Robin Robinson

Safety and Pharmacovigilance: A Moving TARGET

The industry has always been under extreme scrutiny by regulators and the public, but the current business environment creates even more pressure on the pharmaceutical industry to stay compliant.

Regulations and procedures are not only tightening but continually developing and changing in the United States and abroad. Keeping on top of compliance in this dynamic era is a difficult task, and our experts from all sides of the industry offer tips and best practices on how to cope in the turbulent years to come.

There are myriad regulations regarding safety, risk management, and pharmacovigilance. Among the ones that require the most immediate attention from the industry include Extended EudraVigilance Medicinal Product Dictionary, which will be mandatory for all marketing authorization holders in July 2012. The new legislation means that submitting product data to the EVMPD is now mandatory and marketing authorization holders (MAH) will be responsible for providing details of all their authorized products, either via automatic electronic platforms or by manually typing data into a Web portal. The move to electronic transmission of individual case safety reports (ICSRs) and the ICH E2B (R3) are other regulations high on the industry's radar, along with REMS and nonexistent social media guidance from the FDA.

Regulations to Live By

In summary:
1. XEVMPD/EVMPD
2. ICSR
3. REMS for opioids

MARK LOUDON. ARIS GLOBAL. The European regulations regarding EVMPD are the most immediate and, frankly, overtaxing challenge. Companies have to weld together two different functional views of their world — information from regulatory and from safety — and then submit the combined information to EudraVigilance for all of their products by the July 2012 deadline. Not only are the records in many cases quite numerous, but also information is being requested that, in many cases, is not even submitted with the marketing authorization application. This comes at a time when companies were just shifting from one level of maturity — reporting reliably and on time — to another focused more on assessment and balancing of risk. In the future, I think FDA's implementations of HL7 ICSR V3 / E2B (R3) will be interesting. I use the word in the plural, because I worry whether we'll see different implementations in CDRH versus CDER and CBER. The safety reporting regimen is so different for drugs and devices, particularly in the United States, yet companies have an increasing need to handle both. As a simple example, if a MedWatch report contains two devices and two drugs, that means three report numbers — one for each device, and just one for the drugs. This just isn't conducive to consistent processes that would allow a proper risk management focus. I hope these types of issues will get addressed.

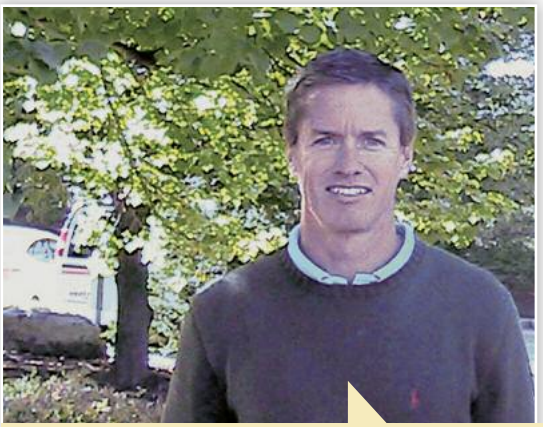
DR. MARTHA BRUMFIELD. RHI. The full implementation of many REMS requirements has

been and continues to be a challenge for pharma companies, both in terms of the execution of safety studies and activities associated with measuring the impact of MedGuides and other REMS elements of safe use. For example, the completion of long-term and sometimes difficult to conduct and expensive safety studies can be challenging and these studies often lead to results that are inconclusive, expensive, and not terribly informative from a labeling perspective. Also, with PDUFA IV, the REMS requirements include assessing the effectiveness of the REMS components, such as use of MedGuides, and there is a lack of clarity as to how to conduct these assessments in a meaningful way.

MICHAEL SUGERMAN. CAREWAVE MEDIA. Today, even the best companies must play catch-up with mandatory safety monitoring and pharmacovigilance reporting requirements. Changes in technology combined with organizational changes resulting from acquisitions and mergers, as well as other factors can profoundly confound safety surveillance operations. Additionally, most safety and pharmacovigilance departments are woefully under-resourced and under-funded. Of course, reporting processes still vary — in subtle and not so subtle ways — across clinical and post-approval processes, across countries' national regulatory authorities, and across companies. From a regulatory point of view, the task of pharmacovigilance is still all about requiring additional trials, or registries as well as meaningful REMs strategies, especially for those products with higher perceived risks.

