Some adverse drug events not reported by manufacturers to FDA by 15-day mark

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About 10 percent of serious and unexpected adverse events are not reported by drug manufacturers to the U.S. Food and Drug Administration under the 15-day timeframe set out in federal regulations, according to an article published online by *JAMA Internal Medicine*.

Health care professionals and consumers can voluntarily report adverse drug events directly to the FDA or the drug manufacturer. Adverse events that are serious (including death, life-threatening, hospitalization, disability and birth defects) and unexpected (any adverse experience not listed in the current labeling) are classified as "expedited" and manufacturers receiving such reports are mandated to forward them to the FDA "as soon as possible but in no case later than 15 calendar days of the initial receipt of the information" under federal regulation, according to background information in the research letter.

Pinar Karaca-Mandic, Ph.D., the University of Minnesota School of Public Health, Minneapolis, and coauthors examined data from the FDA Adverse Event Reporting System for adverse event reports received from January 2004 through June 2014. The final study sample included only initial reports characterized by the FDA as "expedited" and therefore subject to the regulation requiring reports to be submitted within 15 calendar days.

The study, which included more than 1.6 million adverse event reports, estimated that 9.94 percent of the reports (160,383 total; 40,464 with

patient death and 119,919 without patient death) were not received by the FDA by the 15-day threshold. The authors' analysis suggests patient death was associated with delayed reporting.

"Our analysis provided evidence that drug manufacturers delay reporting of serious AEs [adverse events] to the FDA. Strikingly, AEs with patient death were more likely to be delayed. It is possible that manufacturers spend additional time in verifying reports concerning deaths, but this discretion is outside the scope of the current regulatory regime," the authors conclude.

In a related Editor's Note, Rita F. Redberg, M.D., M.Sc., editor of *JAMA Internal Medicine*, writes: "Such reporting delays should never occur, as they mean that more patients are exposed to potentially avoidable serious harm, including death. ... One improvement would be for AE reports to go directly to the FDA instead of via the manufacturer, as recommended by Ma et al. ... Physicians and their patients must be knowledgeable of benefits, harms and alternatives for a wide choice of treatments, especially those recently approved for which clinical experience is limited."

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