

V.C.4.f. *Total benefits.* ERG estimated the total industry savings from more efficient use of resources to be \$38.8 million annually. This estimate, however, accounts for only a modest portion of the potential benefits of the broader set of initiatives that enhance electronic submissions and global harmonization of safety reporting. Table

12 summarizes the estimated annual benefits of this proposed rule. The agency recognizes, however, that the industry savings component will not be fully realized until safety reporting requirements are harmonized internationally. The agency believes that these benefits could be achieved in a relatively short period after this rule

becomes final. The agency is ready to accept PSUR formats and the use of MedDRA for coding of individual case safety reports at the present time (*see* draft guidance of 2001). In addition, the European Union and Japan currently accept PSUR formats and the use of MedDRA.

TABLE 12.—SUMMARY OF THE ANNUAL BENEFITS

Savings category	\$ Million (annually)
Public health benefits for a 2 percent reduction in SADR-related hospital costs:	
Reduced SADR-related hospital admissions	252.2
Reduced in-hospital SADRs	93.6
Indirect benefits from reduced hospitalizations	22.7
Total hospital-related savings	368.5
Expanded safety information on product approvals	(²)
Improved risk communication and product selection	(²)
Future Industry Savings:	
Efficiencies in database maintenance	3.1
Facilitation of PSUR submissions	24.3
Facilitation of intercompany negotiations	4.2
Clinical trial management	7.2
Total Industry Savings	138.8
Economies of Managing Drug Expertise	(²)

¹ Assuming 1/3 of these savings begin in year 2 (\$11.6 million), 2/3 in year 3 (\$23.3 million), and \$38.8 million in years 4 through 10, the annualized present value is \$28.5 million, discounted at 7 percent over 10 years. The 10-year time horizon allows a reasonable projection of current information given the unforeseen progress and impacts of medical and computer technology.

² Not estimated.

V.D. Costs of Compliance

This section presents the estimated compliance costs of the proposed requirements. As explained in the following paragraphs, the proposed rule clarifies and expands existing requirements for submitting premarketing expedited reports, postmarketing expedited initial and followup reports, and postmarketing periodic safety reports to FDA. Drug and biologics manufacturers would be required to use direct verbal contact to collect information sufficient to determine the nature, severity, and outcome of SADRs and to evaluate and describe the safety profile or changes in the safety profile of marketed drugs. The proposed regulation also specifies criteria for reporting individual case safety reports and designates data elements that must be completed as a condition for initial and followup reporting. Each SADR in a postmarketing individual case safety report for human drugs and biologics must be coded using the appropriate “preferred term” in the latest version of MedDRA. The proposal also requires a physician to review the postmarketing expedited and periodic safety reports. The proposed rule would codify the data elements, analyses, and report format of the required postmarketing

periodic safety report submissions and harmonize many of these requirements with ICH initiatives. Applicants holding an approved marketing application would be required to submit semiannual individual case safety reports and more detailed postmarketing periodic safety reports that contain cumulative and comprehensive data, analyses, tabulations, summaries, and other information. The proposed rule also includes revisions to IND safety reporting requirements and bioavailability and bioequivalence study requirements.

V.D.1. Costs of New Recordkeeping and Reporting Requirements

V.D.1.a. *Number of reports.* In 1998, manufacturers and applicants of human drug and biological products submitted approximately 230,000 individual case safety reports of SADRs to FDA. Data from about 130,000 of these individual case safety reports in the agency’s Adverse Event Reporting System (AERS) were analyzed to estimate the annual number of future SADR reports expected to be included as revised expedited and new semiannual submissions. However, not enough data exists to predict the number of new expedited reports the agency may expect each year. For this analysis,

estimates of new expedited reports for human drugs and biological products were based on counts of similar reports received by the agency during 1998. The estimated number of expedited reports for blood products is derived from published studies (Refs. 26 and 27).

The agency does not know how many TPSRs, and PSURs and IPSRs would be submitted annually, because applicants with pre-1998 drug approvals can submit either format. In addition, applicants with ANDAs approved on or after January 1, 1998, may choose to submit a TPSR rather than a PSUR or IPSR if the innovator NDA was approved before January 1, 1998. Despite this uncertainty, this analysis estimates the number of new filings of postmarketing periodic safety reports based on average counts of pre- and post-1998 drug approvals.

The number of affected reports for prescription drugs marketed for human use without an approved application, IND safety reports, bioavailability/bioequivalence safety reports, and other reports were projected from counts of similar reports received by FDA. Estimates for the total number of reports affected by the proposed rule are shown in table 13.