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In my memory, “Emerging countries” have been gathering increasing attention since the early 1990s. This interest, growing gradually but steadily, was expressed by different parties in different ways. The WHO increased its involvement with new concepts of health care provision (organisation, drug lists, focus on specific diseases and others). The global corporate environment started getting involved and investing in scientific and research facilities in parallel to gaining access to the pharmaceutical markets. The gap between the “emerging countries” and the western economies has been shrinking over this time period, which became clearly noticeable since the turn of the century, specifically in Asia/Asia-Pacific region but also elsewhere for example Brazil.

The two subsequent issues of Global Forum, in December and in February 2013, undertake to review aspects of development of medicines, a broad collaboration between countries in emerging and other regions. Following on from the idea of the International Conference of Harmonization, countries of Asia-Pacific region began a closer cooperation of regulatory bodies and exchange of “know how” (e.g. between China, Japan and Korea), which happens in parallel with a clear trend in implementation of existing ICH documents across all of the emerging countries. The latter faces many discussions and obstacles, partly due to the fast evolution of the European and US regulatory environment. These activities however lead to a substantial improvement in understanding the need for harmonized requirements for medicines development and licensing.

To read more of our coverage on topics of interest coming from emerging countries, turn to the Special Topic section of
On that note I would like to thank Jean Soul-Lawton, a member of our Editorial Board and a section editor, for organising this very interesting compilation of informative articles, which greatly increases our knowledge and understanding of developments in these countries.

Frequently, emerging countries are looked at from the regulatory (licensing of medicines) and clinical research perspectives. However when assessing the progress in their health care system, one may notice the changes also seen from the system users’ and providers’ perspectives. Some of the progress we see could be assessed as astounding, even when judged by the standards that we are used to. One example could be the Aravind Eye Hospital in India, where an intraocular lens has been developed that has revolutionized cataract surgery due to the low price. In addition, the provision of the eye service was reorganised so that a single surgeon (with a team of technicians) performs six to eight cataract surgeries per hour with a documented rate of complications of 1.6%. I believe that such efficient and satisfactory results would be appreciated anywhere in the world. Another example, also from India is the “Jaipur Leg,” which is a fully artificial lower limb that allows the “owner” to kneel, squat and climb trees. One can only imagine what a change in quality of life it has delivered.

The other of the Global Forum sections features the interview with Dr T. Kondo, Director and Chief Executive of PMDA. It is good to hear from him how important regulatory sciences and a broad cooperation of all parties (academia, industry, regulators and patients) are for drug development, licensing and the ICH work today and in the future.

Our Special section and the “profile” touch once again on the importance of international cooperation in the areas of scientific development and regulations dictating regulatory processes. We can learn from the experiences gathered over the years by sharing and transferring them from one part of the world into the emerging countries, but we need to recognize also that some experience of those countries could, and hopefully will, benefit health services across other regions of the world. With this thought please keep in mind the second part of our Special Topic section, which will become available early next year. Enjoy reading one of the last paper issues of the Global Forum, and move with us into the new era of publishing starting in 2013.
FROM THE DESKS OF....

LING SU
President, DIA
Board of Directors

PAUL POMERANTZ
Worldwide Executive Director, DIA

DIA Board President &
Worldwide Executive Director

This final issue of the 2012 Global Forum provides a wonderful opportunity for us at DIA to reflect on the hard work and accomplishments of this past year and to anticipate the fruits of that labor in the year to come. As always, we have done much; but, our growth will continue and with that, new goals to set and achieve.

As a knowledge provider for health care stakeholders globally, our commitment to delivering comprehensive information as quickly as possible to our constituency is paramount to who we are and what we do. As such, this year we joined the digital revolution and our development of a more robust website and mobile technologies have completely altered DIA’s information delivery landscape. People can do more things with more information more quickly than ever before; and, our goal is to continue to provide more knowledge, to you, our members, in a variety of formats, effectively positioning DIA as the “go to” information provider in the health care arena.

Our strategic digital initiative has impacted just about every aspect of our operations, and nowhere is that more evident than in our two flagship publications.

This year, we successfully transitioned our 46-year-old, scientific, peer-reviewed Drug Information Journal from a self-published product to SAGE Publishing, whose electronic submission, review, and approval process has resulted in an average turnaround time from manuscript submission to decision of 38 days, well ahead of industry manuscript processing standards. Before receiving your print edition of the DIJ, you are able to access an article within days of acceptance through the link on our website to SAGE’s OnLine First portal. This is important because cutting edge research reaches you, our readers and stakeholders, before it appears in print.

We are very excited to announce that in January 2013, the DIJ will be relaunched as Therapeutic Innovation & Regulatory Science (TIRS). This new title also reflects changing times: When our founders established the DIJ in the mid-1960s, our organization was primarily focused on the scientific and clinical development, and
regulatory review and approval, of drugs. Drug Information Journal was an appropriate and relevant title. DIA has grown to encompass new product types, such as diagnostic devices and drug/device combination products, and new subject areas such as pricing and reimbursement, benefit/risk assessments, comparative effectiveness, health technology assessment, and their supporting scientific and regulatory frameworks. Today’s DIA members are truly immersed in the work of therapeutic innovation and regulatory science, and we’ve adapted this publication to reflect this progress and their interests. Look for broader topic areas in the future with a more global perspective. We’d like to thank Dr. J. Rick Turner, who has spearheaded the DIJ for the past two years, and will be stepping down as Editor-in-Chief, passing the baton to a new editor in 2013. His leadership and vision have guided this publication to its new format and we are grateful for all his contributions.

In February of this year, the Global Forum underwent a redesign to modernize the look and expand the content. This has been well received and readership feedback is better than ever. We have welcomed and heard your comments and recommendations. Based on your input and to align with current publishing trends, the Global Forum will transition in early 2013 to a digital product and we will discontinue mailing of the print edition to membership. This way, DIA and the Global Forum can Reach, Educate, Inform and Advise you no matter where you are- iPhone and iPad digital apps are available for download at the Apple Store and we will continue to provide the digital version of each Global Forum on the “News & Publications” section of our website, as well as email every DIA member a direct link to the publication. You live and work in the electronic environment and we want to be there right alongside you.

Some things to look forward to in 2013 are our regional annual meetings in Brazil, China, Japan and India, whose committees are hard at work creating robust content for our attendees; expanded educational offerings; and a more global approach to all we do at DIA. The EuroMeeting will celebrate its 25th anniversary in March at their meeting in Amsterdam and DIA will kick off its 50th anniversary celebration at our annual meeting in Boston in June. While we are writing this column, we are preparing for our first Board of Directors meeting in Beijing to become more familiar with this key emerging market and to meet with the SFDA and other key stakeholders, thus reaffirming our commitment to building a true global community. At this gathering, the DIA BOD will be completing the scenario planning process started over a year ago and we will be sharing the long-term strategic agenda developed as a result of this exercise with our members in an upcoming issue of the Global Forum.

As always, these advancements would not be possible without our dedicated staff, volunteers, Board of Directors and everyone in our global multidisciplinary network. Thank you for all that you’ve done in 2012 and will continue to do on behalf of DIA in 2013. Our future is bright and we are honored by, and grateful for, your contributions to our mission.
INFORM now houses the Special Sections: Devised to educate and update you on advances in a specific area of research, drugs, diagnostics or devices.
Clinical Drug Development in Emerging Markets

JEAN SOUL-LAWTON

DPhil, is a Director in the Respiratory Medicines Discovery and Development Group at GlaxoSmithKline. She has more than 20 years’ experience working in Clinical departments within the pharmaceutical industry.

CHALLENGES AND OPPORTUNITIES

The involvement of emerging markets in clinical drug development has escalated in recent years. This has provided opportunities for drug development companies, such as increased access to patient populations for clinical trial activities and to the corresponding markets. If emerging countries are becoming involved more and earlier in the clinical trial programme, more clinical data will be gathered in these regions, and will thus facilitate better characterisation of drug handling in the local populations. This should provide the regulatory agencies with greater assurance during the drug review and approval process.

This has been coupled, however, with infrastructure challenges. For example, there may be limited regulatory capability to manage the increased demand and to have the expertise to handle new and evolving processes of clinical trial applications and all the subsequent regulatory involvement in the drug development process. As drug development is new to many of these countries, investigator site capability may be limited, and the local culture may further inhibit the application of the protocol-defined processes for running a clinical trial to GCP standards.
WHAT ARE EMERGING MARKETS?

The precise definition of emerging markets may vary depending on your perspective, but the term can be broadly defined as nations in the process of rapid economic growth. In some cases, the growth rates of these countries has increased such that the standard of living has been raised for many in their populations, and thus created new markets for consumer products and services. In addition, many of these countries have large, low-cost and increasingly educated labour pools, to give these markets competitive advantage in many fields of production and information technology.

The number of countries described as emerging markets has grown over the years and of course will depend on how the term is defined. Approximately 10 years ago, the term “BRIC” was used to represent Brazil, Russia, India and China. However, other countries are now considered as emerging and may include, for example, other South American countries such as Chile and Peru, Asian countries such as Korea and Taiwan, as well as some Eastern European, Middle Eastern and other countries.

IN THIS SPECIAL SECTION

The articles covering this special topic will review some aspects of the practicalities of clinical drug development. As this special topic is extensive, it will be reviewed over two editions of the Global Forum. The Asia Pacific region will be a focus in Part 1. Specifically, there will be a review of fora for collaboration of regulatory agencies and other bodies such as the World Health Organisation (WHO) to address issues emerging in the global drug development environment. We also hear about the innovative approach of co-locating regulatory agencies and science parks. In addition, there are overviews of practical experiences in the regulatory review process and the establishment of investigator sites.
Appropriately preventing, adequately diagnosing, and effectively treating health conditions is a truly global mission. Just as one illustrative example, the World Health Organization (WHO) has observed that cancer is a leading cause of death worldwide accounting for a staggering number of deaths each year (7.6 million or 13% of all deaths in 2008). The WHO also estimates that 1 of 4 people worldwide will suffer from a mental illness at some point in their lives. Over the past several decades, the commonly universal role of disease and its prevention in morbidity, mortality, quality of life, and socioeconomic conditions has secured a heightened emphasis in the global development of medicines.

Attentive to recent environmental enhancements which promote the development of innovative medicines, many multinational biopharmaceutical companies are expanding their presence within emerging regions. As another demonstrative example, the European Medicines Agency (EMA) has reported that 61% of the patients in pivotal trials submitted in Marketing Authorisation Applications (MAAs) to the EMA between January 2005 and December 2009 were from third countries, comprising 35.2% from North America and 25.9% from the rest of the world. However, this extension of geographical reach has led to additional complexities for global drug research and development (R&D). Of particular note, local and regional regulatory processes are oftentimes not specifically designed to account for global aspects of R&D. Also, unique, local intricacies of regulatory procedures may not be updated frequently enough to support evolving global R&D plans. At the same time, advances in science such as biomarkers, diagnostics and novel clinical trial approaches have introduced opportunities for regulators, the biopharmaceutical industry and other stakeholders to better cooperate to enhance global medicines development.

Whilst there are many examples of these types of collaborations between regulatory agencies, industry representatives and other parties, the International Conference on Harmonisation (ICH) is frequently referenced for its progressive approach. Having first launched in 1990, ICH has brought together regulatory agencies from multiple countries and the innovative
industry to achieve common goals. "ICH's mission is to make recommendations towards achieving greater harmonisation in the interpretation and application of technical guidelines and requirements for pharmaceutical product registration, thereby reducing or obviating duplication of testing carried out during the research and development of new human medicines."3

Consistent with this mission and as one example, the ICH Steering Committee agreed upon standardisation for the Common Technical Document (CTD) in 2000. Simply considering this singular ICH initiative and only its impact on U.S. electronic submissions, the Food and Drug Administration (FDA) processed its 160,000 eCTD submission during 2010.2 Even though progress has occurred through ICH and other fora of collaboration (Figure 1), countless challenges and opportunities remain for improving the coordination of global medicines development.

One global R&D topic currently receiving concerted interest is multi regional clinical trials (MRCT). In 1998, the ICH published a guideline entitled, “Ethnic Factors in the Acceptability of Foreign Clinical Data”4 (referred as ICH E5), to establish a general framework for considering the impact of ethnic factors on a potential medicine’s pharmacodynamic effects. Specifically, the Q&A for the ICH E5 guidance notes that MRCT “may be desirable...to achieve the goal of bridging by conducting a multi-regional trial under a common protocol that includes sufficient numbers of patients from each of multiple regions to reach a conclusion about the effect of the drug in all regions.”5

In general, the objectives of MRCT include the improvement of clinical trial administrative, technical, operational and regulatory planning effectiveness across applicable geographies in order to achieve a more concurrent global development strategy. Multinational biopharmaceutical companies have affirmed several important advantages of MRCT including the ability to assess the global treatment effect, improvement in development timeline efficiencies, prevention of duplication of clinical trials in humans, and enhanced cost-effectiveness by using global trial data for parallel registrations. There are however, critical challenges to MRCT that must be recognised and appropriately considered such as the regulatory risk of acceptability of the trial design and results in additional regions. Regulators may also have general questions about the robustness of the overall trial conclusions, if an MRCT is undertaken rather than separate clinical trials in each country.

MRCT efforts have continued to progress since the initial ICH E5 guideline. In 2007, MHLW (i.e. the Japanese Ministry of Health, Labour and Welfare) published the “Basic Principles on Global Clinical Trials”6 guidance which describes principles for global clinical trials including Japan and notes the necessity of considering ethnic factors when planning these clinical trials. The ICH E5 guidance classifies ethnic factors as intrinsic and extrinsic and lists many that should be appropriately considered during clinical trial planning (Figure 2).

In Europe, the EMA’s “Reflection paper on the Extrapolation of Results from Clinical Studies Conducted Outside the EU to the EU-Population” also indicated that particular extrinsic factors, such as medical practice, disease definition and study population, may influence the applicability of foreign data to an EU setting.7 Assisted by these regulatory guidances as well as ongoing engagement between regulators and industry, biopharmaceutical companies are designing MRCT to further prepare for and to mitigate some of the potential challenges noted above. MRCT preparations also allow the study sponsors...
to engage in proactive ethnicity discussions with the involved regulatory agencies and to broadly synchronise consideration of agency advice during the progression of the medicine development strategy.

Whereas it is clear that progress has been made to evolve global development strategies, the topic of MRCT would benefit from continued, targeted fora including the participation of global regulators and industry to further align on optimal approaches and to address unexpected challenges. Considering the numerous fora of regulator and industry collaboration, there are noteworthy benefits achieved for both parties. Collaboration often realises greater resource efficiencies, affords the opportunity to gain expert input from diverse perspectives, results in cohesive agreement on approaches and solutions, and streamlines communications.

All of these advantages should be further leveraged through continued regulator and industry collaboration on the topic of MRCT. Yet, stakeholders must likewise recognise and manage the unintended consequences associated with coalition activities. These include the challenge of reaching agreement or consensus on the path forward, orchestrating the logistics for meetings, maintaining the necessary initiative momentum between face-to-face interactions, and assuring the appropriate involvement of decision makers (Figure 3). Finally, given the preponderance of fora to address R&D-related issues and the need to demonstrate progress on MRCT, it is imperative that priorities be identified and well executed.

Many biopharmaceutical companies have vastly expanded their R&D infrastructures and strategies resulting in the development of an innovative medicine(s) now being considered as a global venture. To achieve the full promise of scientific advances to combat diseases experienced by patients across the globe, regulators and the regulated industry must continue to collaborate to maximise its collective expertise. The ability to develop new medicines depends on it.

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Sophie Viollet is a Senior Regulatory Information Associate at Eli Lilly. She holds a pharmacy degree and a Master degree in Drug Development and International Registration.

References/citations from this article are available upon request.
On August 21, the Asia-Pacific Economic Cooperation (APEC) Life Science Innovation Forum (LSIF) Regulatory Harmonization Steering Committee (RHSC) organized an Awareness Workshop, titled Promoting Public Health & Innovation Through Regulatory Convergence. The workshop, sponsored by the APEC Harmonization Center, featured presentations by a cadre of international regulatory leadership from Canada, Chinese Taipei, Korea, Japan, Mexico, Thailand and the US, and was hosted by the Health Sciences Authority of Singapore.

The APEC LSIF RHSC provides a platform to prioritize and address the regulatory harmonization concerns of APEC-member economies. The RHSC works in partnership with the AHC, an APEC wide harmonization resource established by Korea following endorsement by APEC Ministers in their Joint Ministerial Statement of November 2008: “Recalling our commitment to promoting regulatory reform and harmonization, we welcomed and endorsed the establishment of the APEC LSIF Harmonization Center in Seoul as a key step forward.”

In April 2011, the AHC, DIA and the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA) co-sponsored and presented the first Asia Regulatory Conference: Asia’s Role in Global Drug Development to strengthen cooperation between regulatory...
authorities and the pharmaceutical industry, to facilitate discussion of common Asia Pacific region regulatory and technical issues, and to encourage greater harmonization of regulatory requirements in the Asia Pacific region.

Attendees were welcomed to the AHC RHSC Awareness Workshop by Dr. John Lim, Chief Executive Officer, Health Sciences Authority (HSA), Singapore:

“At the Life Sciences Innovation Forum (LSIF) that was conducted in Singapore in 2009 when the APEC meetings were held here, the keen interest in improving the capacity and efficiencies of regulatory authorities through collective action, and the adoption of international best practices and standards, was very evident,” Dr. Lim began. “These themes resonate with Singapore’s HSA as they are imperative in ensuring that HSA is effective and equipped to safeguard public health and safety in our population, while simultaneously promoting life sciences innovation.”

“The LSIF plays a unique role in promoting a more strategic and coordinated approach to regulatory convergence internationally. It can achieve this by serving as an enabler of convergence and harmonization through promoting a better understanding and use of international standards and practices. It is also worth noting that the LSIF represents a tripartite network comprising government, industry and academia, all of whom play key and complementary roles in this journey.”

In addition to Dr. Lim, scheduled regulatory agency presenters included:

- Health Canada: Mike Ward: Manager, International Program Division, Therapeutic Products Directorate
- Ministry of Health, Labour & Welfare, Japan: Dr. Naoyuki Yasuda: International Planning Director, Pharmaceutical Affairs
- Korea State FDA: Dr. Kui Lea Park: Director, Center for Drug Development Assistance, National Institute of Food & Drug Safety Evaluation; Dr. Joung Weon Oh: Pharmaceutical Safety Information Team; and Dr. Mira Choi: Researcher
- COFEPRIS (Federal Commission for Protection against Health Risks), Mexico: Dr. Raul Ramirez: Executive Director
- Health Sciences Authorities, Singapore: Dr. Srinivasan N. Kellathur: Senior Regulatory Scientist, Advanced Therapy Products, Pre-Marketing Division, Health Products Regulation Group
- Taiwan FDA: Dr. Hsien-Yi Lin: Senior Reviewer
- Thai FDA: Dr. Farsai Chantaruporn: Professional Pharmacist, Bureau of Drug Control
- US FDA: Capt. Justina Molzon, MS Pharm, JD: Associate Center Director for International Programs, CDER; and Michelle Limoli, PharmD: International Programs, CDER

Representatives of industry, scientific and other organizations included:

- Dr. Samvel Azatyan: Manager, Medicines Regulatory Support Programme, Quality Assurance & Safety – Medicines, Department of Essential Medicines & Health Products, World Health Organization (WHO)
- Dr. Patrick Brady: Associate Vice President, Scientific & Regulatory Affairs, PhRMA (Pharmaceutical Researchers & Manufacturers of America)
- Dr. Lila Feisee: Vice President, International Affairs, BIO (Biotechnology Industry Organization)
- Dr. Lindsay Tao: Coordinator, Medical Device Industry Coalition
“As the name suggests, this workshop is meant to promote a greater understanding of the objectives and work of the APEC Harmonization Center and the Regulatory Harmonization Steering Committee so that regulators, industry, academia and other related parties interested in advancing regulatory convergence within the APEC region have the opportunity and channels to do so,” Dr. Lim continued. “Today’s event also marks an important milestone for the APEC LSIF in establishing an extensive base for engagement in RHSC projects and AHC workshops with the launch of the RHSC Regulatory Network and a number of industry coalitions that span the ambit of medical products, including pioneer pharmaceutical products, medical devices, biotechnological products and generic drugs.”

“A newly included area of focus that holds great potential to improve the health of our populations and promote life sciences innovation is that of advanced therapies. This is a broad and diverse category that includes cellular therapies, nanotechnology and other related-technologies that will challenge existing concepts and approaches to the regulation of health products. This is aligned with Singapore’s integrated plan to be an Asia-Pacific hub for biopharmaceutics research and development. This is one key reason why HSA strongly supports and champions the development of an RHSC roadmap on cellular therapies, working together with the US FDA and other interested parties in paving the way for prospective harmonization and information sharing,” said Dr. Lim.

**Associate Professor John C W Lim** is Chief Executive Officer of the Health Sciences Authority in Singapore. A/Prof Lim is a medical graduate of the National University of Singapore, and holds Masters degrees in Public Health from NUS and in Health Policy and Management from Harvard University. He is a Specialist in Public Health and Medicine, a Fellow of the Academy of Medicine, Singapore and Adjunct Associate Professor at the NUS Saw Swee Hock School of Public Health.

He has served as Administrator of the Singapore Blood Transfusion Service, Special Assistant to the Permanent Secretary for Health & Director of Medical Services, Deputy Medical Director of the Institute of Mental Health, and Director, Human Resource in Singapore’s Ministry of Health (MOH). From 1998-2000, he was Director of Higher Education and Director of Public Affairs in Singapore’s Ministry of Education.

In his current position, he oversees HSA’s wide-ranging public health responsibilities as Singapore’s regulator of health products, its national blood service, and also the national forensic science and forensic medicine centre.
INTRODUCTION

“Promoting public health via early access of innovative medicinal products to patients who need them” should be the common goal for Regulatory Authorities (RAs) and pharmaceutical companies alike. However, it takes eight to twelve years, at the cost of $800-1200 million, to bring the medicine from bench to bedside. Moreover, the healthcare industry is one of the most regulated global industries, and during the course of bringing the product to the market, the industry will have multiple interactions with the RA, and that relationship continues over the course of the lifecycle of the product. It has been suggested that some of the delays, and costs, of bringing the medicines to market are due to the complexity of these regulatory interactions which can be daunting, especially for small startup companies. Despite comprehensive guidance documents from the major regulatory agencies and the International Conference on Harmonisation, delays can be caused due to lack of consistency, clarity, transparency in decision making, and poor
FDA relationship. The survey concerns about the industry—recent report identified many sciences industry and a Administration) and the life—United States Food and Drug agency (e.g., on the relationship between studies have been conducted risk assessment. Various changes or changes in benefit—pharmacovigilance, manufacturing compliance/inspections, as advertising and promotion, marketed to discuss topics such continue even after the product is license to manufacture and sell an approval, or rejection, of a clinical trials which culminate in development and continue usually start during preclinical regulatory authorities. These dozen interactions with the (industry) has up to two development, the sponsor biopharmaceutical product During the lifecycle of biopharmaceutical product development, the sponsor (industry) has up to two dozen interactions with the regulatory authorities. These usually start during preclinical development and continue through the various stages of clinical trials which culminate in an approval, or rejection, of a license to manufacture and sell the product. These interactions continue even after the product is marketed to discuss topics such as advertising and promotion, compliance/inspections, pharmacovigilance, manufacturing changes or changes in benefit—risk assessment. Various studies have been conducted on the relationship between the regulatory agency (e.g., United States Food and Drug Administration) and the life—sciences industry and a recent report identified many concerns about the industry—FDA relationship. The survey found opportunities for improving interactions, with nearly 48% of respondents agreeing that greater collaboration with the FDA is needed. So one could ask if a life—science industry and RA co-location, taking the successful model of a “Biocluster,” could be the answer to greater collaboration? A few countries in Asia have taken this concept forward.

Singapore, over a decade ago, was one of the first to experiment with this concept. It located its RA, the Health Sciences Authority (HSA), in a science park called Biopolis which was described as the biomedical hub of Asia. Several other government agencies, publicly—funded research institutes and research laboratories of pharmaceutical and biotechnological companies are located there. It has become a model and others have followed.

Other countries, such as Korea, have started building large planned science parks, one of the largest being the Osong Bio—Health Science Technopolis for the bio—health industry for a research cooperation system with the government institution. Notably, the Korean Food and Drug Administration (KFDA) has relocated from Seoul to Osong along with the other governmental institutions to provide various “one—stop services” regarding clinical trials, new medicines development, patents, and international collaborations.

Taiwan is building a new park called the Nangang Biotech Park, where part of the Taiwan Food and Drug Administration (TFDA) and Center for Drug Evaluation, offering regulatory consultation and training, will expect to be in 2016. This will be alongside the coordination of the newly set up Supra Integration and Incubation Center (SiIC) under the Taiwanese National Science Council. They will use a value creation concept to design its strategy for the biopharmaceutical industry, with the TFDA being in the middle of that development—a novel concept. See previous page for an artist’s rendition of the Park.

