

### E. Benefits of the Proposed Rule

The proposed rule would generate economic benefits both for individuals and for society as a whole to the extent that the reporting of data from all BE studies would prevent product discontinuation and adverse health effects. Also, the data from additional BE studies could provide valuable scientific information, thereby increasing the agency's understanding of bioequivalence and generic drug development issues, and improving the drug approval process. Therefore, this proposed rule would permit FDA to make more informed BE determinations in the future.

### X. Paperwork Requirements

This proposed rule contains information collection requirements that are subject to review by OMB under the Paperwork Reduction Act of 1995 (44 U.S.C. 3501–3520). A description of these requirements is given below with an estimate of the annual reporting burden. Included in this estimate is the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing each collection of information.

With respect to the following collection of information, FDA invites comments on: (1) Whether the proposed collection of information is necessary for proper performance of FDA's functions, including whether the information will have practical utility; (2) the accuracy of FDA's estimate of the burden of the proposed collection of information, including the validity of the methodology and assumptions used; (3) ways to enhance the quality, utility, and clarity of the information to be collected; and (4) ways to minimize the burden of the collection of information on respondents, including through the use of automated collection techniques, when appropriate, and other forms of information technology.

*Title:* Requirements for Submission of In Vivo Bioequivalence Data; Proposed Rule.

*Description:* FDA is proposing to alter the requirements for certain ANDAs, ANDA amendments, and ANDA supplements submitted under §§ 314.94, 314.96, and 314.97. Specifically, FDA is proposing to amend §§ 314.94(a)(7)(i), 314.96(a)(1), and 320.21(b)(1), as well as modify the requirements of § 320.21(c) (which refers to § 320.21(b)(1)), to require an ANDA applicant to submit information from all BE studies, both passing and nonpassing, conducted by the applicant on the same formulation of the drug product submitted for approval under an ANDA, amendment, or supplement.

In addition, FDA is proposing through this rulemaking to interpret § 314.94(a)(7)(ii) as requiring that ANDA applicants who submit ANDAs under a petition approved under § 314.93 submit information on all bioavailability or BE studies conducted on the same drug product formulation submitted for approval.

FDA is also proposing to clarify through this rulemaking that it intends to interpret § 314.81(b)(2)(vi) as requiring the submission of postmarketing reports of all BE studies conducted or otherwise obtained by ANDA applicants in the applicant's annual report. However, as discussed in section IV.C of this document, FDA believes it would be highly unusual that an applicant would conduct a postmarketing BE study. In particular, the agency believes that an applicant would rarely, if ever, conduct a postmarketing BE study, other than one required for an ANDA supplement.

*Description of Respondents:* Persons and businesses, including small businesses and manufacturers.

*Burden Estimate:* Table 1 of this document provides an estimate of the annual reporting burden under the proposed rule.

The proposed rule would affect establishments that submit ANDAs. FDA does not know the precise number of entities, either large or small, that will submit ANDAs in the future. In the year 2000, 57 applicants submitted 346 BE studies in 197 ANDAs, amendments,

and supplements. FDA estimates that this proposed rule would result in a 10 percent increase in the number of BE studies submitted annually, or 35 (346 x 0.10) additional studies. This estimate is based on the assumptions that approximately 20 percent of all BE studies conducted produce results that do not meet bioequivalence limits and that about half of these studies are conducted on formulations that are not submitted for approval.

FDA estimates it would require approximately 120 hours of staff time to prepare and submit each additional complete BE study report and approximately 60 hours of staff time for each additional BE summary report. The agency believes that a complete report would be required approximately 20 percent of the time, while a summary would suffice approximately 80 percent of the time. Based on a weighted-average calculation using the information presented above, the submission of each additional BE study is expected to take 72 hours of staff time  $([120 \times 0.2] + [60 \times 0.8])$ .

In table 1, FDA has estimated the reporting burden associated with each section of the proposed rule. FDA believes that the vast majority of additional BE studies would be reported in ANDAs (submitted under § 314.94) rather than supplements (submitted under § 314.97) because it is unlikely that a sponsor will conduct BE studies with a drug after the drug has been approved. Moreover, drugs approved under an ANDA prior to the effective date of the final rule would only be required to report additional BE studies conducted after the effective date, which should not result in the submission of many BE study reports in supplements. With respect to the reporting of additional BE studies in amendments (submitted under § 314.96), this should also account for a small number of reports because most BE studies would be conducted on a drug prior to the submission of the ANDA and would be reported in the ANDA itself.

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN<sup>1</sup>

21 CFR Section	No. of Respondents	Annual Frequency of Response	Total Annual Responses	Hours per Response	Total Hours
314.94(a)(7)	33	1	33	72	2,376
314.96(a)(1)	1	1	1	72	72
314.97	1	1	1	72	72
Total					2,520

<sup>1</sup>There are no capital costs or operating and maintenance costs associated with this collection of information.