DEAN ERHARDT. RHI. The ability to measure the impact of REMS components to mitigate risks remains an elusive objective. Further, the burdens imposed by REMS on providers, pharmacists, patients, and the healthcare delivery system need to be addressed. Efforts to comply with REMS requirements may also generate information potentially damaging to the defense in litigation, especially in claims of product liability, and to the interests of the industry in the arena of public opinion. It is hoped that some of the proposals within PDUFA V will assist in addressing many of these challenges. The industry is dealing with all these challenges by working with regulators and other MAHs to ensure consolidated REMS and RMPs are developed in collaboration with all MAHs to cost-share based on market share, for example, the opioid REMS group in the United States.

MICHAEL O'GORMAN. SENTRX. Two of the key goals of regulatory changes are to one, improve overall quality of safety reporting, thereby strengthening the agency's ability to review critical safety information; and two, harmonize safety reporting internationally. This means that current guidance on safety reporting procedures will likely continue to evolve and the health authorities will continue to push pharmaceutical companies into an environment that is not only paperless, but provides meaningful and comprehensive safety data relating to their trials or products. There are many recent regulatory changes that need to be reviewed and implemented by pharmaceutical companies, such as the redo of requirements for expedited reporting of serious and unexpected suspected adverse reactions to the IND. Additionally, there are new and clarified definitions for safety reporting and the requirements outline the types of evidence to be reviewed for causal relationships by both the investigator and sponsor. Perhaps one of the more challenging aspects of the new regulations is the proper compilation of the DSUR (Developmental Safety Update Report), which was implemented in September 2011. Sentrx believes that the health authorities will continue to push for more changes relating to data clarification and consistency in reporting. What those changes might be in the future will depend upon the effectiveness of the recent changes and the benefits of those changes realized by the health authorities and overall patient safety.



> **"It is very difficult for pharmaceutical companies, large or small, to fully understand and manage all of the regulatory changes on their own."**
>
> **MICHAEL O'GORMAN** / Sentrx

EXPERTS

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Pharmacovigilance Glossary of Terms

AERS — Adverse Event Report System
CBER — Center for Biologics Evaluation and Research
CDER — Center for Drug Evaluation and Research
CDRH — Center for Devices and Radiological Health
DSUR — Development Safety Update Report
E2B (R3) — The third and most recent version of E2B, the international standard for the transmittal of electronic safety data.
EudraVigilance — European Union Drug Regulating Authorities Pharmacovigilance system
EVMPD — EudraVigilance Medicinal Product Dictionary, a data processing management system for reporting and evaluating suspected adverse drug reactions during the development and post-marketing authorization approval of medicinal products for human use in the European Economic Area
HL7 — Health Level 7
ICH — International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, whose mission is to achieve greater harmonization to ensure that safe, effective, and high-quality medicines are developed and registered in the most resource efficient manner.
ICSR — Individual Case Safety Reports
ICSR V3 — Individual Case Safety Reports, Version 3
IND — Investigational New Drug Application
MAH — Marketing Authorization Holders
PDUFA IV — Renewed Prescription Drug User Fee Act
REMS — Risk Evaluation and Mitigation Strategies
XEVMPD — Extended EudraVigilance Medicinal Product Dictionary, a new legislation requiring mandatory electronic product data be submitted to the EVMPD starting July 2, 2012.

Source: PharmaVOICE. More details on most terms can be found at fda.gov; ich.org; and ema.europa.eu.

