

ENHANCING A CULTURE OF SAFETY IN THE LIFE SCIENCES SECTOR

In its 2007 report, *The Future of Drug Safety*, the Institute of Medicine (IOM) made a series of recommendations to strengthen the overall drug safety system in which it encouraged the U.S. Food and Drug Administration (FDA) to “embrace a culture of safety.”¹ The report detailed 25 specific recommendations designed to “bring the strengths of the preapproval process (data, regulatory authority, organizational function and capabilities, and resources) to the post-approval phase in order to fulfill a lifecycle approach to the study, regulation, and communication about the risks and benefits of drugs.”



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Although the FDA responded to the report thoroughly – and took the opportunity to strongly emphasize its commitment to the drug safety system – the agency limited its response to only those recommendations directed toward the FDA. The FDA’s response clearly acknowledged its need to drive a cultural shift regarding drug safety within the agency itself, but the response fell short in championing a system-wide drug safety model that includes coordinated efforts from every stakeholder in the system. As later noted in a *New England Journal of Medicine* editorial, the “FDA’s response to the IOM report demonstrates a lack of understanding of the magnitude of the changes required to create a culture of safety.”²

The recent change in leadership at the FDA, however, appears to be an encouraging sign that the agency aims to clarify its role as a public health entity. In a June 2009 editorial in the *New England Journal of Medicine*, incoming FDA Commissioner Margaret Hamburg stated that the FDA’s job was to support access to a safe food supply and to innovative, safe and effective medicines, and in doing so, “to promote health, prevent illness, and prolong life.”³ Most significantly, Dr. Hamburg emphasized the agency’s need to collaborate with other stakeholders “to address problems that the agency itself cannot solve alone.” Clearly, drug safety reform fits into this realm.

It should be assumed that regulators, patients, physicians, payers and biopharmaceutical manufacturers all want to bring innovative, life-saving medicines to the market in a safe and cost-effective manner. Reforming drug safety on a wider scale, therefore, must become the responsibility of all these stakeholders within drug safety surveillance.

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For example, biopharmaceutical manufacturers have traditionally regarded drug safety as a *proactive* process for medicines in clinical development, but a *reactive* process for medicines already on the market. To truly create a system promoting safety, there needs to be a proactive approach both before and after medicines are launched. Likewise, action from other stakeholders, including payers, providers and the media, must change to include the voice of the patient regarding systematic drug safety reform. All of these stakeholders should be encouraged to proactively evaluate, determine and define their roles in drug safety.

On the industry side, formal FDA guidance on risk management planning is not expected to be released until 2010, and it appears that most players are waiting until then to see how these programs are evaluated and whether they'll be successful. However, during that time, to reduce risks and minimize lag time, stakeholders can take steps to increase their level of responsibility within an enterprise-wide system for ensuring the safety of medicines.

This includes not only manufacturers but also the key touch-points for patients, primarily the media and payer organizations. The media should aim to obtain a better understanding of how to communicate product risk in context with the product's benefits to the general public. Similarly, payers can make better use of their systems for active drug safety surveillance. These organizations already have numerous databases in which they're collecting information – from appropriate use data to prescribing practices – but the same systems could easily go much further toward investigating patient outcome and adverse event occurrences.

ELEMENTS FOR SYSTEMATIC REFORM

As stated above, drug safety ownership can and should be extended beyond regulators and industry to include multiple stakeholders from the life sciences sector all contributing toward a more effective and efficient system. Realignment of the whole system needs to take place; it is not enough simply to continue making attempts to fix its various components. As such, the following list of suggested best-practices should be considered for developing a systematic solution for drug safety reform.

Accountability: Biopharmaceutical companies should create systems to ensure safety accountability throughout a product's entire life cycle. One such approach is to create and empower an executive-level function with control of an organization's entire safety process. Several companies already have a safety committee, with a remit to lead the charge to ensure accuracy and continuity of safety systems and information and uphold ethical and responsible conduct with regard to safety surveillance and reporting. The establishment of empowered safety committees – or some other similarly structured group or individual – should be encouraged as part of an overall commitment to drug safety.