China, which has seen a prolific growth in science parks in the last decade or so, has incorporated the local or provincial State Food and Drug Administration (SFDA) within the park. One such example is the sprawling China Medical City in Taizhou where the provincial SFDA has its offices to support the local and multinational companies. There are examples of other technology parks that have district or provincial SFDA, such as the Shanghai Pudong FDA covering Shanghai Zhangjiang, and the Tianjin Binhai FDA covering the Tianjin Economic Technology Development Area.

It is worthwhile to note that these science parks attract mostly start—ups or smaller companies as many of them are relatively inexperienced in new drug development and will benefit the most from this set up. This approach, of being completely incorporated into these parks, may not be amenable to the larger research and manufacturing based enterprises, but it is conceptually possible to have part of their organization based in these parks to allow closer proximity to the RA.

These close partnerships can be mutually beneficial in many ways.
The close proximity of industry and RA would provide efficiency, transparency, consistency, clarity, and therefore effectiveness. It would also facilitate a partnership from the beginning of the drug development process and mitigate potential delays in access to important medicines for patients. Reciprocally, the RA can benefit from close interaction with the researchers in paving the regulatory path for emerging new technologies. Ultimately this could result in faster access to medicines, possibly at lower costs to the government and the sponsor, and thus would benefit the patients.

There have been reports in the press that suggest a relationship between the industry and agency as being too close or too close for comfort. To avoid these misconceptions, real or otherwise, there would need to be proper “SOPs and codes” that define “rules of engagement” between the industry and RA to afford opportunities for collaboration during the lifecycle of drug development. This would allow transparency around decision making which is key for a fair and balanced decision making process. There are risks if the RA becomes too integrated into the science park, and that the data assessments might be done by academic third parties co-located in the park or in the industry before submitting the data to the RA. Some may have a concern of the RA “looking over their shoulder.”

Recently there have been some unfortunate examples where drug safety issues (e.g., Mediator in France) have been attributed to a relationship that was considered as being too close, and where a timely benefit-risk assessment of the product was not reported by the company or not evaluated by the RA in a timely manner.²

To curb some of these challenges, the European Medicines Agency (EMA) has recently announced strengthened policies on handling conflicts of interest and encouraging transparency. As part of this initiative there will be continued implementation of the legislation on pharmacovigilance and on falsified medicines, further development of the communication activities of the Agency with increased transparency and better explanation of why decisions are made, ensuring efficient interactions between the committees and increasing the efficiency of the Agency’s operations.³

Similarly the US FDA has published a report where it has adopted eight initiatives aimed at improving transparency by promoting greater access to compliance and enforcement data.⁴

Certainly these initiatives will help but needless to say, the health authorities and companies should foster good relationships with each other based on science, and must maintain a healthy distance by “rules of behaviour” that are not influenced by geographical distance or mindset.

References/citations from this article are available upon request.

The views expressed herein represent those of the author and do not necessarily represent the views or practices of the author’s employer or any other party.
In order to promote a new drug and medical device research and development (R&D) biotechnology industry in Taiwan, and to be an Asian R&D partner for the global community, a top-down national initiative, “Taiwan Biotech Takeoff Diamond Action Plan,” was launched and has been implemented stepwise since 2009, and was further revised in 2012.

The 4 pillars of the action plan are:

1. Translational research (via a national program of medical research for value identification)

2. A Supra Integration and *Incubation Center (SI2C, inaugurated in November 2011, for value creation)

3. The Taiwan Food and Drug Administration (TFDA, inaugurated in January 2010, for regulatory infrastructure)

4. Biotechnology Venture Capital (BVC, for value amplification).

*A “business incubation” is a unique and highly flexible combination of business development processes, infrastructure and people designed to nurture new and small businesses by helping them to survive and grow through the difficult and vulnerable early stages of development.

Among them, Si²C is the key driver to translate innovative research results into commercialized products to benefit patients. This translational effort has not seen much success in Taiwan previously. As part of the recent trend in global pharma R&D decentralization and operational entry into emerging...
markets, Taiwan has taken the opportunity to enter the business and value chain of the biotechnology industry. In this way, it can become a recognized regional leader and global player through the construction of fully integrated centers of excellence in research, development and commercialization for selected diseases with a strong medical need and business potential in Asia Pacific markets. Key elements for building a successful Taiwan biotechnology industry should include value-chain capability building and sourcing of the best possible technologies, funding mechanisms to support efficient R&D and technological transfer activities, connection to, and collaboration with, global Asia Pacific and China networks, and development of new skills through training, and recruitment of domestic and overseas personnel.

Specifically, goals and responsibilities of SI²C include:

1. Initiate value-chain mapping and capability building for new drugs and medical devices R&D
2. Select and incubate early domestic and overseas R&D projects leading to technology transfer and new company formation
3. Establish seed funding, i.e., low level financing needed to establish a new idea to support project work flow before major (venture capital) investment
4. Provide training for future leaders of startup companies.
5. Support biotech park planning
6. Acquire late-stage products in selected disease targets for a fully integrated portfolio including products that can make an impact in the short-term
7. Build international networks and collaborations

In addition, SI²C plays a key advisory role to Taiwan’s National Science Council (NSC) and Board of Science and Technology (BOST). This includes bringing key R&D management concepts and practices into new drug and medical device R&D grant review, approval, and monitoring processes, specifically by:

1. Changing the current “period-based” into “milestone-based” funding for projects sponsored by the government
2. Using the “performance matrix” indicators to evaluate the process instead of the number of patents and publications achieved
3. Setting up an “Intellectual Property sharing principle” for all stakeholders involved as a sustainable business model
4. Introducing portfolio management tools and decision rules into the monitoring of all granted projects.

During the past year, the value chain mapping and capability building have been completed for liver cancer, lung cancer and tuberculosis. These efforts provide Taiwan institutions collectively as global centers of excellence for the new drug discovery and development against these diseases from target identification all the way through clinical trials. Project teams have been formed to search both domestically and overseas for opportunities in academia, startup companies, and big pharma for entry into the SI²C portfolio. These multi-disciplinary teams of SI²C include patent, regulatory, clinical, business and legal staff, who will monitor, facilitate and support the progress of the projects including technology transfer, securing the seed fund investment from public or private sectors, and facilitating the setting up of the startup companies. Portfolio Advisory Groups, composed of experienced domestic and overseas senior experts covering research, drug development, intellectual property, clinical, regulatory affairs, business planning, financing, and manufacturing process development, have also been established to help in reviewing the due-diligence reports in order to select the projects for funding and incubation. SI²C is in discussion with Stanford University in the USA to introduce their SPARK concept of talent development to Taiwan and establish a similar program in local universities. Similarly, the Stanford-Taiwan Biomedical Fellowship Program for medical devices will be expanded locally in Taiwan. In supporting Biotech Science Park planning in content management and capability building, SI²C has worked with the NSC and Academia Sinica to design R & D and incubation centers in three science parks. This includes the Hsinchu Biomedical Science Park (established in 2011 with a focus on medical devices and leveraging the nearby Information Computer Technology industry), Tainan Southern Science Park (with a focus on dental and orthopedics tools and instruments) and NanKang Biotechnology Science Park (expected to be
inaugurated in 2016 with a focus on pharmaceuticals, leveraging nearby Academia Sinica, Taiwan FDA, hospitals and Universities in Taipei). To gain early recognition and support of this initiative, SI2C needs to select a number of “high impact cases” to help illustrate the SI2C business model. Some of these show cases can be late-stage development projects so that success can be seen in the short term. A number of full due diligence procedures have been performed for overseas opportunities during the past year.

There are certainly still many challenges ahead for SI2C. For instance, there may not be enough experienced senior managers or project managers available locally to provide a ‘jump start’ for SI2C. The salary scale and rewarding schemes have no comparison to the private sectors abroad. When it comes to terminating an ongoing project with good scientific merits but inadequate commercial potential, there may be resistance from academia. Finally, the seed fund from the public and private sectors may not be enough to fill the gap in funding and support for the kind of research that moves basic science down the path toward commercialized products.

Despite the many challenges, SI2C is encouraged by the support from the government, academia, and domestic industry to gain its initial footing, and hopes to see a few success stories in the near future.

Herng-Der Chern, MD, PhD, Distinguished Research Fellow, Center for Drug Evaluation (CDE), Chinese Taipei, received his MD from National Taiwan University and his PhD in Pharmacology from the University of Pittsburgh. Dr. Chern served as Executive Director of the CDE until March 2011, in charge of technical review of IND/NDA/HTA. He has played a vital role in promoting ICH concepts, GCP education, good review practices, bridging studies, new drug development and health technology assessments in Asia. Before the CDE, he served as head of the Division of Clinical Pharmacology of National Taiwan University Hospital and associate professor at National Taiwan University.

Whaijen Soo, MD, PhD, is a global pharmaceutical and biopharmaceutical R&D executive with over 25 years of experience in various diverse therapeutic areas. He received his MD from the University of California, San Francisco, and his PhD from the University of California, Berkeley. Before he joined the SI2C, he served as Senior VP and Global Head of R&D, Shire Human Genetic Therapies; as Global Head of Clinical Research & Development, Biogenidec; and as VP & Global Head of Clinical Development, Oncology, Virology & Organ Transplant, Roche.

Ling-Mei Wang, PhD, serves as Chief Operating Officer at SI2C in Taiwan. She received her PhD from the UT Health Science Center at San Antonio, her post-doctoral training at the National Cancer Institute, National Institutes of Health, continued her career as an NIH researcher, and as a senior researcher at Van Andel Research Institute in Michigan. She previously served as SI2C CTO and as Deputy General Director at Biomedical Technology & Device Research Laboratories, Industrial Technology Research Institute, where she led the R&D groups.
THE GLOBALIZATION OF MEDICINES

The clinical development burden to pharmaceutical companies is increasing, currently accounting for around 36% of research and development expenditure and on average, 7 to 8 years of time. Moreover, most medicines are not developed for only one country, and although most regions want to participate in global clinical trial programs, for an increasing number of countries such as China, India, Taiwan, South Korea, Vietnam, and Russia, the conduct of local clinical trials is a requirement for the registration of new medicines.

There are a number of agencies that are trying to reduce the regulatory burden through streamlining/centralizing the ethics review and the use of risk-based approaches, such as a reduction in the time for clinical trial approval in India through the acceptance of trial protocol approval from reference countries, clinical trial waivers, and the adoption of clinical trial notification/clinical trial exemption process that occur in Australia and Taiwan. However at the same time, foreign clinical trials are coming under increased scrutiny and ethical oversight in regions such as Europe and the United States, and as detailed in a reflection paper by The European Medicines Agency Working Group on Clinical Trials Conducted Outside of the EU/EEA, future...
dossiers may predominantly include clinical data from outside the traditional countries of Europe, Japan, and the United States.

Companies looking to ensure good clinical development decision making are also looking to streamline the clinical development process. Participants in a workshop convened by the Centre for Innovation in Regulatory Science – CIRS – developed factors to be considered for the inclusion of countries in a clinical development plan (Table 1). Other considerations include a country’s socio-political business environment, clinical practice and operations regulatory process and requirements and need to be viewed from the perspective of:

- **Internal (company) factors or the way in which a company conducts its business:** Much depends on whether the company is sufficiently informed of a country’s regulatory procedures. In addition, industry must employ a realistic approach in deciding whether a country can assume a role in meeting the company’s global regulatory or marketing strategy.

- **External (local) factors:** These factors relate to the existing environment in the target country that would make it attractive for inclusion in a clinical development program, such as access to the regulatory authority, the regulatory authority infrastructure, in particular the application of GRevPs, a control process that ensures that all reviewers apply same review standards, the transparency of the review process, availability of guidance on regulatory requirements, and adherence to stated regulatory requirements, review practices and timelines.

- **Cross-cutting issues:** These are factors that might allow the company to work alongside the regulatory agency to make the environment more economically attractive such as the mechanisms to encourage feedback from or to agencies to improve working practices or to increase the acceptability of data from other regions.

### THE IMPORTANCE OF GOOD REVIEW PRACTICES

Irrespective of a country’s approval system, good review practices (GRevPs) and control processes within regulatory agencies instill stakeholder confidence in the decisions of those agencies. GRevP is the documented best practice related to the process, format, content, and/or management of a product review. GRevPs provide consistency to the overall review process, as well as improve the quality, efficiency, clarity, and transparency of reviews and review management. GRevP are thought to be of value in that they:

- Ensure completeness and comprehensiveness of the review, describing the critical tasks and required elements
- Detail expectations for the reviewer and the review
- Eliminate the need to reinvent the elements of the review and the format and content of the review document
- Avoid the potential for critical omissions, and make completeness readily visible, by specifying the general format and content of a review
- Recognize that format influences content by imposing a logic to the review
- Build in quality by shaping both the conduct of the review and the presentation of the results

Regulatory agencies are continuously evolving their process and practices to ensure that they are using the best tools and techniques to improve the quality of the review (Figure on previous page). It is well established that the elements of a good quality review are clarity, transparency, predictability and timeliness, and that it is important that the process that an agency undertakes whether to review a new medicine for registration or as part of the clinical trial review process is both efficient and effective. GRevPs and good review management practices (GRevMPs) should be part of the philosophy, behavior, and culture of an agency throughout the review process. Although well established in mature agencies these practices are being actively integrated and adopted across agencies with emerging pharmaceutical markets in Asia, Latin America, the Middle East, and Africa.

### APEC SURVEY

The results of a 2011 CIRS study showed that companies rated the timeliness, predictability, quality, and transparency of the majority of 22 agencies (including 15 Asia Pacific Economic Cooperation (APEC) countries) as fit for purpose across these four specific aspects. However the evolution
of GRevP in emerging market countries will be critical, especially in the APEC region where, under the APEC Life Science Innovation Forum, Chinese Taipei is the sponsoring economy and Canada, China, Indonesia, Korea, Malaysia, Mexico, Peru, Philippines, Thailand and the United States are co-sponsors of a program to develop best regulatory practice for medical products and devices, with a focus on a strategic approach. The objectives of this program are:

1. To promote the adoption of best regulatory review practices in order to improve the quality, consistency and transparency of scientific assessments of medical products and the efficiency of regulatory systems and

2. To recognise the importance of GRevP to a well-functioning regulatory system and to establish mutual confidence in each other’s practices.

As part of this initiative, to examine GRevPs within APEC agencies, to identify gaps and subsequently to develop training to promote and enhance these practices, a detailed survey was undertaken. Fourteen responding APEC agencies indicated that the three main reasons for introducing quality measures in regulatory review are the insurance of consistency, the accomplishment of efficiency and the increase of transparency of those reviews. The early indicators from the study suggest that most of the responding agencies have implemented GRevPs, although the majority of these are informal and most are subject to the need for improvement. In addition, survey results indicated that their agencies would benefit most from training in three main areas:

1. Assessment frameworks, templates, reports and decision tools
2. Overviews of measures and approaches to GRevPs/ GRevMPs
3. Improving performance through target times and project management

The full results of this study will be published, but this initiative bodes well for improvement of the review standards in the APEC region and the enhancement of confidence with which agencies regard each other’s assessments, increasing the possibility for sharing resources and information across the agencies.

References/citations from this article are available upon request.

Table 1. Company considerations: selecting the mix of countries for global clinical trials

- Compliance with good clinical practice
- Institutional Review Board/ Ethics Committee and regulatory approval times and the regulatory environment
- Disease prevalence and standards of care
- Quality and availability of research professionals
- Patient availability, start-up and enrollment times
- Costs
- Potential to assist in the achievement of strategic business and marketing objectives

NEIL MCAUSLANE
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is currently Director of the Centre for Innovation in Regulatory Science (CIRS), an international forum for industry, regulators, HTA and other healthcare stakeholders to meet, debate and develop regulatory and reimbursement policy through the innovative application of regulatory science. Dr. McAuslane completed a PhD degree in Clinical Pharmacology from the University of Edinburgh, an MSc in Toxicology from the University of Surrey and a BSc in Pharmacology from Dundee University. He has initiated a number of key CIRS projects in regulatory strategy and R&D performance and is the author or editor of numerous related publications and reports.

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Challenges and Opportunities for Clinical Trials in Asia Pacific

A pharmaceutical company’s perspective on navigating the regulatory process

CHALLENGES

From an industry perspective, regulatory agencies in Asia Pacific can be broadly viewed as falling into three categories. These are “straightforward” regulatory agencies that adapt to international guidelines, have relatively transparent pathways to drug development and follow a predictable timeline to completion. Japan, Korea, Taiwan, Australia and New Zealand, Hong Kong and Singapore can be viewed in this way.

China and India can be viewed as falling into a second category, and can be termed “complicated” agencies, as they do not have clear requirements or predictable approval guidelines. Regulations may be different in practice to those on paper in these regions. Most South East Asian countries fall into a third, “in-between” category.

A number of challenges in country-specific guidelines have made clinical trial submissions difficult and have therefore been impediments to efficient approvals. These are the differences in allowable submission documents, varying procedures for Clinical Trial Applications and ethics committee approvals in nearly every country, and the number of translations required. The requirements for translations add cost and time to the process. For example, in China, all documents – which amounts to thousands of pages – must be translated. Document translation can add an additional 2-3 months to the review process. In India, all patient materials must be translated into up to 10 local languages.

Trial specimen export adds a further complication in countries such as Taiwan, where regulatory authority and ethics committee approvals are required, and in China, where uncertainty on the exportation application could add an additional four months to the timeline.

The final challenge is the local, country-specific requirements for the Informed Consent Form/
Commitment Letter/Contract that even “straightforward” countries follow. Templates vary from country to country, and in some countries language is non-negotiable.

**POSITIVE TRENDS**

Despite these challenges, there are several positive changes that have occurred in the Asian regulatory landscape.

Agencies are working to shorten the review timeline; for example, the Korean FDA’s simplified Clinical Trial Application process for phase 1 trials was instituted a few years ago. Also, China SFDA started a “special review process” (so called “fast track”) to shorten the Clinical Trial Application approval timeline for innovative products.

Health authorities are becoming more transparent and open to industry. For example, China’s Center for Drug Evaluation (CDE) is advancing reform within the consultation and review process by improving methods for pharma representatives to reach CDE officials to ask questions or monitor application status online through the CDE website. Face-to-face meetings between CDE and applicants are now permitted to help them better understand the product and expedite the review process for innovative product applications.

The Association of Southeast Asian Nations (ASEAN) guidelines and changes to ASEAN Common Technical Document (ACTD) help the harmonization of the submission requirements in those countries. The batch number reduction and document simplification of Chemistry, Manufacturing and Controls (CMC) document requirements for investigational new drugs (INDs) in China are also signs of local harmonization of international regulations. APEC and ICH initiatives reflect trends towards looking at the possibility of mutual recognition of clinical data, with official discussions already begun between China and Taiwan, as well as between China, Korea and Japan.

**HOW CAN INDUSTRY ADDRESS ALL THESE CHALLENGES?**

Industry could work together to try and address the challenges. For example, they could provide more support to health authorities, including the introduction of global guidelines and international practices, they could share industry/associate networks with authorities, and use multiple channels to influence governments to allocate more resources to regulatory agencies. As earlier stage enrollment of Asian subjects will significantly reduce the timeline for product launch in Asian markets in the future, companies should consider involvement of the Asian population in Phase I and II trials when creating a global development plan. Towards this goal, the Taiwan Food and Drug Administration reduced the Certificate of Pharmaceutical Product (CPP) requirement to encourage this early involvement in trials conducted in Taiwan.

The industry as a whole needs to have local expertise to help companies and the industry better address challenges in the region.

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The National Institute of Allergy and Infectious Diseases (NIAID) at the National Institutes of Health in the USA has a strong history of conducting collaborative clinical research in resource-constrained settings overseas. The goal of these collaborations is to strengthen the local research infrastructure by providing support to the existing scientific and operational systems in these countries.

A key strategy for successful partnerships in international research is the development of research networks that bring together medical centers, laboratories, government agencies, and supportive groups that provide statistical, data management, and coordination components. These groups pool their resources and expertise so that multi-center and multi-country clinical trials can function in a streamlined and expeditious fashion. Although a research network can fall prey to bureaucratic slowdowns, with proper attention, networks create greater collaborative opportunities and streamlining of costs than individual sites working in isolation.

Networks are focused on creating common standards across sites during a clinical trial, with all investigators following the common study protocol, receiving common training to ensure consistency of data, setting quality control procedures to ensure the quality of data, standardizing methods for storing specimens, putting standard operating procedures into place, and establishing policies for publication and authorship.
The enhanced quality resulting from the network collaborations benefits all the partners. Networks are geared to address research topics of relevance to the host countries, such as locally emerging epidemics, and they provide mentorship and research experience for young investigators.

In one example, the Collaborative Clinical Research Branch (CCRB) of the NIAID established the South East Asia Infectious Diseases Clinical Research Network (SEAICRN), originally an Influenza Clinical Research Network. The SEAICRN is a collaborative partnership of hospitals and institutions in Thailand, Vietnam, Indonesia and Singapore. The network strives to advance the scientific knowledge and clinical management of infectious diseases in general, and influenza in particular, through integrated, collaborative clinical research in the South East Asia region.

The SEAICRN came into existence in 2005 and is made up of hospitals and institutions with varying degrees of clinical research experience. The mission of the network is to advance the scientific knowledge and management of emerging infectious diseases through integrated, collaborative clinical research.

During the first year of the SEAICRN efforts focused on building the capacity of the network hospitals to conduct research according to international quality and regulatory standards. For the network, the standards chosen included the United States Code of Federal Regulations, International Human Subjects Protection regulations including the Declaration of Helsinki and the Belmont Report, and the International Conference on Harmonization Good Clinical Practice Guidelines (ICH GCP).

Twelve sites joined the SEAICRN, four in Thailand, five in Vietnam and three in Indonesia. Singapore joined the network at a later time and sites there required less support. All initial sites were high level research institutions in their countries but not very familiar with ICH GCP or other standards.

Initial individual site assessments were conducted at the outset, with immediate focus on fielding the first study protocol. Because each site brought varying levels of research experience to the network, there was a differential level of support required for the individual sites.

There were three main areas of operational focus: 1. training, both operational and academic, 2. lab quality, including central/reference labs and local clinical labs, and 3. site development. All the work focused around the first study, an IND treatment study for avian and severe human influenza.

The activities of site development focused on:
- Human resources / Research staff
- Physical infrastructure
- Laboratories
- Pharmacies
- Data management
- Standards for international research

Support to the sites was provided by trained local medical personnel, Clinical Trials Support Specialists (CTSS). They provided large group trainings as well as side-by-side training at assigned sites in their country. Because they spoke both English and their native language they were able to convey new ideas more efficiently than could have been done by translation. They very quickly established themselves as valuable supports to the local clinical research institutions.

Sites varied in their skills at conducting research. At the basic level, a site conducted the protocol following standards set and provided by the sponsor. At a higher level a site was able to function at ICH GCP standards on its own initiative. Two issues that immediately became apparent with the approach of local site supports were that the anticipated use of a research team, with a central study coordinator, was not a generally or easily accepted practice, and that the CTSS was overly relied upon by under-resourced sites.

The network strove to have an inclusive process that avoided a paternalistic "Western" viewpoint, but which treated the sites with the same principles normally applied to the treatment of study participants. At a midpoint assessment (of the first 5 year funding cycle) an effort was made to measure site self-reliance in sites that volunteered for this assessment.

A task force was formed and spent several months developing definitions, categories, and values. The result of this effort was a proficiency skills matrix, identifying skills valued by the network, each with a metric for what constituted proficiency in each skill. A collaborative planning process involved representatives from each country network operations office, Oxford University, NIAID, and the Wellcome Trust, with input from study sites.
The process of creating the site self-reliance program created a shared mission/vision for the program – to provide whatever assistance possible to enable sites to become independent of the CTSS system, and improve the quality of their research to the level they themselves desired. Guidelines were developed to describe the expectations of the program and details on how to implement it.

Site competency/assessment metrics were a large part of the development process – selecting the areas to assess, key elements of a successful site, and metrics for quantifying current levels of core competencies. It was seen as key that this would be a completely voluntary process, built in collaboration with site principal investigators (PIs) and members of their study team. In order to implement this, a determination of the interest of sites was needed.

An assessment team was formed, relying on experienced evaluators who took a teaching perspective, not that of an auditor or monitor. Using site competency metrics, the evaluation intended to provide an initial assessment of capability in key areas: regulatory, clinical study implementation, data management, financial, and site management. The assessment was meant to be kept as simple as possible, with a focus only on the highlights of necessary skills.

After an assessment, the team worked in collaboration with the site PI and staff to develop a “site self-reliance plan” including measurable goals and timelines of activities. The team worked with the site PI to determine what areas would be the primary focus at their site.

The pilot assessment was conducted at one of the Indonesian sites, and was meant to help test the assessment plan and tools as well as evaluate the site. Due to a hold on funding this process was stalled and it is hoped it will be resumed again soon. Having strong research sites available within these countries in SE Asia would be a tremendous strength when a new disease is emerging and a quick start is needed to implement quality clinical research in the region.

