SUPPORTING STATEMENT FOR

Information Program on Clinical Trials: Maintaining a Registry and Results Databank

OMB No. 0925-0586

Introduction

Food and Drug Administration Amendments Act of 2007 [FDAAA, Public Law 110-85] was enacted on September 27, 2007. The statute modified 42 USC 282 to add a new section (j) that expands the existing databank of clinical trials registry information that was established under previous law and to make available to the public a searchable databank of information about certain controlled clinical trials of drugs, biologics and devices, as provided for in the statute. The law mandated the implementation of the revised and expanded clinical trials registry by December 26, 2007.

Effective March 10, 2008, the information collection request for the pre-existing collection of clinical trial registry information,"Information Program on Clinical Trials for Serious or Life-Threatening Diseases: Maintaining a Databank," (OMB No. 0910-0459) has been transferred from the FDA to NIH. The new OMB No. is 0925-0586. See OMB Notice of Action dated 03/10/2008, ICR Reference Number 200803-0925-002. Along with this transfer, the title of the information collection request has been revised to reflect the expansion in the scope of the clinical trials databank that resulted from enactment of the Food and Drug Administration Amendments Act of 2007. The new title is “Information Program on Clinical Trials: Maintaining a Registry and Results Databank.” The expanded program will include information on certain clinical trials of drugs, biologics, and devices, whether or not they relate to serious and life-threatening diseases. This information collection request is intended to expand the prior information collection to reflect the broader scope of clinical trials that are required to submit registration information under FDAAA and the additional data elements that are needed to comply with the new law.

Compelling reason exists for the collection of required information for successful planning and implementation of the expansion of the Clinical Trial Registry, as described in Public Law 110-85. This information collection is essential to the effective stewardship of Federal Funds. After consultation with other agencies and NIH components, NIH has determined that the information is not currently available in any single, reliable, accessible source.

Since the passage of the law, staff at the National Library of Medicine has worked with other NIH officials and representatives of the U.S. Food and Drug Administration to revise the set of data elements needed to register an applicable clinical trial in accordance with the law and to assure smooth transition to the expanded registry.

The statutory deadline requires that clearance of the information collection mandated by P.L.110-85 be approved and operational at the earliest possible time. NIH cannot

reasonably comply with the normal clearance procedures for information collection, because the use of normal procedures will delay the collection and hinder the agency in accomplishing its mission and meeting new statutory requirements, to the detriment of the public good. Emergency clearance approval of the information collection is being requested to ensure the effective implementation of this new law. In accordance with 5 CFR 1320.8(d), NIH published an emergency clearance request with a 15-day comment period for this information collection on March 21, 2008 (Vol. 73, No. 56, page 15163).

1. Circumstances Making the Collection of Information Necessary

This information collection is necessary to comply with new statutory requirements contained in Section 801 of the Food and Drug Administration Amendments Act of 2007 (FDAAA; Public Law 110-85). FDAAA, enacted on September 27, 2007, instructs the Director of NIH to expand the databank of the Clinical Trials Registry that was established under previous law [Section 113(a) of the Food and Drug Administration Modernization Act of 1997 (FDAMA)] and to establish a results databank. Pursuant to the new law [codified in 42 USC 282(j)(2)(A)(ii)] the Director of NIH is to collect and make available to the public in a searchable data base information concerning certain controlled clinical trials of drugs, biologics, and devices that are subject to regulation by the Food and Drug Administration (FDA). The statute permits the NIH to collect information on other types of clinical trials and on trials that were completed prior to enactment of the law or other reporting deadlines established in the law. FDAAA mandates the implementation of the revised and expanded reporting of clinical trials by December 26, 2007. It also requires, beginning on September 27, 2008, the collection of information describing the results of clinical trials. This request is limited to the approval of the collection of registration information authorized by FDAAA Section 801. Collection of results information will be addressed in a separate request.

