

# Exchange

From the Medical Industry Leadership Institute

Winter 2016 • Issue 16

## Deadly Delays

Pharma companies are taking too long to report side effects and adverse events—including deaths—to the FDA. Carlson School of Management professor Paul Ma and his co-authors, Iván Marinovic (Stanford's Graduate School of Business) and Pinar Karaca-Mandic (U of M's School of Public Health and the National Bureau of Economic Research), used data on 10 years of reports to the FDA for their research letter published in the *Journal of the American Medical Association—Internal Medicine*. The numbers were grim.

Ma, a Stanford graduate who studies information economics, says his field is interested in “how (more or less) information affects the behavior of people and firms.” In this case, his team wanted to see how information on the negative outcomes of ongoing patient use of a medication affects companies’ reporting behavior—whether that is to the FDA, investors, or patients. “The decision to disclose is a function of the firm’s perceived costs and benefits and also depends on the regulations concerning what is required or not required for disclosure,” Ma explained.

*“This finding informs regulators on the degree of compliance with the existing regulation and is consistent with a broad literature that suggests that firms’ disclosure of product safety information is strategic.”*

In their study of over 1.6 million adverse-event reports to the FDA, a full 10 percent of the reports were well past their federally regulated submission date, a significant portion more than a full year past due. Ma said, in technical terms, “We found the decision to delay was both non-

### About

*Exchange*, a publication from the Medical Industry Leadership Institute, features dialogue on medical industry research and application. The content is a summary of research from both academia and the medical industry, followed by commentary on the importance of the research and its application. Topics highlighted in the *Exchange* span all sectors of the medical industry and include commentary from leaders in the field, as well as researchers from the University of Minnesota and other academic institutions.

random and correlated with the seriousness of the report—that is, reports of patient deaths were much more likely to be delayed.”

“This finding informs regulators on the degree of compliance with the existing regulation and is consistent with a broad literature that suggests that firms’ disclosure of product safety information is strategic,” Ma continued. FDA enforcement letters the researchers gathered show examples of the selective reporting of negative information, selective disclosure and delays in disclosure of patient deaths, and even tampering with the dates of reports to make them appear more recent. In a generous interpretation, the team writes that companies may delay in order to verify the most serious patient reports. But beyond that, either the FDA isn’t enforcing its regulations stringently enough or the regulations are too onerous.

Either way, the solution they offer is, essentially, to cut out the middle-man (the very heavily invested middle-man, that is): redirect patient and clinical reports of adverse effect events related to a medication directly to the FDA rather than to its manufacturer. This seemingly simple policy change might literally save lives. ■




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Minneapolis, Minnesota 55455-9940

Nonprofit Org.  
U.S. Postage  
PAID  
Twin Cities, MN  
Permit No. 90155

## *Exchange*—A dialogue on medical industry research and application

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 Printed on recycled paper 30% post-consumer fiber

### Commentary

*By Susan Alpert, PhD, MD, Principal, SEA Consulting, Executive in Residence MILI*

It is well known in the healthcare community that the clinical trials upon which FDA drug, device, and biologics approvals are based are not a complete reflection of the patients in whom the products, once approved, will be used. Off-label uses, co-morbidities, and the interaction of the drug with others mean the medication's "real world" results do not always reflect what was seen in the initial trials for approval. That's why there are requirements that manufacturers and some healthcare facilities are required to report deaths and other serious, adverse events after a drug hits the market.

Paul Ma and his co-authors note that 10 percent of these reports have been submitted late, and some of these companies' delays are strategic or intentional. From my experience in both the FDA and the healthcare industry, I would note that a very small number of companies may behave this way. Still, it's the difficulty in obtaining the details the FDA requires for these reports that delay most. Further, back and forth about autopsy notes, copies of hospital records, and patient privacy concerns—all incredibly important on their own—may prevent full information from being gathered or reported in a timely way. And, of course, while healthcare facilities are mandated to report some types of adverse events, individuals using a drug or other product at home may not

tell their doctors about side effects, and their doctors are not mandated to report to the drug manufacturer or to the FDA.

Certainly, the FDA needs to see the numbers of events and the detailed reasons for them so that the agency can communicate with the public and healthcare providers to assure safe and appropriate use. Thus, the MedWatch system, including a web portal set up by the FDA, supports and encourages voluntary reporting of serious adverse events and product quality issues by anyone, be they consumer, health professional, or family member. Voluntary reporting eliminates the middle-man.

A move toward health professionals' mandated reporting to the FDA should be carefully evaluated. The issues that should be considered include how the professional would know that the event occurred, when it took place, and whether there were possible other potential contributors to the event. And which healthcare provider should be mandated to report? The prescribing individual or the individual who spoke to or saw the patient after a serious drug-related event? Both? Who would research, gather records, and write reports? There is no easy answer to these questions, but clearly, they are critical for drug and device development, as well as the safety and health of patients. ■