Products, Animal Plasma or Serum-Derived Products.'' This guidance document provides general information for the preparation of CMC and establishment description sections of the BLA, revised Form FDA 356h, which is currently being implemented for human plasma-derived biological products, animal plasma or serum-derived products. This guidance document supersedes the draft guidance entitled ''Guidance for Industry: For the Submission of Chemistry, Manufacturing and Controls and Establishment Description Information for Human Plasma-Derived Biological Products or Animal Plasma or Serum-Derived Products'' that was announced in the **Federal Register** of January 21, 1998 (63 FR 3145).

In the **Federal Register** of July 8, 1997 (62 FR 36558), FDA announced the availability of a revised Form FDA 356h that will be used as a single harmonized application form for all drugs and licensed biological products. Manufacturers may voluntarily begin using this form for human plasma-derived biological products, animal plasma or serum-derived products. FDA will announce in the future when manufacturers are required to use this form for all products. Use of the new harmonized Form FDA 356h will allow a biologic product manufacturer to submit one BLA instead of two separate license applications (product license application and establishment license application).

This guidance document represents the agency's current thinking on the content and format of the CMC and establishment description information section of a BLA for human plasma-derived biological products, animal plasma or serum-derived products. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both. As with other guidance documents, FDA does not intend this guidance document to be all-inclusive and cautions that not all information may be applicable to all situations. The guidance document is intended to provide information and does not set forth requirements.

II. Comments

Interested persons, may at any time, submit to the Dockets Management Branch (address above) written comments regarding this guidance document. Two copies of any comments are to be submitted, except individuals may submit one copy. Comments should be identified with the docket number found in the brackets in the heading of this document. A copy of the guidance document and received comments are available for public examination in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

III. Electronic Access

Persons with access to the Internet may obtain the guidance document using the World Wide Web (WWW). For WWW access, connect to CBER at ''http://www.fda.gov/cber/guidelines.htm''.

Dated: February 5, 1999.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

[FR Doc. 99–3715 Filed 2–16–99; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 99D–0121]

Draft Guidance for Industry on Waiver of In Vivo Bioavailability and Bioequivalence Studies for Immediate Release Solid Oral Dosage Forms Containing Certain Active Moieties/ Active Ingredients Based on a Biopharmaceutics Classification System; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry entitled ''Waiver of In Vivo Bioavailability and Bioequivalence Studies for Immediate Release Solid Oral Dosage Forms Containing Certain Active Moieties/Active Ingredients Based on a Biopharmaceutics Classification System.'' When final, the guidance will provide recommendations to sponsors of investigational new drug applications (IND's) and applicants submitting new drug applications (NDA's), and abbreviated new drug applications (ANDA's) who intend to perform bioavailability and bioequivalence (BA/BE) studies for immediate release solid oral products during either the preapproval or postapproval periods.

DATES: Written comments on the draft guidance document may be submitted by April 19, 1999. General comments on the agency guidance documents are welcome at any time.

ADDRESSES: Copies of this draft guidance for industry are available on the Internet at http://www.fda.gov/cder/guidance/index.htm. Submit written requests for single copy of the draft guidance for industry entitled ''Waiver of In Vivo Bioavailability and Bioequivalence Studies for Immediate Release Solid Oral Dosage Forms Containing Certain Active Moieties/ Active Ingredients Based on a Biopharmaceutics Classification System'' to the Drug Information Branch (HFD–210), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857. Send one self-addressed adhesive label to assist that office in processing your requests. Submit written comments on the draft guidance to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: Ajaz S. Hussain, Center for Drug Evaluation and Research (HFD–940), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–5927.

SUPPLEMENTARY INFORMATION: FDA is announcing the availability of a draft guidance for industry entitled ''Waiver of In Vivo Bioavailability and Bioequivalence Studies for Immediate Release Solid Oral Dosage Forms Containing Certain Active Moieties/ Active Ingredients Based on a Biopharmaceutics Classification System.'' When it becomes final, this guidance for industry will provide recommendations on when in vivo BA/BE studies may be waived for NDA's and ANDA's submitted to the Center for Drug Evaluation and Research during either the preapproval or postapproval period.

In 1974, the Office of Technology Assessment's Drug Bioequivalence Study Panel made eleven recommendations, one of which stated:

> It is neither feasible nor desirable that studies of bioavailability be conducted for all drugs or drug products. Certain classes of drugs for which evidence of bioequivalence is critical should be identified. Selection of these classes of drugs should be based on clinical importance, ratios of therapeutic to toxic concentrations in blood, and certain pharmaceutical characteristics.

