ESTIMATED ANNUAL REPORTING BURDEN[1]—Continued

	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Hours per Response	Total Hours
≤Requests for Tier-Two Dispute Resolution	5	1	5	8	40
Total					790

[1] There are no capital costs or operating and maintenance costs associated with this collection.

In the **Federal Register** of September 5, 2003 (68 FR 52777), FDA announced the availability of a draft guidance for industry entitled ''Formal Dispute Resolution: Scientific and Technical Issues Related to Pharmaceutical CGMP.'' The notice requested comments on the information collection estimates within 60 days. No comments were received on the information collection estimates. This document requests comments on the information collection burden that FDA estimates will result from the draft guidance.

The draft guidance was drafted as part of FDA's initiative ''Pharmaceutical cGMPs for the 21st Century: A Risk-Based Approach,'' which was announced in August 2002. The initiative focuses on FDA's current CGMP program and covers the manufacture of veterinary and human drugs, including human biological drug products. The agency formed the DR Working Group comprising representatives from ORA, the Center for Drug Evaluation and Research, the Center for Biologics Evaluation and Research, and the Center for Veterinary Medicine. The working group met weekly on issues related to the DR process and met with stakeholders in December 2002 to seek their input.

The draft guidance was initiated in response to industry's request for a formal DR process to resolve differences related to scientific and technical issues that arise between investigators and pharmaceutical manufacturers during FDA inspections of foreign and domestic manufacturers. In addition to encouraging manufacturers to use currently available DR processes, the draft guidance describes a formal two-tiered DR process that provides a formal mechanism for requesting review and decision on issues that arise during inspections:

- Tier-one of the DR process provides a mechanism to raise scientific or technical issues to the ORA and center levels.
- Tier-two of the DR process provides a mechanism to raise scientific or technical issues to the agency's DR Panel for Scientific and Technical Issues Related to Pharmaceutical CGMP (DR Panel).

The draft guidance also covers the following topics:

- The suitability of certain issues for the formal DR process, including examples of some issues with a discussion of their appropriateness for the DR process.
- Instructions on how to submit requests for formal DR and a list of the supporting information that should accompany these requests.
- Public availability of decisions reached during the DR process to promote consistent application and interpretation of drug quality-related regulations.

Dated: January 18, 2005.

Jeffrey Shuren,

Assistant Commissioner for Policy.

[FR Doc. 05–1396 Filed 1–25–05; 8:45 am]

BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 2005D–0004]

Draft Guidance for Industry on Nonclinical Safety Evaluation of Drug Combinations; 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 ''Nonclinical Safety Evaluation of Drug Combinations.'' The guidance provides recommendations on nonclinical approaches to support the clinical study and approval of fixed-dose combination products (FDCs), copackaged products, and adjunctive therapies.

DATES: Submit written or electronic comments on the draft guidance by April 26, 2005. General comments on agency guidance documents are welcome at any time.

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information (HFD–240), 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 Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to *http://www.fda.gov/dockets/ecomments*. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Abby Jacobs, Center for Drug Evaluation and Research (HFD–540), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–2020.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled ''Nonclinical Safety Evaluation of Drug Combinations.'' Drug combinations include FDCs, copackaged products, and adjunctive therapies. An FDC is a product in which two or more separate drug components (active pharmaceutical ingredients) are combined in a single dosage form. A copackaged product consists of two or more separate drug products in their final dosage form, packaged together with appropriate labeling to support the combination use. An adjunctive therapy refers to the situation in which a patient is maintained on a second drug product that is used together with (i.e., in adjunct to) the primary treatment, although the relative doses are not fixed and the drugs need not be given at the same time. Adjunctive therapy products may or may not be labeled for concomitant use. The guidance discusses all three types of drug combinations. However, it is only intended to describe general guiding principles. To receive more detailed

advice regarding a particular drug combination development program, a sponsor should contact the appropriate review division before submitting an Investigational New Drug application. In addition, FDA is in the process of publishing more specific guidance for certain categories of drug combinations.

The guidance discusses drug combinations involving the following items: (1) Previously marketed drugs, (2) one or more new molecular entities (NMEs) and one or more previously marketed drugs, and (3) more than one NME. The nonclinical studies considered important for each type of combination may differ, depending upon the information available on each drug component (active pharmaceutical ingredient). The nonclinical studies that would be appropriate to adequately characterize the combination depend on the toxicologic and pharmacokinetic profiles of the individual drugs, the treatment indication or indications, and the intended population.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the agency's current thinking on nonclinical safety evaluation of drug combinations. 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 statutes and regulations.

