

in the case of a 505(b)(2) application, an effective approved application" with the phrase "under section 505(c) of the act." Although NDAs, including those referred to in section 505(b)(2) of the Federal Food, Drug and Cosmetic Act (the act) (21 U.S.C. 355(b)(2)) are filed under section 505(b)(1) of the act, they are approved under section 505(c) of the act. FDA is proposing to use the phrase "section 505(c) of the act" because it more appropriately references the cite for approval of NDAs.

The agency is proposing to remove the phrase "in the case of a 505(b)(2) application, an effective approved application" because FDA no longer issues approvals with a delayed effective date for 505(b)(2) applications, as it did at the time this regulation was issued. The agency now issues tentative approvals for 505(b)(2) applications when the (final) approval is blocked by patent or exclusivity rights. As described in the preamble to the final rule on "Abbreviated New Drug Application Regulations; Patent and Exclusivity Provisions" (59 FR 50338 at 50351 to 50352, October 3, 1994), a 505(b)(2) application that has a tentative approval is not approved for marketing until a final approval letter for the drug product is received from FDA. Thus, applicants having a 505(b)(2) application with a tentative approval would not be subject to the postmarketing safety reporting

requirements under § 314.80 until final approval of the application is in effect. For consistency, FDA is proposing a similar change to § 314.98(a).

III.C.3. Reporting Requirements

Current postmarketing safety reporting requirements at §§ 310.305(c), 314.80(c), and 600.80(c) state that persons subject to these requirements shall report to FDA adverse drug experience information as described under these sections. FDA is proposing to remove these provisions from its postmarketing safety reporting regulations because they are redundant (see proposed §§ 310.305(c), 314.80(c), and 600.80(c)).

Current postmarketing safety reporting requirements at §§ 314.80(c) and 600.80(c) state that two copies of each report must be submitted to FDA. For drug products, proposed § 314.80(c) would require that applicants submit to FDA two copies of each postmarketing expedited report and one copy of each postmarketing periodic safety report of an individual case safety reports—semiannual submission pertaining to its product (see tables 6 and 7 for proposed postmarketing expedited and periodic safety reports). For nonvaccine biological products, proposed § 600.80(c) would require that applicants submit to FDA two copies of each postmarketing expedited report and each postmarketing periodic safety

report of an individual case safety reports—semiannual submission pertaining to its product. For drugs and nonvaccine biologics, proposed §§ 314.80(c) and 600.80(c) would also require that one copy of a PSUR, IPSR, or TPSR be submitted to FDA along with one copy for each approved application for a human drug or licensed biological product (e.g., NDA, ANDA, BLA) covered by the report (see table 7 for proposed postmarketing periodic safety reports). For vaccines, proposed § 600.80(c) would require that applicants submit to VAERS two copies of each safety report required under § 600.80 and pertaining to its product. These proposed amendments would provide FDA with enough copies of safety reports for efficient review by the agency. Electronic submission of these reports will obviate the need for submission of two copies. At this time, manufacturers and applicants can voluntarily submit certain postmarketing safety reports in an electronic format (see Docket 92S-0251 regarding postmarketing expedited and periodic individual case safety reports; available on the Internet at <http://www.fda.gov/ohrms/dockets/dockets/92s0251/92s0251.htm>). Capabilities for electronic submission of other postmarketing safety reports (e.g., safety reports for vaccines) will be available in the future.

TABLE 6.—PROPOSED POSTMARKETING EXPEDITED SAFETY REPORTS

Expedited Safety Report	Type of Information	Submission to FDA—Timeframe	Persons with Reporting Responsibility	Reference in Section III of this Document
Serious & unexpected SADRs.	Individual case safety reports.	15 calendar days.	Manufacturers and applicants.	D.1
Information sufficient to consider product administration changes.	Information based upon appropriate medical judgment. For example, any significant unanticipated safety finding or data in the aggregate from an in vitro, animal, epidemiological, or clinical study that suggests a significant human risk.	15 calendar days.	Manufacturers and applicants.	D.2
Unexpected SADRs with unknown outcome.	Individual case safety reports of unexpected SADRs for which a determination of serious or nonserious cannot be made..	45 calendar days.	Manufacturers and applicants.	D.3
Always expedited reports.	Individual case safety reports of certain medically significant SADRs whether unexpected or expected and whether or not the SADR leads to a serious outcome.	15 calendar days.	Manufacturers and applicants.	D.4
Medication errors	All domestic reports of medication errors, whether actual or potential..	15 calendar and days.	Manufacturers and applicants.	D.5
30-day followup ...	Followup report for initial serious and unexpected SADR reports, always expedited reports and medication error reports that do not contain a full data set.	30 calendar days.	Manufacturers and applicants.	D.6
15-day followup ...	New information for expedited or followup reports, except initial expedited reports for which 30-day followup reports must be submitted.	15 calendar days.	Manufacturers and applicants.	D.6
SADR reports to manufacturer.	All SADRs	5 calendar days to manufacturer.	Contractors	D.9
SADR reports to applicant.	All SADRs	5 calendar days to applicant.	Contractors and shared manufacturers.	D.9