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 The draft guidance describes when waivers of in vivo BA/BE studies will be allowed under specified circumstances depending on the solubility, intestinal permeability, and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:

Kent R. Johnson, Center for Drug Evaluation and Research (HFD–550), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–2080; or
Jeffrey N. Siegel, Center for Biologics Evaluation and Research (HFM–582), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852, 301–827–5094; or
Sahar M. Dawisha, Center for Devices and Radiological Health (HFZ–410), Food and Drug Administration, 9200 Corporate Blvd., Rockville, MD 20850, 301–594–3091, ext. 196, FAX 301–594–2358.

SUPPLEMENTARY INFORMATION: 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).'' The guidance contains recommendations on the timing, design, and conduct of preclinical and clinical trials for RA products and on special considerations for juvenile RA.

This guidance has been under development since 1995. The first version of the guidance was completed in March 1996. An additional section on juvenile RA was added in May of that year. A second version was completed in January 1997. Two public workshops have been held on the topic, on March 27, 1996, and on July 23, 1996. On February 5, 1997, the draft guidance was discussed at a meeting of the Arthritis Advisory Committee. Another draft version, published for comment on March 18, 1998 (63 FR 13259), incorporated suggestions made during the February 5, 1997, Arthritis Advisory Committee. In developing this final version of the guidance, FDA considered comments submitted to the docket on the March 18, 1998, draft guidance.

This guidance represents the agency's current thinking on RA. 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, at any time, submit to the Dockets Management Branch (address above) written comments on the guidance. Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments and requests are to be identified with the docket number found in brackets in the heading of this document. The guidance and received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

Dated: February 10, 1999.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Health Care Financing Administration

[HCFA–4008–N]

Medicare Program; Establishment of the Citizens Advisory Panel on Medicare Education and Requests for Nominations for Members

AGENCY: Health Care Financing Administration (HCFA), HHS.

ACTION: Notice.

SUMMARY: Pursuant to Public Law 92–463, the Federal Advisory Committee Act (FACA), the Department of Health and Human Services (DHHS) announces the establishment by the Secretary of the Citizens Advisory Panel on Medicare Education (CAP–ME). The Secretary, DHHS, signed the charter establishing the Committee on January 21, 1999. This notice also requests nominations for members for the panel. The Committee shall terminate on January 22, 2001, unless the Secretary, DHHS, formally determines that continuance is in the public interest.

This Committee shall advise and make recommendations to the Secretary, DHHS, and the Administrator of the Health Care Financing Administration (HCFA) on opportunities for HCFA to make more effective use of its National Medicare Education Program and other HCFA programs that help Medicare beneficiaries understand the expanded range of Medicare options available with the passage of the Medicare+Choice program.

DATES: Nominations for members will be considered if we receive them at the appropriate address, as provided below, no later than 5:00 p.m. on April 5, 1999.

ADDRESSES: You may mail or deliver nominations for membership to the following address: Linda Levin, Center for Beneficiary Services, Health Care Financing Administration, 7500 Security Boulevard, Room S1–08–07, Baltimore, MD 21244-1850.

A request for a copy of the Secretary's charter for the CAP–ME should be submitted to Eric Katz, J.D., Center for Beneficiary Services, Health Care Financing Administration, 7500 Security Boulevard, Room S1–08–07, Baltimore, MD 21244-1850, (410) 786–6477, or by e-mail to ekatz@hcfa.gov.

FOR FURTHER INFORMATION CONTACT: Eric Katz, (410) 786–6477.

SUPPLEMENTARY INFORMATION:

I. Background and Legislative Authority

The Citizens Advisory Panel on Medicare Education (CAP–ME) is governed by provisions of Public Law 92–463 as amended (5 U.S.C. Appendix 2), which sets forth standards for the formulation and use of advisory committees. The Secretary, DHHS, has found that the CAP–ME is necessary and in the public interest.

The CAP–ME will consist of 10 appointed members from among authorities in disability and chronic disease interests, minority populations, health consumer interests, seniors' organizations, health communications and policy, research and philanthropic organizations, health insurers and plans, employer groups, and health providers.

The CAP–ME will focus its review on the National Medicare Education Program and our other efforts to help Medicare beneficiaries and those who assist them find accurate and current information about new Medicare options and benefits under the Medicare+Choice program. The committee will also identify best practices in consumer health education that could enhance our efforts to inform and assist Medicare beneficiaries about their health plan options. An annual report to our Administrator will summarize the panel's findings and any recommendations the panel may provide.

We are requesting nominations for voting members to serve on the CAP–ME. We have a special interest in ensuring that women, minority groups, and physically challenged individuals are adequately represented on the advisory committee and, therefore, encourage nominations of qualified candidates from these groups. We also seek to ensure geographic diversity in the composition of the panel.

All nominations and curricula vitae for the CAP-ME should be sent to Linda Levin at the address in the **ADDRESSES** section of this notice.

II. Criteria for Members

Persons nominated for membership should have expertise in one or more of the following areas: disability and chronic disease interests, minority populations, health consumer interests, seniors' organizations, health