DIA DEVELOP INNOVATE ADVANCE

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openFDA: An Open Question

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This past June, the FDA launched openFDA, a new initiative designed to make it easier for web developers, researchers, and the public to access large, important public health datasets collected by the agency.

According to the agency, the initiative is the result of extensive research with internal officials and external developers to identify those datasets that are in recurrent demand and are traditionally fairly difficult to use. Based on this research, the FDA decided to phase in openFDA beginning with an initial pilot program involving the millions of reports of drug-adverse events and medication errors that have been submitted to the FDA from 2004 to 2013. Previously, the data were only available through difficult to use reports or Freedom of Information Act requests.

The crowd-sourcing of adverse event data may or may not yield interesting results, but it's a good place to start. It represents an opportunity for the agency to begin designing a more evolved approach to 21st-century pharmacovigilance.

In the United States, indeed throughout the world, 21st-century pharmacovigilance must be about more than just adverse drug reaction reporting—it must be about leadership in drug safety, in safe use, and in achieving better and more regular positive therapeutic clinical outcomes. Pharmacovigilance in the 21st century is crucial in a regulatory environment that is changing to embrace medically promising and more complicated innovator molecules as well as biosimilars and nonbiologic complex drugs (NBCDs) such as glatiramer (Copaxone) and enoxaparin (Lovenox). To more quickly identify and accurately establish causality, we need to expand our thinking about pharmacovigilance, pharmacoepidemiology, risk management, and communications in various settings (regulatory, academia, industry, and health care systems). The agency's openFDA initiative is at the base of the pyramid.

In addition to the size and scope of modern medicines, new expedited and conditional pathways to approval also require more robust and interactive pharmacovigilance via more regular and creative risk management plans. Postmarketing risk management cannot exist without a more holistic understanding and acceptance of the responsibilities of risk. One key reason the EMA has been able to keep pace with the FDA shorter regulatory review cycles for innovative treatments (in 2013 the FDA reported, of the New Molecular Entitles approved, 10 via fast-track, 3 through breakthrough designation, 10 with priority review [6 months or less], 2 via accelerated approval paths[1]) is the EMA's faith in its various pharmacovigilance programs such as the Pharmacovigilance Risk Assessment Committee (PRAC). This has enabled millions of European patients earlier access to important new medicines that improve, save, and extend their quality of life.

In addition to openFDA, the agency is also placing greater weight on product quality, having just established an Office of Pharmaceutical Quality to improve the agency's scrutiny of brand name, generic, and over-the-counter drugs. The FDA is talking with their industry partners to develop data that may signal which manufacturing plants are straying from standards and need inspection. According to Dr Janet Woodcock, director of the USFDA's Center for Drug Evaluation and Research, "We want to use leading indicators. These people aren't in trouble yet but they could be."[2] And according to FDA Commissioner Dr Margaret Hamburg, "All companies must understand that quality is the basis for the public's trust and confidence in their products and maintaining high quality standards is part of the cost of doing business." Hamburg said the new office will "improve our oversight of quality throughout the lifecycle of a pharmaceutical product."[2]

A 21st-century strategy for pharmacovigilance must also include attention to clinical outcomes, and this means a new focus on a new area—substandard pharmaceutical events (SPEs). In a world with increasingly interchangeable innovator and generic large molecules, critical dose drugs, and narrow therapeutic index products, pharmacovigilance programs must extend beyond the traditional World Health Organization (WHO) definition of "the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem"[3] toward

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the more comprehensive understanding of the United Kingdom's Medicines and Healthcare Products Regulatory Agency (MHRA), which includes "assessing the risks and benefits of medicines in order to determine what action, if any, is necessary to improve their safe use."[4]

SPEs occur when a product does not perform as expected—perhaps because of active pharmaceutical ingredient (API) or excipient issues. SPEs can arise because of an issue related to therapeutic interchangeability. When it comes to 21st-century pharmacovigilance, we have to both broaden and narrow our views about bioequivalence to the patient level; 21st-century pharmacovigilance means doing what's right in addition to what has been traditionally required. Traditional risk management means finding ways to avoid risk, to mitigate it. That's important, but it's tactical—and very 20th century. In the 21st century we have to invent new strategies. For pharmacovigilance to play its appropriate role in the safe use of all regulated products, and particularly of personalized medicines, collection, and investigation, communication and action on issues raised by SPEs must constitute a new pillar of regulatory oversight—and openFDA seems like the perfect entrée into this conversation.

Pharmacovigilance in the 21st century must also include tighter and more regularly monitored postapproval bioequivalence measures. Recent recalls of products such as budeprion (Wellbutrin) and metoprolol (Toprol) offer vivid examples. "We are losing control over what people are swallowing," said Dr Harry Lever, a cardiologist at the Cleveland Clinic.[5] It's a new and difficult task, and it calls for better validated methodologies for both data collection and signal prioritization.

Another key regulatory question is the appropriate role of regulators in coordinating input from crucial partners such as physicians, nurses, pharmacists, disease organizations, patients, and pharmaceutical manufacturers. "Real-world" event monitoring must become as specific and informing as in a clinical trial environment. To borrow a term from the nuclear disarmament discussion, 21st-century pharmacovigilance must work with its various colleagues to "trust, but verify." Again, this fits hand-in-glove with the spirit of openFDA.

Access to data is important—but 21st-century pharmacovigilance must also take into consideration the realities of funding, existing staff levels and training programs, and existing regulatory authority. Accessing increased regulatory budgets is problematic. Should licensing agencies be permitted to charge pharmacovigilance user fees? We don't know the answer—but agency funding is an often overlooked 800-pound gorilla in the room and deserves further discussion. Perhaps creative public use of FDA data via openFDA will help develop not only new solutions but also awareness of the magnitude of the task at hand.

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