Table 1 of this document provides a breakdown of the total estimated annual recordkeeping burden. FDA bases this hour burden estimate on its experience with the application of HACCP principles in food processing.

The burden estimates in table 1 of this document are based on an estimate of the total number of juice manufacturing plants (i.e., 2,300) affected by the regulations. Included in this total are 850 plants currently identified in FDA's official establishment inventory plus 1,220 very small apple juice manufacturers and 230 very small orange juice manufacturers. The total burden hours are derived by estimating the number of plants affected by each portion of this final rule and multiplying the corresponding number by the number of records required annually and the hours needed to complete the record. These numbers were obtained from the agency's final regulatory impact analysis prepared for these regulations.

Moreover, these estimates assume that every processor will prepare sanitary standard operating procedures and a HACCP plan and maintain the associated monitoring records and that every importer will require product safety specifications. In fact, there are likely to be some small number of juice processors that, based upon their hazard analysis, determine that they are not required to have a HACCP plan under these regulations.

Dated: April 27, 2007.

Jeffrey Shuren,

Assistant Commissioner for Policy.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 2007N–0182]

Agency Information Collection Activities; Proposed Collection; Comment Request; Information Program on Clinical Trials for Serious or Life-Threatening Diseases: Maintaining a Data Bank

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing an opportunity for public comment on the proposed collection of certain information by the agency. Under the Paperwork Reduction Act of 1995 (the PRA), Federal agencies are required to publish notice in the **Federal Register** concerning each proposed collection of information, including each proposed extension of an existing collection of information, and to allow 60 days for public comment in response to the notice. This notice solicits comments on the collection of information contained in the guidance entitled ''Information Program on Clinical Trials for Serious or Life-Threatening Diseases and Conditions'' dated March 18, 2002.

DATES: Submit written or electronic comments on the collection of information by July 13, 2007.

ADDRESSES: Submit electronic comments on the collection of information to: *http://www.fda.gov/dockets/ecomments.* Submit written comments on the collection of information to the Division of Dockets Management (HFA–305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number found in brackets in the heading of this document.

FOR FURTHER INFORMATION CONTACT: Jonna Capezzuto, Office of the Chief Information Officer (HFA–250), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–4659.

SUPPLEMENTARY INFORMATION: Under the PRA (44 U.S.C. 3501–3520), Federal agencies must obtain approval from the Office of Management and Budget (OMB) for each collection of information they conduct or sponsor. ''Collection of information'' is defined in 44 U.S.C. 3502(3) and 5 CFR 1320.3(c) and includes agency requests or requirements that members of the public submit reports, keep records, or provide information to a third party. Section 3506(c)(2)(A) of the PRA (44 U.S.C. 3506(c)(2)(A)) requires Federal agencies to provide a 60-day notice in the **Federal Register** concerning each proposed collection of information, including each proposed extension of an existing collection of information, before submitting the collection to OMB for approval. To comply with this requirement, FDA is publishing notice of the proposed collection of information set forth in this document.

With respect to the following collection of information, FDA invites comments on these topics: (1) Whether the proposed collection of information is necessary for the 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.

Information Program on Clinical Trials for Serious or Life-Threatening Diseases: Maintaining a Data Bank (OMB Control Number 0910–0459)—Extension

In the **Federal Register** of March 18, 2002 (65 FR 12022), FDA issued a guidance to industry on recommendations for investigational new drug application (IND) sponsors on submitting information about clinical trials for serious or life- threatening diseases to a Clinical Trials Data Bank developed by the National Library of Medicine (NLM), National Institutes of Health (NIH). This information is especially important for patients and their families seeking opportunities to participate in clinical trials of new drug treatments for serious or life-threatening diseases. The guidance describes three collections of information: Mandatory submissions, voluntary submissions, and certifications.

Mandatory Submissions

Section 113 of the Food and Drug Administration Modernization Act (FDAMA) of 1997 (the Modernization Act) (Public Law 105–115) requires that sponsors shall submit information to the Clinical Trials Data Bank when the clinical trial: (1) Involves a treatment for a serious or life-threatening disease and (2) is intended to assess the effectiveness of the treatment. The guidance discusses how sponsors can fulfill the requirements of section 113 of the Modernization Act. Specifically, sponsors should provide: (1) Information about clinical trials, both federally and privately funded, of experimental treatments (drugs, including biological products) for patients with serious or life-threatening diseases; (2) a description of the purpose of the experimental drug; (3) patient eligibility criteria; (4) the location of clinical trial sites; and (5) a point of contact for patients wanting to enroll in the trial.

Senate 1789, ''Best Pharmaceuticals for Children Act'' (Public Law 107–109) (BPCA), established a new requirement for the Clinical Trials Data Bank mandated by section 113 of FDAMA. Information submitted to the data bank must now include ''a description of

whether, and through what procedure, the manufacturer or sponsor of the investigation of a new drug will respond to requests for protocol exception, with appropriate safeguards, for single-patient and expanded protocol use of the new drug, particularly in children.'' The guidance was updated on January 27, 2004, to include a discussion of how sponsors can fulfill the BPCA requirements.

