

TABLE 13.—NUMBER OF AFFECTED REPORTS BY REGULATORY STATUS

Type of report	Drugs marketed without an approved application	NDA/AND	Biologics	Blood products	IND	Bioavailability and bioequivalence	Total
Expedited:							
Serious and unexpected SADRs	350	50,000	3,000	0	0	0	53,350
Always expedited report	50	1,500	100	0	0	0	1,650
Unexpected SADR with unknown outcome	46	912	25	0	0	0	983
Information sufficient to consider product administration changes ..	5	300	4	0	0	0	309
Medication errors	1,000	100,000	10,000	0	0	0	111,000
30-day followup	340	43,000	3,000	0	0	0	46,340
Serious SARs—blood products	0	0	0	7,000	0	0	7,000
IND Safety							
Information sufficient to consider product administration changes ..	0	0	0	0	600	0	600
Bioavailability/bioequivalence safety report	0	0	0	0	0	200	200
Periodic:							
TPSR	0	1,400	35	0	0	0	1,435
PSUR	0	2,500	35	0	0	0	2,535
ISUR	0	350	3	0	0	0	353
Individual case safety reports—semiannual submission	0	4,726	480	0	0	0	5,206
Other:							
Reports to manufacturer or applicant	4	4,548	100	0	0	0	4,652
Submit safety records to FDA upon request	2	15	4	0	0	0	21
Annual reports	0	2,363	69	0	0	0	2,432

V.D.1.b. *New time burden.* The proposed rule requires manufacturers and applicants to use active query to acquire the outcome (*i.e.*, whether an SADR is serious or nonserious) and required data set for any spontaneously reported individual case safety report that they receive pertaining to their marketed human drug or biological product. Furthermore, the proposed rule requires that every individual case safety report submitted to the agency be assigned an appropriate MedDRA code. Although individual case safety reports are currently submitted for most SADRs, depending on the type of SADR, the proposed rule may impose an additional burden on health professional personnel if active query is not already used routinely by a manufacturer or applicant. Regulatory affairs personnel working with the health professional may spend additional time assigning the MedDRA code and documenting the active query. The agency seeks comment on the reasonableness of the estimates of the time burden and the type of employee anticipated to fulfill the new requirements detailed in the following paragraphs.

V.D.1.b.i. *Expedited reports.* The nature of the SADR (*i.e.*, whether the SADR is expected or unexpected) and whether the outcome is known (*i.e.*,

SADR is serious or nonserious) will determine the data needed and when and if an individual case safety report should be submitted to FDA. At present, individual case safety reports of SADRs that are both serious and unexpected are submitted as 15-day alert reports.

The proposed rule adds conditions for determining expedited reports (*e.g.*, minimum data set required). In addition, it specifies that an expedited report for an individual case safety report must contain a full data set, including MedDRA codes, and that supporting documentation such as hospital discharge records, autopsy reports, or death certificates must be submitted, if available. This aspect of the proposal may impose a new burden estimated at 1 hour each for health professionals and regulatory affairs personnel (see table 14).

The proposal defines new criteria for determining when expedited reports should be submitted. Certain medically significant SADRs as listed in the proposal, whether unexpected or expected, and all domestic reports of actual and potential medication errors would be required to be submitted to FDA in an expedited manner.

Furthermore, when the outcome of a spontaneous, unexpected SADR cannot be determined, an expedited report must be submitted to the agency. In

these circumstances, manufacturers and applicants are assumed to allocate from 16 to 24 hours more time for health professionals and regulatory affairs and clerical personnel to prepare and submit these new reports. Table 14 lists the additional hours each type of employee may spend complying with these new requirements.

In addition to individual case safety reports, manufacturers and applicants may receive safety information from domestic or foreign studies that is judged to be sufficient to consider a change in product administration. In this case, the proposed rule requires that a narrative report of these findings be submitted to the agency as an expedited report. Preparing and submitting this new report may take up to 8 hours of time from health professionals and regulatory affairs and clerical personnel as shown in table 14.

V.D.1.b.ii. *Followup reports.* The proposed rule establishes timeframes and data elements required for submission of expedited individual case safety reports. If required data elements were not submitted with the initial filing of an expedited report of a serious SADR or a medication error report, then the applicant must continue to use active query to obtain the additional information. This information must be submitted to FDA in a followup report