Guidance for Industry

Bioequivalence Recommendations for Specific Products

DRAFT GUIDANCE

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For questions regarding this draft document contact (CDER) Doan T. Nguyen, 301-827-0495.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)

May 2007
OGD

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Bioequivalence Recommendations for Specific Products

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I. INTRODUCTION

This guidance describes FDA's process for making available to the public FDA guidance on how to design bioequivalence (BE) studies for specific drug products to support abbreviated new drug applications (ANDAs). Under this process, applicants planning to carry out such studies in support of their ANDAs will be able to access BE study guidance on the FDA Web site, rather than having to request this information from the Agency and wait for the Agency to respond, as has been the case in the past. The FDA believes that making this information available on the Internet will streamline the guidance process, making it more efficient than the previous process. This process also will provide a meaningful opportunity for the public to consider and comment on BE study recommendations for specific drug products.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

A. What Are BE Studies?

To receive approval for an ANDA, an applicant generally must demonstrate, among other things, that its product has the same active ingredient, dosage form, strength, route of administration and conditions of use as the listed drug, and that the proposed drug product is bioequivalent to the reference listed drug (21 U.S.C. 355(j)(2)(A); 21 CFR 314.94(a)). Bioequivalent drug products show no significant difference in the rate and extent of absorption of the therapeutic ingredient (21 U.S.C. 355(j)(8); 21 CFR 320.1(e)). BE studies are undertaken in support of ANDA submissions

[1] This guidance has been prepared by the Office of Generic Drugs in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration.

with the goal of demonstrating BE between a proposed generic drug product and its reference listed drug. The regulations governing BE are provided at 21 CFR in part 320.

B. How Did the Agency Make This Information Available in the Past?

Previously, the Office of Generic Drugs (OGD) provided guidance on how to design BE studies for specific products only when asked for assistance by interested parties. We had determined that making recommendations to interested parties about how to design BE studies would help the generic drug industry, the innovator drug industry, contract research organizations, academia, and others understand the Agency's expectations with regard to demonstrating bioequivalence. In most cases, the requested information was not available anywhere else, and, in some cases, OGD performed its own research before responding to an interested party's request for product-specific information. In many cases, OGD responded to individual requests for information on BE studies in letter format after specific recommendations were prepared within the Center for Drug Evaluation and Research (CDER). This meant that information about BE studies was only being provided to those specifically requesting such information. In addition, the staff developing the recommendations and responding to requests for information have been the same individuals who are responsible for reviewing the BE data in ANDAs. With the increase in the number of ANDA submissions and in the requests for BE information during the last few years, the process of providing BE recommendations has become extremely time consuming for the Agency.

In 2000, to help address this growing problem, FDA issued the guidance *Bioavailability and Bioequivalence Studies for Orally Administered Drug Products – General Considerations*, which describes general recommendations for demonstrating bioequivalence. These general recommendations were helpful, but many parties have continued to seek assistance from the Agency in designing their product-specific BE studies, as certain drug products may raise BE issues not squarely addressed in more general guidance. As a result, after exploring various mechanisms that would allow us to conserve our resources while responding to the needs of industry and other interested persons, OGD has developed a new approach to making guidance available on product-specific BE studies. As before, BE recommendations will be developed by the agency based on its understanding of the characteristics of the listed drug, information derived from published literature, agency research, and consultations within different offices in CDER as needed based upon the novelty or complexity of the BE considerations. Once developed, BE recommendations for specific drug products will be made available through the process described here.

III. PROCEDURES FOR MAKING RECOMMENDATIONS AVAILABLE

To streamline the process for making guidance available to the public on how to design product-specific BE studies, the Agency intends to use the following process:

- Product-specific BE recommendations will be developed and posted on the Internet on the CDER guidance page in draft to facilitate public comment.
- The recommendations can be viewed by clicking on the URL associated with this guidance on the CDER guidance page or on the Office of Generic Drugs Page (see

www.fda.gov/cder/ogd/index.htm). Users can also search for a specific product BE recommendation using the search tool on the guidance page.

- Newly posted draft and final BE recommendations will be announced in the New/Revised/Withdrawn list, which is posted monthly on the CDER guidance page.
- The Agency will issue a notice in the *Federal Register* (FR) announcing the availability on the FDA Web site of new product-specific draft and final BE recommendations. The notice will identify a comment period for the recommendations.
- Comments on product-specific BE recommendations will be considered in developing final BE recommendations.
- The BE recommendations will be revised as appropriate to ensure that the most up-to-date BE information is available to the public.