Based on this and other recommendations of the panel, FDA proposed and finalized regulations in 1977 entitled ''Bioequivalence Requirements and In Vivo Bioavailability Procedures'' (42 FR 1624, January 7, 1977). In these regulations, now at 21 CFR 320.33, under the title ''Criteria and Evidence to

Assess Actual or Potential Bioequivalence Problems,'' FDA provided criteria to assess actual or potential BE problems. Drug products meeting these criteria were deemed ''bioproblem'' drug products, with the understanding that other drug products would be able to document BA/BE through in vitro studies. FDA applied these criteria to decide whether a Drug Efficacy Study Implementation (DESI) effective drug could demonstrate bioequivalence through in vitro studies alone, or whether a combination of in vivo and in vitro approaches were required. The list of DESI effective bioproblem drug products appeared in § 320.22 (21 CFR 320.22) (1992). Beginning in 1979, DESI effective oral immediate release drug products that were not considered to contain bioproblem drugs were allowed to document BE via in vitro studies and achieved an AA rating in FDA's ''Approved Drug Products with Therapeutic Equivalence Ratings'' (the Orange Book). In a 1981 document (46 FR 27396, May 19, 1981), FDA instituted a policy termed the ''paper NDA policy,'' which provided for approval of some duplicate versions of post-1962 drugs. As part of this policy, FDA required demonstration of in vivo BE for all duplicate post-1962 nonsolution drug products, including locally acting drug products, prior to approval for marketing. With the passage of the Drug Price Competition and Patent Term Restoration Act of 1984 (Waxman-Hatch), this general approach was recommended for all post-1962 nonsolution drug products (54 FR 28872 at 28882 through 28883, July 10, 1989).

Although the approach to require in vivo documentation of BA/BE for many drug products, both pre- and post-1962, has been generally followed, FDA has in some cases allowed in vitro methods for documenting BA/BE even for post-1962 drug products. Furthermore, as noted both at § 320.22 ''Criteria for Waiver of Evidence of In Vivo Bioavailability or Bioequivalence'' and at 21 CFR 320.24 ''Types of Evidence to Establish Bioavailability or Bioequivalence,'' many options exist to allow waivers of in vivo documentation of BA/BE and to demonstrate BA/BE through in vitro methodology. The draft guidance describes when waivers of in vivo BA/BE studies will be allowed under specified circumstances depending on the solubility, intestinal permeability, and dissolution characteristics of the drug substance and the drug product and based on the biopharmaceutic classification system.

To further justify the objective of reducing regulatory burden while maintaining adequate documentation of BA/BE, FDA encourages the submission of data that support or refute the recommendations in the guidance, specifically the submission of in vivo and in vitro data that document bioinequivalence of pharmaceutically equivalent immediate release products that are rapidly dissolving, and contain a highly permeable, and highly soluble drug.

Following receipt of public comments on this draft guidance, FDA intends to discuss the draft guidance before a meeting of the Advisory Committee for Pharmaceutical Science. After receipt of the public comments, the advisory committee deliberation, and further discussion within the agency, the guidance document will be finalized. FDA does not recommend that any provisions of the draft guidance be implemented at this time.

This draft level 1 guidance document is being issued consistent with FDA's good guidance practices (62 FR 8961, February 27, 1997). It represents the agency's current thinking on BA/BE approaches for immediate release solid oral products. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statute, regulations, or both.

Interested persons may submit written comments on the draft guidance to the Dockets Management Branch (address above). Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The draft guidance and received comments are available for public examination in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

Dated: February 10, 1999.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

[FR Doc. 99–3777 Filed 2–16–99; 8:45 am]

BILLING CODE 4160–01–F

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 96D–0067]

Guidance for Industry on Clinical Development Programs for Drugs, Devices, and Biological Products for the Treatment of Rheumatoid Arthritis (RA); Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a guidance for industry entitled ''Clinical Development Programs for Drugs, Devices, and Biological Products for the Treatment of Rheumatoid Arthritis (RA).'' This guidance is intended to assist developers of drugs, biological products, or medical devices intended for the treatment of rheumatoid arthritis (RA). It provides guidance on the types of claims that could be considered for such products and on clinical evaluation programs that could support those claims. The guidance also contains recommendations on the timing, design, and conduct of preclinical and clinical trials for RA products and on special considerations for juvenile RA.

DATES: General comments on agency guidance documents are welcome at any time.

ADDRESSES: Copies of the guidance are available on the Internet at ''http://www.fda.gov/cder/guidance/index.htm'', or ''http://www.fda.gov/cber/guidelines.htm''. Submit written requests for single copies of the guidance for industry to the Drug Information Branch (HFD–210), Center for Drug Evaluation and Research (CDER), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, or Office of Communication, Training and Manufacturers Assistance (HFM–40), Center for Biologics Evaluation and Research (CBER), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852–1448. Call 888–CBERFAX or 301–827–3844 for copies by fax or CBER's Voice Information System at 800–835–4709 or 301–827–1800 for copies by mail. Send one self-addressed adhesive label to assist the offices in processing your requests. Submit written comments on the guidance to the Dockets Management Branch (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852.

FOR FURTHER INFORMATION CONTACT: