

improved information on SADRs is needed to ensure the safe use of products and to monitor early warnings and unexpected risks associated with drugs, drug-drug interactions, drug-food interactions, and risks to certain patient populations.

V.C. Benefits

The benefits of the proposed rule would result both from the public health gains attributable to the improved scope, uniformity, and quality of information and analyses submitted in safety reports and the economic savings attributable to the more efficient use of industry and regulatory resources.

This proposed rule would require improved factual and analytic data underlying safety reporting and analysis, provide for more timely safety information for certain serious SADRs, and would require a common medical dictionary, MedDRA.

The timely identification of SADRs is critical to managing risk information and to the safe prescribing and use of new drugs. Accurate and timely risk information is especially significant in the early months after product launch to develop appropriate prescribing and use behaviors as health care practitioners and consumers are learning about the product safety and use. Newly approved product use can quickly grow from a few thousand patients (the population in clinical trials) to many thousands or millions. Rare but serious SADRs are detected only after exposure to very large patient populations. Forty percent of SADR reports are for drugs approved within the last 3 years. Compounding this need for timely serious SADR information, U.S. patients are increasingly the first in the world to have access to new medications (49 percent of new drugs were first approved in the United States between 1996 and 1998, compared with 31 percent in 1991–1995).

More timely and improved factual information would also enhance the identification of other important factors associated with the risks of SADRs. These factors include subpopulations that may differ from clinical trial participants, patients taking multiple medications or medications that require therapeutic monitoring, and patients with concurrent comorbidities.

This rule would require affected entities to complete either a minimum or full set of data in safety reports, reflecting levels of risk. That is, more detail is required for higher risk events and reduced reporting for lower risk events. This rule would also require the use of MedDRA, a medical dictionary

developed by the ICH, in coding SADR terms. MedDRA will provide a uniform, consistent and specific presentation of medical terms. By eliminating the use of multiple dictionaries, MedDRA would facilitate the retrieval, presentation, and summarization of SADR data and enhance the global communication and acceptance of safety information and reports. The use of a single dictionary will substantially upgrade the quality of safety analysis by incorporating uniformity of terms. MedDRA will aid in more expeditious and broader international drug use comparisons within a class, and prescribing and use decisions. Providing more complete information and more timely safety assessments would enhance the ability of the manufacturers to more quickly identify, monitor, and communicate the potential risks and benefits of marketed drugs and biologics.

It is well recognized that drug safety information is a critical element in the risk management of marketed drugs and biologics. In addition, the medical literature provides substantial documentation of avoidable hospitalizations associated with SADRs. Improving the quality and timeliness of safety information and accelerating the communication of risk information will enable health care practitioners and consumers to take appropriate corrective actions (in the case of medication errors) and to make more informed decisions about treatments. Moreover, the management of risk information is an essential component of risk-based decisions that determine the continued marketing or withdrawal of effective products with newly identified serious SADRs. We discuss benefits more fully below and show that a small reduction in the number of hospitalizations due to SADRs (as low as 0.85 percent), due to improved prescribing and use decisions, would result in the annual benefits outweighing the total costs.

V.C.1. Expanded Safety Information

New drug approval decisions are based on safety and testing information derived from clinical trials that typically include several thousands of patients. However, the number of individuals tested in preapproval trials is not sufficiently large to reliably detect rare, serious SADRs. Patient exposure can quickly grow from thousands to millions after product launch. Thus, especially in the first few years after product launch, postmarketing surveillance is a critical component of the overall continuing review and assessment of drug safety (Ref. 1). Recent studies have identified common

factors associated with increased risks of SADRs. These factors include subpopulations who differ from the clinical trial participants, e.g., the elderly, patients taking multiple medications or medications that require therapeutic monitoring, and patients with concurrent comorbidities (Refs. 2 through 5). The proposed rule would require companies to collect proactively more complete safety information, improving the factual and analytical data underlying the safety analyses. This expanded risk information would enable health care practitioners and consumers to take appropriate corrective actions (in cases of avoidable medication errors) and to make more informed decisions about treatments.

V.C.2. Improved Uniformity and Quality of Safety Information

For years, numerous health care organizations, teaching hospitals, health care professionals, and educators have recognized the importance to public health of monitoring SADRs. Substantial evidence demonstrates that effective monitoring and analyzing of SADRs facilitate the identification of trends and warning signals that result in improved medication use and patient care (Refs. 6 through 10). Yet, the current drug and biologics safety reporting system, encompassing raw material suppliers, manufacturers, health care providers, and consumers, is fragmented with respect to its oversight and lacks common reporting procedures and tools for evaluating SADRs. For example, FDA oversees mandatory safety reporting by manufacturers of drug and biological products and voluntary reporting from health care providers and consumers. Health care facilities, on the other hand, may be subject to safety reporting oversight by individual state regulatory programs, although not all states have oversight systems. The Joint Commission on Accreditation of Health Care Organizations (JCAHO), which accredits health care facilities, has had standards for establishing SADR reporting systems for hospitalized patients for many years. Hospitals may establish their own systems independently and almost all conform to the JCAHO standards (Ref. 11). Despite growing evidence that avoidable SADRs and serious SADRs are important public health problems and widespread acknowledgment that monitoring SADRs provides public health benefits, FDA continues to receive reports of only a small percentage of the serious and avoidable SADRs that occur in health care facilities (Ref. 12). This proposed rule would improve safety reporting by drug