As part of the resubmission process for OMB approval, this information collection request (ICR) has been revised to include the burden associated with new requirements imposed by the Centers for Medicare and Medicaid Services (CMS). On September 19, 2000, the Health Care Financing Administration (now CMS) implemented a Clinical Trial Policy through the National Coverage Determination process. The Clinical Trial Policy was developed in response to a June 7, 2000, executive memorandum, issued by President Clinton, requiring Medicare to pay for routine patient costs in clinical trials. The original policy suggested that a registry be established into which studies meeting the criteria for coverage under the policy would be enrolled for administrative purposes. This registry was never established.

On July 10, 2006, CMS opened a reconsideration of its national coverage determination on clinical trials. The purpose of the reconsideration is to further refine the policy to rename it the Clinical Research Policy (CRP) to address several ambiguities, including the link between the CRP and the Coverage with Evidence Development concept, and the authority to allow the agency to pay for the costs of limited investigational items. One requirement to qualify for coverage of clinical costs under the proposed policy is that the study must be enrolled in the NLM Clinical Trials Data Bank.

Voluntary Submissions

Section 113 of the Modernization Act also specifies that sponsors may voluntarily submit information pertaining to results of clinical trials, including information on potential toxicities or adverse effects associated with the use or administration of the investigational treatment. Sponsors may also voluntarily submit studies that are not trials to test effectiveness, or not for serious or life-threatening diseases, to the Clinical Trials Data Bank.

Certifications

Section 113 of the Modernization Act specifies that the data bank will not include information relating to a trial if the sponsor certifies to the Secretary of Health and Human Services (the Secretary) that disclosure of the information would substantially interfere with the timely enrollment of subjects in the investigation, unless the Secretary makes a determination to the contrary.

Description of Respondents: A sponsor of a drug or biologic product regulated by the agency under the Federal Food, Drug, and Cosmetic Act or section 351 of the Public Health Service Act (42 U.S.C. 262) who submits a clinical trial to test effectiveness of a drug or biologic product for a serious or life-threatening disease.

For the purposes of CMS, the respondents will be providers that are conducting or sponsoring clinical trials that are seeking to have the clinical costs of their studies reimbursed by Medicare.

Burden Estimate: The information required under section 113(a) of the Modernization Act is currently submitted to FDA under 21 CFR part 312, and this collection of information is approved under OMB Control Number 0910–0014 until May 31, 2009, and, therefore, does not represent a new information collection requirement. Instead, preparation of submissions under section 113 of the Modernization Act involves extracting and reformatting information already submitted to FDA. Procedures (where and how) for the actual submission of this information to the Clinical Trials Data Bank are addressed in the guidance.

The Center for Drug Evaluation and Research (CDER) received 4,858 new protocols in 2005. CDER anticipates that protocol submission rates will remain at or near this level in the near future. Of these new protocols, an estimated two-thirds[1] are for serious or life-threatening diseases and would be subject to either voluntary or mandatory reporting requirements under section 113 of the Modernization Act. Two-thirds of 4,858 protocols per year is 3,239 new protocols per year. An estimated 50 percent[1] of the new protocols for serious or life-threatening diseases submitted to CDER are for clinical trials involving assessment for effectiveness, and are subject to the mandatory reporting requirements under section 113 of the Modernization Act. Fifty percent of 3,239 protocols per year is 1,620 new protocols per year subject to mandatory reporting. The remaining 3,238 new protocols per year are subject to voluntary reporting.

The Center for Biologics Evaluation and Research (CBER) received 474 new protocols in 2005. CBER anticipates that protocol submission rates will remain at or near this level in the near future. An estimated two-thirds[1] of the new protocols submitted to CBER are for clinical trials involving a serious or life-threatening disease, and would be subject to either voluntary or mandatory reporting requirements under section 113 of the Modernization Act. Two-thirds of 474 new protocols per year is 316 new protocols per year. An estimated 50 percent[1] of the new protocols for serious or life-threatening diseases submitted to CBER are for clinical trials involving assessments for effectiveness. Fifty percent of 316 protocols per year is an estimated 158 new protocols per year subject to the mandatory reporting requirements under section 113 of the Modernization Act. The remaining 316 new protocols per year are subject to voluntary reporting.

The estimated total number of new protocols for serious or life-threatening diseases subject to mandatory reporting requirements under section 113 of the Modernization Act is 1,620 for CDER plus 158 for CBER, or 1,778 new protocols per year. The remainder of protocols submitted to CDER or CBER will be subject to voluntary reporting, including clinical trials not involving a serious or life-threatening disease as well as trials in a serious or life-threatening disease but not involving assessment of effectiveness. Therefore, the total number of protocols (5,332) minus the protocols subject to mandatory reporting requirements (1,778) will be subject to voluntary reporting, or 3,554 protocols.