Previously, this information collection was established to comply with the requirements of FDAMA, which specifies that "The Secretary, acting through the Director of NIH, shall establish, maintain, and operate a databank of information on clinical trials for drugs for serious or life-threatening diseases and conditions…The Secretary shall establish the databank after consultation with the Commissioner of Food and Drugs, the directors of the appropriate agencies of the National Institutes of Health (including the National Library of Medicine), and the Director of the Centers for Disease Control and Prevention…the Secretary shall collect, catalog, store, and disseminate the information described in such paragraph" (Section 113, Information Program on Clinical Trials for Serious or Life-Threatening Diseases, Food and Drug Administration Modernization Act of 1997, Public Law 105-115, 105th Congress).

In complying with these statutes, the proposed information collection addresses an important public health need by providing patients, family members, clinicians, and researchers with timely access to up-to-date information about clinical trials. The collection of information about clinical trials is considered a mechanism for enabling patients and their family members to learn about relevant clinical trials and facilitate possible enrollment. In addition, trial registration can reduce inadvertent and unnecessary

duplication of clinical research studies, help reviewers detect incomplete reporting of the results of specific trials, allow comprehensive analysis and reporting of the results of many trials of specific therapies, and therefore provide regulators, scientists, health professionals, and the public a more accurate picture of the benefits and potential harms of specific therapies and a more solid foundation for decision-making. For several years, the National Institutes of Health (NIH) and the Food and Drug Administration (FDA) have initiated efforts to encourage the registration of clinical trials in publicly-accessible databanks, as such information is not otherwise easily accessible to the general public.

2. Purpose and Use of the Information Collection

Information will be submitted electronically at the Website http://www.clinicaltrials.gov. The information in the databank will be available to patients, other members of the public, health care providers, and researchers. FDAAA Section 801 explains that the purpose of the clinical trials registry databank is to enhance patient enrollment and provide a mechanism to track the progress of clinical trials. The information is intended to provide current and reliable information on the broadest possible scale to members of the public, including to physicians and researchers, about the existence, nature, enrollment status, location, eligibility criteria, sponsorship and progress of clinical trials. Members of the public, their physicians and health advisors will use the information to identify locations where the clinical trials are conducted. The registry will provide basic information about the trials, their implementation, and how to enroll. Progress of the trials will be updated so that individuals will have current information on initiatives to intervene to treat, cure, ameliorate or prevent the health conditions with which they are afflicted or at risk. In some instances, registration information will be used for the purpose of facilitating enrollment in clinical trials of drugs intended for the treatment of patients with serious or life-threatening diseases and conditions. Facilitating enrollment will hasten completion of clinical trials, leading to faster and potentially more thorough testing of the safety and efficacy of new treatments, accelerating and expanding availability of promising treatments for serious and life-threatening diseases and conditions.

This information will be of immediate value to patients with a variety of diseases and conditions. Safe and effective treatments are not available for all diseases and conditions (including those that are serious and life-threatening), and clinical trials represent patients' first opportunity to receive new treatments, some of which are ultimately found to represent therapeutic breakthroughs. Information regarding opportunities to participate in such clinical trials is often not publicly available, and patients who may wish to participate in a clinical trial may have difficulty finding such trials. The databank will expand public availability of such information for patients. This expanded patient access to information about clinical trials will increase patients' therapeutic options while enabling them to contribute to development of therapeutic advances in the treatment of serious and life-threatening diseases and conditions.

Data Elements for Clinical Trials Databank

The required registration data elements for this information collection are listed in Table 2-1. Collection of much of this information was previously approved under a earlier information collection request, OMB No. 0910-0459 (items included in the earlier clearance request are marked with an asterisk). The elements include items of information that are specifically enumerated in FDAAA as authorized and required to be collected for the registry *[PL 110-85, Section 801(a), adding new 42 U.S.C. 282(j)(2)(A)*]. The collection includes additional data elements that are necessary to meet other requirements of FDAAA and to enable effective management and operation of the database. For example, FDAAA requires that the databank enable searching by "the safety issue, if any, being studied in the clinical trial as a primary or secondary outcome" and by the location of the clinical trial [*PL 110-85, Section 801(a), adding new 42 U.S.C. 282(j)(2)(B)]* Information is collected to support these functions. FDAAA also establishes compliance and enforcement requirements that apply to mandatory submissions of information. Information is collected to distinguish between mandatory and voluntary submissions. The Law also requires that the registry be easily used by the public and that entries be easily compared [*PL 110-85, Section 801(a), adding new 42 U.S.C. 282(j)(2)(B)(iv)],* making necessary the collection of structured data to ensure consistency and completeness of entries (e.g., requiring information on intervention model, number of arms, masking, and allocation as elements of Study Design)**.** The list of items encompasses those that are necessary to fulfill the requirements established by FDAMA.