MARK SENAK. FLEISHMAN-HILLARD. From a communications perspective, the issue is less about regulatory requirements and more about the fact that there isn't any established set of guidelines for operating within the new changed communications environment. One of the challenges is that in the past five years, communications have fundamentally changed, and I don't mean just that we have new platforms like Facebook and Twitter to deal with, but that those platforms have fundamentally changed the way we communicate. In the past, if we wanted to get a message out, we would broadcast it with broad brushstrokes so that it could go out in radio, or in the newspaper, or on TV, and hopefully out of all the people who heard it, some of those people would act on it. We used to put messages on buses and hope that out of all the people who saw that message that it would matter to at least some. Today, we still do some broadcasting, but we also have the opportunity through social media to do a lot of niche casting, which is very specific messages at very targeted audiences. This in turn has changed the way we might pick up on adverse events because there are now new vehicles from which one may learn about an event, but there is still no regulatory guidance on how to operate within this new framework. The environment keeps changing, but there's no sure footing for the industry on how it should proceed within the communications environment.

Prepare for the Future Today

In summary:
1. Don't ignore new regulations
2. Open source information sharing is increasing
3. Outsourcing is a good first step

MARK LOUDON. ARIS GLOBAL. I'm not sure that all of the industry is really preparing for new regulatory changes. If past performance is the best indicator of future behavior, many companies will, unfortunately, put their collective heads in the sand and hope the issue passes. This is what happened the last time EVMPD was put in place. The difference this time is that there are solutions available, not just to submit EVMPD entries, but to combine them effectively with safety reporting and analysis. Last time, companies depended more on manual data entry, either online, or via a Microsoft Access database that one could populate and send. This time, things are more firmly focused on transactional electronic data exchange.

MICHAEL SUGERMAN. CAREWAVE MEDIA. There are entities around the world, within pharma and outside of pharma, collecting and providing data, information, and knowledge about the molecular basis of human diseases. This knowledge base promises to become the foundation behind the delivery of personalized medicine. Today, most companies are harnessing this knowledge base to identify and develop candidate therapies. However, the expertise necessary to effectively manage and use this information even for drug development is still a highly valuable and an eminently scarce resource. Even more scarce are sufficient resources available to apply this knowledge to pharmacovigilance activities. In the not too distant future, pharma companies, and even the FDA and the European Medicines Agency, will have to accommodate this paradigm shift. One likely development is the further creation of innovative public-private partnerships that bring together collaborative groups of industrial and academic entities each contributing their unique knowledge base to a much larger open source-like repository.

> **"The European regulations regarding EVMPD are the most immediate and overtaxing challenge today."**
>
> **MARK LOUDON** / Aris Global

DEAN ERHARDT. RHI. We believe that one of the most important steps is to assure that the sponsor has a culture and accompanying procedures to support benefit-risk assessment. That culture, and those procedures, should be well-documented so that they can be demonstrated if need be. After that, skilled resources are required. In addition, access to full data sets — clinical trial data and postmarket data and registry data — for signal detection risk assessment would require collaboration and cooperation across pharma companies and regulators.

MICHAEL O'GORMAN. SENTRX. It is very difficult for pharmaceutical companies, large or small, to fully understand and manage all of the regulatory changes on their own. Accordingly, regulatory affairs and pharmacovigilance departments are turning to experts whose business revolves around compliance with safety regulations. We believe that this dynamic is making outsourcing pharmacovigilance more compelling as the knowledge of regulatory changes, relationships with health authorities evolve, and audit readiness can be leveraged across multiple companies. In addi-

SOUND BITES FROM THE FIELD

Within the ever-changing regulatory environment, all functions within the drug development process face a moving target. Experts share tips on what the industry should be focusing on and preparing for in the near future.

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"All signs continue to point toward the growing importance of electronic health record data as a means of identifying and monitoring adverse events for approved drugs. The FDA's recent classwide REMS guidance for long-acting and extended-release opioids, which requires manufacturers to use secondary data analysis to assess how effective REMS activities are at reducing inappropriate prescribing and abuse, represents the agency's most current thinking on how best to monitor for risk and abuse. As the FDA's Sentinel Initiative progresses, and more and more robust EHR data becomes available, the agency will put more emphasis on the use of real-world data as a better way to track postmarketing safety and outcomes."

RICH GLIKLICH is President, Outcome, and Global Head of Late Phase, Quintiles, a fully integrated bio and pharmaceutical services provider offering clinical, commercial, consulting, and capital solutions. For more information, visit quintiles.com.