Our total burden estimate includes multi-center studies and accounts for the quality control review of the data before it is submitted to the data bank. The number of IND amendments submitted in 2005 for protocol changes (e.g., changes in eligibility criteria) was 7,597 for CDER and 855 for CBER. The number of IND amendments submitted in 2005 for new investigators was 11,287 for CDER and 532 for CBER. The number of protocol changes and new investigators was apportioned proportionally between mandatory and voluntary submissions. We recognize that single submissions may include information about multiple sites.

Generally, there is no submission to FDA when an individual study site is no longer recruiting study subjects. For this analysis, we assumed that the number of study sites closed each year is similar to

[1] Estimate obtained from a review of 2,062 protocols submitted to CDER between January 1, 2002, and September 30, 2002.

the number of new investigator amendments received by FDA (11,287 CDER and 532 CBER).

Generally, there is no submission to FDA when the study is closed to enrollment. We estimate the number of protocols closed to enrollment each year is similar to the number of new protocols submitted (4,858 CDER and 474 CBER).

The hours per response is the estimated number of hours that a respondent would spend preparing the information to be submitted under section 113(a) of the Modernization Act, including the time it takes to extract and reformat the information. FDA has been advised that some sponsors lack information system capabilities enabling efficient collection of company-wide information on clinical trials subject to reporting requirements under section 113(a) of the Modernization Act. The estimation of burden under section 113(a) reflects the relative inefficiency of this process for these firms.

Based on its experience reviewing INDs, consideration of the information in the previous paragraphs, and further consultation with sponsors who submit protocol information to the Clinical Trials Data Bank, FDA estimated that approximately 4.6 hours on average would be needed per response. The estimate incorporates 2.6 hours for data extraction and 2.0 hours for reformatting based on data collected from organizations currently submitting protocols to the Clinical Trials Data Bank. We considered quality control issues when developing the current burden estimates of 2.6 hours for data extraction and the 2.0 hours estimated for reformatting. Additionally, the Internet-based data entry system developed by NIH incorporates features that further decrease the sponsor's time requirements for quality control procedures. The Clinical Trials Data Bank was set up to receive protocol information transmitted electronically by sponsors. Approximately 10 percent of sponsors electronically transmit information to the Clinical Trials Data Bank. If the sponsor chooses to manually enter the protocol information, the data entry system allows it to be entered in a uniform and efficient manner primarily through pull-down menus. As sponsors' familiarity with the data entry system increases, the hourly burden will continue to decrease.

A sponsor of a study subject to the requirements of section 113 of the Modernization Act will have the option of submitting data under that section or certifying to the Secretary that disclosure of information for a specific protocol would substantially interfere with the timely enrollment of subjects in the clinical investigation. FDA has no means to accurately predict the proportion of protocols subject to the requirements of section 113 of the Modernization Act that will be subject to a certification submission. To date, no certifications have been received. It is anticipated that the burden associated with such certification will be comparable to that associated with submission of data regarding a protocol. Therefore, the overall burden is anticipated to be the same, regardless of whether the sponsor chooses data submission or certification for nonsubmission. Table 1 of this document reflects the estimate of this total burden.

FDA estimates the burden of this collection of information as follows:

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN[1]

New Protocols	Recruitment Complete	Protocol Changes	New Investigators	Site Closed	Total Responses	Hours per Response	Total Hours
CDER (mandatory)	1,620	1,620	2,507	3,725	13,197	4.6	60,706
CBER (mandatory)	158	158	282	176	950	4.6	4,370
CDER (voluntary)	3,238	3,238	5,090	7,562	26,690	4.6	122,774
CDER (voluntary)	316	316	573	356	1,917	4.6	8,818
Total							196,668

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

CMS Burden Estimate:

The burden associated with CMS' requirements is the time and effort necessary for the provider to extract the data elements from the study protocol and reformatting and entering the information into the data bank. We estimate that approximately 745 clinical research studies will register on the NLM data bank. The number was derived from a search of the database on September 1, 2006 restricting the search by age (e.g., > 65 years of age); sponsor (e.g., NIH, industry, other federal agency, university/organization); Phase II, III or IV; and by type of study (e.g., cancers and other neoplasms, diagnosis, and devices). The age, sponsor, and study phase was applied to each of the three separate searches by type of study. The following number of studies by study type, including trials no longer recruiting was 562 for diagnosis, 164 for cancers and other neoplasms, and 19 for devices. In determining the total number of hours requested, the CMS estimate uses the same assumptions used by the FDA to estimate its total number of burden hours. Therefore, the total annual burden associated with this requirement is 27,480 hours (5,974 responses x 4.6 hours per response).

We believe the combined estimate of burden attributable to FDA and CMS requirements, 224,148 burden hours (196,668 burden hours + 27,480 burden hours) accurately reflects the total burden associated with this information collection request. We recognize that companies who are less familiar with the data entry system and the Clinical Trials Data Bank will require greater than 4.6 hours per response. However, as sponsor familiarity with the system increases, the hourly estimate will decrease.

Dated: May 8, 2007.

Jeffrey Shuren,

Assistant Commissioner for Policy.

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