

unexpected, whether foreign or domestic, as soon as possible, but in no case later than 15 calendar days after receipt by the manufacturer of the minimum data set for the serious, unexpected SADR. If a full data set is not available for the serious and unexpected SADR report at the time of initial submission of the report to FDA, the manufacturer must submit the information required under paragraph (c)(1)(iv) of this section and also submit a 30-day followup report as required by paragraph (c)(2)(vi) of this section.

(ii) *Information sufficient to consider product administration changes.* The manufacturer must also report to FDA information, received or otherwise obtained, whether foreign or domestic, that would be sufficient, based upon appropriate medical judgment, to consider changes in product administration. The manufacturer must submit this information to FDA, as soon as possible, but in no case later than 15 calendar days after determination by the manufacturer that the information qualifies for expedited reporting. Examples of such information include any significant unanticipated safety finding or data in the aggregate from an in vitro, animal, epidemiological, or clinical study, whether or not conducted under an investigational new drug application (IND), that suggests a significant human risk, such as reports of mutagenicity, teratogenicity, or carcinogenicity, or reports of a lack of efficacy with a drug product used in treating a life-threatening or serious disease. The manufacturer must maintain a record of its efforts to determine whether the information required to be reported under this paragraph qualifies for expedited reporting.

(iii) *Unexpected SADR with unknown outcome.* The manufacturer must also report to FDA each SADR that is unexpected and for which the determination of an outcome is unattainable (*i.e.*, SADR with unknown outcome) within 45 calendar days after initial receipt by the manufacturer of the minimum data set for the unexpected SADR. The manufacturer must document in the expedited report the reason(s) for the inability to determine the outcome.

(iv) *Always expedited report.* (A) The manufacturer must also report to FDA each SADR, received or otherwise obtained, whether foreign or domestic, that is the subject of an always expedited report. These reports must be submitted to FDA as soon as possible, but in no case later than 15 calendar days after receipt by the manufacturer of the minimum data set for the report.

The following medically significant SADRs, which may jeopardize the patient or subject and/or require medical or surgical intervention to treat the patient or subject, are subject to an always expedited report:

- (1) Congenital anomalies,
- (2) Acute respiratory failure,
- (3) Ventricular fibrillation,
- (4) Torsades de pointe,
- (5) Malignant hypertension,
- (6) Seizure,
- (7) Agranulocytosis,
- (8) Aplastic anemia,
- (9) Toxic epidermal necrolysis,
- (10) Liver necrosis,
- (11) Acute liver failure,
- (12) Anaphylaxis,
- (13) Acute renal failure,
- (14) Sclerosing syndromes,
- (15) Pulmonary hypertension,
- (16) Pulmonary fibrosis,
- (17) Confirmed or suspected

transmission of an infectious agent by a marketed drug or biological product,

(18) Confirmed or suspected endotoxin shock, and

(19) Any other medically significant SADR that FDA determines to be the subject of an always expedited report (*i.e.*, may jeopardize the patient or subject and/or require medical or surgical intervention to treat the patient or subject).

(B) SADRs that are the subject of an always expedited report must be submitted to FDA whether unexpected or expected and whether or not the SADR leads to a serious outcome. If a full data set is not available for an always expedited report at the time of initial submission of the report to FDA, the manufacturer must submit the information required under paragraph (c)(1)(iv) of this section and also submit a 30-day followup report as required by paragraph (c)(2)(vi) of this section.

(v) *Medication errors*—(A) *Actual medication error.* The manufacturer must also submit to FDA each domestic report of an actual medication error, received or otherwise obtained, as soon as possible, but in no case later than 15 calendar days after receipt by the manufacturer of the minimum data set for a report of an SADR or, if an SADR does not occur, the minimum information described under paragraph (c)(1)(iii)(B) of this section (*i.e.*, identifiable patient, identifiable reporter, and suspect drug product).

(B) *Potential medication error.* The manufacturer must also submit to FDA each domestic report of a potential medication error, received or otherwise obtained, as soon as possible, but in no case later than 15 calendar days after receipt by the manufacturer of the minimum information described under

paragraph (c)(1)(iii)(C) of this section (*i.e.*, identifiable reporter and suspect drug product).

(C) *Full data set.* If a full data set is not available for an actual or potential medication error report at the time of initial submission of the report to FDA, the manufacturer must submit the information required under paragraph (c)(1)(iv) of this section and also submit a 30-day followup report as required by paragraph (c)(2)(vi) of this section.

(vi) *The 30-day followup report.* The manufacturer must use active query to obtain additional information for any expedited report under paragraphs (c)(2)(i), (c)(2)(iv), and (c)(2)(v) of this section that does not contain a full data set and must submit a followup report to FDA within 30 calendar days after initial submission of the expedited report to FDA by the manufacturer. If a full data set is still not obtainable, the 30-day followup report must contain the information required under paragraph (c)(1)(iv) of this section. Any new safety information in the 30-day followup report must be highlighted. Any new information, received or otherwise obtained, after submission of a 30-day followup report must be submitted to FDA as a 15-day followup report under paragraph (c)(2)(vii) of this section.

(vii) *The 15-day followup report.* The manufacturer must report to FDA any new information, received or otherwise obtained, for any expedited or followup report (except for initial expedited reports under paragraphs (c)(2)(i), (c)(2)(iv), and (c)(2)(v) of this section that do not contain a full data set) within 15 calendar days of initial receipt of the new information by the manufacturer. Expedited reports under paragraphs (c)(2)(i), (c)(2)(iv), and (c)(2)(v) of this section that do not contain a full data set at the time of initial submission of the report to FDA are subject to the 30-day followup reporting requirements under paragraph (c)(2)(vi) of this section rather than the 15-day followup reporting requirements under this paragraph.

(viii) *Supporting documentation.* (A) If the patient dies, the manufacturer must submit a copy of the autopsy report to FDA, if it is available. If an autopsy report is not available, the manufacturer must submit a death certificate to FDA. If an autopsy report becomes available after the manufacturer has submitted a death certificate to the agency, the autopsy report must be submitted to FDA. If the patient was hospitalized, the manufacturer must submit a copy of the hospital discharge summary to FDA, if it is available. If any of these documents is not in English, the document must be