

within 30 calendar days of the previous filing. If the full data set is still not obtainable, the 30-day followup report must include all safety information obtained, highlighting new information and stating the reasons for the inability to obtain complete information. The agency estimates that 8 additional hours, as shown in table 14, are needed for these followup reports.

Applicants must also submit any new safety information to FDA for any other expedited or followup report within 15 days of receipt of the new information. This provision is currently required; therefore, no additional hours are allocated to this provision.

V.D.1.b.iii. *Blood products.* Collection and transfusing facilities are currently required to investigate, prepare, and maintain written reports of complaints of SARs arising as a result of blood collection or transfusion. Furthermore, if a fatality occurs as a complication of blood collection or transfusion, facilities must notify FDA as soon as possible and follow up with a written report within 7 calendar days after the fatality occurs. The proposed rule will require that all written reports submitted to the agency use the individual case safety report format. This change in reporting format is not expected to increase the time needed to prepare and submit reports of fatalities. In addition, the proposed rule will require that any serious nonfatal SAR related to collection or transfusion of blood and blood components be submitted as a expedited report within 45 calendar days. As shown in table 14, blood facilities may spend up to 16 hours more preparing and submitting each of these expedited reports.

V.D.1.b.iv. *IND and bioavailability/bioequivalence safety reports.* Sponsors of an IND are currently required to submit written and telephone safety reports. The proposed rule will add some conditions for reporting and require that reportable SADR include the minimum data set. Sponsors of INDs will be required to submit written safety reports to FDA and all participating investigators of: (1) Any SADR that, based on the opinion of either the sponsor or investigator, is both serious and unexpected and (2) any information that might materially influence the

benefit-risk assessment of an investigational drug or that would be sufficient to consider a change in either product administration or in the overall conduct of a clinical investigation. The agency is also expanding the current requirement for telephone and facsimile transmission of safety reports of unexpected death or life-threatening SADR to include those that meet these criteria based on the opinion of either the sponsor or investigator. In addition, the agency is making minor changes to align current IND safety reporting requirements with the proposed changes to postmarketing safety reporting.

The agency anticipates that very few investigator-initiated reports would be submitted under the proposed rule. Because the number of new reports (*i.e.*, approximately 10 per year) would represent less than 0.2 percent of all individual IND safety reports submitted to the agency in a year, no additional burden is estimated. However, up to 4 hours may be needed for sponsors to accommodate the new requirements for written safety reports for information sufficient to consider a change in product administration (see table 14).

In addition, the agency would require submission of expedited safety reports for certain bioavailability and bioequivalence studies that are exempt from submission of an IND. The agency estimates 14 hours per report are needed to comply (see table 14).

V.D.1.b.v. *Semiannual submissions of postmarketing individual case safety reports.* The current regulations require that postmarketing individual case safety reports from domestic marketing experience for serious expected adverse drug experiences, nonserious unexpected adverse drug experiences, and nonserious expected adverse drug experiences be submitted to the agency in postmarketing periodic safety reports. Under the proposed rule, most individual case safety reports not submitted to FDA as an expedited report would be submitted as a separate report twice a year. All reports of actual or potential medication errors, whether or not an SADR occurs, would be submitted as expedited reports and not submitted semiannually. Individual case safety reports of nonserious SADR

that are expected or listed would no longer be submitted to the agency. Exceptions, for vaccines, would be reports of nonserious, expected SARs and expected SARs with an unknown outcome, which would be submitted semiannually. Nevertheless, applicants would be expected to maintain these reports and include them in tabular summaries provided in the postmarketing periodic safety reports (*e.g.*, PSURs).

Whereas the current postmarketing periodic safety reporting regulations do not apply to foreign reports of SADR, the proposed rule would require that foreign individual case safety reports of serious and expected or listed SADR be submitted semiannually. The agency is unable to predict how many foreign reports may be submitted. For the purpose of this analysis, therefore, the number of nonserious and expected or listed individual case safety reports is assumed to be equal to the number of serious and expected or listed foreign reports, and the overall number of individual case safety reports submitted in a year would remain unchanged.

Although the number of individual case safety reports submitted annually as a postmarketing periodic safety report is expected to remain stable, the timing of these submissions may change. Reports will be submitted less frequently (semiannually rather than quarterly) for products that have been on the market for less than 3 years and more frequently (semiannually rather than annually) for products that have been on the market for more than 3 years. Furthermore, additional time may be needed for an active query to obtain a full data set for reports of serious and expected or listed SADR and a minimum data set for all SADR. Based on reports to AERS in 1998, the agency estimates that, on average, approximately 35 individual case safety reports may be submitted semiannually for each drug product. Regulatory affairs personnel and health professionals might spend up to 10 additional hours each to obtain and process information for each semiannual submission (see table 14).

TABLE 14.—ESTIMATED NEW BURDEN FOR EXPEDITED AND SEMIANNUAL REPORTS

Type of report	New or revised	New burden (hours)			
		Health professional	Regulatory affairs	Clerical	Total
<i>Expedited:</i>					
Serious and unexpected SADR .....	Revised .....	1	1	0	2
Always expedited report .....	New .....	2	12	2	16
Unexpected SADR with unknown outcome .....	New .....	3	18	3	24