"While the regulatory environment is shifting, its shifts are being driven by increasing awareness of the need for real-world data and the role of multiple stakeholders. As a result, to be better prepared for the future, the industry needs to adopt a more multistakeholder view of its products and the questions that it answers as new evidence is developed; and, it needs to consider how to access and leverage real-world and late-phase data in a more systematic way throughout the product life cycle. This ranges from understanding background safety signals through disease registries to adding relevant health economic endpoints to late-phase studies to adding cohorts of patients not studied in the trials to address specific subpopulation questions."

KAREN GOSS is Global Pharmacovigilance Director of PharmaNet/i3, a provider of drug development services, with a global infrastructure, therapeutic expertise, and commitment to quality. For more information, visit pharmanet-i3.com.

"As evidenced by the changes in European pharmacovigilance legislation, the industry should focus on proactive risk-based approaches toward medicinal product safety, versus traditional passive and reactive pharmacovigilance programs. Active pharmacovigilance programs, which encompass risk management and mitigation strategies, postauthorization studies and registries, robust periodic safety reports, and signal evaluation can lead to more informed and rapid decisions concerning safety. Pharmacovigilance involves the entire life cycle of the product from discovery through postauthorization and regulatory legislation is supporting this more proactive approach, for eample FDA's recent classwide REMS guidance for long-acting and extended-release opioids."

tion to the consideration of outsourcing the expertise associated to safety reporting, we have noticed a significant move by pharmaceutical companies part to become paperless and accordingly, use best-of-breed safety reporting tools such as Oracle Argus Safety and Oracle Interchange. But pharmaceutical companies also know that use of databases and other tools is not the sole answer for effective handling of these regulatory changes.

MARK SENAK. FLEISHMAN-HILLARD. The industry has been operating in an undefined, yet very dynamic, communications environment for a long time. If the FDA isn't going to act on issuing a communications guidance then it is incumbent on the industry to define for itself, as individual companies or a trade associations, what best practices have developed over time with respect to the Internet, social media, and pharmacovigilance, and talk about those best practices. While there are different levels of interaction with social media and the Internet within the industry, somewhere within that experience a body of knowledge is developing about what is good practice and what is not good practice with respect to pharmacovigilance in a digital era. Some companies have developed digital assets and their own specific rules and this may be the best guidance the industry has while waiting for FDA. This way, individual companies can start moving forward in terms of developing digital assets that take in to consideration applying some standards to how adverse events might or might not get reported.

Addressing Shifting Regulatory Requirements

In summary:
1. Standardization would smooth the waters
2. Processes need to catch up with science
3. Don't be caught by surprise

MARK LOUDON. ARIS GLOBAL. Standardization through bodies such as ICH has brought, at long last, a period of operational consolidation, whereby companies are able to shift their gaze from mere compliance, for example, reporting cases reliably and on time, periodic reporting, etc. This standardization meant they could start to focus on analyzing what all the data mean, and how best to mitigate it. My personal fear is that for countries to diverge again from these standards, and in the new EU framework, for periodic reports, etc., to be done differently based on differing risk profiles, will detract from the actual work of understanding the data and cause people to focus again on low-level operational tactics. This will be especially true if the same product ends up with different risk categorizations in different places and under different conditions. If I could wave a magic wand, it would be to have all cases processed at the same time, all periodic reports to be processed the same, and for the people in the equation to be able to look regularly and thoughtfully at the information, and turn it into meaningful knowledge.

DR. MARTHA BRUMFIELD. RHI. One of the largest challenges for industry is to accommodate the similar but different requirements from regulatory authorities around the world, for example clinical trials that may require a placebo comparison arm in the United States and an active comparator in the EU or Risk MAPS in the EU and REMS in the United States. The area of comparative effectiveness is handled very differently in European countries than in the United States, yet the call for more comparative information in a real-world setting is becoming a global trend. The types of

New Organization to Address Divergent Regulatory Practices

In an effort to address key issues that are outside the scope of similar organizations, several leaders in the healthcare space recently formed the Regulatory Harmonization Institute. RHI is a nonprofit association dedicated to the global harmonization of regulatory requirements with a mission to influence the development and introduction of meaningful therapies to patients across the globe. Its focus is to provide an open and transparent venue for public and private stakeholders to identify divergent regulatory practices that meaningfully affect the availability of medical products to patients, and to develop and sustain educational and other work plans that will assist in harmonizing those practices.