Table 2-1. Information collected for expanded clinical trials registry

Data Element		**Justification** [Statutory References are to 42 USC 282(j) as added by *PL 110-85, Section 801(a)*]
1. Descriptive Information		
	Brief Title*	(2)(A)(ii)(I)(aa) specifies a brief title, intended for the lay public
	Brief Summary*	(2)(A)(ii)(I)(bb) specifies a brief summary, intended for the lay public
	Primary Purpose*	(2)(A)(ii)(I)(cc) specifies the primary purpose
	Study Design* *For interventional studies, includes:* • *allocation,* • *arm description,* • *arm designation,* • *arm number/label,* • *arm type,* • *intervention study model,* • *masking,* • *number of arms.* *For observational studies, includes:* • *group/cohort description, group/cohort number or label,* • *number of groups/cohorts,* • *observational study model,*	(2)(A)(ii)(I)(dd) specifies study design. Requested information under this heading is intended to meet the statutory and practical requirements ensure complete and consistent collection of information to describe the design of interventional and observational studies.

	• *sampling method, and* • *time perspective.*	
	Study Phase*	(2)(A)(ii)(I)(ee) specifies for an applicable drug clinical trial, the study phase
	Study Type (record type)*	(2)(A)(ii)(I)(ff) specifies “study type”
	Primary disease or conditions; Focus of Study*	(2)(A)(ii)(I)(gg) specifies the primary disease or condition being studied, or the focus of the study
	Intervention Name* *Includes FDA approval status, intervention description, other intervention names, and intervention type (e.g., drug, device, surgical procedure)*	(2)(A)(ii)(I)(hh) specifies intervention name and intervention type. FDA approval status collected to determine eligibility of device trials for public posting in accordance with section (2)(D)(ii) and to assist in identifying trials for which results information will subsequently be required.
	Study Start Date	(2)(A)(ii)(I)(ii) specifies study start date
	Expected Completion Date	(2)(A)(ii)(I)(jj) specifies expected completion date. Completion date is defined in the statute as the date that the final subject was examined or received an intervention for the purposes of final collection of data for the primary outcome
	Target Number of Subjects (Enrollment)	(2)(A)(ii)(I)(kk) specifies “the target number of subjects”
	Primary Outcome Measures (including specific measure and time of outcome measurement)	(2)(A)(ii)(I)(ll) specifies “outcomes, including primary and secondary outcome measures”
	Secondary Outcome Measures (including specific measure and time of outcome measurement)	(2)(A)(ii)(I)(ll) specifies “outcomes, including primary and secondary outcome measures”
	Safety Issue? (Yes/No)	(2)(B)(ii) requires the database to enable “searching by safety issue, if any, studied as primary or secondary outcome.”
2. Recruitment Information		
	Eligibility Criteria* (*includes study population description for observational studies*)	(2)(A)(ii)(II)(aa) specifies “eligibility criteria”
	Gender*	(2)(A)(ii)(II)(bb) specifies “gender”
	Age Limits*	(2)(A)(ii)(II)(cc) specifies “age limits”
	Healthy Volunteers Acceptance*	(2)(A)(ii)(II)(dd) specifies “whether the trial accepts healthy volunteers”
	Overall Recruitment Status*	(2)(A)(ii)(II)(ee) specifies “overall recruitment status”
	Individual Site Status*	(2)(A)(ii)(II)(ff) specifies “individual site status”
	Expanded Access Information	(2)(A)(ii)(II)(gg) specifies “...whether or not there is expanded access to the drug and how to obtain information about such access”
3. Location and Contact Information		
	Name of sponsor*	(2)(A)(ii)(III)(aa) specifies “the name of the sponsor”
	Responsible Party (*name,*	(2)(A)(ii)(III)(bb) specifies “the responsible party, by official