Julia Welch, MS, supported the National Institute of Allergy and Infectious Diseases (NIAID) as a Clinical Project Manager II with SAIC-Frederick, Inc. She is a clinical trials specialist for the Southeast Asia Infectious Disease Clinical Research Network (SEA ICN). Prior to this position, she managed clinical trials research projects for over twenty years at Family Health International (FHI). At FHI she served as the Director of Research Operations for the Clinical Research Department, training staff and setting policy for the research management and monitoring division. She has extensive experience conducting and supervising clinical trials in resource-poor settings. Julia is currently a JD Candidate at UNC School of Law, Class of 2015.

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The South East Asia Infectious Disease Clinical Research Network (SEAICRN) is a collaborative partnership of hospitals and research institutions in Thailand, Vietnam, and Indonesia formed in September 2005. Representatives from clinical sites, academic centers, governments and philanthropic organizations from Vietnam, Thailand, Indonesia, United States, United Kingdom, and the World Health Organization (WHO) identified the need for advanced preparation, coordination and increased capacity in order to quickly respond and conduct clinical trials in the context of outbreaks or epidemics of emerging infectious diseases. The Network was created in order to develop the necessary partnerships in the region to conduct collaborative clinical research addressing emerging threats, to increase scientific knowledge and directly contribute to improved clinical management of infectious diseases of public health importance.

The Ministry of Health (MOH) of Vietnam was selected as a partner in the SEAICRN. Within Vietnam there were five hospitals identified as research sites for the network. All five were leading institutes in Vietnam and were already conducting research, though all were unfamiliar with the use of ICH GCP to guide the conduct of human subject research.
Clinical trials that are conducted under a standardized ethical review process are relatively new in Vietnam. The country experiences emerging diseases such as severe acute respiratory syndrome (SARS) and highly pathogenic avian influenza. While other infectious diseases are endemic, chronic diseases, related to life-style, tobacco use and a rapidly changing diet, are increasingly burdening the healthcare system. Many parties, including the MOH, academia, international development partners, and the pharmaceutical industry have a strong interest to conduct clinical trials and other research in Vietnam to support health development work and reform of the sector. Especially with trials of experimental new drugs and medical devices, the MOH is faced with an urgent challenge to develop a system of oversight that follows the Principles of Good Clinical Practice (GCP), which protects the rights and well-being of human subjects. Joining the network provided an excellent chance for Vietnam to improve its system of clinical trials provision and oversight.

Vietnam’s healthcare system is hierarchical, with clear levels of division under the Ministry of Health. This hierarchy in many ways makes it easier to work within the system and to effect change, as responsibilities are clearly at the top. Leadership is accepted within the system and among people in the community.

It became difficult however to add in a new role, such as a Principal Investigator or a Study Coordinator. Since these are positions of importance on a study team, the local hospitals saw it as critical that these roles be assigned to high level personnel within the hospital, such as the Director. There was a strong resistance to having a nurse be the study coordinator and most hospitals assigned the task of completing case report forms to a higher level physician, often the director of the ICU or Infectious Diseases department within the hospital.

To make these studies possible in accordance with national and international standards, the SEAICRN embarked on a significant clinical research capacity building. The key objective was to establish an experienced clinical research team comprising of doctors, nurses, study coordinators, research pharmacists, laboratory technicians, data management and administrative personnel. To support this program, the SEAICRN developed a new model for clinical trials support by establishing local Clinical Trials Support Specialists (CTSS) and contracting with FHI 360 (a non-profit human research and development organization providing clinical research services in the region), to provide staff to fulfill this role.

Local CTSSs were located in each city where studies were conducted. In Vietnam, those cities were Hanoi and Ho Chi Minh City. In Vietnam, 2 CTSSs and 1 Lead CTSS supported the 5 Network sites in Vietnam. Their role was generally defined as to provide day-to-day support to the investigator and his/her study team to conduct the study according to the protocol and all regulations. In short, the CTSS served as a local and easily accessible clinical trials expert to help guide the site study team through all aspects of the study. In Vietnam, both CTSSs were local medical doctors and were trained in operations of research under ICH GCP and then were leaders in training the partner sites.

Training focused on developing clinical trials knowledge, operational implementation of one IND protocol and site specific preparations and tracking. Training topics included: GCP and Research Ethics, Study Procedures, and Protocol Specific Implementation. CTSSs visited their assigned sites several times each week to help site staff navigate Vietnam’s ethics and regulatory approval processes. Side by side training was provided in many areas, including Source Record Keeping, case report form (CRF) completion, Investigator Regulatory File set up, pharmacy storage and accountability, and laboratory tracking and accountability.

Successes were many. Using local health professionals, based in the same time zone, provided a reliable access point to the site for the sponsor. CTSSs could do more than translate; they could learn and explain the new ideas for study personnel and observe and address cultural challenges that were met.

As the SEAICRN developed a core of well-trained Clinical Research Site Staff, they developed a core within each country of clinical research experts, with an understanding of Research Ethics and Good Clinical Practice, with a capable approach to conducting a clinical trial within these guidelines. Many
of these first CTSSs have moved into higher positions, including working with the MOH as advisors in development of clinical trial regulations.

There were also areas of concern. Hospitals did not initially accept staffing requirements; this was limited by system structure. However, it has improved with time. An over-extended hospital staff relied too heavily on CTSSs and tried to recruit them to do the work of the site such as completing case report forms, though they were not allowed to do the site’s work for them. Understanding of local regulations was poor at sites, and required extra support and time investment from CTSSs.

The site self-reliance assessment process was optional and only one site opted for it initially in Vietnam. The assessment process was thorough. The immediately obvious barriers were within their own institution regarding acceptance of staffing a clinical study team.

As the CTSSs worked with the sites in Vietnam, it was obvious that development was also needed for the local ethics committees. There were a number of ethics committees in Vietnam which had registered with the Office of Human Research Protection (OHRP), but only one was found that was transparently following SOPs and a routine system of operation. That one ethics committee was the Hanoi School of Public Health. It was structured, had SOPs, and was able to follow GCP but was not in a clinical medicine center.

Additional approval was required by the MOH in order to gain approval to import study product and review was also required by each hospital’s approval committee and the ethics Committee of the US NIH.

At about the same time that the SEAICRN was being established in Vietnam, the MOH issued a call for support to international development and research organizations to help them improve their system of oversight of clinical trials. From 2006 through 2008 the US FDA offered a long term partnership to provide in-depth GCP Training in how to conduct a Regulatory Inspection. The FDA also joined with FHI 360 to provide training on institutional review board (IRB) operations to monitor compliance with human subject protection.

During this same time, the MOH developed and issued the following regulations for clinical trials: No 36/2006/QD-BYT for Medical Device and 01/2007/ QD-BYT for Medicine. They issued GCP Guidelines for Vietnam following ICH/ GCP Guidelines and a training strategy was established for MOH ethics committee members and for PIs, Investigators and Health Officers.

In 2008, the MOH Ethics Committee was funded for the new term until 2012. It provided definitions of roles and tasks, and a regular meeting was established one day each month for review of clinical trial protocols. In July 2008 the MOH EC held 2-day SOP workshop with FHI 360 resulting in completion of thirteen SOPs for the operation of the committee. They also worked with FHI 360 to provide GCP training for EC members & PIs as well as GCP training for investigators at sites throughout Vietnam.

In Vietnam, with varying degrees of development there are now 21 IRBs registered with OHRP. The new regulations in Vietnam require that the MOH Ethics Committee reviews all clinical trials. Their approval is required for an import permit and also for ethical oversight.

In Vietnam, the influx of focused and sustained site support provided by the SEAICRN was synchronous with an effort by the MOH to achieve even broader benefits for their system of clinical trials oversight. Regulations are now clearer and there is a GCP guidance document in place as well. Sites have improved proficiency in clinical trials and ethics and regulatory systems are improving. Challenges still exist related to culture and existing systems, but they will gradually be given the chance to improve with support from this network.

Peggy Coyle, RN, MES, worked more than six years in FHI 360’s Vietnam country office as Senior Manager of their Clinical Research Program, supervising 11 staff to initiate and develop this new program area within FHI Vietnam. The team developed the Clinical Trials Support Specialist role in Vietnam and provided key support to research institutions in Vietnam. Peggy also had a lead role in partnership with Ministry of Health in development of their system of Good Clinical Practice, ethics and regulatory oversight of clinical trials in Vietnam.
ADVISE includes the “how to” articles you have become accustomed to reading in the former Best Practices section: Time management, skill development, technology, software topics and more are examined for day-to-day implementation in your own jobs and offices.
Identifying the Right Study Sites

At the 2012 DIA 48th Annual Meeting, the team at The Biomedical Research Alliance of New York (BRANY) booth took an informal poll of attendees to learn what were the biggest, most vexing challenges in their day-to-day jobs. One issue came up repeatedly – how to identify and properly vet a study site. This article reviews the issues around finding appropriate study sites and tips for reviewing them.

Identifying high quality clinical research sites is imperative in running a successful trial. From patient recruitment through compliance and appropriate data collection, the success of a trial is largely dependent on the quality of the investigator and the site. Identifying and managing clinical trial sites represent a significant investment for sponsors. Some studies have estimated that it costs pharmaceutical companies approximately $20,000 per study site to start a study.\(^1\) Having a clearly defined vetting and evaluation process can go a long way in expediting study start-ups and increasing productivity for sites.

The overall pool of investigators who have filed 1572s with the FDA has been narrowing. This increases the challenge as study sponsors are selecting from an ever-shrinking pool of investigators. Past performance is often the best evidence of how a study site will do in a clinical trial. Sponsors should conduct the compliance equivalent of a background check - have there been any FDA warning letters issued to the investigator in the past? Are there any pending lawsuits against the investigator?

Historical data on enrollment success can be a strong predictor of future success. However, it is important to consider site-specific factors such as the investigator’s experience, the availability of resources, and the site’s past performance in similar trials. By carefully evaluating potential study sites and implementing a robust vetting process, sponsors can increase their chances of success and ensure the integrity of their clinical trials.
of whether an investigator has the tools and resources necessary to meet enrollment goals. Several studies have reported the impact of study delays on the increasing costs of conducting clinical trials. While there are a number of drivers that cause trial delays, patient enrollment still stymies many investigative sites. Identifying quality study sites is critical to successful patient enrollment and retention.

Sponsors should have a clear understanding of the investigator’s past performance – the number of patients he or she contracted and whether they met their goals.

A site may be perfect for a particular protocol, but changes can shift the match. It is important for the study protocol to be as final as possible when a sponsor selects the sites. A change or amendment to a protocol – for example, revised inclusion or exclusion criteria – could render a clinician’s patient population ineligible to enroll.

An investigator’s expertise in the study’s clinical area can also be an indicator for success. However, experience with a particular disease can be a double-edged sword. An investigator who has done several cardiovascular disease trials, for example, might have experience in that field, but may also be tapping out his or her patient population pool.

A quality study site will also have the appropriate infrastructure in place, from the right staffing to clearly defined policies and procedures regarding subject protection. Site inspectors should also evaluate the processes for recording and maintaining study material and data, as well as the storage of any study drugs or devices.

A thorough evaluation of the staff resources at the site study is also critical. The ratio of research staff to the number of active clinical trials is an important statistic. Two-thirds of industry-funded clinical trials in the United States involve community-based investigators. While many academic medical centers may have dedicated and specially trained study coordinators on staff, independent physician practices might not have the dedicated resources necessary for conducting many clinical trials. This can be a Catch-22 for investigators, as their ability to pay a study coordinator is based on how many trials are conducted at that site.

It is not only a matter of FTEs, however. Evaluating the coordinator’s qualifications should be part of the vetting process. The study coordinator’s experience and training, particularly for highly specialized trials, are important considerations. The study coordinators should have an understanding of the complexities of clinical trials, the importance of subject protection, and the best practices of data collection.

The involvement of the investigator is also an important assessment to consider. Even a highly qualified study coordinator cannot compensate for a disengaged investigator. How quickly an investigator responds to inquiries, or submits documentation, can indicate how enthusiastic he or she is. It can also indicate how busy he or she is and how much time and energy will be available to dedicate to the study.

Although study sponsors have a tendency to return to investigators with whom they have worked in the past, they cannot always rely on experienced investigators. In 2010, 44 percent of investigators conducting clinical trials were novices. This represents a significant challenge because novice investigators may need additional coaching through the process to ensure success. This investment of time and resources, however, can yield good results in the longer term as sponsors develop relationships with newer generations of investigators.

The selection of high-quality study sites will continue to grow in complexity as protocols and regulatory hurdles become increasingly detailed and complex. If study sponsors have a clearly defined pathway and standardized evaluation criteria, they can mitigate some of the risks inherent in site selection.

References/citations from this article are available upon request.

Carmela Houston-Henry is Director of Sales for BRANY. Her responsibilities include Developing CRO/Pharmaceutical/Device company relationships and marketing BRANY services including; investigator networks by clinical specialty, study procurement, education programs, Central IRB, auditing and monitoring services.

She is a graduate of North Carolina Central University where she completed her MS in Family and Consumer Science.
Auditors are required by the nature of their jobs to develop a strong technical knowledge of their chosen disciplines. Auditors who are well trained in one area of pharmaceutical compliance, such as manufacturing, preclinical/clinical research, labeling, pharmacovigilance, or marketing, develop in-depth knowledge of those areas. Switching from one area to another, however, requires the auditor to develop a new knowledge base. The techniques of auditing don’t change, but the technical knowledge underlying the audit does change. Due to increasingly stringent regulatory requirements as well as more holistic approaches to agency inspections, auditors are often tasked with audits outside of, or encompassing elements outside of, their primary area of expertise.

One of the problems labeling teams run into is inexperienced auditors from other disciplines conducting labeling audits. This article is designed to educate auditors unfamiliar with the labeling process. It is designed to give a general overview of the pharmaceutical labeling process. The labeling process is broader and much more detailed than auditors from other disciplines may be familiar with:

- The labeling processes discussed here involve the development and updating of medical safety labeling that goes beyond a “one in-one out” change control activity as commonly seen in manufacturing processes, or the detailed analysis of clinical records as seen with GCP audits.
- The labeling process typically allows for a grouping of changes from multiple sources, affecting multiple departments within the pharmaceutical life cycle process.

Before proceeding, however, we should note that pharmaceutical labeling is much more complex than this overview. There are multiple industry programs available for more in-depth study. If you get deeply involved in labeling auditing, we recommend that you take advantage of these resources.

WHAT IS LABELING?

To those unfamiliar with the process, labeling seems simple, but it isn’t simply a sticker on a box or bottle. The development, maintenance, and implementation of pharmaceutical labeling is complex. Labeling is a definition of how a pharmaceutical product is to be used, when it should not be used, its usage and effectiveness limitations, and most significantly, the risks associated with its use.
Simply put, labeling is a dynamic process that results in the printed product information that physicians and consumers receive with the product. Some basic terminology:

- There is labeling, the **act** of providing product information.
- The word **Labeling** may also be used to mean the carton or container labels of a product. This is how the term is typically understood in the European Union.

In this article, we use the term labeling to mean the entire set of product information that, per regulatory license, must be provided for a product. From an auditing perspective, labeling has 2 basic elements:

- First, it defines a product’s use:
  - Its Indications – what it is intended to be used for and
  - Its Contraindications – when it is not to be used, even if the patient had the right indication.
- It also defines the product’s safety profile:
  - Warnings and Precautions for its use and
  - Common adverse events / reactions and interactions.

Typically, these characteristics are defined by the company in a reference document product dossier, usually referred to as a **Core Labeling Document or Company Core Data Sheet**. They may be called other names. They are not subject to approval by regulatory authorities. These documents are typically NOT public, but are provided to some regulatory authorities.

**THE LABELING PROCESS**

“Labeling” as we use it here includes the detailed summary of information which describes the product. The system or process which ensures that the definition of the product’s use and safety profile, and other elements, are accurate, appropriate and up-to-date, and which directs their implementation in local labeling, is the labeling process. Labeling audits primarily deal with the labeling process.

The labeling process extends throughout the pharmaceutical life cycle (Figure 1.)

When a product is first developed, a dossier which also defines the safety and usage profile of the product is developed. This dossier is submitted to regulatory authorities in each of the countries targeted for marketing. After review, regulatory approval is given in the form of marketing authorizations specific to each market country.

Marketing authorizations determine the claims that can be made by the company, and the labeling information that must be disclosed to healthcare professionals and the patient or consumer.

The labeling information contained in the marketing authorization is implemented by business units in the form of, for example, prescribing information documents, patient or consumer leaflets, and – not to forget – advertising, and promotional materials.

**Figure 1**

The Labeling Process extends throughout the Pharmaceutical Life Cycle

<table>
<thead>
<tr>
<th>Safety and usage information related to the pharmaceutical product is defined and updated as needed</th>
<th>The labeling information contained in the marketing authorization is implemented by business units and processes are updated as needed.</th>
<th>The cycle repeats as new information becomes available</th>
</tr>
</thead>
<tbody>
<tr>
<td>Safety and usage information is summarized and submitted to regulatory authorities and a marketing authorization is granted. Supplemental submissions are made as needed for updated authorizations.</td>
<td>The cycle repeats as new information becomes available</td>
<td>The cycle repeats as new information becomes available</td>
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The cycle repeats as new information becomes available.
Labeling information is not static. When new information becomes available, the Core Labeling document Dossier is updated. Local labeling is then updated accordingly and submitted to regulatory authorities as supplemental submissions, and after approval, new marketing and manufacturing materials are developed with the new information.

This process repeats throughout the product’s life cycle.

LABELING INVOLVES MULTIPLE DISCIPLINES

The labeling process requires a coordinated effort from multiple departments within the company at both the headquarters and affiliate levels:

- At Headquarters
  - The Labeling department
  - Pharmacovigilance
  - Medical
  - Clinical Research
  - Regulatory Affairs.

- At the affiliate level whoever is involved in the submission and implementation of labeling, usually
  - Regulatory affairs
  - Medical
  - Pharmacovigilance
  - Sales and Marketing
  - Sales Training
  - Manufacturing.

If properly implemented, labeling systems (policy, process, organization, and staff) can help:

- Ensure appropriate and timely evaluation of emerging safety information,

- Define when and how information about new suspected risks needs to be communicated to users of the product and the medical community, and

- Drive and verify timely implementation of new information into local labeling in all affected markets.

An effective labeling process has several key components:

- Putting effective mechanisms in place to ensure timely decision making on the need for labeling changes.

- Maintaining up-to-date Core Labeling documents which summarize, include information on
  - product usage, and
  - safety

- Distributing these Core documents to affiliate offices for implementation.

- Timely Implementation by the affiliate offices
  - Submit labeling changes to local regulatory authorities
  - Incorporating updated labeling authorizations into promotional materials in use by the sales and marketing departments
  - Package Inserts produced by the manufacturing sites.

First, each country has unique regulatory requirements. There is a common misperception that the US FDA has the most rigorous requirements and, if you meet FDA requirements, you will be in compliance everywhere in the world. Not true. FDA has indeed very rigorous requirements, but many of them are unique to the US, and other markets may require different or additional information in labeling, not to speak about marked differences in how information needs to be presented in labeling. The variations between countries are too numerous to list here. They warrant a training course in themselves.

Second, each country also has different regulatory processes. Some have relatively simple processes which allow for rapid adoption of new safety information into local labeling. Others have complex processes which can delay labeling updates for months, if not years.

Another barrier is that staffing levels vary in branch offices. Some have dedicated labeling personnel which make timely implementation easy. Other affiliates do not.

However, after the Core labeling document is prepared and the affiliates receive the information, there are additional barriers to overcome. (Figure 2)
Finally, labeling updates compete with Affiliate resources needed for other projects such as:

- New drug applications for other products
- AE reporting for all marketed products
- Promotional material review and approval for all products
- Other regulatory submissions
- Staff Training
- Clinical trials

SO, IN SUMMARY:

- Labeling defines how a product is to be used, its limitations, and its risks.
- Failure to disclose product safety information, failure to give it sufficient prominence, or delaying the communication of such information can be detrimental on several levels. Such delays can:
  - put the patient/consumer at significant health risk,
  - severely damage the image of a company with regulatory authorities and the public,
  - be extremely costly to the company, and
  - diminish shareholder value.

Effective Labeling systems are designed to minimize these issues. Auditing can help ensure that the labeling systems are working as intended. To be effective, the auditor must understand the process.

**Joseph McMillian**, BS, MA, has extensive experience in the pharmaceutical industry. McMillian spent 9 years with American Hospital Supply in sales and sales management and 21 years with Aventis Pharma in sales, professional education, scientific communications, and regulatory compliance. Since 1989, he has been heavily involved in international auditing of adverse event reporting, labeling, advertising and promotion, and privacy. In 2000, he joined Wyeth Pharmaceuticals to develop a labeling, advertising/promotion, pharmacovigilance, and privacy compliance function.

**Robert Quinty**, BS, MBA, has had extensive pharmaceutical industry experience during his career with Wyeth Pharmaceuticals as an analytical medicinal chemist, a research supervisor and then in Regulatory Affairs and the Global Compliance Auditing Division. His areas of expertise include the global and local processes and activities for pharmacovigilance, labeling, marketing/promotional programs, and employee/clinical trial privacy. Since January 2012, Quinty has been working as a private consultant in the pharmaceutical industry.

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On September 19, ten leading biopharmaceutical companies – Abbott, AstraZeneca, Boehringer Ingelheim, Bristol-Myers Squibb, Eli Lilly and Company, GlaxoSmithKline, Johnson & Johnson, Pfizer, Genentech a member of the Roche Group, and Sanofi – announced that they have formed TransCelerate BioPharma Inc., a non-profit organization to accelerate the development of new medicines.

Through TransCelerate, these ten founding companies will combine financial and personnel resources to collaboratively identify and solve common drug development challenges with the end goals of improving the quality of clinical studies and bringing new medicines to patients faster.

“There is widespread alignment among the heads of R&D at major pharmaceutical companies that there is a critical need to substantially increase the number of innovative new medicines, while eliminating inefficiencies that drive up R&D costs,” said Acting CEO of TransCelerate BioPharma, Garry Neil, MD, Partner at Apple Tree Partners and formerly Corporate Vice President, Science & Technology, Johnson & Johnson.

“Our mission at TransCelerate BioPharma is to work together across the global research and development community and share research and solutions that will simplify and accelerate the delivery of exciting new medicines for patients.”

TransCelerate has identified clinical study execution as the initiative’s initial area of focus and selected five specific projects for funding and development:

1. Development of a shared user interface for investigator site portals;
2. Mutual recognition of study site qualification and training;
3. Development of risk-based site monitoring approach and standards;
4. Development of clinical data standards;
5. Establishment of a comparator drug supply model.

In the following Q&A, Dr. Neil shared thoughts about the potential of these and related projects with the Global Forum.

How and why were these five funded projects selected for funding?

“We had senior clinical operations people from all of our member companies create a list of potential projects and came up with a list of 30 that we thought were worth considering. We narrowed it down to five,
prioritizing on ‘doability,’ value to the ecosystem, whether or not we could demonstrate some short-term wins, and also the potential interest of other partners in them. FDA and EMA were high on that list, as were some of our academic partners such as the Critical Path Institute and the Clinical Trials Transformation Initiative."

What are some areas in which you believe TransCelerate can make immediate progress?

"Right off the bat, we’re looking at things like data standards and so we’re working with the Clinical Data Interchange Standards Consortium. CDISC has already promulgated some data standards that have not yet been adopted as industry standards, and we’re looking at doing something there. They have a whole series of more specific, narrow standards that are related to individual diseases or conditions that need to be studied – they call those CFAST, the Coalition for Accelerating Standards & Therapies, standards. We think there’s some low hanging fruit there, where we can provide some ‘industry muscle,’ if you like, to work that’s already going on. We’ve already been participating in these efforts as individual companies but collectively can make a more concerted and aligned effort and prioritize getting these standards adopted by our industry members."

"We think another place where things could happen pretty fast is setting standards for investigator training and certification, and then working to expand the number of qualified and well-trained investigators. Right now, a lot of really good projects are not being done quickly because there are not enough qualified investigators; for example, five percent or less of cancer patients who are eligible to enroll in cancer trials actually do. Why is that? A lot of that answer is that there just aren’t enough investigators who are offering them a chance to participate."

Would you like to see clinical investigator training offered in medical schools?

“Yes. Every physician should have a basic understanding of clinical trials including what it takes to be an investigator. Today we have a lot of physicians in practice who would like to be clinical investigators but don’t necessarily know how to do it or haven’t had that training. A certification pathway would be a great advance. With certification in place, each sponsor wouldn’t have to certify each individual investigator site over and over again. Many of investigators do trials for many different sponsors so there are a lot of efficiencies to be gained for everyone."

Conversely, what are some areas that you believe will require more long-term efforts to identify, develop and improve?

“Here we start talking about what it would take to build an infrastructure for clinical trials: A national infrastructure, centralized IRBs and safety monitoring boards, standardized contracts for investigators would be a great start. We also need to work with patient advocates and with policy makers, to get them to recognize the importance of clinical trials and clinical investigation to our national security, prosperity, and national health."

How can individuals get their companies involved in this initiative?

