belgium*
December 8–11	American Society of Hematology Annual Meeting *Atlanta, Georgia*

2013

March 5 – 6	International Plasma Protein Congress (IPPC) *Dublin, Ireland*
March 19 – 22	33nd International Symposium on Intensive Care and Emergency Medicine *Brussels, Belgium*
June 11-12	Plasma Protein Forum *Reston, VA*

Cambridge, Massachusetts

THINKSTOCK

FORUM DELIVERS KNOCK OUT PUNCH FOR PATIENTS

BY LISA LOVULLO

The 2012 Plasma Protein Forum delivered on its *"Commitment to the Community"* promise which was reflected in two days of presentations that highlighted the unique nature of orphan diseases and drugs with an emphasis on patient access to care. Global Board Chairman, Paul Perrault set the tone by challenging all to "become ambassadors" and create awareness about rare diseases and plasma protein therapies.

Representative Michael Burgess (R-TX) provided a brief overview of key federal issues and legislation. The Congressman suggested that the Affordable Care Act was passed without proper debate and revision. Members in both parties believe that the legislation could be improved to ensure a more fiscally sound means of providing access to health care to greater numbers of people.

The Forum's patient driven focus began with a keynote address by National Health Council President, Myrl Weinberg, who made a compelling case for involving patients in research and development and the regulatory decision-making process. In particular, she argued that patients can provide valuable input on benefit-risk assessments based on individual experience.

Involving patients in policymaking is also on the agenda of Mary Cobb, Senior Vice-President of Membership and Organizational Strategy, National Organization of Rare Diseases (NORD) who suggested that "there is a significant unmet need for collaboration" and that "patient voices can get the attention of policymakers and regulators".

As the Orphan Drug Act celebrates its 30th anniversary this year, Francesca Joseph, M.D., FDA Office of Orphan Product Development (OOPD) provided an overview of how the Agency identifies, evaluates and designates treatments for rare diseases. Since its inception, OOPD has approved nearly 400 drugs. Tom Mullin, Senior Vice-President, Xcenda provided food for thought on communicating with payers by suggesting a risk-value-partnership model, "The sweet spot is where clinical, economic, and humanistic benefits align and the best possible patient care is also good business." He advised industry and patients to work together to educate payers.

Attendees also learned that "economics is about value, not money" and that health technology assessments must be patient centered. Panelists John F. Bridges, Johns Hopkins Bloomberg School of Public Health; Albert Farrugia, Ph.D , Vice President Global Access; and Scott Gross, Ph.D., Centers for Disease Control and Prevention reviewed the current principles around cost-effectiveness assessments for rare population treatments. New approaches that engage patients are believed to be more relevant. Policy decisions drawing from cost-effectiveness models need to ensure the appropriate use of concepts such as willingness to pay for chronic treatments, which is often higher in the general population than in the payer agencies.

Keynote Speaker: Myrl Weinberg, National Health Council

The economics of affordable care and the impact of health care reform in the States were debated by Ryan Faden, State Patient Access Coalition (SPAC), Western Region Chairman/ Manager State Affairs CSL Behring;, Larry LaMotte, Vice President, Public Policy, Immune Deficiency Foundation; and Matt Salo, Executive Director, National Association of Medicaid Directors.

The Forum concluded with an excellent historical overview of twenty years of plasma collection by outgoing Source Board Chair, Ileana Carlisle, Vice President, Plasma Operations, Biotest Pharmaceuticals. Mario Macis, MD delivered an insightful presentation based on a field study that demonstrated the effectiveness of incentives in motivating blood donors.

Finally, David Morad, President Southern Blood Services, Inc., and Albert Farrugia, Ph.D., Vice President, Global Access, paid homage to hyperimmune immunoglobulins, an often neglected segment of our industry, "We don't give enough attention to hyperimmunes, which are used to treat significantly greater numbers of people than the populations of rare chronic disorders." Hyperimmune immunoglobulins are used to protect against hepatitis, tetanus, and rabies when healthy people are at risk of having been exposed to these illnesses. Rhesus immunoglobulin is used in to protect rhesus negative women and their children after birth. Recently, hepatitis B immunoglobulin has increased success in liver transplants.

Larry LaMotte, said, "The Plasma Protein Forum always energizes me as I continue to learn more about this industry. It also allows me the opportunity to reconnect and compare notes with fellow stakeholders. The varied sessions, including new research, public policy issues, benefit-risk assessment issues, trends – you name it - of the plasma industry and user communities, cover a wide range of interests and I always come back with ideas that will benefit our patients. This year was fantastic!"