	organization, contact information)	title" [*Note*: *contact information not made public)*
	Facility Name (*facility location – city, state, country, zip/postal code*)*	(2)(A)(ii)(III)(cc) specifies "the facility name and facility contact information (including the city, State, and zip code for each clinical trial location, or a toll-free number through which such location may be accessed)"
	Facility Contact (*name and phone or email*)*	(2)(A)(ii)(III)(cc) specifies "the facility name and facility contact information (including the city, State, and zip code for each clinical trial location, or a toll-free number through which such location may be accessed)"
	Central Contact (*name, title and toll-free telephone number of email address*)*	(2)(A)(ii)(III)(cc) specifies " ...or a toll-free number through which such location may be accessed"
4. Administrative Data		
	Unique Protocol ID*	(2)(A)(ii)(IV)(aa) specifies "the unique protocol identification number"
	Other Protocol IDs	(2)(A)(ii)(IV)(bb) specifies "other protocol identification numbers, if any"
	FDA IND/IDE Protocol? (*including grantor name, IND/IDE number and IND/IDE serial number*)*	(2)(A)(ii)(IV)(cc) "the Food and Drug Administration IND/IDE protocol number". IND/IDE grantor, IND/IDE number, and IND/IDE serial number are considered the components of a complete IND/IDE protocol number.
	Record Verification Date*	(2)(A)(ii)(IV)(cc) specifies "record verification date"
5. Other Necessary Information		
	Applicable Clinical Trial? (including FDA-Regulated Intervention and Section 801 Clinical Trial?	Collected to distinguish between mandatory submission of Applicable Clinical Trials [defined in (1)(A)(i)] and voluntary submissions authorized in [(4)(A)] and to help users determine if their trial is an applicable clinical trial.
	Pediatric Post-market Surveillance	Collected to identify studies that are post-market pediatric surveillance studies that are required to register, even if they are not standard interventional or observational studies.
	Delayed Posting?	Collected to identify trials of unapproved/uncleared devices for which information is to be withheld from public posting in accordance with (2)(C)(ii)(I)
	Institutional Review Board Approval Information (including Board Approval, Approval Status, Approval Number, Board Name, Board Affiliation, and Board Contact)*	Collected to ensure that registered trials conform with international human research protection policies [not required for federally funded or IND/IDE studies because they are subject to procedures that verify compliance with such polices].
	Oversight Authorities*	Collected to determine which organization (domestic or international) has authority over the trial, which is essential to verifying that any listed trial conforms with relevant regulations

		regarding human subjects research.

* Data element was included in OMB No. 0910-0459

In addition to the items listed in Table 2-1, respondents may submit optional data elements to provide a more complete record of the clinical trial or to enable compliance with the requirements of other clinical trial reporting policies (such as that of the International Committee of Medical Journal Editors, which requires registration as a precondition for considering research papers for publication). Optional information consists of those elements listed below. Those optional elements that were previously approved for collection under OMB 0910-0459 are indicated with an asterisk.

- links to related Web-based information (e.g., publications regarding the trial, additional enrollment information)*,
- keywords to facilitate search and retrieval*,
- overall study official* [required by the ICMJE]
- official title of the trial (in contrast to the "brief title" required by law) and acronym [required by the ICMJE],
- study completion date [formerly completion date] (as opposed to primary completion date as specified in FDAAA)*
- study classification [formerly endpoing] (e.g., safety, efficacy, bioequivalences -- for interventional studies only)*
- biospecimen retention and biospecimen description (for observational studies only)
- detailed description of the trial/study*
- names of collaborators [required by the ICMJE],
- whether or not a data monitoring committee has been established for the trial, and
- why recruitment stopped?

The clinical trials registry data base, ClinicalTrials.gov has been in operation since 2000 and has incorporated elements and features to facilitate use by affected stakeholders with each successive OMB approval. The most recent approval was in January 2008 – OMB Control Number: 0910-0459 [ICR Reference No: 200711-0910-004]). The proposed information collection for the expanded clinical trials registry established by FDAAA incorporates many of the same data elements and is intended to supersede the existing information collection.