“We are actively looking to expand beyond our ten original charter members. We’re very interested in having other companies join us – not just large ones but medium- and small-size companies too. We’ve seen a lot of interest from such companies and several have asked for membership agreements. We’ll soon have our website running through which interested companies can request a membership agreement."

“Second, we’re very interested in partnering with other groups who share our goals and mission to streamline biopharmaceutical R&D. We’re reaching out to create those partnerships and associations. We’re starting to engage with regulatory agencies, with CROs, and with some of the major academic groups that have already been established to address these problems, but we know that there’s going to be broader interest."

“We all have to understand, and I think we do, that biopharmaceutical R&D is an ‘ecosystem’ that works for societal good. We share the responsibility – the social contract, if you like – to provide new medicines for patients who want and need solutions to their health problems. We want to figure out the best way for us to work together to be able to achieve that. The problem is bigger than any individual company or even an association of companies could solve on their own.”
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**REACH**: Reflects the global nature of DIA and exposes readers to what we are doing around the globe and how advances in each region can have a worldwide impact. This is where Upcoming Events now resides, in an easy-to-read sidebar box for each region outlining their educational offerings.
On September 20, DIA and the Food & Drug Law Institute (FDLI) collaboratively presented a conference that provided one of the first systematic looks at the Food & Drug Administration Safety & Innovation Act (FDASIA) signed into law by the President in July.

In October, DIA and FDA collaboratively presented a subsequent DIA/FDA Industry PDUFA V Conference that provided an opportunity for FDA, industry, technology vendors, and representatives of patient, consumer and healthcare professional groups to more fully discuss key PDUFA V commitments and implementation strategies. Sessions at both conferences were recorded and efforts are underway to make them available as archived webinar presentations on www.diahome.org.

Unwrapping FDA’s UFA Package: What’s Inside the Statute – What’s Next? examined the content of the fifth reauthorization of the Prescription Drug User Fee Act (PDUFA V), the third reauthorization of the Medical Device User Fee Act (MDUFA III), and implementation of the new Generic Drug User Fee Act (GDUFA) and Biosimilars User Fee Act (BsUFA). The content of these UFA packages will shape the timely development and review of life-saving medicines and medical devices.
This conference included a special “PDUFA, GDUFA & BsUFA Highlights” panel discussion led by key FDA officials’ presentations on the drug, generic drug and biosimilar user fee packages. Manju Thomas (Office of Planning & Analysis, CDER) discussed the biosimilar package, and subsequently noted that, “All negotiated provisions are considered helpful in this new program, and more experience will be necessary to determine the most helpful provisions.”

Nancy Bradish Myers, JD (Catalyst Healthcare Consulting) served as moderator for this panel session. After the meeting, she explained what new topics or stakeholders we might expect to come forward when it comes time to begin discussing PDUFA VI.

“Clearly it is too early to really know what will be the theme for the next round but, for good or for ill, interested parties are already sowing seeds for potential issue candidates for the next go-around in 2017. Given that issue identification leading up to the new round of negotiations may begin as early as 2014, it may be useful for all sides to give some thought to issues that could be on the table,” she began.

“Data is already being captured that will feed into issue identification from the perspective of industry and FDA. For example, the drug industry has asked its trade groups to develop a review tracking system to monitor FDA progress. FDA has processes in place to capture experiential data, too.”

“The political environment leading into the 2017 negotiation will also impact the next group of issues to be negotiated. But no matter who is running the agency, Congress, or advocacy organizations, there are a few topics that will likely command attention in the next PDUFA negotiation cycle and its legislative vehicle,” she concluded. Nancy provided these in the below list.

1. Refine provisions of the current agreement: The bulk of the agreement will likely be refinements to the premarket review process, drug development process, and post-market safety oversight. This is what we have seen historically throughout the PDUFA life cycle; its focus will be determined by the experiences and data generated by industry and FDA over the next two plus years.

2. Additional financing, and exploring how to ensure user fee dollars do not get caught up in Congressional issues (such as sequestration) or become a substitute for Congressionally appropriated dollars: One of the major issues we’re already seeing, only a few months after the commitment letter was ratified, is that user fees could become a political victim of sequestration. For the next negotiation or in the legislative wrapper that surrounds it, FDA, industry and possibly members of Congress may look for ways to ensure all the user fees collected are spent as intended.

3. Build on clinical trial improvement efforts: FDA leadership has been investing in cooperative efforts to improve biopharmaceutical clinical trials through groups like the Duke Clinical Trials Transformation Initiative and the recently launched TransCelerate effort. Insight will come out of these efforts right when the data can feed into user fee issue identification.

4. Speed access to promising medicines & medical technologies to vulnerable populations: Through each go-round, interest groups have proposed ways to speed the development, and more tangibly the review process, to help promising products reach critical vulnerable populations faster. These types of provisions have been included in the FDA/industry commitment letter language, as well as the legislative wrapper. This may be in the form of a Progressive Approval-type approach, or one similar to the proposal for a Limited Population Antibacterial Drug (LPAD) approval pathway that FDA is currently considering. An expanded LPAD approach might allow for smaller, faster clinical trials to support initial approval of therapies in subpopulations of patients with serious diseases, with strong limitations on prescribing.

5. Improve policies & processes to facilitate co-development of drugs & companion diagnostics and encourage development of targeted, personalized medicines: FDA has made attempts at improvements in these areas, including draft guidance. However, confusion and lack of clarity persists among product developers, despite the fact that it is an area often touted as holding promise for the future of oncology and personalized
outside of FDA and industry to grant more groups a seat at the negotiating table, such as members of Congress or advocacy/consumer groups. While this would complicate an already complex negotiation, some might argue the only way a strong negotiation happens is if all interested parties, not just those with a financial interest, are at the table.

6. Expect the unexpected issue with safety undertones: Be prepared for a surprise issue that will slide in, seemingly at the last minute, to address a current crisis. For example, given the current crisis with fungal meningitis infections and deaths linked to contaminated injectable steroids, if negotiations were still under way for PDUFA, we could see a last-minute effort to expand FDA’s authority over compounding pharmacies.

We may also see some broader process-type issues raised across the UFAs, including:

7. Simplify the multi-user fee negotiation process: Negotiating multiple unique user fees at the same time with diverse but sometimes overlapping interests is a very complex process. Each effort takes up significant FDA, industry and advocacy group staff time. Negotiators may also approach similar problems with different solutions, creating confusion inside and outside the agency. We have heard one FDA negotiator suggest that negotiators should find ways to simplify the negotiations and find synergies.

8. Consider expanding the list of who sits at the negotiation table: We may see efforts

DIA & NORD Present
“Shaping the Future Now”

From October 22-24, the Capital Hilton in Washington DC hosted the second annual DIA/NORD US Conference on Rare Diseases & Orphan Products: Shaping the Future Now presented in collaboration with the US FDA, the National Institutes of Health (US), the Duke Department of Pediatrics (Duke University School of Medicine) and EURORDIS, the voice of the rare disease patient community in Europe.

Shaping the Future Now was aligned along three meeting themes – Research & Regulation, Impact of the Food & Drug Administration Safety & Innovation Act (FDASIA) on Orphan Product Development, and Special Challenges in Rare Diseases – that were reinforced by keynote addresses and plenary and special sessions. (Please see this issue’s Regulatory Roundup for a regulatory report from this Rare Disease & Orphan Products conference.)

HIGHLIGHTS OCTOBER 22

NORD President & CEO Peter Saltonstall formally opened the conference by thanking the planning committee, the collaborating/cosponsoring organizations, and leadership from industry, the FDA, academic health centers and patient organizations for their contributions to the conference program. “Our commitment at NORD is to ensure that the 30 million Americans with rare diseases have the products, services and treatments they need,” Peter said.

Anne Pariser, MD (Associate Director for Rare Diseases, Office of New Drugs, CDER), noted that 2013 will mark the thirtieth anniversary of the original Orphan Drug Act of 1983. “Investment in orphan products has never been higher and interest has never been greater,” said Anne.

“One these conferences demonstrate the strategic partnership between EURORDIS and NORD,” explained Flaminia Macchia (Director, European Public Affairs, EURORDIS). Other fruits of this partnership include RareConnect.org, a web portal which hosts more than thirty different online rare disease communities from 55 different countries, and...
“The change we need in this space is not mathematic, it is logarithmic,” he suggested. “The only way around this problem is you: Patient advocates.”

Don’t be afraid to advocate for change – those of us who are driving for change need you,” encouraged Chris.

RESEARCH & REGULATION KEYNOTES

Robert Califf, MD, MACC (Director, Duke Translational Medicine Institute – DTMI), opened by referring back to an expression often heard at 2011’s DIA/NORD conference – the “valley of death” into which most products that enter clinical R&D disappear. “We have now ‘amassed the troops’ on the border of this ‘valley of death,’” he explained. “What happens if we successfully invade this space?”

Robert summarized several major trends in clinical research 2012 which unfortunately include the consensus that, as trial start-up times continue to lengthen and costs continue to escalate, the clinical research enterprise is “broken.” “If we could reduce the cost of clinical research, investors would take a lot more ‘shots on goal’ and they’d come up with a few more ‘winners,’” he suggested.

Robert noted that technological and organizational innovation drive cost and quality improvement in most markets. In the orphan product space, global information and communication networks can connect and integrate clinical research sites into a clinical research network that facilitates more efficient research and create a framework within which patients, physicians and scientists can form true research communities. “It’s obvious to me that we are at a tipping point. We can do things this year that we couldn’t do before,” he said. “The window is open now for people who want to take advantage of this technological revolution.”

Chris Austin, MD (Director, National Center for Advancing Translational Sciences (NCATS), National Institutes of Health (NIH)), chaired the keynote on the NCATS’ Therapeutics for Rare & Neglected Diseases program. “It’s really great to be here because I feel like ‘you are my people’ in a very real way,” he began.

Chris reviewed the NCATS Mission Statement: “To catalyze the generation of innovative methods and technologies that will enhance the development, testing, and implementation of diagnostics and therapeutics across a wide range of human diseases and conditions.” NCATS was created to be a connector and enabler through such programs as the chemical rescreening of 3500 existing compounds to identify candidates for repurposing, under the auspices of the NIH Chemical Genomics Center, and other initiatives.

“Don’t be afraid to advocate for change – those of us who are driving for change need you,” encouraged Chris.

RESEARCH & REGULATION PLENARY

Stephen C. Groft, PharmD (Director, Office of Rare Diseases Research, NIH), chaired the Shaping the Future Research & Regulation plenary that focused on two current innovative initiatives.

Bonnie B. Dunn, PhD (Program Director, NCATS) overviewed the NIH Drug Repurposing Program. A 2011 NIH and industry roundtable on “Exploring New Uses for Abandoned and Approved Therapeutics” identified opportunities for NIH to serve as a clearinghouse for discontinued compounds, biologics and data that could
potentially be repurposed for unmet healthcare needs. As a result, the NCATS Therapeutics Discovery Pilot was launched to identify new therapeutic uses of 58 proprietary compounds and biologics by matching these agents with innovative ideas for new indications. To qualify, these agents must have gone through significant R&D (including safety testing in humans), have a well-characterized method of action and a well-understood safety profile, and be ready for Phase 2a studies.

Citing data which illustrated that success rates for new phase 2 development projects have recently fallen from 28% to 18%, Danilo A. Tagle, PhD (NCATS) explained the need for better evaluative tools: For safety/toxicity, to predict adverse events and allow for earlier mitigation or prevention; and for efficacy, to more quickly identify the population who will respond to a new drug. To meet this need, the DARPA-FDA-NIH Microphysiological Systems Program has developed human microsystems, or organ “chips,” to screen for safe and effective drugs before human testing. Tissue Chips to Predict Drug Safety provide an in vitro platform of both individual organs, and organs integrated into a microsystem, on a chip. It is envisioned that these microsystems will soon result in a ten-organ system mimetic that provides the physiological equivalent of a “human on a chip” that can be entered into clinical trials.

RESEARCH & REGULATION LUNCHEON SPEAKER

Preston W. Campbell III, MD (Cystic Fibrosis Foundation) overviewed Challenges in Developing Therapies for Orphan Diseases: The Cystic Fibrosis (CF) Experience. In 1955, most children with CF did not live long enough to go to school; today, nearly one half of all CF patients are adults with median survival of almost 40 years. FDA has approved eight CF therapies, including one that treats the basic defect, and more are in the pipeline. What happened?

“The most important thing,” he explained, was the formation of the CF Foundation in 1955. Because many doctors did not even know how to treat CF patients at the time, the CF founded the CF Care Center Network in 1960, which published evidence-based guidelines that ensured standard care. The CF Foundation Patient Registry followed soon thereafter. “Registries are essential tools for orphan diseases,” said Preston.

The CFF subsequently launched its Therapeutics Development Program and corresponding Therapeutics Development Network. These provide financial and resource support to pharmaceutical partners to encourage the development of new CF drugs – to “de-risk the industry to come into the field of CF,” he suggested. Since then, the TDN has completed 70 clinical trials. All this work, of the TDN, TDP, industry and science, came together with the CFF-funded Vertex program which resulted in the 2012 approval of Ivacaftor (kalydeco).

HIGHLIGHTS OCTOBER 23

POLICY KEYNOTE

Keynote Speaker Stephen P. Spielberg, MD, PhD (Deputy Commissioner, Medical Products & Tobacco, Office of the Commissioner, FDA) immediately noted that he spent much of his academic career caring for children, so rare pediatric diseases are a subject dear to his own heart. “Pediatricians by definition are optimistic,” he began, “and I’ve never been more optimistic about this field than I am now.”
Stephen explained how stakeholders throughout the healthcare continuum are currently struggling with how to integrate pharmacogenomics, personalized medicine and rare disease therapies into our policy and regulatory frameworks. “At no time in human history has the pace of change been so great,” he suggested. “So it’s a hard time for policy. It’s a hard time for regulators.”

“We’re in a time of enormous complexity, and in a time of enormous complexity, this is a team sport,” he concluded. “We need to be together on this, and we need to keep this dialogue going.”

POLICY PLENARY

Moderator Cole Werble, MA (Prevision Policy, LLC), explained that the Shaping the Future of Health Policy Now plenary would present “two distinctly different perspectives” and placed these perspectives in the context of “four consecutive policy wins for rare disease patients”:

- Passage of Affordable Care Act in 2010 confirms special status of rare disease patients and orphan products
- 2010 Institutes of Medicine Rare Diseases & Orphan Products: Accelerating Research & Development Report sets forth the elements of an integrated national strategy to promote rare diseases research and product development
- NIH establishes the National Center for Advancing Translational Sciences in 2011 “to re-engineer the process of translating scientific discoveries into new drugs”
- Passage of FDASIA in 2012 features more than fifty citations of rare diseases or orphan products, including the new consultation process for rare disease drugs, the new priority review voucher for pediatric rare diseases, and special consideration of rare diseases in reports and guidelines.

Charles A. Mohan, Jr. (CEO/Executive Director, The United Mitochondrial Disease Foundation – UMDF) spoke of the essential importance of the mission to any patient advocacy organization. “The mission cannot change. It can only become sharper,” he said. “We want to continue to focus on that which got us involved to begin with.”

Charles also spoke of the importance of organizational consistency. At one point, he explained, there were six or seven different “mito” organizations geographically dispersed throughout the US. These have now been consolidated into the UMDF. In the rare disease community, our similarities are greater than our differences, he noted, yet it often seems that we are all going down the same road – in different directions.

David P. Meeker, MD (President & CEO, Genzyme) delivered industry’s perspective on rare disease policy. “Orphan diseases are not immune to the pressures of the world we live in,” he began. “One of the things I’m most concerned about is that these discussions get framed in the wrong way.”

In today’s healthcare system, there are three basic ways to control cost: Preventive therapies; better use of existing technologies,
treatments and therapies; and hope from new and innovative therapies. To be honest, the hope that one project team will identify the one out of ten thousand molecules that actually makes it to market is quite low. Academic science is best equipped to discover these molecules, but they’re not prepared to develop it – the biopharm industry is. Recently, payers have become one of the most unpredictable parts of this process, and market approval without market access is little more than an award to display. “We have proven that you cannot BUY the next drug,” he observed.

To overcome these challenges, David presented four proposals:

1. If we do not fund the NIH, this entire system will collapse. Academic research needs NIH funding.

2. We need to help patient organizations prepare for their cure: Set up your registries and clinical networks so that you can readily provide patients for clinical trials as soon as your molecule is discovered.

3. FDA is overwhelmed and under-resourced and regulatory review is hard. FDA is located in Washington, DC. The NIH is located in Washington, DC. Can the NIH help the FDA with the scientific aspects of regulatory review?

4. For this review process to be right, the benefit/risk assessment must be right; the best way to get the benefit/risk assessment right is to get patients involved in that assessment. How do we build this voice into the formal process? And as we look toward personalized medicine, can we let individual patients make their own risk/benefit determination?

POLICY LUNCHEON SPEAKER

Jonathan S. Leff, MBA (Managing Director, Warburg Pincus) looked at Facing the Crisis in Biomedical Innovation: A Venture Investor’s Perspective.

Because it now takes, according to most estimates, between ten to fifteen years and between one and two billion dollars to get a new drug product to market, return on investment in pharmaceutical R&D continues to spiral downward. As a result, he explained, the number of venture capital groups that reduced their investments in pharma over the past three years is three times greater than the number that increased it. Fewer new companies are being funded, fewer clinical trials are being started, and venture investors expect to continue to pull back.

The economics of drug development and approval just don’t work anymore, he said. It is past time to have a “grown-up conversation” about patients’ expectations, tolerance and uncertainty, and specifically include the burden in time and cost as part of regulatory policy and decision making for drug development and approval. This model is obviously unsustainable. Here, Jonathan quoted Herbert Stein’s law: “If something cannot go on forever…it will stop.”

Innovation in rare diseases demands even greater regulatory flexibility and clarity, Jonathan said. “FDA tends to be a magnet for criticism and it’s not because they don’t do their job well but because their job is so important,” he suggested.

There IS good news, he pointed out, such as the NORD report “Quantum of Effectiveness Evidence in FDA’s Approval of Orphan Drugs: Cataloguing FDA’s Flexibility in Regulating Therapies for Persons with Rare Disorders,” presented on the first day of last year’s DIA/NORD Rare Disease & Orphan Products conference, which indicated that 67% of the orphan product approvals from 1983 to 2010 demonstrated flexibility in assessing effectiveness. In addition, 60% of surveyed life science venture capitalists view FDASIA as a positive development, and view the regulatory environment as more positive and getting better.

“The biopharma innovation ecosystem is in grave danger,” Jonathan concluded. “This is not anyone’s fault, but it is everyone’s problem.”
HIGHLIGHTS OCTOBER 24
SPECIAL CHALLENGES IN RARE DISEASES KEYNOTE

John J. Castellani (President & CEO, Pharmaceutical Researchers & Manufacturers of America – PhRMA) spoke of PhRMA's enduring commitment to the rare disease community and relationship with NORD. He noted that there were only about ten orphan drugs when the ODA was passed in 1983; as we approach the Act's thirtieth anniversary, nearly 500 drugs are approved for rare disease treatments and hundreds more are in development pipelines. “It’s good news that the research muscle of our largest companies have joined the rare disease fight,” John said.

“The effort to reauthorize PDUFA as part of FDASIA is a wonderful example of what we can do together,” he continued. “Now, the trick, of course, is its implementation.”

John also mentioned the cost of drug development and reimbursement systems as the two biggest challenges for rare disease patients and orphan product development: “We have to find a way to shape the reimbursement system,” he said. “It focuses on short-term cost instead of long-term benefit.”

SPECIAL CHALLENGES IN RARE DISEASES PLENARY

During the plenary panel discussion on Access & Reimbursement, Mark McClellan, MD, PhD (Engleberg Center for Health Care Reform; The Brookings Institution) spoke about budget and technology considerations impacting healthcare reform, and corresponding opportunities in healthcare financing reform. He noted that government spending on healthcare is projected to double over the next five years. “There’s a tremendous amount of financial pressure on our healthcare system today,” he began. “This is why the work you’re doing to change the trajectory of healthcare spending is so important.”

He encouraged attendees to support the alignment of healthcare policy with healthcare financing reform. Expanding insurance coverage while squeezing down prices won’t bring about or even support the innovation this system needs, Mark explained, but better performance measures will help design more responsive insurance programs and benefits. Healthcare policy, financing and delivery reforms that turn away from paying for volume and intensity and shift toward paying for what’s best for patients through demonstrated outcomes can tie both price and coverage to demonstrated impact and not just the volume of product used.

It takes an ecosystem – government supported research, academic research, investors, life science companies, patients, regulatory bodies, and the rest – to bring new treatments to patients, said Richard H. Bagger (Celgene Corporation). In this ecosystem, clinical trials have become complex, time-consuming and costly. “While the number of ‘shots on goal’ seems to be increasing, the ‘degree of difficulty’ seems to be increasing as well,” he said.

“The orphan drug incentive model should be both preserved and strengthened to protect the progress that has already been made,” Richard concluded. He suggested expanding the seven year orphan drug exclusivity in the US to the ten year exclusivity period currently allowed in the European Union, and further suggested changing insurance
plans to no longer differentiate between IV treatments and oral treatments that provide the same benefit: Oral treatments are covered by prescription, not healthcare insurance, plans, often with higher co-pays, he explained.

Miriam O’Day (Alpha-1 Foundation) described more specific Alpha-1 patient-industry interactions. She noted that the Alpha-1 Foundation Research Registry has contributed to ten clinical trials this year and close to one hundred clinical trials since its 1997 inception. Getting an accurate diagnosis is generally just the first of many access problems for Alpha-1 patients. So are the site of service (most Alpha-1 disease treatments are an IV infusion that can generally only be done in the oncology department of a qualified hospital) and $100K-$150K annual treatment cost. To help patients meet these challenges, the Foundation offers online tools that allow patients to compare and select insurance plans, patient assistant programs and Medicare plans that meet their specific needs. In addition, being able to track where, how and when people have been treated help quantify and ultimately determine treatment and payment plans. “Data has made a huge difference for us,” Miriam explained.

SPECIAL CHALLENGES IN RARE DISEASES LUNCHEON SPEAKER

Christopher Jennings (President, Jennings Policy Strategies) placed his luncheon presentation squarely in the current context of budgetary sequestering. “The environment is tough, and if I’m honest with you today, I have to tell you that it will get tougher,” he began.

In the absence of any other budget agreement, sequestering that will automatically cut approximately 8% of every federal budget line item, including allocations for the FDA and NIH, will become effective in January 2013. “If we really care about the ways we’re going to save money over time, these are the areas in which we’re going to have to invest,” he said. This may seem like ridiculous policy, but it is designed to motivate budget discussions in a serious way. “Literally hundreds of millions of dollars are at risk for FDA,” he said.

NORD understands that every aspect of the word “access” needs to be on the table in this budget process and that the word “access” has many meanings, Christopher continued. “They really understand how the process works at each stage,” he said.

“Access also means that all American must have access to the coverage and the medicines they need,” he said. “And they get that ‘access’ is also related to the word ‘affordability.’

“Most patient representatives here are a living breathing example of ‘pre-existing conditions,’” he continued. “Access is all these things.”

Christopher called for the patient community to demonstrate and articulate the potential impact of these budget cuts for patients living with rare diseases to their congressional representatives. “You worked so well together and so hard together on the PDUFA legislation because you were all committed to the same vision,” he said. There is no group better suited to do that then the people gathered here in this room, he concluded.

CLOSING PLENARY: WHAT THE FUTURE LOOKS LIKE FOR THE RARE DISEASE PATIENT

Moderated by Wayne Pines (APCO Worldwide, Inc.), the closing plenary session featured Peter Saltonstall, Jonathan S. Leff, Dr. Anne Pariser, Tamir Orbach (PNH Research & Support Foundation; Aplastic Anemia & MDS International Foundation) and Maria Mavris (Director, Therapeutics Development, EURORDIS) and simultaneously reviewed this three-day conference and looked forward to the year’s work ahead.

Maria revisited many of the same challenges heard throughout this conference, most notably how to translate scientific innovation into innovative products, and the question of who gets to define the “value” of a therapy. She also overviewed important next steps for the rare disease patient and orphan product development community, such as better and broader collection of relevant data, early dialogue between industry and health authorities, fairness and transparency in cost construction and pricing for long-term sustainability. “‘Collaboration’ was the keyword that came out of this conference,” she concluded.

“We’ve been told that medical research is broken. We’ve been told that the venture community is skeptical about this area of drug development generally. We’ve been told that Washington is broken. Those are not problems
– that’s an agenda,” Wayne reflected. “We hear the word ‘collaboration’ and that seems to be the theme of this meeting. That is, if the medical community, the patient community, if the government and industry, if everybody pulls together, then the future really is bright because biomedical research continues and new cures are being found.”

“One of the themes that emerged for me here is in contrast to what we talked about last year. Last year, there was a lot of discussion about FDA and how FDA was the hurdle; at this meeting, we have heard a lot of good things about FDA, about the efforts that it has made to work collaboratively with everybody and to try to make sure that it is NOT a hurdle.”

