

V.C.3.d. *Sum of SADR-related costs.* Summing these estimates, the total annual direct and indirect benefits of reducing avoidable SADR-related hospitalizations and longer hospital stays by 2 percent would lead to economic benefits of \$368.5 million per year. Varying the assumption of a 2 percent reduction in hospital costs with a 1, 3, and 5 percent reduction, would yield annual benefits of \$184 million, \$553 million, and \$921 million, respectively. A reduction of only 0.85 percent in the hospital costs associated with SADRs would be needed to outweigh the annualized industry costs of \$155 million. Furthermore, under any of these scenarios, the total SADR-related hospital savings would outweigh the costs of this rule. With a 2 percent or greater reduction, the annual benefits would outweigh the costs beginning in the first year. Nonetheless, the agency seeks comment on our estimates of expected reductions in hospital-related costs, including the potential for reducing the incidence and length of stay of hospital-related SADRs.

In contrast to focusing only on hospital costs of SADRs, one study estimated the direct costs of drug-related morbidity and mortality for the ambulatory population at \$76.6 billion annually, with the largest component \$47.4 billion for drug-related hospitalizations (Ref. 24). The remaining cost components included: \$14.4 billion for long-term care, \$7.5 billion for physician visits, \$5.3 billion for emergency department visits, and \$1.9 billion for additional prescriptions. Again, assuming a 2 percent reduction, savings are approximately \$948 million annually.

V.C.4. Cost Savings and More Efficient Use of Resources

The proposed rule is intended to complement and formalize international efforts by industry representatives and major international regulatory bodies to achieve a more uniform and global approach to safety reporting. The content, analyses, and timing of SADR report submissions would closely align with international initiatives and recommendations. To the extent that U.S. requirements become harmonized within a global context, companies that compete internationally would benefit from this proposed rule. Multiple international due dates for safety report submissions and reformatting of the same information to meet different regulatory requirements represent opportunity costs that could be allocated elsewhere. Companies would accrue savings through a substantial reduction or elimination of the

reformatting of postmarketing periodic safety report information to meet varying international requirements and by synchronizing report frequencies and due dates internationally. Thus, as the international community harmonizes, companies would achieve efficiencies, eliminate duplicative processes, and reallocate those resources more efficiently.

The agency contracted with the Eastern Research Group, Inc. (ERG), an economics consulting firm, to estimate the potential benefits that would accrue to drug and biologics companies in the long run, as international harmonization efforts align and generate cost savings. These savings include more efficient regulatory safety reporting, more efficient sharing of safety information, and a common medical terminology. ERG estimated the following specific categories of benefits: More efficient management of drug safety data, more efficient intercompany agreements, and international harmonization of the postmarketing periodic safety report format (*i.e.*, use of PSUR format). ERG applied estimates of savings by category and firm size to the number of affected firms within each affected industry. The methodologies and procedures for deriving these estimates are fully presented in ERG's final report (Ref. 25).

V.C.4.a. *Savings related to maintaining and building data bases of SADRs and intercompany transfers of drug safety data.*

Drug and biologics companies maintain safety data bases of all domestic and foreign SADRs involving their products. The management of these data bases can be quite complex depending on the individual circumstances of manufacturing and marketing. Companies may have foreign subsidiaries, domestic and foreign manufacturing sites, and varied licensing agreements with other companies for marketing products. Foreign subsidiaries and licensees generally submit SADR reports to U.S. companies by fax. U.S. companies then reenter the reports into their own databases. Use of standardized safety report formats and content internationally will lend itself to electronic transmission of safety information. In these cases, intercompany and intracompany sharing of safety information will be substantially facilitated. ERG estimated these benefits at \$3.1 million annually.

V.C.4.b. *Savings related to greater ease in entering into intercompany agreements.* As requirements for drug and biologics safety reporting become harmonized, drug and biologics companies will find it easier to

coordinate safety reporting efforts when entering into various agreements with other manufacturers or sales organizations. In the current organizational structure of the industry, companies are frequently negotiating licensing agreements, mergers, joint ventures, and other contractual matters with other companies. For these arrangements, companies must develop, share, and merge drug safety reports from around the world. At present, negotiation of drug safety data sharing is often complicated by reporting formats and requirements that differ between regions. ERG estimated the potential savings that would accrue from simplified negotiation of licensing agreements due to standardized reporting formats and requirements at \$4.2 million annually.

V.C.4.c. *Savings related to eventual international harmonization to the PSUR format.* ERG estimated the potential savings to industry of preparing a single PSUR that would be accepted by regulatory authorities internationally on the same date. Currently, companies are faced with many inconsistent requirements and must meet the individual requirements and timeframes of each country. ERG estimated these savings at \$24.3 million annually.

V.C.4.d. *Potential savings in clinical trial management.* Some companies noted that they would convert medical terms from clinical trials to MedDRA whether or not it was required by FDA. Assuming that this transition will gradually apply to future clinical trials, a single medical terminology, internationally developed, accepted, and applied, would allow companies to more easily transmit, integrate, and analyze clinical trial data from global sites. Subsequent reductions in time and resources would contribute to reduced costs during drug development. Based on input from industry, ERG developed a narrow focus of savings associated with clinical trial data management valued at \$7.2 million annually.

V.C.4.e. *Leveraging specialized knowledge.* This proposed rule also provides the groundwork for establishing focused centers of technical information on drug safety. Global companies and regulatory agencies will have the opportunity to create economies of expertise by concentrating specialized knowledge of global drug use and product risks and benefits in centralized locations. To the extent that safety information is better managed, understood, and shared with interested parties, substantial benefits will accrue. Neither ERG nor FDA could quantify these benefits.