3. Use of Improved Information Technology and Burden Reduction

The clinical trials registry data base utilizes the latest software and Internet technologies for registration and searching capabilities. Information can be uploaded automatically or entered into electronic

forms available on the ClinicalTrials.gov website. It can be viewed at http://clinicaltrials.gov/. The Law itself directs the Director, NIH to make the information available via the Internet, stating that "The Director of NIH shall ensure that the registry databank is made publicly available through the Internet." [*PL 110-85, Section 801(a), adding new 42 U.S.C. 282(j))(2)(A)]*.

4. Efforts to Identify Duplication and Use of Similar Information

The Clinical Trials Registry Databank is unique and encompasses information on nearly 50,000 clinical trials in more than 150 countries. No comparable listing of clinical trials exists in the world. While some companies make clinical trial information available through commercial databases and choose to designate the organization as a data provider for the company, these efforts are not as comprehensive as ClinicalTrials.gov and contain limited information on only a select subset of trials.

Much of the information to be collected under FDAAA is currently submitted to FDA in a different format by sponsors of Investigational New Drug (IND) and Investigational Device Exemption (IDE) applications under Federal Regulations, but is not publicly available. IND/IDE submissions are confidential and proprietary, and are not subject to release under section 552 of Title 5, United States Code (Freedom of Information Act). Information about non-IND/IDE or IND/IDE-exempt studies is typically contained in clinical trial protocol documents, which are not generally submitted to the FDA nor made available to the public. The specific processes for submission of trial information by responsible parties under FDAAA provide for public availability of clinical trial information while being sensitive to the needs of registrants, e.g., by minimizing reporting burden and protecting FDA submissions from unauthorized release. Considerable attention has been devoted to development of the processes for registering trials with ClinicalTrials.gov to minimize the possibility for duplicate submission of registration information for multi-site trials.

5. Impact on Small Business or Other Small Entities

This activity is anticipated to have minimal impact upon small business. While a number of the parties registering clinical trial information will be small businesses and entities (e.g., physician practices, start up or small companies that produce medical devices), the preparation and submission of the required information for the databank is anticipated to represent a small proportion of the total administrative burden for any business (large or small) conducting a clinical trial. Organizations involved in conducting clinical trials must sustain a substantial administrative burden. These efforts far outweigh the effort needed to register and update records in the clinical trial registry. Because much of the information to be supplied to the registry is already compiled for the study protocol, scientific and ethical reviews, other regulatory purposes, and recruitment of subjects to participate in the trials – or to comply with policies of the International Committee of Medical Journal Editors (ICMJE) and World Health Organization, the additional burden of this information collection (on large and small entities) is greatly reduced. The fact that many such organizations list their clinical trial information voluntarily in the ClinicalTrials.gov

registry further suggests that the benefits of registration outweigh the costs of the effort involved**.**

6. Consequences of Collecting the Information Less Frequently

Reporting of registration information is conducted on an ongoing basis as new trials are initiated and conducted. In general, the law requires that trials be registered within 21 days of recruiting the first patient [*PL 110-85, Section 801(a), adding new 42 U.S.C. 282(j)(2)(C)]*. Information must be updated at least once every 12 months if there are any changes to report; changes in recruitment status must be reported within 30 days of such change [*PL 110-85, Section 801(a), adding new 42 U.S.C. 282(j)(4)(C)(i)]*. Less frequent reporting is inconsistent with the Congressional mandate and would cause delays, gaps, and errors in the publicly available information about clinical trials, compromising the databank's utility as a resource for patient recruitment and for providing reliable, up-to-date information to the public about ongoing trials.

7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

This collection fully complies with 5 CFR 1320.5.