“And so what I would like to do is to remove FDA as being the problem – FDA is now clearly part of the solution,” Wayne concluded.

“We are really on the brink of tremendous change, and we certainly hope that there’s tremendous growth for rare diseases. We obviously have momentum, the interest is certainly there, and the potential, and certainly the unmet needs that are really propelling us forward,” said Anne. “This is really a unique time to be in rare diseases and we really have the potential to pull this together and move forward.”

“‘Learn from experiences’ has been another major theme and I think that’s what we tried to really hit on here, and tried to show examples of what has worked: Where are the trailblazers? What is the path forward? What has been done? What can we learn from it? What can we apply?”

“The result of our collective labor is always moving toward the direction of benefit for the patient because that’s ultimately what matters,” Anne concluded.

“I’m trying to put a positive spin on everything at the end of the day,” Peter began. “We have real issues around costs for our patients right now, and we’re seeing a tremendous amount of pressure on drugs being tiered into categories now, where they’re no longer available to patients.”

“I am really concerned for all of us in this room around the crisis that we’re facing in this city, the inability of this city to make decisions that impact all of us,” Peter continued. “I’m talking primarily about the sequestration that’s staring us in the eyes right now and the impact that it’s going to have not only on the FDA, on NIH, on science, on everything that’s going to move forward to help patients whether they’re rare disease patients or not rare disease patients, who are just patients in general.”

“All of the plans that we’re talking about for the future essentially aren’t going to happen if the sequestration piece moves forward in any kind of fashion. I recognize that our economy is difficult right now, but the sequestration piece basically pulls the rug out from under us in lots of different ways.”

“So, for me, I’m looking between now and January 2 as my window, because everything else on my game plan changes based upon what happens that day. I want to end on a positive note and say that everything else we’re talking about here is good. But we all need to pay attention to that, and we’re going to be back in touch with every one of our groups, because we need to take a leadership role,” Peter concluded.
From October 8-11, DIA hosted our EDM & ERS/eCTD: The Content Continuum from Document Authoring through Submission Delivery, a new and yet familiar program that combined DIA’s traditional standalone conferences for Electronic Document Management (EDM) and Electronic Regulatory Submissions, including the electronic Common Technical Document (ERS/eCTD), into a unified educational forum that provided continuity and synergy between these two topics, as well as fostered enhanced networking opportunities with both EDM and ERS audiences.

NANCY SMERKANICH
Octagon Research Solutions

What are some of the primary topics of overlap between the two EDM and ERS/eCTD conferences that were better addressed by this combined conference?

“The ERS conference in the past has primarily been a two-track conference, divided into essential and advanced topics specific to electronic submissions, so we added a track this year that focused specifically around issues more related to document management. But one of the things to recognize as we look forward is that the whole idea of content management is becoming much more prevalent, and that content management occupies both spaces, the document management and the submission space as well. One of the things we want to look at possibly adding to the conference is the whole regulatory information management concept, which bridges EDM and ERS. It shows the natural progression of where content management and regulatory information management are taking over spaces previously occupied by traditional document management or traditional regulatory submissions management.”

“But, in addition to having topics overlap, it’s important to recognize from a sponsor’s perspective that the people who attend the EDM and ERS conferences tend to be the same people. The audience we surveyed at the beginning of our October conference was essentially split in half between regulatory affairs and regulatory operations. These are primarily the people who are responsible for electronic document management as well as electronic regulatory submissions, so we wanted to present a conference that addressed all their concerns and topic areas.”

“The DIA EDM conference has always been held in February in Philadelphia and the ERS conference has always been held in San Diego in November. We’ve...
been using a survey tool to fully assess whether the conference met the needs of our participants – How was the timing? How was the location? These responses will impact the planning of the conference for next year. This was the first time that we combined them in this particular location at this particular time of year – we’ve had the ERS conference earlier but we’ve never had the EDM conference so late.”

“The content is another survey topic: We’re surveying both groups who would have attended this conference separately. I generally go to both conferences, and it is a lot of the same people. In these days of cost-cutting, I think people are having to choose their ‘one meeting a year.’”

Did the Exhibit Hall represent this combined conference and if so how?

“Yes, very much so. To be honest, I think DIA did exhibitors a favor because instead of having to exhibit at two shows, a lot of companies could just exhibit at one show. This allowed for other people more from the document management side, who are more concerned with document authoring and document management systems, and collaborative working environments. There were even a few exhibitors who do cloud computing; cloud computing affects people doing document management as well as people offering software as a service, because it has the ability to do both. Certainly, the booth representation reflected the theme of the conference, which is what we were going for: This whole idea of creating a continuum from where a document is created to where it ends up in the submission. That was really the idea. So I do think that it reflected the combined conference.”

“If you’re strictly a document management person – you’re in charge of eArchiving or eRecords or whatever – you typically won’t get FDA at your conference. When FDA has spoken at the EDM conference, it’s been on submissions – they won’t necessarily talk to companies about how they should be managing company documents. But they were very prevalent throughout this combined conference. Every day we had regulators, and we had regulators at our collaborative sessions. The collaborative session is something we’ve done at the ERS conference but I think it was new for people who had been to the EDM conference.”

What changes can we expect to see in the content continuum between this year’s conference and the next?

“There are a number of FDA initiatives around the regulatory submissions side that have a tremendous impact on the document preparation side, specifically around the implementation of a new Module One in the eCTD framework that will encompass promotional materials for drugs and biologics. That is going to have document management effects. Promotional materials are typically created by outsourcing or by a different group within your company, so now you have to kind of bring them in and educate them about electronic submission and controlled document management techniques, that whole idea of authoring with the end in mind. That’s what this continuum is reflective of. I see that as a big topic.”

“There may be some other subtle things from the PDUFA V reauthorization. Certainly, with the addition of user fee programs for generics and biosimilars, there may be some new topic areas once those programs have a little bit of time under their belts. Globalization is something that every pharma company has to worry about, so creating documents and managing documents and creating submissions and managing submissions in a global framework continues to be a very important and big topic.”

In March 2013, DIA will present our Medical & Scientific Communications Forum 2013, which will expand the annual Medical Communications Workshop into a must-attend annual forum for Medical Communication, Medical Information, Medical Science Liaison, and Medical Writing Professionals. This meeting includes content to meet the needs of those who work in pharmaceutical based medical and scientific communications into a single unified offering by offering three tracks specific to these areas. Presented in Chandler, AZ, this Forum is being collaboratively developed by the DIA Medical Communications, Medical Science Liaisons, and Medical Writing Special Interest Area Communities (SIACs).
In 2011, Jürgen Venitz, MD, PhD (School of Pharmacy, Medical College of Virginia Campus of Virginia Commonwealth University), was awarded a Patient Fellowship to represent the Myasthenia Gravis Foundation of America at our Annual Meeting in Chicago, one of fifteen Fellowships awarded in the first year of DIA’s Annual Meeting Patient Fellowship program.

A pharmaceutical scientist, Professor & Vice Chairman of the Virginia Commonwealth University Department of Pharmaceutics, and still an advocate for myasthenia gravis patients, Dr. Venitz will also serve as Chair of the Rare & Neglected Disease track for our DIA 2013 49th Annual Meeting: Advancing Therapeutic Innovation & Regulatory Science next June in Boston. He spoke of his service to MG patients and to DIA in the following interview.

What has your Annual Meeting journey – from attending the Annual Meeting as a Patient Fellow to serving on the Program Committee as a Track Chair – taught you about the healthcare industry? About DIA? About yourself?

“I am representing the Myasthenia Gravis Foundation of America (MGFA) and was selected as one of the inaugural DIA Patient Advocate Fellows (PAF) and attended the 2011 DIA Annual Meeting. As pharmaceutical scientist by profession, I had attended several DIA meetings in prior years. My experience as a patient fellow was truly inspirational. I met fellow patients and patient advocates at a global forum that I had previously associated with only scientists and regulators in drug/medical device development. I want to commend DIA not only for giving my current fellow PAF and me this opportunity, but also for formally incorporating a patient perspective into our Annual Meeting programming. I hope and believe that, in the long run, this addition will help drug/device developers and global regulatory agencies to customize their development programs and regulatory decision-making to patients’ needs by considering patient input along the way. The PAF program has also encouraged me personally to volunteer my service for the DIA Program Committee for 2012-2014 on the Rare and Neglected Disease track.”

How would you like to see DIA and patients working together five years from now?

“I would like to see DIA continue their outreach to patient advocacy organizations not only through the DIA Annual Meeting but also by supporting the ad-hoc PAF alumni program that grew out of our inaugural meeting in 2011 and has resulted in monthly virtual meetings, as well close interactions among the various patient advocacy representatives and patient input into several national and international meetings. I also hope to see more individual patient representatives on DIA Program Committees, not only for the Annual Meeting, but also for more targeted DIA meetings and joint meetings, e.g., with the National Organization for Rare Disorders.”
“Having participated in the ‘Voice of the Patient’ panel at the 2011 DIA Meeting, which was well attended and equally as well received by the diverse DIA audience, I would like to encourage more formal programming (symposia, sessions, presentations) across the board with actual patients discussing their experiences with the disease they are afflicted with, existing treatment options and participation in clinical, therapeutic trials in order to more explicitly provide the patient perspective into designing more effective and efficient development programs for novel therapeutics, especially for rare and neglected diseases. Based on informal feedback I received in 2011, I think that the treatment developers and regulators are actively seeking and appreciate this unique but essential perspective.”

What has been the most surprising thing you have learned while serving on this Committee?

“I am mostly impressed by the diversity of expertise and interests among committee members as well as their sincere commitment in putting together attractive, innovative and broad-scope programming intended to address the interests and needs of a very diverse audience at the Annual Meeting (including patients and patient advocates!)."

The MGFA is the only national volunteer health agency in the US dedicated solely to the fight against myasthenia gravis (MG). While there is no known cure, effective treatments allow some – but not all – persons with MG to live full lives. To learn more about the MGFA, please visit http://www.myasthenia.org.

DIA Offers Opportunities for Patients & Students

While the healthcare landscape and DIA’s role within it continues to evolve, patients and students remain key stakeholders as DIA works toward our collective mission and vision. Through the Patient Advocate Fellowship Program, DIA works to ensure that the “voice of the patient” is heard globally throughout every facet of the life cycle management of pharmaceuticals, medical devices, and related health care products through a program designed to develop, strengthen and support patient collaborations with policy makers, health professionals, industry representatives and academia.


But DIA’s commitment to patients and their advocates does not end upon the conclusion of these meetings. Patient fellows are invited to join the Patient Advocate Fellowship Alumni program, a community of members for networking and achieving common goals that foster the mission of DIA. Open to all organizations who have received Patient Fellowships, this alumni network aims to increase knowledge about key issues central to patient-centered health care, and presents one more avenue to share best practices, identify opportunities for collaboration and nurture relationships between current and future participants.

DIA Worldwide Executive Director Paul Pomerantz expressed the importance of patients in DIA’s global mission and vision: “With all the changes that we are seeing in healthcare development and delivery, the patient is becoming the primary driver behind drug development, access to drugs and health policy. It’s through the engagement of patients in our global multi-stakeholder network that we are able to adequately address and in fact get to the heart of these matters.”

DIA’s annual Clinical Forum in Europe, and annual Rare Disease meetings presented in collaboration with the National Organization for Rare Disorders (NORD) in North America, and with EURORDIS, the Voice of the Rare Disease Patient Community,
Beat Widler, PhD (Widler & Schiemann AG) and Jennifer L. Riggins, PharmD (Eli Lilly & Company) co-chair the Member & Volunteer Engagement (MVE) of the DIA Board. “Patients rightly claim to be better involved in health care decisions and also in the development of new therapies,” said Dr. Widler. “DIA in Europe is proud to have been active in this area and have started a dialogue with patients and patient groups already some years ago. DIA wants to build on this rewarding experience and foster this dialogue more actively.”

DIA keeps students up to date through programs and events that deliver a practical understanding of how education can be applied directly to their professional careers, including several unique opportunities at DIA 2013. Eligible students are invited to submit poster abstracts for the Student Poster Program at our 2013 EuroMeeting and 2013 Annual Meeting, an opportunity to present their research to a diverse group of scientific, academic and industry professionals who work each day in the discovery, development and life cycle management of pharmaceuticals, biotechnology, medical devices and related health care products.

Students can take advantage of special discount registration fees and can participate in the Student Forum designed to provide real-world workplace and job-seeking information to students as well as the Speed Networking session designed to maximize their professional contacts.

“Our student programs are vitally important to DIA,” Jennifer said. “Students represent the next generation of clinicians, investigators, and scientists – the individuals making the healthcare decisions of the future.”

To learn more about opportunities for students and young professionals at our 2013 EuroMeeting, please visit http://www.diahome.org/EM2013. For more information about opportunities for students at our DIA 2013 Annual Meeting, please visit http://www.diahome.org/DIA2013.

### Upcoming Events

**NORTH AMERICA**

- **Pharmacovigilance and Risk Management Strategies 2013**
  - January 13-16 | Washington, DC
  - Register by December 19 to Save!

- **Three-Part Online Training Series: Art of Writing a Clinical Overview**
  - Begins January 28 | Online

- **Three-Part Online Training Series: Development of a Clinical Study Report**
  - Begins February 5 | Online

- **Five-Part Online Training Series: Clinical Statistics for Nonstatisticians**
  - Begins February 13 | Online

- **Marketing Pharmaceuticals 2013**
  - February 19-21 | Washington, DC
  - Register by January 30 to Save!

- **Premarketing Clinical Safety & Pharmacovigilance**
  - February 25-26 | Horsham, PA

- **Assessing the Benefits and Risks of Medicines: A Webinar Series for Practitioners**
  - Part 3: Framing for Benefit-Risk Assessment and Communication
  - February 27 | 11:00AM-12:30PM ET

- **Leadership Experience**
  - March 5-7 | Horsham, PA

- **Regulatory Affairs Part I & II: The IND and NDA Phases**
  - March 17-20 | Irvine, CA

- **Risk Management and Safety Communication**
  - March 18-19 | Horsham, PA
  - Register by February 25 to Save!

- **Medical and Scientific Communications 2013 Annual Forum**
  - March 18-21 | Chandler, AZ
  - Register by February 25 to Save!

- **NEW COURSE! Advanced Clinical Vendor Oversight: Vendor Lifecycle Management**
  - March 26-27 | Horsham, PA
  - Register by February 25 to Save!

- **CMC Workshop 2013**
  - April 15-17 | Washington, DC
  - Register by March 25 to Save!

- **DIA/FDA Statistics Forum 2013**
  - April 28- May 1 | North Bethesda, MD

To take advantage of high-visibility exhibiting opportunities at DIA Events in 2013, visit diahome.org/exhibit for details.
I was fortunate enough to attend the 6th DIA Clinical Forum – Empowered Patient (The Hague 8th – 10th October) as a Student Fellow, despite graduating as a pharmacist (at the Faculty of Pharmacy, University of Lisbon) very shortly. My application to this meeting had several motivations: the interest in the themes addressed, a huge curiosity to experience the professional environment that I am aiming for in the near future, and DIA’s prestige. I would like to start my testimony about my presence in 6th DIA Clinical Forum by stating that, in each one of these aspirations, my expectations were outdated.

As part of DIA’s commitment to the students’ participation and professional evolution we (both Students and Young Professional Fellows) participated in Student Special Sessions, in which I acquired essential lessons for the future. We have learned about networking, job application techniques, employers’ expectations and other related subjects. In one of these Sessions we also had the chance to gain more insight into DIA and its activities. DIA’s mission was there described as “to be the global forum for knowledge exchange that fosters innovations, raising the level of health and well-being worldwide.” Although the Clinical Forum is only one of the DIA events, it was more than enough to understand that its mission is being successfully accomplished. On one hand the programme was multidisciplinary and covered the pharmaceutical industry’s current issues and future challenges in clinical operations, drug safety, medical information and data management, from the several stakeholders point of view. On the other hand, it was consistent in the dynamic of the sessions and in standard quality and transparency of the information provided. Surely, those two and a half days contributed to the spread of global development trends as well as to bring together industry members, regulators, academia and patient groups’ knowledge and thinking.

However, and despite the greatness of DIA’s mission as described above, I dare to say that DIA’s impact is much broader than that. I can speak, at least, about the impact of this
experience with DIA for me, as a student. The amazing experience of seeing the huge world of Pharma put together, and to take part of it, will definitely play a role in my future choices. The chance to network with everyone, as even the ‘senior professional of the big company’ was very kind to give me some tips, allowed me to develop the important soft skills. All I have learned about the scientific topics, as even when the sessions were too complex for my understanding, my questions were welcome. I found myself participating in workshops where my group colleagues were such experienced professionals, or discussing the controversial theme at the plenary debate with someone in the next chair, without fearing who would that person be, because I knew that my opinion would be respected. I have experienced that the common interests and the fascination that participants shared there made them become closer, as everyone breathed knowledge and innovation, and everyone had something to learn or to teach.

A further benefit of this conference was the chance to meet people in similar situations with similar aims, and share thoughts and emotions with them. I consider that I can speak on behalf of my Fellowship colleagues, and for us this DIA Clinical Forum was more than “raising the level of health and well-being worldwide.” It was mostly about finding out the driving force of each one of those professionals that brought them together in that event. It was to acquire the motivation that will make us try hard, work hard, create and innovate, to get to the level of knowledge and know how that we’ve seen represented there. It was to discover the speakers and other participants’ enthusiasm, or the patients’ tenacity, in their everyday subjects, and to realize that also for them DIA activities refresh their passion for what they do. It was to understand that to have a unique, recognized, independent, global forum for collaboration and exchanging knowledge as DIA makes the difference, to face the daily professional needs or in each one of those individuals’ careers course. In this way, DIA mission goes further than the impact in the global pharmaceutical and medical products landscape and life cycle management, as it offers an impact in each person who takes part on this community, in advancing skills, providing resources or implementing leading practices.

I’ve returned home willing to be present in more DIA events, willing to know more about the hot topics discussed or about the health sciences underlying the presentations I have attended. I have returned home willing to get a job in the areas represented there, so that I can contribute to the innovation stream at the clinical use and development of pharmaceutical and medical products. As for me, I believe that the other participants, from industry to policy makers, academia or patient and advocacy groups have returned home with refreshed ideas and extra expertise to commit to their everyday practice. We all have returned home knowing that, until next DIA Clinical Forum, our everyday contributions can keep the level of health and well-being world-wide being raised.

I’ve heard of DIA through EPSA (European Pharmaceutical Students’ Association) and explored DIA’s website and learned DIA supports students and young professionals by giving fellowships for the first time for Clinical Forum 2012. I was very excited about this conference because it was the first time that I was going to an event where health professionals, public health authorities, policy makers, academia and patients were coming from all over the world to exchange their knowledge and experiences and I was glad to be accepted as a fellow.

The three-day conference started in World Forum in The Hague and the first tutorial which I attended was about personal data protection in clinical trials.

MARKO RADOVIC
is a Student in the Faculty of Pharmacy at the University of Belgrade, Serbia
and pharmacovigilance. There I met fellow students and young professionals and we were all encouraged by the instructors to ask questions, encourage debate and join groups of professionals for discussion. It was a perfect time to relax, start conversations and network with people who are deeply involved in this topic and career.

The next day for the first time at this conference, fellows and other students had an opportunity to attend special student sessions with professionals who are deeply involved in their professions. These sessions helped us to learn how to get the most out of our attendance at The Clinical Forum and gave us better understanding about available activities (clinical researches, drug safety, and medical information). The second special student session was more dedicated to how to get the most out of DIA and DIA membership, the job-seeking landscape and what’s behind hiring decisions. All of them were very open and answered our questions.

The gap between the sessions we used for networking with other professionals and young students. It was a perfect example of how to start to build your career through networking with other people. These gaps I used to share my own idea about a future career in pharmacy with experienced professionals and asked for personal opinions and advice on how to get started.

For the first time in my life, at the Clinical Forum I participated in sessions with patients (one of the key people in clinical research) and had direct communications with some of them about how they struggle with life and diseases and the relationships between doctors and pharmacist.

As a student and future young professional, I concluded after this forum that networking and connections between colleagues and patients who are deeply involved in clinical research is really a very important factor and that DIA provided an excellent opportunity for all of these different groups to get involved.

DIA Celebrates 25th Annual EuroMeeting in Amsterdam

DIA's 2013 Annual EuroMeeting, to be held 4-6 March in the Amsterdam RAI, is global in scope and will attract more than 3,000 medicines development professionals from around the world. It will bring together experts from the biopharmaceutical industry, contract research and service organisations, academic research centres, regulatory agencies and health ministries as well as delegates from patient organisations. This convergence will afford participants the opportunity to network with professional colleagues from around the world. With an appealing range of topics set in 17 themes the co-Chairs, Beatriz Vícen Banzo and Peter Bachman, anticipate fruitful and engaging discussions that will serve to improve further healthcare systems everywhere.

With a focus on better public health protection, greater transparency of the processes and the rational use of medicinal products, the proposed areas for discussion for this, the 25th Annual EuroMeeting, are classified into general disciplines including Pharmacovigilance and Regulatory Affairs for medicinal products and medical devices, R&D and Clinical Trials.
The scope of the presentations will cover the experience gathered after the implementation of the new Pharmacovigilance legislative framework, as well as from the patients’ and Health Technology Assessment (HTA) perspective. Experts and authorities in the fields will be presenting their considerations for debate.

HIGHLIGHTS OF THE 2013 EUROMEETING INCLUDE:

• Speakers from the European Medicines Agency, the European Commission, the FDA and other regulatory agencies from European countries and other regions of the world
• Unparalleled multi-disciplinary networking opportunities
• Student and professional poster sessions
• Active involvement of patient organisations
• Pre-conference tutorials led by expert faculty
• Hot topic sessions
• More than 200 exhibitors on one of the largest exhibition floors in Europe

OPENING PLENARY DEBATE – LACK OF MEDICINAL PRODUCTS

The globally recognised shortage of medicinal products could be due to a number of factors such overregulation, reduced R&D or an overall decrease in investment – among others.

Whatever the reasons, a panel of thought leaders from industry, regulatory authorities and patient organisations will debate the hot issues around this thought provoking subject. The discussion will be moderated by a journalist with an in-depth knowledge of medicines development.

PANELISTS INCLUDE:

• Jan Geissler, Director, EUPATI, Belgium
• Kemal Malik, Head of Global Development, Member of the Bayer HealthCare Executive Committee and Chief Medical Officer, Bayer HealthCare Pharmaceuticals, Germany
• Pat O’Mahony, Chief Executive, Irish Medicines Board, Ireland
• Luca Pani, Director General, AIFA, Italy
• Andrzej Rys, Director of Public Health and Risk Assessment, European Commission, EU
• Harpreet Singh, Managing/CSO, Immamics Biotechnologies, Germany

For more information on the DIA EuroMeeting, go to www.diahome.org/EM2013 or contact us at diaeurope@diaeurope.org.
For more information about how to enjoy Amsterdam please visit www.iamsterdam.com.

Report on DIA Europe Training Course

Quality by Design for Chemical and Biotech Products – A hands-on course for the pharmaceutical industry and regulators

This new course, held in Vienna, Austria at the end of September 2012, provided a comprehensive description of strategies for developing a product according to the ICH guidelines ICH Q8, Q9, Q10 and also the brand-new released ICH Q11 guideline ‘Development and Manufacture of Drug Substances (chemical entities and biotechnological/biological entities)’.

During this interactive course, the key elements of Quality by Design for small molecules and biotech products were discussed. Participants learned, with practical work on case studies (solid dosage form of a small molecule and manufacturing process for a biotech product), how to use Quality Risk Management (QRM), Process Characterization, Design of Experiments (DoE), Development of a Design Space and Control Strategy.
One case study demonstrated that a systematic approach to pharmaceutical development is faster, needs fewer resources and leads to robust processes.

The trainers, Dr Siegfried Adam, QA Manager, Hermes Pharma, Austria, Dr Fritz Erni, a Switzerland-based industry expert with considerable experience in research, development, QA/QC and manufacturing, Dr Erich Hochuli, ICB Consulting, Switzerland, an expert in Biotech manufacturing, Prof. Dr Johannes Khinast, Head of the Institute for Process and Particle Engineering, University of Technology and Scientific Director of the Research Centre for Pharmaceutical Engineering in Austria together with Dr Christa Wirthumer-Hoche, Head of the Unit for Marketing Authorisation and Life-Cycle Management of Human Medicinal Products at AGES PharmMed (Austrian Medicines and Medical Device Agency) led the case studies for small molecule tablet formulation and a monoclonal antibody drug substance.

Dr. Erni reinforced that “a systematic approach to pharmaceutical development with science based tools and adequate use of Quality Risk management could make a big difference for competitive manufacturing of drug substance and drug products, for new drugs and for generics, for small molecules and for biotech products. There was a lot of very positive feedback from the participants. They are very keen to use the newly learned QbD approach in their daily life.”