LISA LOVULLO, *Senior Manager, Communications*

GLOBAL QUALITY/COMPLIANCE REGULATORY WORKSHOP EDUCATES AND ENTERTAINS

BY MARY CLARE KIMBER

Nearly eighty people converged on the day before the 2012 Plasma Protein Forum (PPF) for a Regulatory Workshop *"US/EU Quality/Compliance Challenges and Solutions."*

The Workshop aimed to provide education on the focus of regulators overseeing and performing inspections, the use of quality tools to reduce errors in manufacturing facilities, and the value of effective communication during and after

Roger Brinser, Baxter Regulatory Policy Steering Committee

inspections. Workshop presenters and attendees included Association members, regulators and policymakers, colleagues from the blood community and other stakeholders.

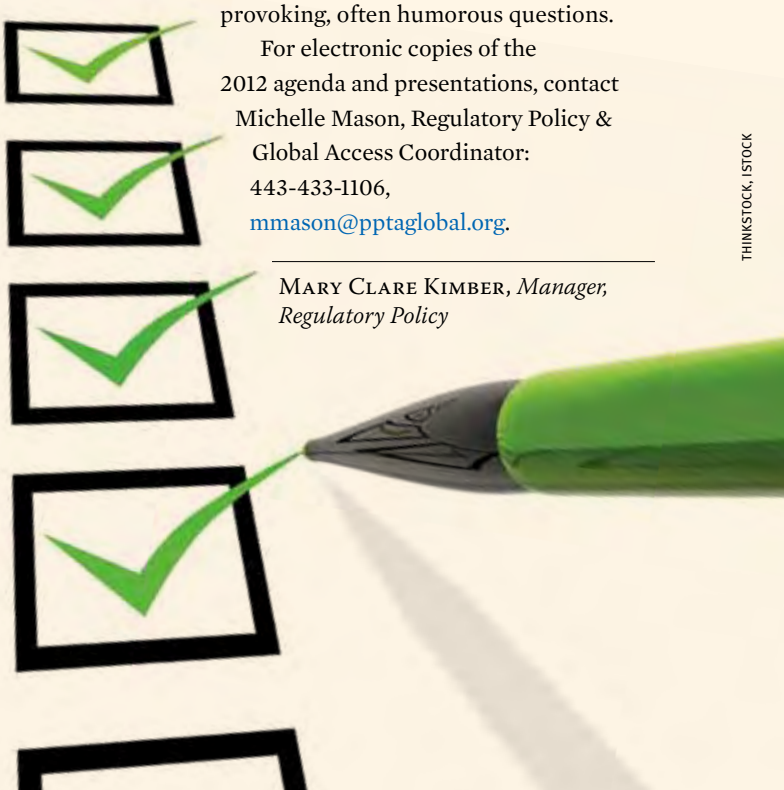
Attendees appreciated the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) regulators' openness and willingness to present and discuss thorough, up-to-date information on inspection trends. In particular, Director Gilliam Conley, FDA, Center for Biologics Evaluation and Research's (CBER) Division of Inspections and Surveillance (DIS) presented 2011 data on Source Plasma inspections and regulatory actions and offered insights into the Agency's next steps for CBER's Direct Recall Classification (DRC) program. Importantly, Director Conley acknowledged that DRC reports of relatively high raw numbers of biologics recalls can be "misleading" unless tempered with denominator data. Scientific Administrator Brendan Cuddy, EMA complemented Director Conley's US-focused presentation with an EU perspective, prefacing his remarks by applauding the performance of US facilities during EMA-coordinated inspections.

The PPTA Regulatory Policy and Compliance Steering Committee conducted the event and served as both presenters and moderators. Nancy Geer, Manager, Regulatory Affairs, Ortho Clinical Diagnostics and Bryan Silvey, Director, Quality and Regulatory Compliance, Baxter Healthcare Company shared their quality/compliance challenges and solutions through case studies on the use of quality tools to reduce human errors. The successful session was reflected in an attendee's sentiment that the Workshop "identified tools/models new to me – all good!"

For many, the highlight of the afternoon was "*How to Resolve Conflict with FDA During and After Inspections.*" The anecdote-peppered, interactive presentations of Investigator/Biologics National Expert Kip Hanks, FDA Division of Domestic Field Operations, and Corporate Director Patrick Ooley, Quality Operations, Blood Systems, Inc., delighted attendees. Hand-held polling devices allowed attendees to answer the duo's thought-provoking, often humorous questions.

For electronic copies of the 2012 agenda and presentations, contact Michelle Mason, Regulatory Policy & Global Access Coordinator: 443-433-1106, mmason@pptaglobal.org.

