

and biologics manufacturers, which may serve to provide a national framework for improved data collection and analysis of safety reports from a variety of sources.

The proposed rule would also require the use of MedDRA, a single, medical terminology developed by ICH that can be used for the coding of SADR terms. MedDRA is a broad-based dictionary, developed for international use, that combines both SADR and morbidity terminology to 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. In addition, the use of a single comprehensive medical dictionary by drug safety reporters and reviewers would substantially upgrade the quality of safety analysis by incorporating uniformity of terms. Standardizing the terms and improving the quality of the roughly 250,000 safety reports submitted annually to FDA would lead to better and more timely safety assessments and to improved communication of risk information. The widespread use and acceptance of standardized SADR information by regulators would ultimately enhance drug comparisons within a class and drug prescribing and use decisions.

V.C.3. Potential Savings From Reduced SADR-Related Hospitalizations

Improved timeliness and analysis of SADR data would lead to a better understanding and a more rapid communication of the risks of SADRs. By providing such improvements, the proposed rule would reduce the incidence of SADRs. An agency estimate of the potential economic benefits of the rule is presented below and reflects the value of the expected hospital cost savings and the avoided lost wages that might result from reduced numbers of SADRs.

V.C.3.a. *Reduced rate of SADR-related hospitalizations.* Numerous studies have documented drug-related hospitalizations (60 FR 44182 at 44232, August 24, 1995). A comprehensive review of 36 articles focused specifically on SADRs as the primary cause of hospitalization. This study counted the number of reactions attributed to unintended consequences of drug therapy, excluding admissions due to overdose, intentional poisoning, attempted suicides, drug abuse, or intoxication. The percentage of hospitalizations due to SADRs ranged from 0.2 to 22 percent, with a mean of

5.5 percent. FDA adjusted this figure to 5 percent to remove over-the-counter drugs (Ref. 13). Based on 27.8 million hospital admissions reported in 1997, excluding obstetrical admissions (Ref. 14), the agency estimates the annual number of SADR-related hospitalizations at about 1.4 million (5 percent \times 27.8 million). Absent available data, the agency assumes the costs associated with SADR-related hospitalizations are similar to the average cost of a hospital stay, but requests comments and supporting data on this assumption. Therefore, applying an estimated cost of \$9,177 for an average hospital stay (Ref. 15) implies total annual SADR-related hospital admission costs of about \$12 billion ($\$9,177 \times 1.4$ million).

If the improved reporting and analyses of SADRs led to the avoidance of only 2 percent of these hospitalizations, the economic savings would amount to \$252.2 million annually.

V.C.3.b. *Reduced rate of in-hospital SADRs.* Bates et al. conducted a random sample of nonobstetrical admissions to two large tertiary care hospitals in Massachusetts over a 6-month period (Ref. 16). His prospective investigation of SADRs included interviews with medical staff and daily reviews of all medical charts. He estimated the incidence of all SADRs, including medical errors, at 6.5 percent with an average increase in hospital costs of \$2,595 per case. Extrapolating these findings, FDA estimated the annual number of in-hospital SADRs at 1.8 million and the total additional hospital cost at \$4.7 billion annually. If this proposed rule led to a 2 percent reduction, the economic benefits would be \$93.6 million annually.

In a comprehensive review of studies that estimated the incidence of SADRs and/or the magnitude of hospital costs due to SADRs, the U.S. General Accounting Office cited substantial variation in estimates (Ref. 17). These differences may be due to inconsistent definitions of SADRs, different study methodologies (active prospective investigation versus retrospective review of patient records), representativeness of the samples, and particular methods used to extrapolate study findings to a national level. For example, Lazarou et al. and Classen et al. estimated the incidence of serious SADRs using the WHO definition of SADR and excluding other factors such as poisonings, intentional overdoses, and therapeutic failure (Refs. 18 and 19). These two studies had findings similar to Bates et al. On the other hand, Thomas et al. reviewed randomly

selected hospital discharge records in two states and found a lower incidence of "drug injury". However, he used a particularly restrictive definition of SADR, one that resulted in prolonged hospitalization or disability at discharge (Ref. 20). Despite the uncertainties of estimating the incidence and cost of hospital related SADRs, FDA believes that the \$4.7 billion estimate for in-hospital SADRs derived above provides a plausible estimate.

V.C.3.c. *Indirect benefits of reducing the hospital costs of SADRs.* The indirect benefits of reduced drug-related illnesses are derived from estimates of the costs of missed work or reduced productivity. Several studies on SADR-related hospital admissions stratified findings by patient age. Roughly 58 percent of SADR admissions were for patients aged 20 to 59. The remaining 42 percent were for patients under 20 years (less than 10 percent) and over 59 years old (Refs. 21 through 23). To calculate productivity losses, the agency assumed 56 hours per admission for patients aged 20 to 59 years (40 hours of lost work per hospitalization plus 16 additional hours for recovery and followup doctor visits)² and 14 hours for the remaining groups (to account for lost volunteer time or for time away from work for the care givers of dependent patients). The wage rates used are the average hourly production workers earnings of \$15.96 for patients aged 20 to 59 (\$12.28 plus 30 percent for benefits), and \$12.28 for the remaining patients or their care givers (Ref. 14). The estimated value of this lost productivity is \$812 million.

To estimate similar indirect benefits for in-hospital SADRs, the agency assumed the same distribution of patient ages. Related productivity losses are assumed to be 16 and 6 additional hours respectively, for patients aged 20 to 59, and for the remaining groups. The estimated value of this lost productivity is \$323 million.

A 2 percent reduction in costs of SADR-related hospitalizations and prolonged hospitalizations would yield indirect benefit savings of \$22.7 million. These estimates may somewhat overstate the value of lost productivity for the 20 to 59 age group because all patients are assumed to be employed. On the other hand, indirect benefits for the remaining age groups are understated because many of these patients are in the workforce and for those who are not, data are inadequate to measure their contribution to society.

² The agency used 40 hours to estimate work productivity losses. This estimate is consistent with current hospital discharge data and with the length of stay for drug-related hospitalizations (Ref. 21).