II. Comments

Interested persons may submit to the Division of Dockets Management (see **ADDRESSES**) written or electronic comments on the draft guidance. Two copies of mailed 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 Division of Dockets Management between 9 a.m. and 4 p.m., Monday through Friday.

III. Electronic Access

Persons with access to the Internet may obtain the document at either *http://www.fda.gov/cder/guidance/index.htm* or *http://www.fda.gov/ohrms/dockets/default.htm*.

Dated: January 18, 2005.

Jeffrey Shuren,

Assistant Commissioner for Policy.

[FR Doc. 05–1394 Filed 1–25–05; 8:45 am]

BILLING CODE 4160–01–S

DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Institutes of Health

National Heart, Lung, and Blood Institute (NHLBI); Opportunity for a Cooperative Research and Development Agreement (CRADA) to Identify and Explore Epigenetic Regulatory Elements for Diagnostic and Therapeutics Purposes

AGENCY: National Institutes of Health, Public Health Service, HHS.

ACTION: Notice.

SUMMARY: The National Heart, Lung, and Blood Institute (NHLBI) is seeking Cooperative Research and Development Agreement (CRADA) collaborator(s) to work with investigators in the Laboratory of Molecular Immunology (LMI) to identify epigenetic regulatory elements that may be involved in the disease development of T and/or B cell leukemia/lymphoma and other cancers via genome-wide analysis of acetylation islands using the Genome-Wide Mapping Technique (GMAT). Representative disease-specific acetylation islands will be explored for diagnostic and therapeutic purposes.

SUPPLEMENTARY INFORMATION: Epigenetics play a critical role in cellular development and cellular transformation in many pathogenic processes. For example, many cancers are correlated with changes of their chromatin structure and are sensitive to drugs that modulate the levels of histone acetylation. Epigenetic regulation refers to the modification of chromatin including posttranslational modification of histones, which does not involve change of DNA sequences of target genes. MHLBI investigators have mapped the genome-wide distribution of histone H3 acetylation in human T cells and discovered over 40,000 acetylation islands using a technique called GMAT. This tool combines Chromatin immunoprecipitation (Chip) of hyper-acetylated histones, with Serial Analysis of Gene Expression (SAGE). The acetylation islands are epigenetic markers for transcriptional regulatory elements and chromatin controlling elements. Changes of the acetylation islands may be correlated with early development of T cell lymphoma or leukemia. Therefore, this discovery may be applied to early diagnosis and/or treatment of these diseases.

The NHLBI is seeking capability statements from parties interested in entering into a CRADA to identify, explore and further develop epigenetic regulatory elements/acetylation islands for diagnostic and therapeutic purposes. The role of the CRADA collaborator(s) will include, but not be limited to, the following:

1. The ability to collaborate with NHLBI on further research and development of this technology. This ability can be demonstrated through experience and expertise in this or related areas of technology indicating the ability to contribute intellectually to on-going research and development.

2. To assist with obtaining specimen/tissues (patient and normal controls) for the Genome-Wide analysis as diagnostic and therapeutic markers.

3. To assist to further developing the epigenetic regulatory elements markers/acetylation islands as new targets for novel drug-development strategies.

The collaborator may also be expected to contribute financial support under this CRADA for personnel, supplies, travel, and equipment to support these projects. The collaborator is also expected to cooperate with the NHLBI in the timely publication of research results and to accept the legal provisions and language of the CRADA with only minor modifcations, if any.

DATES: CRADA capability statements should be submitted to Vincent Kolesnitchenko, Ph.D., Technology Transfer Specialist, National Heart, Lung, and Blood Institute (NHLBI), Office of Technology Transfer and Development, National Institutes of Health, 6705 Rockledge Drive, Suite 6018, MSC 7992, Bethesda, MD 20892–7992; Phone: (301) 594–4115; Fax: (301) 594–3080; E-mail: *vk5q@nih.gov*. Capability statements must be received on or before March 28, 2005.

The NHLBI has applied for patents claiming the core of the technology. Non-exclusive and/or exclusive licenses for these patents covering core aspects of this project are available to interested parties.

Licensing inquiries regarding this technology should be addressed to John Stansberry, Ph.D., Technology Licensing Specialist, Office of Technology Transfer, National Institutes of Health, 6011 Executive Boulevard, Suite 325, Rockville, Maryland 20852–3804, Phone: (301) 435–5236; Fax: (301) 402–0220; E-mail: *stansbej@od.nih.gov*. Information about Patent Applications and pertinent information not yet publicly described an be obtained under the terms of a Confidential Disclosure Agreement.

Respondents interested in submitting a CRADA Proposal should be aware that it may be necessary to secure a license to the above-mentioned patent rights in order to commercialize products arising from a CRADA.