Buoyed by the success of this QbD training DIA Europe will be holding the next training course on QbD, with the same trainers, in November 2013 in Dubai. There is also a special CTD (Common Technical Dossier) course planned towards the end of 2013.
The 4th Latin American Regulatory Conference: Supporting the Industry through fostering regional regulatory convergence

The 4th DIA Latin American Regulatory Conference (LARC 2012) was held on October 1-2nd, 2012 in Mexico City with great success. Compared to the previous meetings, this year’s meeting had 10% more participants and attracted participants from 17 countries in Latin America, Europe and the US. Justina Molzon, MS Pharm, JD, Capt. USPHS, Associate Director for International Programs, CDER, FDA co-chaired the event together with Mike Ward, Manager, International Programs Division at Health Canada. In order to support the meeting locally, LARC’s Scientific Committee for the first time included 3 local members of DIA’s Regional Advisory Council for Latin America in addition to the Council’s Chair, Sergio Guerrero, MD.

The first day featured an opening plenary session debate on Regulatory Convergence for Promoting Public Health, featuring...
high-level speakers working actively on regional convergence such as QFB Jose Daniel Peña-Ruz, Senior Advisor, Essential Medicines and Biologicals, Pan-American Health Organization; Lembit Rago, MD, Coordinator for Quality and Safety of Medicines, World Health Organization; and Anthony Ventura Pfizer’s Head of the Latin American Region.

This excellent two-day program featured 8 sessions, covering topics such as Emerging Issues in Clinical Research, Trends in Education and Certification of Clinical Research Professionals, Integrity of Supply Chain/Good Manufacturing Practices (GMP), Biosimilars and Pharmacovigilance, among others. Over 27 expert speakers and panelists attended the meeting, including officials from the regulatory agencies of Venezuela, Cuba, Mexico, US and Canada.

The Plenary Closing panel session, “Increased Collaboration and Catalysts for Regulatory Convergence: Next Steps Planning Discussion for the 5th LARC,” was especially energetic, given its interactive design and dynamics between the meeting participants, faculty and Conference Chairs. There was a lively discussion that will shape the program for LARC 2013.

SAVE THE DATE
The 5th DIA Latin American Regulatory Conference will be held May 15-16, 2013, in Bogota, Colombia. For more information contact Alejandro Bermudez-Del-Villar at Alejandro.Bermudez@dialatinamerica.org.
Moriyuki Miyasato, MBA, is the program chairperson for this workshop, a member of Biostatistics SIAC of DIA Japan and a manager of Biostatistics Dept in R&D of Janssen Pharmaceutical K.K.

The first trigger for this Basic Statistical Concept workshop was an e-mail to me about a basic statistics educational course for non-statisticians that was offered by DIA in the US. We thought it might be useful to provide a similar educational course for the Japanese audience.

During the planning phases, the program committee members found that there would be many additional needs for non-statisticians, who reported that they felt they had a weak consciousness for statistical concepts, including help understanding when and what (not “how”) to apply statistical concepts within the context of clinical development (especially in the regulatory environment in Japan), and how to work with their statisticians productively and smoothly, rather than being a “beginner” statistician on their job. The program committee was excited and challenged by the task of creating materials to meet the needs of this audience.

Held October 9-10, the 1st Basic Statistical Concept Workshop for All Clinical Research Professionals drew even more participants than expected. The conference room, which had a capacity of 150 seats, was almost full. The first session of the workshop focused on phase 3 confirmatory clinical trials, presented by Ayano Takeuchi (Researcher, National Institute for Environmental Studies). She carefully instructed about issues in each scene (study design, study conduct and interpretation of results) of phase 3 clinical trials (such as hypothesis testing, sample size calculation, random allocation, analysis population, point and interval estimates, etc), as well as basic statistical framework. This first session was very important, since it provided the audience with a clear understanding for all subsequent sessions which referred to the basic framework, and focused on issues in each clinical development context.

The next session focused on exploratory phase 2 study, presented by Dr. Yoichi M. Ito (a member of Biostatistics SIAC of DIA Japan, Associate Professor, Department of Biostatistics, Hokkaido University Graduate School of Medicine). In his lecture, dose finding learning study was
selected as a representative case of exploratory phase study, and explained several basic points to consider estimation of dose response curve, differences between general drugs and oncology drugs as representative of drug for life-threatening diseases, multiplicity in dose selection for phase 3 trial, validity and reliability of rating scales, proof of concept, etc. Of course his lecture was also in line with each scene of clinical trials.

The last session of the first day was about safety data from early clinical development to post-marketing, presented by Osamu Komiyama (a member of Advisory Council of DIA Japan, Chairperson of Data Science Expert Committee of JPMA, Clinical Statistics of Pfizer Japan Inc.). He referred to the good textbook for safety data (Original: Drug Safety Data: How to Analyze, Summarize, and Interpret to Determine Risk, Michael J. Klepper, MD, Barton Cobert, MD), which he and his colleagues recently translated into Japanese. He provided not only the essence of this textbook, but also his own opinions and statistical concepts to understand safety data.

On the second day of the two-day workshop, all sessions focused on the application and reality of clinical trials. The focus of the first day was designed to concentrate more on basics, principles and ideal situations, but the second day centered on applications of basic statistical concept in reality.

The first session on the second day focused on phase 3 trials by Dr. Satoru Fukinbara (a member of Biostatistics SIAC of DIA Japan, Director of Data Science in Ono Pharmaceutical Co., Ltd.). He talked mainly about “Mitigation of Uncertainty” in each scene of phase 3 trials, such as sensitivity analysis, hypothesis setting in superiority trials and non-inferiority trials, how to consider robustness, choice of randomization method, missing data, interim analysis, data quality, subgroup analysis and etc.

The second session was my session, focusing on exploratory phase 2 trials. In my session, the main topics were issues in study design, study conducting and interpretation of results in dose-ranging clinical trials for an earlier stage and later stage (ie, just before go decision of phase 3 trials). Topics included Controls, Prognostic factors, choice of statistical method, multiplicity, data review, level of blinding, etc. My point was the importance of phase 2 to reach success in phase 3 trials.

The last session was about safety data, presented by Komiyama-san again. In the first half, he focused on the meaning of numbers in safety data and understanding relationships between sample size and what we can observe, including not only an explanation of the concept but also learning the binominal distribution “Rule of Three.” In the latter half, he talked about the way of thinking in the global development environment, such as causality assessment of AE, all data vs. individual data, and local pharmacovigilance. He also provided closing remarks for the workshop.

In his closing remarks, he emphasized that it’s more important to understand basic statistical concepts for clinical trials and to have a good sense of which matter should be consulted by a statistician, rather than being able to do complicated statistical calculation and/or understanding choice of statistical methodology with delicate difference. Those are the statistician’s job!

Functional areas of participants seemed wide-spread from all clinical development, including clinical research physicians, clinical scientists, regulatory specialists, medical writers, safety or pharmacovigilance, data managers and some statisticians. The workshop seemed to be very well received. At the end of every session, audience members asked questions to each presenter directly and very intently. We have received comments from participants after the workshop, that say it was well-planned and the content of sessions were unified on the same context.

The survey to participants (total 114 participants responded) after the workshop also indicated that more than we expected. Over 80% of participants indicated that the contents were relevant to their job (“Strongly agree” plus “Agree”), and almost 70% were indicated that contents were met their expectations both for the first day and the second day. For the easiness to understand, 78.1% of participants indicated “Strongly agree” or “Agree” for the first day (about basic concepts), 70.2% was for the second day (about more applications). In the free text field for suggestion to this survey, many participants (more than 20) clearly commented “wish to hold sequel to this workshop,” and some participants also suggested concrete ideas for a sequel workshop.

Finally, I would like to express my special appreciation to all participants of this workshop; all personnel supporting the program committee in planning and coordination, including Ko Sekiguchi-san (Director of DIA Japan, for providing this opportunity), Keiko Cambridge-san and Yoshiko Takahira-san (DIA Japan Office), Eri Sekine-san (bringing the first trigger of this workshop, Leader of Biostatistics SIAC of DIA Japan), Director of Biostatistics and Data Management in Novartis Oncology Japan); and all members of the program committee (Takeuchi-san, Ito-san, Fukinbara-san and Komiyama-san).
Upcoming DIA India Meetings 2013

- **e-CTD Hands on Training Workshop**
  - FEBRUARY | BANGALORE/MUMBAI

- **Pharmacovigilance**
  - MARCH | BANGALORE

- **6th Regulatory Conference**
  - APRIL 5-6 | AHMEDABAD

- **Technological Advancements To Meet Regulatory Challenges**
  - APRIL 25 | MUMBAI

- **Biosimilars**
  - JUNE | MUMBAI

- **2nd IT Life Sciences**
  - JULY | BANGALORE

- **Generics/ APIs**
  - AUGUST | HYDERABAD

- **8th Annual Conference**
  - OCTOBER | MUMBAI

To know more on the upcoming DIA India meetings write to DIAIndia@diaindia.org
EDUCATE does just that: Keeps you abreast of the association, membership, regulatory, and legislative news while including features such as career advice, book reviews, patient perspectives and more.
In less than six months, the newly launched DIA.HBA Leadership Project has established a vibrant community of women in the regulatory, legal, compliance and medical functions.

This month’s Women in Healthcare section shares benchmark data to advance the Project’s key goals:

Goal: Accelerate leadership talent through skill building.
The first article summarizes data on leadership skill building priorities for these four functions. Watch for registration information on our custom-fit leadership skill building workshop being planned one day prior to the 2013 June DIA Conference in Boston.

Goal: Accelerate leadership impact by positioning these functions as high value partners to the overall business.
The second article shares data on why regulatory, legal, and compliance leadership makes promotional reviews more efficient, saving time and money. HBA Steering Committee members are quoted, along with male DIA members – as functional value transcends gender.

Please join our dedicated LinkedIn community to learn more about how this initiative benefits you and to share your perspectives (www.hbanet.org/companies/alliances/DIA).
Which leadership skills do women in regulatory, legal, compliance and medical want to improve in order to accelerate their careers? This was the question posed by a benchmark survey conducted at the DIA/HBA Leadership Project launch event in June 2012. The findings of this research are summarized below.

PROFILE OF THE RESPONDENTS

Survey respondents largely work in pharmaceutical/biotech (78%) followed by clinical research services, devices and government (Figure 1).

It’s important to note that the majority of the survey participants (70%) currently work in Regulatory (Figure 2).

Nearly 70% of the women have been working in the industry for over ten years (Figure 3).
### Skill Building Needs

Regarding the top developmental needs among all respondents, skills related to executive presence (54%), more innovative thinking (50%), strategic thinking (43%), coaching/mentoring (43%) and delegating (33%) were cited. A further breakdown of the desirable skills can be found below.

The survey also determined the level of agreement with the following statements on a scale from 1-5. Statements below ranked at 3 or above:

- There still remains some unconscious bias against women
- Women tend to hold themselves back, sometimes talking ourselves out of professional opportunities
- There are few mentors or sponsors for women in leadership positions
- Men must play a greater role in dismantling barriers to career advancement for women
- Women still hold a traditional role, making work/family integration a barrier to career advancement
- Regulatory, medical, legal and compliance are not valued as business partners because they don’t manage P&Ls

The last statement is the focus of the following article entitled **Regulatory, Legal and Compliance are High Value Partners for Companies That Want to Achieve Marketing Excellence in a Compliant Culture.**

#### Percentages of Respondents Identifying Development Needs

![Diagram showing the percentages of respondents identifying development needs](chart.png)
Regulatory, Legal and Compliance can now make a business case to management that demonstrates their value to the commercial organization. Specifically, these functions help Marketing fuel marketing excellence – a key strategy for an industry that strives to excel within a compliant, transparent culture.

Marketing excellence occurs when promotional review committees (PRCs) are more efficient so corporations don’t waste time and money during the review process. As a result, more effective, balanced promotion gets into the field more quickly to protect and enhance public health and patient care.

Benchmark data below diagnose three key drivers of inefficiency and spotlight why a partnership between Commercial and Compliance contributes to ‘smarter’ promotion.

According to Abbott’s Divisional VP of Regulatory Affairs, Tracy Rockney, who serves on the DIA/HBA Leadership Project Steering Committee, “These findings make clear what many of us have known in Regulatory for years – partnership is essential for success. What these finding also bring to the surface is the role of educator within a company – what function(s) should be responsible for educating on critical regulatory requirements? And should companies consider minimal threshold requirements across all functions in order to make decisions for the approval of promotional materials.”

THE DATA*

Knowledge Gaps - When asked to pass an exam developed by former FDA officials that covers regulatory fundamentals, marketing professionals often incorrectly answered basic test questions in numerous categories, including risk communication; pre-submission requirements; reminder and disease state awareness ads; and use of spokespeople. Promotional agency staffers tend to fail questions on websites, press releases and use of spokespeople.

Schism – Given these knowledge gaps, internal marketing professionals and promotional agencies don’t often agree with Regulatory on how to implement the following tactics within regulatory guidelines: digital initiatives, public relations activities (e.g., media tours, press releases); promotional education (e.g., speaker’s bureaus, and slide kits); and advisory board meetings. Disagreements about compliant claims can increase interdepartmental tension, which results in less streamlined decision-making.
Alignment and knowledge sharing between Marketing, Regulatory and Compliance can also create powerful business benefits, asserts Kristin Rand, Executive Director of Compliance at Seattle Genetics. Rand, former Director of Compliance at Genentech, and a member of the DIA.HBA Project Steering Committee, describes how the compliance function can supply competitive intelligence to the marketing and regulatory members of PRC.

“When assessing and managing risk, especially in grey areas, compliance functions often benchmark what other companies are doing. The insight gained from these environmental scans can provide additional value to review committee members, not only regarding compliance and regulatory matters, but also business strategy.”

2013 requires a new business model where marketers embrace Regulatory, Legal, and Compliance as high-value partners instead of seeing them as policemen (or proverbial “sales prevention/suppression” departments).

“This three-point plan delivers:

**Efficiency** – by reducing the number of rewrites for heavily redlined materials submitted by marketing and agency professionals that are not versed in regulatory fundamentals. Fewer rewrites shorten review cycles and reduce the overall number of cycles. When time isn’t wasted rewriting, associated savings could fund more marketing materials or support a new hire.

**Effectiveness** – by freeing up time for Regulatory to focus on improving quality of claims. Educated marketers are better equipped to present creative ideas in compliant terms, reducing ‘non-starter’ concepts so more big ideas are executed. Fewer disagreements about compliant claims mitigate tension, streamlining decision-making. Sales materials get into the market more quickly because rewrites don’t delay the review process.

**Impact** – by accelerating the transfer of accurate and non-misleading information about drugs and devices; deepening healthcare professional knowledge/insight on appropriate interventions; and enhancing patient/consumer decision-making.

*For survey data, analysis and sources, contact ilevins@CommunicationCompliance.com*
REGULATORY ROUNDPUP
DIA / NORD Rare Disease & Orphan Product Conference

Several sessions at the second annual DIA/NORD US Conference on Rare Diseases & Orphan Products, presented in October, addressed the regulatory aspects of orphan product development, review and approval.

IMPACT OF FDASIA ON ORPHAN PRODUCT DEVELOPMENT

John K. Jenkins, MD (Director, Office of New Drugs, CDER) explained that this fourth reauthorization of PDUFA (PDUFA V) means that we’re in the 21st year of the drug user fee program, expanded by this reauthorization to introduce similar user fee programs for generics and biologics. Having safe and inexpensive (generic) and innovative (biologics) products are just as if not more important to the rare disease community, he said. John also noted that, “There’s a lot of focus in the legislation on innovation in general.”

John reviewed the aspects of PDUFA V’s new review program that aim to improve and increase communication and transparency not only between the agency and industry but within and between agencies. He also presented the six specific rare disease commitments made in PDUFA V (see accompanying box). He concluded by reviewing other aspects of the FDASIA/PDUFA V legislation related to innovation and orphan products, such as the “Accelerated Approval” and “Breakthrough Therapy” designation, for which FDA has already received several requests.

As she assessed The Impact of FDASIA on Orphan Device/HUD Development, Cassie A. Scherer, JD (Office of the Center Director, CDRH), reviewed the definitions of a Humanitarian Use Device (HUD)

Six Rare Disease Commitments of PDUFA V:

- Increase CDER rare disease staff by five, and establish rare disease liaison in CBER
- Develop and disseminate guidance and increase outreach to industry and patient representatives and organizations
- Conduct public meetings to discuss complex issues
- Develop training in orphan product development, review and approval for FDA staff
- Develop an evaluation tool to assess impact of rare disease interventions
A HUD is a medical device intended to benefit patients in diagnosis and/or treatment of a condition that annually affects fewer than 4,000 people in the US. “HDE approval is based on safety and probable benefit,” she explained, and authorizes the applicant to market their device subject to certain profit and use restrictions: The FDAAA of 2007 (PDUVA IV) previously incentivized the development of pediatric HUDs by removing the profit restriction if the device is labeled for pediatric use; FDASIA expands this profit prohibition. New Draft HDE Guidance is hoped for as early as 2013; in early 2014, there will be a public meeting on the orphan device implications of FDASIA to be followed by a written summary report.

Andrew J. Emmett, MPH (Biotechnology Industry Organization – BIO) was the industry representative most involved in PDUFA V negotiations. “We’re extremely proud and enthusiastic about the innovation provisions of FDASIA,” Andrew allowed.

PDUFA V will support the development of rare diseases through focused policy development, training of FDA review staff on unique scientific issues related to rare diseases, and education and outreach to industry, patient and investigator communities, Andrew explained. It was designed to encourage innovative clinical trial designs for drug products AND to ensure that FDA has the scientific expertise and training to adequately assess them. During these negotiations, BIO also focused on modernizing and expanding the accelerated approval process, which has mostly been used for cancer and HIV/AIDS treatments: “We really want to expand that to other disease areas, including rare diseases,” he said.

“A predictable, consistent, and efficient regulatory system will help drive investment in the rare disease area,” Andrew concluded.

THE NEW RELATIONSHIP WITH THE PATIENT COMMUNITY: FDA & THE PATIENT

Moderator Jayne C. Gershkowitz (Amicus Therapeutics), who also served on the program committee, framed this session with the question: “How can rare disease patients and their community leaders access the FDA and impact its processes?”

The FDA Approach to Drug Benefit/Risk Assessment is organized around five key considerations, explained Theresa M. Mullin, PhD (Associate Director, Office of Planning & Informatics, CDER): The Analysis of Condition and the Current Treatment Options provide regulators with the clinical context for weighing benefits and risks; the Benefit, Risk and Risk Management considerations incorporate expert judgments based on evaluation of the efficacy and safety data and the expected impact of efforts to reduce and further characterize risks.

“How do we make this process most useful to patients?” she asked. She answered by reviewing the patient-focused drug development provisions of PDUFA V. These include supporting additional review staff to expand activities that provide review divisions with patient input; convening meetings with review divisions and relevant patient advocacy communities; and holding four public workshops each year, over the next five years, each focusing on a different disease area and identifying areas of unmet need within it.

Richard Klein (Director, Patient Liaison Program, Office of Special Health Issues, FDA) said that patient representatives have been serving in FDA advisory committee meetings through the Patient Representation Program since 1991. Currently, approximately 175 patient representatives representing approximately 70 diseases/conditions serve in this program; as mandated by FDASIA, this program will now expand to give patients the opportunity to provide input earlier in the drug development process. Patient representatives provide great input to clinical trial designs, enrollment, gender/age/race issues, and real-world product use, and further help by overlaying value judgments on top of measurable, empirical clinical evidence, Richard explained.

“Traditionally, industry and regulators have clearly defined roles in the regulatory process,” said Phillip R. Desjardins, JD (Associate Director for Policy, CDRH). “The role of patients is a little less well-defined by statute and by regulation.” Phillip placed patient interactions with FDA in the context of the regulatory process: Because the ultimate decision-makers when it comes to treatment options are the patients themselves, incorporating the patient voice into the device approval process will help guide
providers and regulators to the best healthcare decisions.

Diane Edquist Dorman (Vice President Public Policy, NORD) noted that you can see the importance of patients grow through the successive reauthorizations of PDUFA, culminating in the many patient provisions of PDUFA V. “If you’re not familiar with the FDA review process, if you’re not familiar with the rules and regulations they must abide by, I strongly encourage you to learn more about them,” she suggested. Benefit/risk is one of the most important areas in which patients can provide valuable input, she noted; especially rare disease patients, who may be willing to accept more risk than a patient with a less life-threatening disease.

WORKING WITH THE FDA

“Instead of talking about what the FDA demands, we’re going to talk about what the FDA can give you,” said session chair Kathryn O’Connell, MD, PhD (Medical Officer, Rare Disease Program, OND, CDER). What can FDA do early in the process to help get your project to the point where it becomes the purview of the appropriate review division?

Gayatri Rao, JD, MD (Director, Office of Orphan Products Development – OOPD) discussed how to apply for Orphan Designations & Grants. “What can the FDA do to promote the development of orphan products?” she asked. “We provide incentives for these products which within FDA is pretty unique.”

“These are really strong incentives for the promotion of products, particularly drugs or biologics, in this space,” suggested Gayatri, which contributed to the approval of 26 orphan products in 2011 (see accompanying box).

Gayatri stressed that the OOPD is cross-agency and not in one review division – they review drugs, devices, biologics, foods, etc. – so sponsors should submit their request for Orphan Drug Designation to the OOPD first, and thereafter submit their NDA or BLA to the appropriate review division.

Gayatri also overviewed the FDA’s Orphan Drug Grant Program, which encourages clinical development of drugs, devices, biologics, and medical foods for use in rare diseases; and helps to advance marketing approvals and generate publications that impact rare disease care. She concluded by describing the pathways for the Humanitarian Use Device (HUD) designation, the Humanitarian Device Exemption (HDE), and the FDA’s Pediatric Devices Consortia Grants Program.

Larry Bauer, RN, MA (Office of New Drugs, Rare Diseases Program) explained the Importance of Meetings with the FDA. “The pathway to softening regulatory uncertainty is through communication,” he began.

Why are meetings with the FDA early in your clinical development program important? “It’s an opportunity to discuss your drug development plan that may eventually support your NDA or BLA regulatory submission,” he explained.

“The point of contact within the review division is the project manager,”Larry continued. “Your meeting request should be consistent with the phase of development for which you’re seeking advice” (see accompanying box).

What impact can meeting with the FDA have? Larry cited a study of the mean clinical development times for new molecular entity (NME) and new biologics applications for rare disease therapies: Clinical programs with pre-IND meetings averaged 6.3 years, but those without averaged 16.9 years; programs with end of phase 2 meetings averaged 9.8 years but those without averaged 14 years. “Everyone’s so interested in expediting drug review – this is important data,” he enthused. “This is IMPORTANT data.”

“Ensure that you are getting what you want from the meeting,” he encouraged attendees in conclusion. “This is YOUR meeting.”

RISK TOLERANCE FOR THE RARE DISEASE PATIENT

Patrick Frey (Director, Office of Planning & Analysis, CDER) reviewed CDER’s Benefit-Risk
FDA Meeting Types

- **Type A Meetings**: Immediately necessary for an otherwise stalled development program to proceed; FDA commits to responding in 14 days and conducting the meeting within 30 days.
- **Type B Meetings**: Generally pre-NDA/BLA or pre-IND meetings or at the end of phase 2 / beginning of phase 3; FDA commits to responding within 21 days and conducting the meeting within 60 days.
- **Type C Meetings**: General advice regarding product review and development; FDA commits to responding within 21 days and conducting the meeting within 75 days.

In his conclusion, Markham directed attendees to the “Factors to Consider When Making Benefit-Risk Determinations in Medical Device Premarket Approval and De Novo Classifications” Guidance that was issued in March 2012, and from which he quoted: “FDA recognizes that patient tolerance for risk and a patient-centric assessment of risk may reveal reasonable patients who are willing to tolerate a very high level of risk to achieve a probable benefit, especially if that benefit results in an improvement in quality of life.”

Kevin Romer (Board President, National Tay-Sachs & Allied Disease Association – NTSAD) further discussed Understanding Risk Tolerance for the Rare Disease Patient. He explained that NTSAD has a two-part mission – family support and advancing research – and that patient advocacy groups can be the most useful data providers as scientific research progresses to clinical trials in humans. “It’s really about family services and research being harmonized,” he suggested. “It’s a really measured and fair way of making important decisions that need to be made.” Patient advocacy groups can provide unique insights to other drug development stakeholders, including and especially the FDA, he concluded.

Markham Luke, MD, PhD (Deputy Director, Office of Device Evaluation, CDRH; Acting Director, Cosmetics Staff, Office of Cosmetics & Colors, CFSAN), presented Risk Tolerance for the Rare Disease Patient: An FDA Medical-Device/Surgical Perspective. Markham began by exploring the concept of risk tolerance: For a specific therapy, risk tolerance is acceptance of “perceived risk” due to expectation of “perceived benefit” in the setting of alternative therapies. “Perceived risk” is based on “real” risk as modified by your personal biases and filters; “perceived benefit” is based on “real” benefit as modified by your internal values and external influences.