MARY CLARE KIMBER, *Manager, Regulatory Policy*



THINKSTOCK, ISTOCK

PPTA EXHIBITS AT THE EUROPEAN CONGRESS FOR RARE DISEASES

In May, PPTA exhibited at the European Congress for Rare Diseases 2012 (ECRD) held in Brussels, Belgium, an event organized by EURORIDS, the voice of rare disease patients in Europe. A multicultural audience included nearly 700 delegates from 55 countries primarily from Europe but also from North America, Asia and Australia. The event was structured around seven thematic pillars of strategic importance to the European rare disease community:

- National Plans for Rare Diseases
- Centres of Expertise and European Reference Networks
- Information and Public Health
- Research
- Access and Regulation of Orphan Drugs
- Therapies
- Patient Empowerment

PPTA distributed educational material, as well as, books on rare diseases, immunodeficiencies and plasma proteins, edited by José Luis Valverde, Ph.D., Professor of Pharmaceutical Law and History of Pharmacy, University of Granada, Furthermore, PPTA promoted initiatives such as the European and German recommendations for the better diagnosis of primary immunodeficiency and the German FIND-ID initiative aiming at increasing the level of PID diagnosis in Germany. The Staff spoke with over 200 patients, policymakers and regulators who visited the PPTA exhibit.

GLOSSARY OF TERMS

AERS	Adverse Event Reporting System
ASRM	American Society for Reproductive Medicine
CDC	Centers for Disease Control and Prevention
CHMP	Committee for Medicinal Products for Human Use
EPA	Environmental Protection Agency
EMA	European Medicines Agency
ECRD	European Congress on Rare Diseases and Orphan Products
EUCERD	European Union Committee of Experts on Rare Diseases
EAC-VHP	Expert Advisory Committee on the Vigilance of Health Products
FDA	Food and Drug Administration
IRDiRC	International Rare Disease Research Consortium
NCA	National Competent Authorities
NIH	National Institutes of Health
NORD	National Organization of Rare Diseases
OOPD	Office of Orphan Product Development
ODA	Orphan Drug Act
PCORI	Patient-Centered Outcomes Research Institute
SART	Society for Assisted Reproductive Technology
TRND	Therapeutics for Rare and Neglected Diseases
WHO	World Health Organization

MEET THE PPTA

STAFF

Menso Bult

Manager, Global Access, PPTA Europe

How long have you served at PPTA?

I joined the Brussels staff in September 2000 to manage the European activities within the Albumin Program, initiated after the publication and impact of the Cochrane meta-analysis in 1998.

What do you focus on in your role as Manager, Global Access?

I started as coordinator of the European Albumin Task Force and in 2003, when PPTA established the Immunoglobulin Task Force, management of this new task force became part of my activities. In my role as manager, I contribute to the development and execution of activities within the different programs to achieve our strategic goals. PPTA's Global Access team is committed to the job and it is a pleasure to contribute to the program and achievements.

Besides Global Access, I am also involved in the Dutch Industry Working Group which allows me to further develop skills in the area of health policy and maintain contacts with patient organizations.

Tell us about your background.

In 1986, I started my career in the pharmaceutical industry. I worked as a sales representative for BYK Gulden and Bayer in the cardiovascular business units. In 1991, I was asked by Astra, now AstraZeneca, to join the products specialist team for cardiology in The Netherlands. This team was involved in marketing and sales activities, but was also part of the medical department. At the University Hospital of Groningen, the head of the Department of Cardiology, Prof. Dr. H.Lie, was my supervisor where I continued my medical education in cardiology and clinical research.

What is your proudest professional achievement?

When PPTA became a sponsor of the annal International Symposium on Intensive Care and Emergency Medicine (ISICEM) in 2001 in Brussels, it was extremely difficult to find any physician to speak on albumin. Today, we have established excellent contacts with key opinion leaders in North America, Europe and Australia who share their views on albumin and its clinical uses at scientific meetings and medical congresses at a global level. This achievement is of great value for PPTA: and yes, I am proud of it.

What is most rewarding about working in this industry?

It is most rewarding to contribute to the improvement of awareness and sharing knowledge about plasma protein therapies among stakeholders, patients, physicians and policymakers. I realize that patients all over the world struggle with access to care and the best available treatment. I learned this through personal experience. I played football, tennis and golf at a high level until a ski-accident sidelined me 5 years ago. It has taken me four years to get a correct diagnosis and treatment plan. After years of struggling, I am now making good progress. Despite achievements and progress many patients all over the world still struggle to get access to proper treatment or recognition. There is a lot more that can be achieved. This is what we have to keep in mind when we see the achievements and progress made. It is unacceptable that, despite all efforts made so far, many patients all over the world still struggle to get access to proper treatment or recognition. Or to quote John Lennon from his song, *Imagine,* "You, you may say I'm a dreamer, but I'm not the only one."

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