8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

In accordance with 5 CFR 1320.8(d), NIH published an emergency clearance request with a 15-day comment period for this information collection on March 21, 2008 (Vol. 73, No. 56, page 15163). A single public comment was received in response to the Federal Register Notice which was not directly related to this information collection request and did not address any of the items contained in the notice. No further action in responding was taken subsequent to the initial acknowledgement to the sender that the comment had been received and would be reviewed for further consideration. In addition, FDA published a 60 day notice for public comment in the Federal Register on May 14, 2007 (72 FR 27140) to request an extension of the pre-existing clearance for the information collection under FDAMA. No comments were received on that notice.

Development of this information collection has nevertheless benefitted from considerable public consultation. The FDAMA and FDAAA legislation that established and expanded the clinical trials registry resulted from extensive Congressional hearings that included input from a range of stakeholders. The preceding information collections have been in effect for nearly 10 years and have won wide acceptance from the affected communities. NIH staff participate regularly in conferences, meetings, monthly conferences, and other discussion forums with affected stakeholders in industry, academia and the general public. They have also published articles about the system and its requirements in widely disseminated peer-reviewed journals. Users of the registry may submit comments and questions to a dedicated email address (register@clinicaltrials.gov). In addition, the National Library of Medicine (NLM) organized two workshops on clinical trials registration and results reporting that included representatives of the affected stakeholder

communities. The first was held in Warrenton, Virginia on November 8-9, 2006; the second in Bethesda, Maryland on July 16-17, 2007. Since passage of FDAAA, NIH staff redoubled its efforts to consult with affected stakeholders, participating in meetings and conferences with representatives of the drug and device industries, FDA law community, academic medical centers, and the library community, among others. Draft versions of the data element definitions were posted on the NLM website several weeks in advance of the statutory deadline, and the NLM Board of Regents Working Group on Clinical Trials held an open meeting on February 11, 2008. As a result, development of the expanded clinical trials registry data base was carried out with considerable understanding of the issues and the concerns of the public and professional and industry groups.

9. Explanation of Any Payment or Gift to Respondents

No gifts or payments are to be offered in regard to this information collection.

10. Assurance of Confidentiality Provided to Respondents

No personally identifiable information is to be sent to the databank, other than contact information for designated points-of-contact. This information is required by law to be made public, in keeping with the policy objectives of FDAAA and FDAMA.

11. Justification for Sensitive Questions

No questions of a sensitive nature are included in this data collection.

12. Estimates of Annualized Burden Hours and Costs

The burden associated with this information collection is the time and effort necessary for the data provider to extract the data elements from the study protocol, reformat them and enter the information into the databank. The burden calculations below include the burden associated with information collection under FDAAA and FDAMA, as compliance with these policies requires submission of the same information. References below to mandatory and voluntary reporting refer only to FDAAA, but all necessary reporting is captured in the estimates.

To determine the annual reporting burden for mandatory submissions of registration information, estimates were made of the number of applicable trials of drugs, biologics, and devices. It was estimated that approximately 3,500 applicable clinical trials of drugs and biologics and 445 applicable trials of devices would be registered annually in accordance with FDAAA. The drug and biologic estimates were based information showing that in 2005 some 5,332 new clinical trial protocols were submitted to the FDA Center for Drug Evaluation and Research and 474 new protocols were submitted to the Center for Biologics Evaluation and Research. FDA expects that submission rates will remain at or near this level in the near future. Of the drug and biological protocols received in 2005, an estimated 50% -- approximately 2,900 protocols -- were for trials involving assessments of effectiveness, which would be subject to the provisions of

FDAAA. This figure was raised to 3,500 drug and biological trials per year to account for IND-exempt trials that are required to register in the expanded registration databank, but for which a protocol might not be sent to FDA. For devices, the estimated 445 new applicable device clinical trials per year includes trials related to pre-market applications (approximately 50 applications to FDA containing 75 clinical trial protocols in 2005), 510(k) submissions (approximately 360 submissions to FDA containing clinical trial protocols in 2005), humanitarian device exemptions (9 in 2005). The estimates of drug, biologic, and device trials computed using this approach are consistent with the numbers of relevant trials that were registered with the ClinicalTrials.gov registry in calendar year 2007.

