Drug Safety in Europe: A Model for the United States?


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Two of the leading players in the global pharmaceutical market are the United States, where the Food and Drug Administration (FDA) regulates drug safety, and the European Union (EU), where a network of regulators in the 27 EU member states oversee drug safety – both directly and through EU-level approaches coordinated by the European Commission and the European Medicines Agency (EMEA).

In the United States, an intense debate about the adequacy of FDA authority and programs to ensure drug safety has erupted. Among those involved are the agency itself, a broad array of stakeholders, prestigious bodies like the Institute of Medicine, and above all, the US Congress.

The core question is whether the FDA drug safety program is in need of legislative repair. The jury is still out on the question but, with the shift in Congressional control from Republicans to Democrats, enactment of legislation to tighten drug safety control (whether needed or not) seems more likely.[1]

Drug Safety à la Europe?

Have countries in Europe, or the EU as a whole, managed to fashion regulatory approaches worthy of adoption by the United States and other countries? The short answer is "perhaps."[2] Certainly, the United States is not alone in having many stakeholders who are dissatisfied with the current state of affairs and interested in better regulation. For pharmaceutical regulatory comparisons, the system most often benchmarked against the FDA's is that of the EU's EMEA.

Certainly, the EU has been among the leaders in developing elaborate "pharmacovigilance" approaches. As defined by the World Heath Organization (WHO), pharmacovigilance is the science and activities relating to the detection, assessment, understanding, and prevention of adverse effects or any other medicine-related problem. Traditionally, drug regulators have relied heavily upon receipt and analysis of adverse event reports to monitor whether marketed drugs continue to enjoy a favorable benefit-to-risk ratio. Although pharmacovigilance is sometimes treated as synonymous with adverse event reporting and analysis, it actually is a broader concept that encompasses both event analysis and other tools such as postapproval studies and patient registries.

Without question, obtaining and interpreting postmarketing safety data is complex, involving the analysis of later-received clinical data, adverse experience in relation to the estimation of unreported events and overall drug usage, consideration of background rates of adverse events in the relevant patient population, and other confounding variables. Complicating this already difficult process is the fact that decisions about how to address a safety concern are often a matter of scientific judgment, and conflicting opinions are commonplace.

Despite holding similar views on many subjects, the FDA and the EMEA are dissimilar in many ways, among them, their role in how adverse incidents are reported and handled. As the sole pharmaceutical regulatory body in the United States, the FDA has established a centralized pharmacovigilance system, including a single and unified reporting system. Meanwhile, in Europe, the European Commission (EC) and EMEA are unable to exercise the same degree of control. Rather, analysis of adverse event reports and associated pharmacovigilance activities are carried out by the individual member states and is merely coordinated by the EMEA.

Nobody's Perfect

Despite the differences in the rules governing the reporting of adverse incidents in both the United States and the EU, both systems have recently been criticized by their respective governmental bodies, for distinct reasons.

In February 2007, the European Commission published an assessment of the EU's system of pharmacovigilance (the Commission Assessment) based on the results of a European Commission Public Consultation, in which it made a number of observations. It is clear that the difficulties inherent in the EU framework are largely attributable to the lack of harmonization in the member states implementing the EU pharmacovigilance rules. These rules impose only the minimum requirements to be enforced in each of the member states, leaving the door open to stricter or different national-level standards. Hence, many member states have exceeded the EU requirements through the implementation of their

[1] To read more about product safety legislation in the United States, see pages 24–25.
[2] To read more about product safety risk management plans in the EU, see pages 22–23.

own national rules. A prime example is the fact that several member states demand an in-country person as a pharmacovigilance focal point.

A by-product of the disparate reporting mechanisms that exist in the individual member states is the enormous duplication of work that this entails. Equally problematic is the circuitous route in which reports of adverse incidents make their way to the member states in the first place.

The Commission Assessment observed that many respondents, including regulators, industry, academia, and patient and consumer groups, explicitly call for the introduction of consumer reporting of adverse incidents as a way to streamline organization. The utility of this proposition is obvious in times of serious crisis.

The Commission Assessment also stated that a significant step toward remedying the various reporting bottlenecks in the EU would undoubtedly be the implementation of a single European Council Regulation on pharmacovigilance to replace all existing EU laws. The benefit of this could be seen in the interim if transitional harmonization measures were set out in the EU guidance. It is beyond question that the EU would benefit from a unitary reporting procedure more closely approximating that in the United States.

Interestingly, the Commission Assessment raised the possibility of trying to improve the EU pharmacovigilance system through the establishment of regional "Centres of Excellence." The ideal Centre of Excellence would capitalize on experts in all of the specialized categories of drugs and medicinal products.

Outlook

There are many other emerging issues in the drug safety debate with no easy answers and no one solution on either side of the Atlantic. For example, the FDA is coming under criticism about monumental shortcomings in the agency's computer system, which is the foundation of its adverse event system. Yet another challenge to drug regulators – the EMEA and the FDA alike – involves communicating drug safety information to the public. Neither one seems to have achieved complete success on this front.

Clearly both the US and EU drug safety frameworks are still works in progress. One option is for FDA and EU regulators to discuss a joint initiative combining certain FDA Critical Pathway initiatives with the European Commission's Centres of Excellence proposal. If EU authorities decide to move forward with Centres of Excellence, they will need sufficient resources and official support, as well as an open line of communication with industry and regulators so that their advice is practical and not perceived as theoretical.

In formulating any new drug safety measures, the FDA and the EU should proceed through the International Conference on Harmonisation process rather than unilaterally so that regulators and industry are working together and aligned with key players from Japan, Canada, Switzerland, and the WHO.

[3] At the time of this report, the US House of Representatives passed legislation addressing drug safety; the US Senate is scheduled to vote on companion legislation by the end of July 2007. Assuming the Senate bill is passed, a reconciliation bill would be sent to the President for his signature or veto.