

V.E. Small Business Analysis

The following analysis along with other sections of this preamble constitute the agency's regulatory flexibility analysis as required under the Regulatory Flexibility Act.

V.E.1. Need for and Objectives of the Rule

A primary objective of this proposed rule is the harmonization of FDA's safety reporting requirements with international initiatives. The proposed rule would also improve the quality of information contained in postmarketing safety reports for marketed human drug and biological products. By providing more complete information for individual case safety reports, the revised reports would enhance the ability of manufacturers, applicants, and the agency to identify, monitor, and communicate the risks and benefits of marketed drug and biological products. Monitoring these risks and benefits is especially critical for recently approved products introduced to large and diverse patient populations following market approval.

V.E.2. Description and Estimate of Small Entities

The proposed rule applies to manufacturers, applicants, and contractors of drug and biological products, and persons involved in blood collection and transfusion. The Small Business Administration (SBA) defines a small business in Standard Industrial Classification (SIC) 2834 (or North American Industry Classification System (NAICS) code 325412) as one employing fewer than 750 employees and in SIC 2836 (or NAICS code

325414) as one employing fewer than 500 employees. According to 1996 U.S. Bureau of the Census statistics, almost 90 percent of the firms under these SIC codes are considered small businesses. A review of 1998 AERS data, which contain postmarketing 15-day and periodic safety reports from manufacturers and applicants of marketed drug and biological products, found that about 200 firms submitted at least one individual case safety report for a trade name product and that the majority of these firms were considered large under the SBA definitions. However, the number of firms submitting reports vary from year to year. Therefore, using the 1998 AERS data, estimates of the percentages of reporting firms by size were distributed to the number of firms in each SIC, suggesting that about 230 drug and 72 biologics firms would be affected by the proposed rule, of which 190, or about 60 percent, would be considered small.

FDA estimates that about 3,200 blood facilities would be affected by the proposed regulation. Approximately 3,000 are hospitals with blood collection and/or compatibility testing operations, classified in SIC 8062 (or NAICS code 62211), and 200 are blood banks or non-hospital blood and plasmapheresis centers, classified in SIC 8099 (or NAICS code 621991). The SBA defines businesses in SIC 8062 and 8099 with annual revenues of \$25 million and \$7.5 million or less, respectively, as small. ERG estimated the number of small businesses affected in SIC's 8062 and 8099 at 1,786 and 188, respectively. This is approximately 60 and 94 percent of the blood facilities in SICs 8062 and 8099, respectively, that will be

implementing the MedDRA requirements.

V.E.3. Projected Reporting, Recordkeeping, and Other Compliance Requirements

V.E.3.a. Reporting and recordkeeping requirements. The proposed rule may impose an additional burden on manufacturers of human drug products for which SADR are reported. In any year, SADRs may be reported for about half of the products marketed in the United States. AERS data from 1998 suggest that small firms manufactured less than 12 percent of the products for which SADRs were reported. Moreover, during this same year, only about 2 percent of the postmarketing 15-day alert reports submitted to the agency were from small firms. Nevertheless, the proposed changes to the postmarketing safety reporting requirements may impose a substantial burden on a significant number of small firms, especially small startup firms with only one product on the market. The extent of the impact will depend on the time that has elapsed since the drug was approved and the number and types of individual case safety reports received in a reporting period.

To illustrate the impact of the safety reporting and recordkeeping requirements of the proposed rule, table 19 shows the hypothetical first-year burden for a drug approved 6 months prior to the effective date of the final rule. Under this scenario, the first-year burden incurred for a newly approved product might be as much as \$19,600, assuming 26 expedited and 6 followup reports, two semiannual reports, and two PSURs had been submitted.

TABLE 19.—HYPOTHETICAL FIRST-YEAR REPORTING AND RECORDKEEPING BURDEN FOR NEWLY APPROVED DRUG PRODUCT

	Expedited (serious, unexpected SADR)	Expedited (medication errors)	Expedited (unexpected SADR with unknown outcome)	Always expedited report	30-day follow-up	Individual case safety report—semi-annual submission	PSUR	Total
Per report new burden ¹	\$104	\$612	\$919	\$612	\$367	\$1,042	\$1,564	
Number of reports	8	16	1	1	6	2	2	36
Totals ²	\$834	\$9,799	\$919	\$612	\$2,202	\$2,084	\$3,128	\$19,578

¹ Only whole dollar values are shown.

² Values rounded to the nearest whole number.

V.E.3.b. Implementing MedDRA. Implementing MedDRA would impose additional significant one-time and recurring costs on drug and biological product manufacturers. Costs would vary among individual firms depending

on circumstances, including the number of products manufactured, the frequency of SADRs, and the extent of legacy data converted. Table 20 displays ERG's estimates per firm of revenues, annualized compliance costs and costs

as a percent of revenues. Costs for small entities are 0.15 percent and 0.28 percent of revenues for drug and biological product manufacturers, respectively. Similarly, average compliance costs for small entities are