The registration databank also receives a large number of voluntary submissions of information from registrants who wish to make their information public for purposes of recruitment or compliance with other policies (e.g., International Committee of Medical Journal Editors). Voluntary registration is explicitly authorized in P.L. 110-85 [*PL 110-85, Section 801(a), adding new 42 U.S.C. 282(j)(4)(A)],* and the statute places certain requirements on parties that voluntarily register clinical trials of drugs and devices that are subject to FDA regulation but not subject to the reporting requirements of the law. Nevertheless, for all voluntary submissions, information is collected in accordance with the specifications established for mandatory registrations. The number of voluntary registrations is estimated by subtracting the anticipated annual number of mandatory registrations from the total number of trial registrations expected during the year, based on historical averages. In calendar year 2007, there were approximately 13,300 new trials registered in the ClinicalTrial.gov registry databank, of which some 8,000 were trials with drugs or biologics as an intervention, 900 were trials with a device as an intervention, and 4,400 were other types of trials (e.g., observational studies, procedural interventions, behavioral interventions). These figures are consistent with the numbers of trials registered during calendar year 2005. Subtracting the anticipated number of mandatory trial registrations (from Table 12-2) from the anticipated number of total registrations (2007 statistics) produces estimated numbers of voluntary registrations of 4,500 trials of drugs and biologics, 445 trials of devices, and 4,400 trials of other intervention types. To account for a possible increase in voluntary submissions resulting from the heightened level of attention being devoted to clinical trials information, these estimates were raised by 20 percent to 5,400 trials of drugs and biologics, 545 trials of devices, and 5,280 trials of other intervention types.

The hour burden accounts for time required to register trials and provide necessary updating over the course of the study. Based on previous experience, it is estimated that each new registration record will be updated an average of 8 times during the course of the study (e.g., to reflect protocol changes, additions of investigational sites, updates of recruitment status, trial completion). This estimate is consistent with the statutory requirement in FDAAA that clinical trial information be updated at least once annually if there were any changes in the previous 12-month period and within 30 days of any change in the recruitment status of individual sites. The time to complete an initial (new) registration for trials of drugs, biologics, or devices is estimated to be 7 hours (including time to extract, reformat and submit information which has already been produced for

other purposes), an increase of 50% above the 4.6 hours that was estimated for the smaller set of information collected under previous law (FDAMA), and which was based on FDA's experience reviewing INDs and consultation with sponsors who submit protocol information to the Clinical Trials Databank. The estimate incorporates 4 hours for data extraction and 3 hours for reformatting, consistent with the proportions that were used in the estimates for the smaller data collection under FDAMA, which were, in turn, based on data collected from organizations submitting protocols to the Clinical Trials Databank. The time required for subsequent updates of registration information is expected to be significantly less than for the original registration (as less information must be provided), and is estimated at 2 hours per update.

Applying these figures to the anticipated numbers of trials produces a burden estimate for mandatory, new trial registrations of 348,910 hours. Of this total, 90,735 hours are associated with mandatory registration requirements and 258,175 hours are associated with voluntary reporting. These estimates are summarized in Table 12-1. These figures would be expected to decline over time as registrants become more familiar with the registration processes and refine their data submission systems. The Internet-based data entry system developed by NIH incorporates features that decrease the data provider's time requirements for quality control procedures. The Clinical Trials Databank is set up to receive protocol information transmitted electronically by sponsors. 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. Some data providers lack information system capabilities enabling efficient collection of company-wide information on clinical trials subject to reporting requirements under FDAAA. The estimation of burden reflects the relative inefficiency of this process for these firms. As sponsor's familiarity with the data entry system increases, the hourly burden will continue to decrease.