Root Cause Analysis: When a safety lapse does occur, we need to identify not *who* was responsible for the lapse, but rather *why* the lapse happened and what actions need to be taken to correct the underlying cause. This includes an enterprise-wide safety system in which safety audits and inspections are geared toward determining the root cause of safety concerns through root cause analysis, and empower individuals at all level to identify and report safety concerns without fear of retribution or blame. This is similar to the Corrective And Preventive Action system used in manufacturing and should be more widely implemented in the biopharmaceutical industry.

Risk Communication and Transparency: All stakeholders should promote communication of drug safety information to the public and professional community in a fully open process that includes all available data presented in an easily understood manner. At minimum, the industry should embrace more open disclosure – perhaps in a standardized format – of a medicinal product's risks and benefits. Indeed, properly communicating risk is a core business function that actually strengthens a company's credibility rather than weakens it. For example, Johnson & Johnson (J&J) took immediate action in July of this year to address safety concerns regarding Tylenol. Less than a week after an FDA Advisory Panel recommended lowering the maximum dosage of the drug for concerns about potential liver damage, J&J ran full-page advertisements in several major newspapers acknowledging the panel's concerns, yet reassuring a confused public that taking acetaminophen at the recommended dosage was indeed safe. The company stressed the notion of *appropriate use* for its product, emphasizing to consumers that drug misuse could pose serious risk. This type of quick action and consumer engagement should be applauded and encouraged as an appropriate response to a valid drug safety issue.

Professional Development: A key element of sustaining drug safety best practices is to implement them early during the education of new clinicians and other health care professionals. The clinical educational process should encourage a better understanding of pharmacoepidemiology, pharmacoepidemiological principles and pharmacovigilance. Many medical students today receive very little education in these areas, and may not fully grasp how their roles as physicians fit into the overall system of safety. As part of continuing education in this dynamic environment, industry professionals might also benefit from a more thorough understanding of the risks and benefits of medicinal products, accepted risk

management processes as well as the numerous legal and ethical dimensions involved in safety compliance to stay abreast of new developments and therapies.

New Methods to Improve Safety: Finally, as new mechanisms for collecting and disseminating safety data are established, they should be embraced and supported by all stakeholders across the life sciences spectrum to ensure optimal drug outcomes and benefits. As proposed by Waller and Evans⁴, a new model for pharmacovigilance should include data from randomized controlled trials, as well as meta-analyses of both observational data and random controlled trials. The current system – over-dependent as it is on adverse event reporting – is simply not adequate in today’s complex environment. Additionally, advancing the use of new technologies such as electronic health records will help better identify and communicate emerging safety concerns on a prescriber and patient level.

One such example is the FDA’s Sentinel Initiative, a post-marketing drug safety surveillance program which would “access the capabilities of multiple, existing data systems” such as electronic health record systems and medical claims databases. Although still in the development phases, a fully operational safety system with the ability to capture electronic health data from more than 100 million people could have a significant impact on safety signal detection and confirmation. But again, large-scale cooperative efforts between all relevant stakeholders – government agencies, providers, payers, academia, patient groups and the biopharmaceutical industry – will be required to fully capitalize on this initiative’s potential.

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CONCLUSION

As part of the biopharmaceutical industry, we all are striving to ensure that medicines are used appropriately and in their most effective manner to ensure the best outcomes, and we can help that cause through our analytical capabilities. The systems and procedures for establishing an enterprise-wide culture of safety are already available; and with a concerted, coordinated effort among multiple stakeholders, far-reaching reform can be realized.

¹ Institute of Medicine, *The Future of Drug Safety: Promoting and Protecting the Health of the Public*. IOM, National Academies Press, September 26, 2006. Institute of Medicine, <http://www.nap.edu>

² Smith, SW. Sidelining Safety – *The FDA’s Inadequate Response to the IOM*. *N Engl J Med*. 2007 Sep 6;357(10):960-3

³ Hamburg MA, Sharfstein JM. *The FDA as a public health agency*. *N Engl J Med*. 2009 Jun 11;360(24):2493-5

⁴ Waller PC, Evans SJ. *A model for the future conduct of pharmacovigilance*. *Pharmacoepidemiol Drug Saf*. 2003 Jan-Feb;12(1):17-29.

⁵ *The Sentinel Initiative: a national strategy for monitoring medical product safety*. <http://www.fda.gov/downloads/Safety/FDAsSentinelInitiative/UCM124701.pdf>