

0.01 percent and 0.03 percent of revenue for SICs 8062 and 8099, respectively.

TABLE 20.—COMPLIANCE COSTS AS A PERCENT OF ESTIMATED REVENUES FOR SMALL ENTITIES

Industry classification	Number of employees	Number of affected firms	Per firm estimated revenues (\$000)	Per firm annualized compliance costs (\$000)	Compliance cost as a percent of estimated revenues
SIC 2834 Pharmaceutical preparations	< 750	146	44,265	66.9	0.15
SIC 2836 Biological products	< 500	44	15,752	44.4	0.28
SIC 8062 General medical and surgical hospitals	< 500	1,786	13,366	0.6	0.01
SIC 8099 Blood banks (Health and allied services, NEC) ..	< 500	188	1,320	0.3	0.03

The reporting, coding, and analysis of SADRs are standard procedures that manufacturers routinely conduct under current regulations. No additional professional skills would be necessary to comply with this rule. However, current safety reviewers, analysts, and IT personnel would need training to implement MedDRA.

V.E.4. Alternatives and Steps To Minimize the Impact on Small Entities

The major objectives of this proposed rule are to harmonize FDA's safety reporting requirements with international initiatives and to improve the quality of safety reports. With these objectives in mind, the agency considered alternatives to this proposed rule.

V.E.4.a. *Do nothing.* The agency considered but rejected the option of not proposing this rule. The proposed rule would align FDA's safety report terms, formats and requirements for human drugs and biological products with the recommendations of ICH. With regard to use of a medical dictionary for safety reporting purposes, at the present time, major problems exist with comparing safety data globally because multiple medical dictionaries are being used internationally for coding of SADRs (see section III.F.2 of this document). In this rule, the agency proposes to require the use of MedDRA, the medical dictionary developed by ICH. FDA believes that "to do nothing" would be inconsistent with the agency's efforts to harmonize safety reporting with international initiatives.

Another objective of this proposed rule is to improve the quality of safety reports. In this preamble, the agency cited a substantial number of studies that estimate the number of SADRs that have resulted in a hospitalization or that occur in a hospital and the hospital costs related to SADRs. Safety reports that are complete are critical and necessary to reduce SADRs, medication errors, and hospital costs. This proposed rule would improve the agency's ability to monitor the safety of human drugs

and biological products. In light of this information, "to do nothing" would be inconsistent with the agency's mission of protecting public health.

V.E.4.b. *Do not require a medical dictionary.* The agency considered but rejected the alternative of not requiring the use of MedDRA terms in individual case safety reports. MedDRA is an integral part of the postmarket safety reporting system that was developed jointly with international stakeholders. Requiring MedDRA terms in safety reports will enhance the analysis of drug safety information. Moreover, MedDRA is a medical dictionary designed to translate terms in multiple languages, thus aiding in more expeditious and broader international drug use comparisons and analysis. Not requiring MedDRA would compromise the agency objective of improving drug safety reporting and analysis. In addition, continued use of multiple medical dictionaries to code SADRs will perpetuate the major problems with comparing safety data globally that currently exist.

V.E.4.c. *Do not require medication errors as expedited reports.* The agency considered but rejected the alternative of not requiring medication errors as expedited reports. Requiring expedited reports of medication errors would allow the agency to review critical information and take appropriate and more timely action on SADRs that are preventable. Not requiring expedited reports of medication errors would ignore a key step in reducing medical errors.

V.E.4.d. *Do not require blood establishments to submit reports for all serious SADRs associated with blood collection and transfusion.* The agency considered but rejected the alternative of not requiring blood establishments to submit reports for all serious SADRs associated with blood collection and transfusion, in addition to the current requirement to submit reports of fatalities. Because these establishments are currently required to conduct

investigations and prepare and maintain reports of serious SADRs, this proposal would impose minimal costs. However, only some serious SADRs must be reported in a timely manner. The agency believes it is critical that we receive all such reports. This would improve the agency's ability to take appropriate action to protect the blood supply more consistently, to enhance donor safety and to ensure the safety, purity and potency of blood and blood components for administration to patients.

V.E.4.e. *Do not require certain bioavailability and bioequivalence reports as expedited reports.* The agency considered but rejected the alternative of not requiring expedited reports of SADRs for bioavailability and bioequivalence studies not subject to an IND. This requirement would allow the agency quicker access to information and would facilitate appropriate action to protect those enrolled in clinical trials.

V.E.4.f. *Waivers for economic hardship.* The agency recognizes that requiring individual case safety reports to be coded using MedDRA will likely impose significant costs on some small firms (see section III.F.2 of this document). One alternative would be to consider the option of allowing companies to request a waiver from MedDRA coding, based on economic hardship. The agency is seeking comment on ways to reduce economic hardships of implementing MedDRA while maintaining adequate procedures to monitor and assess the safety of products.

V.E.4.g. *Small business outreach, training, and assistance.* The agency has received both written and verbal input from interested parties, including small businesses, on the recommendations of ICH regarding safety reporting for human drugs and biological products (e.g., the ICH E2A guidance, the ICH E2C guidance, and ICH M1). These public comments addressed published draft versions of the ICH guidances as well as numerous agency presentations