RHI's scope differs from other similar organizations in that it will include all emerging markets, address administrative, compliance, and global consistency issues around manufacturing implementation, and will solicit engagement from the industry.

"By enabling strategic capacity building among both regulatory authorities and regulated industries, we will be able to leverage regulatory harmonization efforts already under way, and empower them through dialogue, training, and external communications to non-regulatory stakeholders," says Dean Erhardt, president of RHI and principal at D2 Pharma Consulting.

RHI encourages the industry to become involved and to follow the workings of the organization, as it strives to broaden the understanding of international companies on regulatory issues across the globe and bring clarity and uniformity to the process.

"We are working with manufacturers across multiple fronts to assist in the educational process related to regulatory issues, including multiple international companies to assist in their understanding of the U.S. market," Mr. Erhardt says. "We are also working with various government agencies to support educational programs for companies looking to expand from local to multinational status."

Members include government organizations, public/private companies, patient advocacy organizations, not-for-profit entities, academic professionals and other industry groups. Funding for RHI is provided by a combination of annual fees, workshop fees, and grants from supporting companies, associations and other organizations.

Source: RHI. For more information, visit regulatoryharmonization.com.

trials that are required to provide truly meaningful information on effectiveness of various treatment options will be long and expensive, an issue of particular significance in this era of cost constraints, and will require the endorsement of multiple stakeholders. This leaves the industry in a quandary as to what the appropriate next steps might be.

PATRICK CAUBEL. SANOFI. The biggest challenge for industry is the increasing lack of harmonization between regions while more and more countries are becoming strongly regulated. The need to allocate resources to track and meet local regulatory requirements diverts resource allocation and efforts from the most crucial tasks: safety signal characterization and risk-management. The need for a more harmonized "safety world" is crucial for industry, for regulators and ultimately for the public, which has legitimately an increased desire for transparency. The second challenge is the emergence of diversified and non-conventional sources of safety information — social media — and the need to integrate these data sources into our practice. The public is taking an active role in safety reporting, and partnering within the social world will require total transparency from industry.

MICHAEL SUGERMAN. CAREWAVE MEDIA. I believe all of these issues are minor speed bumps on the road ahead. Much more concerning and daunting is the fact that the underlying scientific paradigm governing our understanding of disease has profoundly shifted. Current pharmacovigilance processes are essentially rooted in an earlier notion of disease: a relatively static clinical framework that underestimates and, perhaps even grossly simplifies, the dynamic complexity of the molecular basis of human disease. The new, evolving paradigm suggests that health and disease, and therapeutic intervention, exists in a complex biological ecosystem with multiple, complex interactions, redundant networks, signaling pathways, and receptors. This knowledge base about the molecular basis of disease, of these networks, pathways and receptors, is growing exponentially. Single molecules often affect a wide range of pathways, including ones with a pluralism of effects that we do not yet understand or even know about. In light of this evolving understanding, and in the context of our growing knowledge of genomics, epigenetics, proteomics, signaling and metabolomic factors, current pharmacovigilance reporting requirements, tools and processes are, by default, archaic and outmoded, and so are the regulations governing those reporting processes.

> "The ability to measure the impact of REMS components to mitigate risks remains an elusive objective."
>
> **DEAN ERHARDT** / RHI

MICHAEL O'GORMAN. SENTRX. Pharmaceutical companies realize that they carry the burden of regulatory requirements since their products and trials impact patient safety. Accordingly, none of the regulatory requirements should be surprising. Being well-prepared for regulatory changes is a challenge that all of these companies face and some companies are much more prepared than others. Also, preparedness strategies tend to differ significantly from company to company, but there is no doubt that the drug safety experts will continue to play a significant role in helping companies be prepared. The key is to take fast action on implementing steps to stay in compliance with regulatory requirements.