He then examined risk in the context of medical devices: Unlike drugs, devices do not rely on chemical action or being metabolized within or on the body for their function, so, unlike drugs, medical device risk may not decrease over time due to metabolic adjustments after initial administration. “We follow a risk-based review paradigm for devices,” he explained as shown below:

- **Class I**: Simple, low-risk devices (such as hospital beds) are subject to “general controls” and are mostly exempt from premarket review: “These are not always without risk, but they have very low risk,” he said.
- **Class II**: More complex devices with higher risks are subject to general plus special controls; most require premarket notification and must meet the regulatory standard of “substantial equivalence”
- **Class III**: The most complex devices with the highest risk must go through bench, animal and clinical testing and may also have post-approval study requirements; their regulatory standard is “reasonable assurance of safety and effectiveness.”
During two sessions at DIA’s 48th Annual Meeting: Collaborate to Innovate in Philadelphia, a panel consisting of Guido Rasi, MD, Executive Director of the European Medicines Agency (EMA), Hans-Georg Eichler, MD, MSc, Senior Medical Officer of the EMA, and Aginus A.W. Kalis, MD, Executive Director of the Netherlands’ Medicines Evaluation Board, demonstrated how the European regulatory network provides a unique example of incorporation, building on common results in drug development and approvals.

This network serves more than 500 million users of medicinal products via 27 EU member states, plus 3 European Economic Area (EEA) countries, Iceland, Liechtenstein, and Norway. Within these member states, 44 national agencies cooperate with each other and with the EMA to serve patients and innovation.

The network allows for an optimal use of resources, promoting work-sharing and reducing duplication of work. Examples include:

- **Common European Submission Portal**, through which industry can submit new product applications and reach up to 15 member states at once.

- **European Benchmarking of Medicines Agencies**, whose aim was to contribute to development of world-class medicines through a regulatory system based on a network of agencies (human and/or veterinarian) operating to best practice standards.
The EMA is keenly aware of challenges to product development, such as rising costs leading to declining productivity. Its own mandatory regulation causes some of these challenges; however, the EMA’s mission remains to support research and innovation in order to stimulate development of better medications. The EMA attempts to act not only as a gatekeeper, but also as an enabler. Panelists discussed several initiatives that support this, including:

- **Innovative Medicines Initiative (IMI)**, described as the most important public-private partnership in the world. Uses a broad range of pre-competitive projects from biomarker development to combating antibiotic resistance to address bottlenecks in drug development.

- **European Network of Centres of Pharmacoepidemiology and Pharmacovigilance (ENCEPP)**, which focuses on building infrastructure and developing rules of engagement for better monitoring of drugs.

- **Pharmacoepidemiological research on outcomes of therapeutics by a European consortium (PROTECT)**, an IMI-sponsored initiative that aims to develop innovative tools and methodological standards to enhance safety monitoring of medicinal products, and better evaluate and communicate.

- **EMA’s Benefit-Risk Toolkit**, aims to increase the predictability of decision-making for industry, and “de-risk” decision making, as drug development is a risky business.

The IMI Research Agenda (http://www.imi.europa.eu/sra_en.html) describes research bottlenecks in the drug development process and identifies four strategic pillars:
- Predictivity of safety evaluation
- Predictivity of efficacy evaluation
- Knowledge management
- Education and Training.

With these topics, IMI aims to accelerate the discovery and development of new medicines in the field of cancer, inflammatory and infectious disease.

**INTERACTING WITH THE EUROPEAN SYSTEM**

Coordinating efforts to efficiently produce innovative, safe, and efficacious drug products for patients who need them remains a challenge in Europe.

The Voluntary Harmonization Procedure (VHP) was cited by panelists as a successful and efficient tool to achieve harmonized and quick approvals of clinical trials in many EU member states. For multinational clinical trials, the VHP offers a simple and flexible administrative process, including a single dossier, a single repository, mandatory electronic submission, with all business conducted only in English. The VHP produces a standardized procedure for coordinated assessment with a leading member state, as well as reliable timelines for sponsors.

A next step for this process includes a new regulation for all multinational clinical trials; with one vote per concerned member state.

**DEVELOPMENTS IN PEDIATRICS**

Panelists briefly discussed challenges in pediatric development, including the main challenge of scientific coordination with other committees involved in the cycle of medicines.

In order to make pediatric clinical research feasible, collaboration is necessary. On January 26, 2007, the Pediatric Regulation came into force in the EU, with an objective to improve European children’s health by:
- Facilitating the development and availability of medicines for children aged 0 to 17 years;
- Ensuring that medicines for use in children are of high quality, ethically researched and authorized appropriately;
- Improving the availability of information on the use of medicines for children.

The regulation aims to achieve this without subjecting children to unnecessary trials or delaying authorization of medicines for use in adults. The EMA is currently working on a 5-year report on implementation of the Pediatric Regulation, with hopes to publish a final report in January 2013. To date, data has been received for about 1,000 active substances, and 18,000 reports on studies in children.
The most feared thing in the world is not spiders, heights, death, or even the number thirteen. Unbeknownst to many, the most common phobia in the world is glossophobia or fear of public speaking. For the past several years, the DIA Professional Education Training Development (PETD) SIAC has been coordinating volunteers among SIAC members to offer a solution for people who have this fear by offering The New Presenter Training Sessions. The vast majority of people who utilize these sessions just want to practice and get feedback prior to their presentations.

The people utilizing this program may be first time presenters or even seasoned veterans. The sessions are usually available Sunday through Tuesday of the annual DIA meeting in two time slots per day. They are held in a room allocated for the program with equipment to project presenters’ power point slides and microphones to practice speaking.

The primary purpose is for individuals to practice their presentations with PETD professionals who can offer feedback in both content and presentation skills such as posture, voice projection, and even pacing the timing of the presentation. Oftentimes, simple things like standing straight with head up and speaking clearly are overlooked and attendees are reminded of the basics.

Sometimes, over gesturing is noticed or improper stance is corrected. The time that is taken during the practice session shows the commitment the presenters have to ensure they are making the best presentation possible. If the content of one of the slides is a little confusing and may be corrected by a simple change or two that input is available, but due to the time constraint that is not a primary objective.

Oftentimes the purpose is to familiarize oneself with the technical equipment and hear oneself in a room comparable to the actual presenting room. Guidance is provided on minute details such as hand signals for emphasis, body posture, and proper placement of the microphone.

The individuals that come to these practice sessions may request the amount and type of feedback they would like from the volunteers. On occasion, it is simply to have a neutral third party provide an ear to the content and provide reassurance and help gain confidence.

Session chairs also come to learn how to better time the individual presentations in their session. The advice we usually give to chairs is to have a question prepared for each presenter to get questions started from the audience. The DIA sessions are also recorded so the session chair also makes sure the volume is audible for that purpose. Prior familiarity with the equipment is also reassuring.
and boosts confidence during the actual session.

Since the DIA Annual Meeting is a global conference, many international presenters have sought help in making sure their presentations are clear in content and convey the intended message. Input is provided in proper enunciation of difficult and tricky words. For local presenters, the feedback is to avoid vernacular that is specific to one locality. Sometimes, references to local sports teams or slang which is not widely used may appear in a presentation and may not be understood by the diverse global audience.

In one instance, several years ago a presenter was eager to make his presentation casual and unintentionally used the phrase “to kill a bird with two stones” instead of “to kill two birds with one stone” to describe their new process that saved time.

Fortunately, his practice session prevented the error and improper usage!

Most presenters may have at one time or another made a presentation before in their professional career, but the Annual Meeting is a very large venue which carries prestige and the sheer number of possible attendees in a session makes the task seem daunting. The primary aim of the PETD SIAC is to provide presenters an opportunity to get feedback and provide guidance on good presentation practices (GPP).

Most of the volunteers notice a significant improvement in presenters after they have practiced and incorporated their feedback. In fact, they leave more assured, taller (metaphorically speaking), confident, and relaxed than when they came into the practice session.

Whether you are a first time presenter and do not like experiencing sweaty palms, perspiring forehead, and butterflies in the stomach, or a seasoned veteran or even somewhere in the middle there is an opportunity to rid one-self of these ails. The solution is to attend the PETD SIAC New Presenter Training Sessions. The times and room location are always announced by DIA prior to the annual meeting.

The continued commitment and efforts both the presenters put forth and the dedication of the volunteers has resulted in a high quality conference with standards that result in the success of the DIA Annual Meeting.
DIA’s efforts to foster local geographic communities in the Latin American region have yielded results recently. Under the auspices of the 9th Latin American Conference of Clinical Research (9th LACCR), the DIA SIAC Leadership Council Representative for Latin America, Veronica Lezano, B. MT-BS, Eng, CEO, General Manager, ACTIVA8 Clinical Research along with DIA’s Worldwide Deputy Executive Director, Carlos Fulcher, hosted the first SIACs Latin American Breakfast in Mexico City, Mexico.

Twenty-five 9th LACCR participants attended this successful event, which marked the kick-off for the SIACs Initiative in the region. After a showing a video invitation from the DIA SIAC Leadership Council’s Chair, Deborah Dolan, Dr. Veronica Lezano informed the audience that the Special Interest Area Communities (SIACs) are discipline-specific, global community where DIA members can share common experiences and knowledge and connect with others in their particular field. Likewise, Mr. Fulcher provided a brief interactive explanation on how the Communities work online and on the list of SIACs available.

The audience was also informed on the next steps of this initiative, which is the formation of three specific communities in Latin America: Regulatory, Pharmacovigilance and Project Management. By the same token Dr. Lezano encouraged all participants to take advantage of all DIA’s membership benefits through becoming part of a SIAC, regionally or globally.
Benefit/risk assessments – and related discussions about whose risk and benefit, who is best equipped to define risk and assess how much is acceptable, and the structures and processes underlying these assessments – are the focus of much current discussion among the global healthcare network and its industry, legislative, regulatory and patient constituencies.

To help members and other interested stakeholders navigate these churning waters, DIA’s Clinical Safety & Pharmacovigilance Special Interest Area Community (SIAC) recently unveiled a special Benefit/Risk Working Group specifically dedicated to these and related issues. This working group is chaired by Rebecca Noel, DrPH, MSPH (Eli Lilly & Company), who explained its context and importance in the following interview.

**Title X of PDUFA V directs FDA to develop and implement a five year plan for implementing a structured benefit/risk assessment in the new drug approval process. What characteristics do you hope to see in this five year plan, and in this structure?**

"FDA has put forward their initial benefit/risk assessment framework. As FDA progresses in this area, we would like to see a framework that supports and is harmonized with other leading frameworks, such as the one the EMA uses. We think that harmonization will be a significant, key issue moving forward. In addition, we would also like to see a benefit/risk framework that helps structure and inform consistent high-quality decision making, as well as communication, among both the regulatory agencies and sponsors."

**Why is this Working Group important to DIA’s member and volunteer community?**

"Benefit/risk assessment has been a significant focus of activity for both regulators and industry for at least the past five years. We’ve seen individual initiatives and individual groups working on various elements of the benefit/risk question, but they’ve been just that – individual elements or initiatives. Initiatives like the PhRMA BRAT (Benefit-Risk Action Team), the EMA Benefit/Risk Methodology Project, initiatives being spearheaded by the Center for Innovation & Regulatory Science (CIRS), and the Innovative Medicines Initiative, have typically..."
Benefit-Risk Analysis that will be moderated by Bennett Levitan (Johnson & Johnson), who also serves in our Working Group, who will speak to the PBRER requirements and best practices. We’re going to lay out an overview of benefit/risk assessment from qualitative to quantitative. The qualitative elements will speak to where people are right now with benefit/risk assessment and help address their very short-term needs.”

“Then, other speakers will address needs that will emerge downstream: As we all grow more comfortable with this transition, additional analytic requirements are going to be brought to bear. We hope that this panel will help orient people around the changes implemented by PDUFA and the EU GVP legislation. Those changes have come on quite quickly. It is a whole new world, but we want to make people aware of the tools we have at our disposal and that these tools can help you right now, as well as position you for the future state.”

What is the short-term and long-term vision for this Benefit/Risk Assessment Working Group?

“In the short-term, we have an educational focus. We want to make this larger base of potential practitioners aware of what is happening in the external environment. We must make our membership aware of regulatory requirements that may be changing, of the FDA framework, the EMA framework, the CIRS framework, and of the requirement for PBRERs and the qualitative approach to benefit/risk assessment that can be used across the life cycle to meet the EU GVP requirement. Our short-term focus will be to push out the knowledge we have embedded in our core committee and working group, and sharing that with what we hope is an up-and-coming group of new practitioners. To support this educational component, we’re designing a series of webinars that lay out how we got to where we are, the external environment and some benefit/risk assessment approaches. We hope to eventually turn our long-term attention to more fully developing existing tools that don’t get applied as often because the environment may not yet be as aware of, and therefore as receptive, to them.”

In what ways will this working group inform the content of our upcoming Pharmacovigilance & Risk Management Strategies 2013 conference?

“I will be speaking at this conference by participating in the panel debate on Will We Ever Move Towards Fully Quantitative

DIA will present Pharmacovigilance & Risk Management Strategies 2013 (#13002), January 13-16, 2013, in Washington, DC.

The tentative Benefit/Risk Webinar Series schedule is shown below. Please continue to visit “Meetings & Training” on www.diahome.org for more detailed and updated information on these and other educational and networking opportunities.

- December 6: Introduction to Benefit/Risk Assessments
- January 30: Regulatory & Industry Benefit/Risk Initiatives
- February 27: Framing for Benefit/Risk
- March 20: Unweighted Analyses
- TBD: Conjoint Analysis
- TBD: Multi-Criteria Decision Analysis (MCDA)
- TBD: Quality Adjusted Life Years (QALYs)
- TBD: Visualization & Communication
The clinical research enterprise comprises many different facets that help therapies progress from laboratory bench to patient bedside. Like many other contributors, the roles nurses play in clinical research have evolved to meet the needs of our changing current scientific, clinical and regulatory environments.

Correspondingly, the DIA Clinical Research Special Interest Area Community (CR SIAC) has evolved to meet these needs through the recent formation of a special Nursing Working Group. Susan Nunchuck, PhD, RN (Actelion Clinical Research), who serves as CR SIAC Chair, and Tim Fish, RN, MBA, (Baxter Healthcare Corporation), who serves as lead for this Nursing Working Group, explained the recent evolution of nursing in clinical research and this new working group in the following interview.

**What roles have nurses traditionally played in clinical research and in what ways have those roles evolved over the past five years?**

**TF:** “I’ve been an RN for about twenty years, in hospital-based nursing (bedside and management) for about fifteen years. I have been in a medical information/medical affairs department for the last five. I don’t participate in or facilitate clinical research myself, but I regularly collaborate with partners who do and help facilitate some of the nuances that make clinical research work more smoothly.”

“In my hospital days, I saw nurses serving as research foot soldiers – collecting data, documenting it and sharing it back up through the principal investigator and research coordinators. Now, especially on the pharma side, I’m seeing nurses in a much more sophisticated capacity: Taking the data, doing some of the analysis and collaborating with the principal investigators at each clinical site.”

“I read an article a few years ago about the notion of nurses becoming principal investigators. There are certainly an increasing amount of advanced-practices nurses – at both the Master’s and Doctorate levels – who are qualified to perform research themselves. This would be an emerging trend to look at over the next five to ten years.”

**SN:** “Nurses have played a very large role in different facets of drug development for years. I started in industry, as nurse with a Master’s degree, as a monitor and have held several different..."
positions within drug development that have required my nursing background from time to time. A nursing background frequently helps in a lot of different aspects. In industry, a very large group of nurses are involved as site managers. They’re typically study coordinators but they’re directly involved with patients and with the clinical research monitors.”

“Nurses who come into industry evolve into a lot of different roles: Into project management, into clinical research as monitors, regulatory affairs, medical writing and drug information. They’re also involved in data management, clinical research drug safety and pharmacovigilance. There are also a number of nurses who are involved as medical science liaisons; as well as sales representatives. So nursing in drug development is very well-represented across a lot of disciplines. I’ve had one site which had a certified nurse practitioner – who also had a PhD – as a principal investigator. For the most part, this has not been an industry shift because of the different roles that a physician must play and decisions that a physician must make. That’s not to say this won’t be a future trend.”

From the nurses’ perspective, what is the most common and biggest misconception about clinical research, and what can nurses do to help alleviate that misconception?

SN: “Probably one of the biggest things you hear when you’re working with clinical trial sites is the amount of time that a patient must commit for their study participation, from the number of visits required in a certain period of time to telephone calls between visits. They look at the activities they might have to undergo or they don’t necessarily feel comfortable participating in a trial. Most patients, if they’re participating in a trial, want to fully participate – they don’t want to consent for and get into a trial and then not completely understand what they need to do and when they need to do it. Oftentimes, other logistical issues get in the way: Distances patients have to travel, if their parking is going to be paid for, if they’re going to be remunerated for their visits, if they have to stay for an all-day visit, how they’re going to eat during that visit, their transportation costs, and so on. A lot of different questions come up when patients are asked to review and sign their informed consent. So I see the study coordinators and study nurses very attuned to the concerns that the patients are voicing so they fully participate in the study. It’s incumbent on that person getting the informed consent and working with the patient, whether it’s the study coordinator directly or a nurse who’s assisting with the study, to keep the patient informed about what they need to do as they move successfully through a trial. If that great communication isn’t there, if that care for the patient isn’t there, and if they don’t get their questions answered in a timely fashion, patients could certainly drop out. Onsite nurses keep the trial moving on schedule and help to make sure that patients are well cared for and well informed.”

TF: “Patient misconceptions occur when there’s a lack of education or communication about the trial. Susan spoke of the remuneration perspective. If patients think they are going to receive free product – and many times they will if they’re part of a study – the concern is, are they pursuing the study to get free product? Especially if the study has a placebo arm or is blinded: To not know if they’re on placebo or the study drug can be a huge dissatisfaction for a patient.”

“And if compensation is the concern and they have a larger disease process going on, at what point does the study pay for other treatments to manage their disease process, either in general or specific to the intervention of the study drug? If adverse events happen in the sequence of the study, who covers that? Patients also need education on their entire disease process and continuum of care and not only what a very specific trial may be targeting.”

“There may be misunderstanding as to what trials are and the different strengths that the trials can be designed – whether you have a randomized control, a blinded study or simply a case study that the patient is being interviewed for. Each has different significance to the contribution of knowledge and the patient may not have a full understanding of what that means. Patients sometimes distrust a pharmaceutical company: Is what’s going to be done ethical and will it produce a good product that will improve the population as a whole, or is it just trying to take advantage of my situation?”

“Nurses who have good awareness of the clinical research process can certainly collaborate to find the best ways to educate patients on all of these topics, so
they walk away with the highest level of confidence that the study they’re considering is being conducted in an ethical manner, in a manner that’s consistent with what the FDA requires, that it’s not something done off the cuff, and that a lot of thinking goes into the development of these studies.”

**What is your vision for the short-term and long-term goals of this working group?**

**TF:** “Nursing seems to be an emerging field within pharma in general, whatever the role. This whole notion of being on the research side within pharma is somewhat novel for a nurse, so there’s a lot of disparity and inconsistencies in how the industry applies the nursing talents that we bring to the table. There’s a little bit of a push to fit into a pharmacist or medical model for the delivery of care when there’s a unique nursing theory that provides for the delivery of care and care for the patient. Nurses bring that to the table, but we’re still developing what that looks like within pharma. So I think a great goal for the first year is to develop that idea: What is the nursing role in pharma? Can we learn best practices from one another and bring our unique nursing talents and vision for patient care to light within our respective employers? We have a really good opportunity to better define the role of the nurse in pharma.”

“In five years, I would like to see nurses have a greater capacity to influence the pharma industry from the non-promotional research and development side. Nursing theories on patient care can be incorporated into the way that pharma operates. That might be kind of aggressive but that’s what I think we can contribute to DIA and to industry in general.”

**SN:** “One of our most important short-term goals was to set up a page on the DIA ConneX section of our SIAC website for nurses. Now we can start to develop contacts and use that portal to connect us with the Clinical Research SIAC. From a long-term perspective, we must first and foremost identify the nurses within DIA. Most physicians or scientists have a doctorate that you can query a database by degree, but nurses are a little bit more elusive. This is a different group for DIA; we’ve got to be able to find them and get this message out. Through this article, they can see that this working group has started and can contact us. And what I’d like to see us doing in five years is presenting programs about best nursing practices.”

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**JOIN A SIAC!**

Joining a SIAC is easy, convenient, and free as part of your DIA membership.

SIACs are discipline-specific global communities of industry, academic, and regulatory professionals who collaborate with one another and share best practices.

To become a DIA member, go to [www.diahome.org/membership](http://www.diahome.org/membership).

Go to [www.diahome.org/SIACs](http://www.diahome.org/SIACs) to join the SIACs of your choice.
PATIENT PERSPECTIVE

Listen to Us: Patient Impact on the Drug Approval Process

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The Code of Federal Regulations guarantees that people like Susan Gregory get the chance to tell their stories at FDA public meetings. Gregory’s son, Denny, overdosed on heroin in a grocery store restroom in 2006. An addict, Denny had been clean 8 months—but heroin’s persistent pull won. Two buddies were with Denny but panicked, fearing police prosecution. They ran from the shop without calling 911 or alerting anyone to the 20-year-old man unconscious on the bathroom floor. Denny died alone.

Gregory talked about Denny—his “quick spiral” at 16 from marijuana to Oxycontin addiction to heroin—at a crowded FDA public workshop in Silver Spring, Maryland. The FDA convened the meeting to discuss the benefits of expanding public access to naloxone, a mu-opioid antagonist that reverses opioid overdose. Gregory was one of 28 people registered to speak during the meeting’s open public hearing. She represented Families Against Narcotics, a grass-roots community action group in Fraser, Michigan.

“We wanted to reduce the stigma that’s attached to [opioid addiction],” Gregory explained later. At a meeting filled with medical professionals and empirical data, Gregory sought to “share the personal side” of overdose death. “They didn’t need another expert testimony.”

Title 21 of the Code of Federal Regulations instructs the FDA to devote a portion of every public meeting to oral presentations from the public: an opportunity for non-experts to voice concerns, assert experiences, and relay their stories. For meetings of FDA advisory committees, chairs must devote at least 60 minutes to the open public hearing; they can extend the time when necessary to accommodate a larger-than-usual response. Chairs may neither interrupt nor cut off speakers, who learn in advance how long they may present. At the naloxone workshop, the large
number meant that registered speakers received just two minutes each.

The FDA typically announces upcoming public meetings in the Federal Register approximately two weeks in advance, including registration instructions for the open public hearing. Gregory described a “systematic” process with “guidance every step of the way” before the naloxone workshop: from learning that she’d been granted a slot to receiving an information packet about local transportation and hotels. While she characterized herself as “overwhelmed” at the crowded meeting, “I felt very well received,” she said. Some panel members listened to her in tears. Other speakers at the same meeting expressed less enthusiasm for their reception, but said they shared Gregory’s adamance that their stories must be told, over and over, until the FDA “hears” them. The naloxone meeting was the third time that Joanne Peterson, of Raynham, Massachusetts, had spoken before a panel convened by the FDA. The founder and executive director of Learn to Cope, a support group, Peterson sought—like Gregory—to represent “the human piece” of addiction.

Just over a decade ago, the father of a teenage friend invited Peterson’s 18-year-old son to try Oxycontin for the first time. He liked it. While he survived years of addiction, Peterson’s son—now the father of two young children—is always in danger of relapse, she said. At FDA public hearings, Peterson has demanded a coordinated federal response to the rising number overdose deaths, which she calls an epidemic. “It’s my responsibility because of the carnage,” she said after the naloxone meeting. Where Gregory felt empowered before the FDA, Peterson felt patronized. “They say, ‘oh, you’re so brave,’ and then they go on with their lives. They don’t listen,” she said. A panel of experts may have extraordinary data and decades of professional experience on which to support (or decline) approval of a new drug, but patients and families live and suffer a disease. They’re the ones who can attest to the reality behind the numbers. Gregory has been to the funerals of too many addicts to keep quiet, she said.

“I’ll always go back [to testify] because I’ll never stop trying,” Gregory explained. “I’m okay with saying what needs to be said.”

In addition to guaranteeing time for open public hearings, the FDA has developed a pool of 160 patient representatives to bring “the patient perspective” to public forums. More and more often, patient reps are invited to sit on panels at public workshops like the naloxone meeting, according to Andrea Furia-Helms, coordinator of the FDA Patient Representative Program. Patient reps may also be invited to attend confidential discussions between FDA officials and the developer of a proposed medical product. And every meeting of every FDA advisory committee includes one patient rep with a vote equal to that of the permanent advisory committee members, typically medical and research experts. “Their role is the patient perspective,” Furia-Helms explained. “These are the end users of the product. They know how it affects them.”

Patient rep candidates go through a lengthy, “pretty intensive” review process. Furia-Helms seeks candidates with personal experience of a disease or condition, whether as a patient or a patient’s family member, friend, or caregiver. She also looks for “alternate disease experience” that would enable a rep to serve on more than one advisory committee. Connections to the broader patient community are also important. All patient reps must be legal US residents at least 18 years of age.

