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A New Approach to Reporting Medication and Device Adverse Effects and Product Problems

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UNFORTUNATELY, many health professionals do not think to report adverse events that might be associated with medications or devices to the Food and Drug Administration (FDA) or to the manufacturer. That needs to change, and the FDA is taking steps to encourage that to happen.

Reports from health professionals of adverse events or product quality problems are essential to ensure the safety of drugs, biologicals, medical devices, and other products regulated by the FDA once they are introduced into the US market.

Even the large, well-designed clinical trials that are conducted to gain pre-market approval cannot uncover every problem that can come to light once a product is widely used. A new drug application, for example, typically includes safety data on several hundred to several thousand patients. If an adverse event occurs in perhaps one in 5000 or even one in 1000 users, it could be missed in clinical trials but pose a serious safety problem when released to the market. Moreover, patients taking marketed drugs in conjunction with other drugs may experience interactions not revealed during the premarketing phase.¹

In response to voluntary reports from physicians to the FDA or the manufacturer, the FDA has issued warnings, made labeling changes, required manufacturers to conduct postmarketing studies, and ordered product withdrawals that have ultimately prevented patient deaths and suffering.

Adverse drug reports from physicians, for example, prompted the FDA to determine that torsades-de-pointes ven-

tricular arrhythmias could occur when the antihistamine terfenadine (Seldane) was taken in combination with the antifungal medicine ketoconazole or the antibiotic erythromycin.² This episode also increased recognition that individual variability in drug metabolism can account for significant differences in patient response³ and underscored the importance of postmarketing studies and physician observations and reports.

Other examples of FDA actions prompted by reports of adverse events include the 1986 recall of suprofen,⁴ the 1991 alert to health professionals on potentially fatal latex hypersensitivity,⁴ the 1992 boxed warning and alert to physicians regarding use of angiotensin-converting enzyme inhibitors during the second and third trimesters of pregnancy,⁵ and, most recently, the recall of temafloxacin.⁶

Just as reports enable us to respond to serious adverse events, lack of reporting can delay problem detection. Silicone breast implants are one example. Although these devices have been on the market for some 30 years, only recently has evidence accumulated about a possible association with autoimmune-like disorders.^{7,8} If reports from physicians who diagnosed autoimmune-like disorders in patients with breast implants had been received years ago, the possible connection might have been identified much earlier.

Aside from adverse events associated with specified vaccines (listed in the National Childhood Vaccine Injury Act⁹), most reporting by health providers is voluntary. Manufacturers of drugs and devices and device distributors are required to report adverse events,^{10,11} and soon manufacturers of biologicals will face similar requirements. Device manufacturers and distributors are also required to report to the FDA product problems that may cause death or serious injury if the malfunction were to

recur.¹¹ Health care facilities are required to report certain adverse events associated with devices.¹¹ However, these groups, like the FDA, depend on health care professionals' surveillance and voluntary reporting.

Although the FDA receives many adverse event reports, these probably represent only a fraction of the serious adverse events encountered by providers. A recent review article¹² found that between 3% and 11% of hospital admissions could be attributed to adverse drug reactions. Only about 1% of serious events are reported to the FDA, according to one study.¹²

There are probably several reasons why some serious events are not reported to either the FDA or the manufacturer. First, when confronted with an unexpected outcome of treatment, physicians may not consider drug-induced or device-induced disease, but rather consider the event to be related to the course of the disease.

Unfortunately, this may be due to the limited training medical students receive in clinical pharmacology and therapeutics. A 1985 survey of US medical schools found that only 14% of them had required courses in core skills and principles of therapeutic decision making and clinical pharmacology. Of the remainder, 87% taught only a few hours of clinical pharmacology, and most of the teaching occurred in the early years of medical training.¹⁴

Another factor inhibiting physician reporting is that it is not an ingrained practice—it is not in the culture of US medicine to notify the FDA about adverse events or product problems. In other countries such as the United Kingdom, adverse drug reporting is more frequent.¹⁵ A patchwork of reporting forms and systems may make it difficult to file reports in the United States and may discourage even the most conscientious professionals. Finally, physi-

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A complete list of the participants in the Working Group appears at the end of this article.

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