MARK SENAK. FLEISHMAN-HILLARD. I recently participated in a series on the movement toward increased transparency in terms of the financial relationship toward physicians and pharma and part of that has do with the Sunshine Act in the United State. In France, there is a new proposed legislation that would prohibit sales reps from having a one-on-one discussion with any physician. That means a sales rep who is representing a device manufacturer couldn't sit down one on one with a physician to tell him or her how to use the device. Sales reps can instruct or meet with physicians in a group of physicians, but not one on one. I'm wondering what kind of impact the lack of one-on-one instruction, for example, will have in France — it's definitely something to think about. PV

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Best Practices *in* Pharmacovigilance

As with most processes in the industry, there is no one-size-fits-all solution, but best practices and lessons learned can facilitate a more efficient process.

Pharmacovigilance is becoming more critical as the need to ensure safety of medicines and manage risk increases with the changing global regulatory pressures and public and government scrutiny. According to Mark Loudon, director, regulatory compliance, Aris Global, once companies get the process down, they can streamline processes and allow for greater focus on risk management.

"When companies are self-disciplined, and impose consistent processes on all their safety cases, whether serious, nonserious, postmarketing, clinical, etc., they will be able to make these processes second nature," Mr. Loudon says. "They can also avoid the safety system configuration and customization that has become second nature to a lot of companies that think their safety processes are somehow unique."

This, in and of itself, is critically important when new regulatory mandates have timescales of nine months to a year. It is important that implementations and upgrades aren't taking twice that long, based on requirements of a year ago, he says.

"Unfortunately, that has been de rigueur for some time, but some companies are overcoming this tendency, and building best-practice approaches that seriously accelerate these projects, while simplifying process and operation."

Best-practice approaches are best built through ongoing evaluation of all data, both clinical and postmarket surveillance, throughout a medicine's life cycle, according to Dean Erhardt, president, RHI. This requires a particular skill set, adequate analytical capability, robust internal procedures, and dedicated staff, he adds.

"Assessment of benefit-risk should begin before FIH and should continue throughout the entire life cycle of the medicine," Mr. Erhardt says. "The ability to access complete datasets across industry, government, and academic trials — clinical trial data, postmarket surveillance data, and registry data — for signal detection risk assessment would require collaboration and cooperation across multiple stakeholders but would contribute substantially to having a more thorough body of knowledge of both benefit and risk."

As more medicines move into the generic sector, the ability to monitor data across the various sectors becomes more challenging. Should a company's decision-making be challenged, taking steps such as these will help it to demonstrate what it knew at any given time, how it analyzed what it knew, and how it reached the conclusions it reached, Mr. Erhardt says.

"Such a showing will go far toward advancing the company's interests, and by extension the industry's, in the eyes of regulators, legislators, and courts," he says.

By its very nature, the evolving knowledge base of science challenges established medical dogma and commonly held notions of health and disease, and of risk and benefit. The science behind new molecule development and medical intervention has started to shift in a material way, says Michael Sugerman, president and co-founder of CareWave Media. "Ultimately, it will impact government regulation and pharmacovigilance practices. Yet, most active stakeholders in the marketplace are still operating under an older paradigm and set of assumptions."

For instance, vast resources are focused on harvesting meaningful data from growing numbers of electronic medical records in order to standardize treatment. There are still unsolved, non-trivial issues in this latter endeavor that encompass everything from interoperability, data standards, semantics, as well as the hardware platforms and form factors and data entry task inappropriately assigned to HCPs. It is unclear how much impact this endeavor will have until we better understand the subtle differences in systems biology from one patient to the next, Mr. Sugerman says.

According to Mr. Loudon, statistical power in data is something that comes with time and volume. In the meantime, companies need to be able to assess other large pools of data and the primary one has been the FDA AERS data, but other sources are coming online too. But companies lack regular routine and documented processes for the entire chain of events that lies between safety case and periodic report production, and eventual action being taken to mitigate, monitor, or redefine risk.