Candidate interviews examine the potential for conflicts of interest: situations in which serving as a patient rep might bring them (or seem to bring them) personal benefit. Decisions about conflicts of interest can be a “gray area,” according to Furia-Helms. A candidate might not receive money directly from a pharmaceutical company, for example, but serving as president of an organization that gets pharma money can constitute imputed interest. Once the FDA fully vets and clears candidates, they receive training in the drug development process, and in pertinent regulations and FDA policies. First-time reps attend a two-day workshop, and the FDA broadcasts monthly webinars on current issues and events, such as drug shortages. Reps serve 4- to 5-year terms; many seek and receive reappointment for additional service.

While patient reps do not need formal scientific training, they should be up-to-date with treatment options and research
related to their disease. In other words, they should be “curious,” explained rep Amy Celento of Nutley, New Jersey, who attended her first meeting of the FDA’s Pediatric Advisory Committee in 2007. Diligence helps as well.

About three weeks prior to a scheduled meeting, patient reps receive confidential information about the issues and data to be reviewed. Information from both the FDA and the manufacturer of the product under review can include a detailed description of the clinical development program, trial outcomes, and the product’s proposed indication. Briefing documents frequently number in the hundreds of pages; even a cursory review of briefing documents can require many hours, if not days, of study.

While patient reps receive an hourly, “special government employee” wage for the time spent in meetings (currently about $62 per hour), and the FDA pays for lodging and meals, reps are not compensated for meeting preparation and travel time. Being a patient rep demands determination, Celento stressed. Reps must be determined to wade through briefing documents methodically and thoughtfully; determined to make the trip to the DC suburbs and back; and determined to deal with the red tape that swathes a federal agency.

Some patient reps describe advisory committee meetings that invigorated them and underscored their significance as patient advocates. At Celento’s first meeting, convened for a review of cough and cold medicines marketed for children, she unexpectedly “walked into a media circus.” Although initially shocked, Celento said she quickly found her voice, asking pointed questions about issues such as product packaging, the potential for mis-dosing young children, and the use of cold products to sedate children. Only on her way home, as friend after friend called her cell phone, did Celento learn that her comments had appeared on the evening news.

Patient reps discuss the importance of being part of the regulatory and drug approval process, a role that feels particularly satisfying when the FDA approves a much-needed treatment—such as when the FDA approved Daliresp, a drug for COPD, in 2011. At a 2010 meeting to consider the drug’s safety and efficacy, the majority of the Pulmonary Allergy Drugs Advisory Committee voted against supporting approval. Patient rep Edna Fiore voted for the drug, repeatedly asserting its promise, particularly for raising patient quality of life. When the FDA ultimately went against the committee’s advice and approved the drug, Fiore, of Littleton, Colorado, felt victorious. Results like that can be a high for patient reps—but other results can be heartbreaking.

In February 2012, the Anesthetic and Analgesic Drugs Products Advisory Committee reviewed the Qutenza 8% dermal patch, which was proposed as a treatment for neuropathic pain due to HIV-associated peripheral neuropathy. Almost one-third of people with HIV/AIDS experience peripheral nerve damage, and the pain (which typically affects toes and soles of the feet, but may also extend to fingers, hands, and wrists) can be excruciating. Patient rep Matthew Sharp, of San Francisco, was keenly aware of the lack of FDA-approved medications specifically indicated for this kind of pain. HIV-positive since 1988, Sharp has witnessed many friends suffer without relief. He had high hopes for Qutenza.

But while committee members repeatedly stated that the drug showed potential, they found discrepancies in the efficacy results presented. In the end, the committee voted unanimously that the data did not constitute “substantial evidence” of Qutenza effectiveness.

“I was devastated. I got on the plane and I felt like I had betrayed my community,” Sharp said. He had wanted clear and convincing data, but the sponsor didn’t provide it. “I had to vote based on the evidence,” he says. “You don’t want to do anybody harm.”

Sharp’s disappointment continued, even leading him to reconsider his role as a patient rep. But in the end, the value he and his patient colleagues bring to FDA discussions defeated that sense of frustration. “I am an expert on the patient experience,” he explained, with real-life understanding of product risks and benefits. “It’s critical for us to be there, to be at the table.”

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In 2012 the CPE Monitor, a national electronic system of tracking continuing pharmacy education credits for pharmacists and pharmacy technicians, was implemented in a collaborative effort by the Accreditation Council for Pharmacy Education (ACPE) and the National Association of Boards of Pharmacy (NABP). The CPE Monitor allows pharmacists and pharmacy technicians to track their completed continuing pharmacy education (CPE) credits. It also provides boards of pharmacy the opportunity to electronically authenticate the CPE units completed by their licensee, if applicable. Any pharmacist who has not already set up their profile and obtained their NABP e-Profile ID is encouraged to do so by visiting the NABP’s website at www.nabp.net.

It is the responsibility of the pharmacist and pharmacy technician to obtain and submit their NABP e-Profile ID to accredited providers when requesting CPE credit. ACPE has required accredited providers to have their credit tracking systems in place to support the collection of pharmacists and pharmacy technicians NABP e-Profile ID and date of birth. DIA has updated its credit tracking system, “My Transcript” to capture and store pharmacist and pharmacy technicians NABP e-Profile ID and date of birth. This information will be recorded in DIA’s database and will be uploaded to the CPE Monitor for each activity in which CPE credit is requested.

Beginning January 1, 2013, accredited providers must submit all ACPE certified activity credit requests through the CPE Monitor within 60-days post date of participation in the activity. To receive ACPE credit for participation in a DIA activity, learners must submit their request by logging into www.diahome.org and clicking on “My Transcript.” DIA encourages learners to submit their ACPE credit requests through My Transcript within 45-days post activity to allow DIA to transfer their CPE claimed credit through the CPE Monitor.

Any questions regarding the CPE Monitor should be submitted by email to karen.wetzel@diahome.org.
Since 2008, Dr. Tatsuya Kondo has been the Chief Executive of the Pharmaceuticals and Medical Devices Agency (PMDA) in Japan and oversees all operations of PMDA including, but not limited to, relief for adverse health effects of drugs, drug/medical devices reviews, and post-marketing safety measures.

Before taking this current position, he spent most of his career as a neurosurgeon after he graduated from Medical Department of the University of Tokyo in 1968. He worked at various medical institutions, including the First National Hospital and Faculty of Medicine, the University of Tokyo, and was a visiting staff surgeon at the China-Japan Friendship Hospital in Beijing, helping to establish its Department of Neurosurgery under the JICA project. In addition, Dr. Kondo has worked internationally at the Max-Planck Institute in Germany for biological research on brain tumors in 1977. From 1978 to 2008, he worked at the International Medical Center of Japan, where he served as Hospital Director from 2003-2008 and was responsible for management of the 900-bed hospital. During that period, he was positively engaged in R&D activities as a surgeon scientist, and invented the stereotactic treatment system for cancer, and discovered the fibroblast growth factor (FGF)-9 in brain tumors.
Of his choice of career, Dr. Kondo comments that, “My father was a doctor so I decided on medical school and decided on a field of study that would allow me to perform at the highest level of science without limitations. I also wanted to work with patients. That is why I chose the field of surgery, and, specifically neurological surgery.” Always interested in research, his choice of a surgical career seemed reasonable. “I am basically of a research mind and surgery is based on research. The essence of research is about how to eliminate excess, to cut through fat to get to the heart of the matter. Science is precisely of that nature — it is not accomplished by adding various weird elements, but rather by stripping out meaningless details to see the true nature of things.”

This philosophy of returning to true meaning aligned with the revitalization of the PMDA. Dr. Kondo was identified as an obvious choice for Chief Executive in 2008. “I have always welcomed challenges. Change is necessary as antibody medicines and more sensitive medicines are coming out. I think the way of conducting clinical trials has changed thanks to the establishment of the ICH GCP guideline. I sympathize with ICH’s mission. When I took office as Chief Executive of the PMDA, the agency faced many challenges such as drug lag, device lag and the hepatitis problems. I considered how we could be trusted by citizens. It was not enough to carry on as before or to speak haphazardly. Philosophical aspects had to be thoroughly incorporated, and I wanted all the PMDA staff to work with high motivation because they are distinguished people. When I came to think of it, I reached one answer; that is, science.” During the past 5 years at the PMDA, Dr. Kondo’s approach has been based on making academic science applicable to society. “I found a concept of regulatory science, and I suggested that we should pursue it. Taking one example for it, automobiles have brakes, as well as an accelerator, a handle, lights and wipers. It is about learning how to appropriately use all of those parts. Some things are positive, some are negative, and some are revolving. I understood that regulatory science was the science to seek how to use such parts appropriately. That was the start. We need philosophy to work in a unified direction. Because our staff is gathering from various fields, it is important to have common direction. To develop a cohesive mission, I spent a half of a year building a philosophy for the PMDA, giving first priority to life and health of our citizens.” Over time, Dr. Kondo’s approach gained popularity and he received positive feedback on his philosophy.

“The organization became unified with my establishment of philosophy,” he states. “I put a focus on science and strengthened the collaboration with graduate schools. What we had to do next was to act in a more concrete manner. In other words, we could not be all talk; rather we had to have a strong practical core. I formed the Science Board and new review mechanisms. I also wanted to take a more active approach. Drug regulations are essentially passive. In other words, we only review drugs submitted to us for marketing authorization. So PMDA started ‘Pharmaceutical Affairs Consultation on R&D Strategy.’ We needed to provide more active support in order to develop better medical products. Research has to benefit society, but many researchers do not know how to make their research beneficial. They do not have the idea of compliance. Research supports Japanese industries. I would like to stress that there needed to be more collaboration between industry and academia if the research is funded by the Japanese government.”

“The unification of industry, government, and academia is compliance. Regulatory science is the science of compliance and each party needs to carry out its specific job duties for the benefit of society. Drug regulations are precisely the science of compliance, upheld by the three pillars of quality, effectiveness, and safety. Regulators must ensure them”

As noted above, one of Dr. Kondo’s accomplishments at PMDA was the establishment of the Science Board appointing new committee members from a variety of universities throughout Japan, with people from medical, pharmacy, and engineering sciences. “The purpose of this is to infuse the PMDA with academia’s advanced scientific knowledge and also to disseminate, simultaneously and continuously, the concept of the three pillars mentioned above. In doing so, I think we can advance the quality of Japan’s science,” he explains.

Collaboration amongst industry, government, and academia should be closer, expanded and
strengthened to develop better medicines and realize better benefit-risk balance for patients, believes Dr. Kondo. There are several areas where he sees opportunity. “The field of drug discovery is plateauing. Generally speaking, drugs are developed in the laboratories of pharmaceutical companies. I am a medical doctor and know there are many biomarkers. They are a gold mine and that is why I think that it is very important for doctors who discover seeds of new drugs in the medical field to collaborate with pharmaceutical companies in order to make medicine useful for patients. I think that the pharmaceutical company laboratories should become more directly connected with the medical field.”

Communication between universities and regulatory agencies is another opportunity for collaboration and information sharing. “Until now, even though funding from the Japanese government is provided to universities, they do not know the expectation of regulatory agencies. If they have the correct understanding of what is important, then they understand the process of drug discovery and drug development,” explains Dr. Kondo.

Dr. Kondo believes Japan can become a leader in developing new medical products and in reviewing them. He cites the following example to support his position: “In February of this year, Mexico confirmed that the Japanese medical device regulatory requirements are equivalent to its own. Applicants can reduce the amount of documentation of applications for their medical device registration in Mexico if the products have already been approved or certified in Japan. It could occur because Japan’s emphasis on quality was recognized by the Mexican regulatory agency. Another aspect is quantity. Approval by Japanese regulatory authority implies a brand of quality and quantity, for Japan has the universal healthcare system which insures 120 million of its citizens. I have a renewed sense of the importance of Japan’s approval system.”

Following this experience, Dr. Kondo “thought that we have to do the same thing for medicines — that we should aim at a direction where Japan becomes the first country which approves new drugs.” To do so, he concludes, “We should promote phase 1 studies and first-in-human studies in Japan. It takes courage to be the first country which approves a new drug. I want to make a full use of our scientific background, and strengthen it more and more. Such discussion resulted in the establishment of the Science Board.”

It is clear that the main agenda for Dr. Kondo is ensuring patients’ well being. “Since becoming a doctor, I have thought about many things; and there are situations when your judgment on a patient differs from other doctors or nurses. At the final call you have to decide—based on what is best for the patient. The idea can be traced back to the Helsinki Declaration, and The Hippocratic Oath is the origin of medical ethics. The Hippocratic Oath was formed in a time when the society was consisted of everyone from slaves to kings; but Hippocrates did not discriminate, even against slaves. There is an unchanged principle, ‘one must never do harm against patients.’ This is passive. Most doctors work for the patient with willingness. It is also the motivation behind drug and medical device development. But, there are some blind spots, and they could be bad for the patients. In that respect, drug regulations become the embodiment of the Hippocratic Oath— ‘One must not cause harm to the patient.’ One must work for the patient and not do anything which is not beneficial to the patients. We must ensure quality, efficacy and safety of medical products, which is the origin of medical practice as well as drug regulations.”
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Your needs are unique. Choose the IRB with the flexibility to fit your needs, with ethics and integrity.
As announced in our October Global Forum, Sandra Milligan, MD, JD (Vice President, Global Regulatory Therapeutic Area Head for Inflammation, Virology & Ophthalmology, Genentech – A Member of the Roche Group) will serve as Program Chair for DIA 2013 49th Annual Meeting: Advancing Therapeutic Innovation & Regulatory Science, June 23-27, 2013, in Boston (MA). A member of the DIA Board of Directors and the Annual Meeting Program Committees for 2010, 2011 and 2012, Dr. Milligan provides an update on the planning and progress of this committee, and other thoughts about our industry’s largest and most respected annual event, below.

Advancing Therapeutic Innovation & Regulatory Science is the theme of our DIA 2013 Annual Meeting. What is your vision for this theme, and what makes it so appealing for this meeting?

“When we were considering the 2013 theme, one thing that struck me about previous Annual Meetings is that the focus on innovations occurring in specific diseases or therapeutic areas is often light. My colleagues in industry often report back from scientific congresses that healthcare authority representatives presenting at the meeting provided insight on how companies and researchers might better develop products in specific diseases – for example, acceptable endpoints for clinical trials in a disease area that’s rapidly evolving. Coming to our DIA Annual Meeting, you may not get that same information. But DIA is the place that brings together scientists, clinicians, regulatory professionals, clinical operations (ClinOps) professionals and global health authorities, so we could have this dialogue with all constituent cross-functional groups around that specific therapeutic area or disease. That is one of the gaps we are hoping we might address through our programming.”

Can you share more about what attendees might expect from this disease or therapeutic area focus?

“We’ve decided to pilot a program focused on Alzheimer’s Disease for the 2013 Annual Meeting. I’m working with a small team of experts from our Program Committee and DIA, and although we just started, we are hoping and planning to deliver impactful
sessions focused on this significant disease."

**How does the magic happen in planning each Annual Meeting?**

"During the year prior’s Annual Meeting, we get all of the program track chairs together and preview what to expect as far as the abstracts coming in, timelines, review expectations, tactical directions and such. This year, instead of reviewing process mechanics, we split the program committee up into smaller groups and challenged ourselves to identify what we thought went well at DIA 2012, where we thought we could improve, and what some of the taboos are. What are the elephants in the room that haven’t changed year after year? The program committee provided great output on what they thought might improve the Annual Meeting. We do take the all of the feedback we got from attendees at last year’s Annual Meeting quite seriously and critically look at ways we can continuously improve the experience for attendees and the scope or depth or level of our offerings."

"Later in the fall, in October, we bring together the program committee to review the theme and direction of the annual meeting, review the submitted abstracts, examine strengths and gaps in the expected program, and further define the objectives of the annual meeting."

**How long have you been involved in the Annual Meeting program committee?**

"I was co-chair of the Public Policy, Healthcare Compliance/Regulatory Law Track for a three-year term which was the start of my involvement in program planning for the Annual Meeting. Then I was elected to the Board last year, in 2011, and this year I was asked to chair the Annual Meeting. Hmm… I think I say ‘yes’ too often!"

**Why did you agree to serve on the committee, in that track?**

"I have a background in both medicine and law. Even though it’s not a predominant part of our Annual Meeting offering, I really like the fact that DIA presents an Annual Meeting program track that wrestles with some of the more difficult questions, whether they be ethical or legal, and also some of the more current hot topics that don’t fall into a larger Town Hall or one of our plenary sessions. There may be a sticky or thorny issue that keeps bubbling up and this particular track can address and provide a forum for those discussions. Some of the offerings we’ve had in this track just didn’t meet or fit into the more traditional tracks. This track nicely blends current public policy, health law and regulatory perspectives, as well as patient and ethical perspectives leading to discussions and sessions on a variety of interesting topics, often at the intersection where healthcare, regulatory, policy and law intersect."

**What do you hope building an Annual Meeting around the theme of Advancing Therapeutic Innovation & Regulatory Science will provide attendees?**

"It will provide the fundamental pieces of the program that everyone comes to the DIA Annual Meeting for: The networking opportunity to interface with regulators and vendors; the opportunity to hear about the latest trends in regulatory thinking, trends in clinical operations, in programming and statistics, all of the important topics that the meeting addresses every year. But I’m hoping we can also highlight rapidly progressing fields in specific disease areas. For instance, FDA is developing a new breakthrough therapy designation program, authorized by the FDA Safety and Innovation Act enacted last year and we know that there is at least one company who has requested such designation. This is just one of example of an area of regulatory uncertainty where we could generate a dialogue between clinicians, patients, industry and FDA. There are other examples where increased dialogue would be beneficial to all stakeholders, perhaps in a therapeutic area where a region’s guidance document has been withdrawn or never published, or generate some other type of input that we can provide to developers in the area so that they can continue to progress their science."

**Are you excited about traveling to our host city of Boston?**

"I am looking forward to going to Boston and exploring the history around the area. I think it’s a great place for people to bring their families if they can. I’m looking forward to bringing my kids. I’ve got a son who’s a real government buff – he loves all things government. He loves the states. He loves the presidents. He loves coins. He loves monuments. He loves all things government! Boston is one of the largest and most important hubs for the life sciences industry in the
US, and one of the most popular destinations for our DIA Annual Meeting, too. I think it’s going to be a great experience.

**Qualitatively or quantitatively – or a combination of both – how will you determine if DIA 2013 was successful?**

“I would like to see a way of bringing people together that improves networking. A lot of people come to the DIA Annual Meeting and they know people from their company or prior company, but they only know a limited circle folks. Is there a way to stimulate conversation and interaction? We are brainstorming ways of communicating during the meeting – is there a way to have a ‘Question of the Day’? An intriguing ‘Question of the Day’ where, if I met you at lunch or in the vendor hall, we could start a discussion with likely different points of view? ”

“All day, I’d like to hear people talk about a program or a speaker or a Town Hall. Referring back to DIA 2012, I went to the opening plenary with only a vague sense of Dean Kamen and his achievements, but his presentation was amazing. I walked out of that opening plenary session and everybody was talking about Dean Kamen – every single person. Two days later, people were still talking about him and it was my opening question for every new person I met: ‘Did you see Dean Kamen? What did you think?’ I could have an immediate conversation with that person that was interesting and carried different viewpoints.”

“One success factor for 2013 is: Can we build on topics and themes presented as early as the opening plenary session? Can we find that feeling of ‘unifying electricity,’ if you will, every day of DIA 2013? We’ll be challenging the program committee to do that. What is the buzz of the day? The networking and the energy level of the meeting will help determine its outcome.”

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Dr. Daniel Kraft to Deliver Keynote

DIA is pleased to announce that Dr. Daniel Kraft will deliver the keynote address at our *DIA 2013 49th Annual Meeting: Advancing Therapeutic Innovation and Regulatory Science*. Dr. Kraft is a Stanford and Harvard trained physician-scientist, inventor, entrepreneur and innovator.

Dr. Kraft has over 20 years of experience in clinical practice, biomedical research and healthcare innovation. Daniel chairs the Medicine track for Singularity University and is Executive Director for FutureMed, a program which explores convergent, exponentially developing technologies and their potential in biomedicine and healthcare.

Dr. Kraft recently founded IntelliMedicine, focused on enabling connected, data driven, and integrated personalized medicine. He is also the inventor of the MarrowMiner, an FDA approved device for the minimally invasive harvest of bone marrow, and founded RegenMed Systems, a company developing technologies to enable adult stem cell based regenerative therapies.

Following undergraduate degrees at Brown and medical school at Stanford, Dr. Kraft was board certified in the Harvard combined Internal Medicine and Pediatrics residency program at the Massachusetts General and Boston Children’s Hospital, and completed Stanford fellowships in hematology/oncology & bone marrow transplantation, and extensive research in stem cell biology and regenerative medicine. He has multiple scientific publications (including in Nature and Science), medical device, immunology and stem cell related patents through faculty positions with Stanford University School of Medicine and as clinical faculty for the pediatric bone marrow transplantation service at UCSF.

He is also an avid pilot, serving in the California Air National Guard as an officer and flight surgeon with an F-16 Fighter Squadron. He has conducted research on aerospace medicine that was published with NASA, with whom he was a finalist for astronaut selection.
**ASSOCIATION NEWS**

**DIA India Director Elected FIP Associate Executive Committee Member**

Kaushik Desai, Director, DIA India, has been elected as an Associate Executive Member to the committee of Industrial Pharmacy Section of the International Pharmaceutical Federation (FIP), for the year 2013. The announcement was made at the recent FIP 2012 Centennial Conference held in Amsterdam.

As an associate executive committee member, Kaushik will take responsibility in assisting regulatory affairs activities and identifying the program content for the development of the industrial pharmacy profession. The Executive Committee members met in November to discuss the way forward.

"The International Pharmaceutical Federation (FIP) is the global federation of national organizations of pharmacists and pharmaceutical scientists dedicated to improving global health through the work of the Members, Officers and via official partnerships with WHO and other global health leaders," Kaushik explains. "Such affiliations inform and update the members of these organizations, help to share best practices internationally, expand our respective professional networks and potentially present opportunities for future collaborative events. DIA's representation in the FIP also aligns with DIA's vision, mission and strategic plan."

**ASSOCIATION NEWS**

**Associate Director for International Programs, CDER, Named to Global Forum Editorial Board**

Capt. Justina A. Molzon has been selected to serve on the Global Forum Editorial Board. Justina is currently the Associate Director for International Programs, Center for Drug Evaluation and Research, FDA. One of her primary responsibilities is coordination of CDER’s efforts related to the ICH. Justina is a pharmacist and attorney, and a commissioned officer in the U.S Public Health Service. She received her BS and MS in Pharmacy with a concentration in pharmaceutics and pharmacognosy from the University of Rhode Island, and her law degree from the Chicago-Kent College of Law/Illinois Institute of Technology.

Editorial board members serve a one-year renewable term starting each year in June.
KATHLEEN FINDLEN was appointed Director, Clinical Operations, for Collegium Pharmaceuticals. Prior to joining Collegium, Kathleen managed US clinical operations for a UK-based CRO, and served as Executive Director of Clinical Operations for Syndax Pharmaceuticals. She is currently serving on the DIA Annual Meeting Program Committee.

SHAYESTEH FÜRST-LADANI, MSc, MBA, received the Open University Business School's 2012 Alumni Award for an Outstanding Contributions to an Organization. Shayesteh serves as Managing Director and founder of SFL Regulatory Affairs & Scientific Communication Ltd. She has served on the Program Committee for several DIA EuroMeetings and as leader for the EuroMeeting's “Drugs, Devices, in vitro Diagnostics & Their Combinations” theme, and also Chairs the DIA Devices & Diagnostics SIAC. She also serves as Chair of the Combination Products Topic Group at EuropaBio and of the Medical Device Working Group at EUCOPE. Shayesteh earned her MSc in Microbiology from the University of Vienna (Austria) and her MBA from the Open University Business School, Milton Keynes, UK.

ERNEST A. KOPECKY, PhD, MBA, was appointed Vice President, Clinical Development, and Head of Neuroscience, for Collegium Pharmaceutical. Dr. Kopecky most recently served as Head of the Pain Group at Endo Pharmaceuticals. Dr. Kopecky serves on the FDA AAACTION Executive Committee, is on Faculty at the Pharmaceutical Education Research Institute, and is appointed as a Research Fellow at the Hospital for Sick Children, Division of Clinical Pharmacology and Toxicology, Toronto, Canada. He previously served on the IMMPACT Steering Committee and was a Subteam Lead on the PhRMA Neonatal and Pediatric LDKITs. Dr. Kopecky received his PhD in Pediatric Clinical Pharmacology from the University of Toronto (Canada) and his MBA from the University of Connecticut.
Drug Information Journal is Being Relaunched in January 2013
The Official Publication of DIA

Upcoming January 2013 Articles
• Practice-Based Research Network Infrastructure Design for Institutional Review Board Risk Assessment and Generalizability of Clinical Results
• Influence of Clinical Research Investigator Fraud on Clinical Trial Participation
• How FDA Advisory Committee Members Prepare and What Influences Them
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Contact the Managing Editor, Judy Connors, at judy.connors@diahome.org with questions on article topics and/or submission deadlines.

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