"The general principles of establishing a routine, repeatable, and reliable process are the same as for any other processes, but some of the entities being managed in this area lack precedent and terminology in the industry," Mr. Loudon says. "As a simple example, if there is an emerging risk with multiple symptoms and no defined medical syndrome name, how does one give the risk a working name while still exploring the hypotheses? And is it a risk, a hypothetical risk, or topic of interest, etc.?

Mark Senak, senior VP, partner, at Fleishman-Hillard, says a best strategy when devel-

oping digital communications would include the concept of a two-way exchange.

"The brand is no longer the communicator talking to the audience, so strategies must take into account channel appropriate reporting for things like adverse events," he says. "Getting this right will be very important in terms of being successful in creating digital content."

Like existing pharmacovigilance processes, EMR design is essentially rooted in an earlier notion of health and disease, designed around a relatively static clinical framework that underestimates and, perhaps, even grossly simplifies the dynamic complexity of the molecular basis of human disease.

"Right now, most EMRs are built around an archaic data model; they are designed to be nothing more than glorified digital data forms," Mr. Sugerman says. "One of the many challenges to be tackled will be how to best integrate and make use of complex system biology data from different sources at the point of care."

In the near future, EMRs will have the potential to become far more powerful tools, designed to support dynamic interactions and exponentially more complex information. By design, this will necessitate a new data model that manages and supports the delivery of personalized medicine, including but not limited to the use of applicable genomic, epigenetic, proteomic, and signaling and other data necessary to enable highly specific therapeutic intervention decisions and monitor related outcomes.

Products or trials with a higher risk profile should receive greater attention and therefore greater funding for their pharmacovigilance programs since noncompliance can significantly impair a pharmaceutical company's business model, says Michael O'Gorman, CEO, Sentrx.

"Such impairment could come in the form of sanctions, such as approval delays or pulling products off the market," he says. "Understanding the risk profile is the most challenging part of that dynamic for early-stage drug discovery."

Accordingly companies turn to the best available information relating to the compound under trial, or in the event of a commercial product, analysis of both internal and available external safety data, including data from historical clinical stages.

One of the technologies commonly used to understand the number of and demographics related to adverse events within a specific drug or compound category is Oracle's ESignal product, which provides a clean representation of the FDA's AERS database. But understanding the number of and demographics of adverse events is just one of many areas for which companies analyze the risk-benefit balance of pharmacovigilance.

"We would like to believe that all companies that carry the regulatory burden of pharmacovigilance have an understanding that there is a baseline cost plus incremental costs associated to the risk profile," Mr. O'Gorman says. "And such costs need to be built into the company's business model, not only during the commercial phase, but also the clinical trial period. Understanding this cost can be quite complicated and judgmental given all of the variables involved. The variable nature of adverse events makes evaluating the risk-benefit quite difficult in the clinical stages since trials typically operate under a fixed budget.

"To combat this, we see many companies making an attempt to be conservative and overestimate SAEs during a trial, but to support estimates to management or shareholders, projected SAE data must be derived from a reliable source," he adds.

Communications isn't what it was five years ago so pharmacovigilance isn't what it was five years ago and the development is not static, Mr. Senak says.

"In five more years it will be different, so the industry is under a continual challenge to evaluate and calibrate and recalibrate how to do things given an environment that is changing so dynamically," he says. "I'm not sure that I know where we are going, but it is clear that the balance of power of communication shifted from communicator to the audience in the last five years so that there are strategic ramifications for pharmacovigilance adverse event reporting and virtually every aspect of what we do in production of medical products." PV

Safety and Risk Management Best Practices

- Utilization of a global safety database with electronic reporting capabilities
- Maintenance of a validation unit that can quickly implement technology changes
- Utilization of experts, not just in pharmacovigilance, but also in specific therapeutic areas and epidemiology
- Well-documented SOPs, working practices and work instructions
- Tight adherence to documented policies and procedures
- Maintenance of solid company-wide risk management plans and pharmacovigilance plans that support the overall risk management of the company
- Effective use and analysis of patient safety data, not only within company records, but also use of publicly available information
- A company culture that views patient safety teams as an asset to the business as opposed to just a regulatory necessity

Source: Michael O'Gorman.
For more information, visit Sentrx.com.

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