Table 12-1 Estimated Burden for Newly Registered Trials

Type	Respondents	Frequency	Total Responses	Average Time per Response	Annual Hour Burden
Mandatory Submissions					
Drug & Biologic	3,500	1 Initial	3,500	7 hrs	24,500
		8 Updates	28,000	2 hrs	56,000
Device	445	1 Initial	445	7 hrs	3,115
		8 Updates	3,560	2 hrs	7,120
Subtotal	3,945		35,505		90,735
Voluntary Submissions					
Drug & Biologic	5,400	1 Initial	5,400	7 hrs	37,800
		8 Updates	43,200	2 hrs	86,400
Device	545	1 Initial	545	7 hrs	3,815
		8 Updates	4,360	2 hrs	8,720

Other	5,280	1 Initial	5,280	7 hrs	36,960
		8 Updates	42,240	2 hrs	84,480
Subtotal	11,225		101,025		258,175
Total	15,170		136,530		348,910

During the first year after enactment of FDAAA [i.e., between September 27, 2007 and September 27, 2008] there is an additional mandatory reporting burden associated with the collection of information for applicable trials of drugs, biologics, and devices that were ongoing as of December 26, 2007 and had been previously registered with ClinicalTrials.gov. These respondents already provided information under the previous OMB clearance, but must provide the additional elements required by FDAAA that are subject to this clearance. It was estimated that there were 7,650 entries in the ClinicalTrials.gov registry in December 2007 for ongoing, interventional Phase 2-4 studies of drugs, biologics, and devices that would need to have updated information. Of this total, 7,000 were previously registered trials of drugs and biologics and 650 were previously registered trials of devices. It is anticipated that information collection required to bring these trials into compliance with the new information collection requirements will be significantly less than for a new trial registration and is estimated as 3 hours. The number of updates for these trials is estimated to be 4, which is half of the updates estimated for new registrations. Each update is estimated to require 2 hours, consistent with the updates for newly registered trials. The total burden associated with the updating of information for ongoing trials is 84,150 hours, as shown in Table 12-2.

Table 12-2 Estimated Burden for Mandatory Updating of Information for Ongoing Trials

Type of Respondents	**Number of Respondents**	**Frequency of Response**	**Average Time per Response**	**Annual Hour Burden**
Drugs and Biologics	7,000	1 Compliance Update	3 hrs	21,000
		4 Subsequent Updates	2 hrs	56,000
Devices	650	1 Compliance Update	3 hrs	1,950
		4 Subsequent Updates	2 hrs	5,200
Total	7,650			84,150

13. Estimates of Other Total Annual Cost Burden to Respondents and Record Keepers

There are no capital costs associated with this collection.

14. Annualized Cost to the Federal Government

The operating budget for the clinical trial registry databank in FY2008 is approximately $3 million, which includes NIH staff salaries, costs of software development and maintenance, and quality assurance. Additional costs will be entailed in operating the expanded registry and the future results database due to the increased volume of information to be processed. Such costs are not known at this time.

15. Explanation for Program Changes or Adjustments

The program changes reflected in this request respond to new statutory requirements contained in Section 801 of Public Law 110-85. The law expands the types of clinical trials that must be registered in the registration databank and increase the number of data elements that must be submitted. The result is an increased annual burden of approximately 152,250 hours above the previous information collection.

16. Plans for Tabulation and Publication and Project Time Schedule

Submitted data is made available to the public via a website operated and maintained by NIH: <http://www.clinicaltrials.gov>. Deadlines for public posting of such information are established in FDAAA. Most registration information is posted within 30 days of receipt, but information for applicable clinical trials of devices is not posted publicly until after the device is cleared or approved. The databank is subject to public search and review, and the statute identifies certain criteria by which the databank must be searchable by the public, including by disease or condition being studied, location of the clinical trial, study phase, and safety issue being studied as a primary or secondary outcome.

The overall project will proceed in accordance with statutory milestones. FDAAA requires that the expanded registry be operational 90 days after enactment [i.e., by December 26, 2007]. The law further requires that the registry databank be expanded using a phased approach to include results information. Starting 90 days after enactment (i.e., December 26, 2007), links are to be established from registry records to specified FDA and NIH results information. Such linking is not expected to entail additional collections of information. Not later than 1 year after enactment [i.e., September 27, 2008], FDAAA requires that the databank be expanded to include basic results information related to the demographic and baseline characteristics of the patient sample and to primary and secondary outcome measures. Compliance with this statutory requirement will entail an additional collection of information that will be announced via a separate public notice. FDAAA also requires that the Secretary of HHS expand the registry and results databank by regulation within 3 years of enactment (i.e., September 27, 2010). The regulations are to consider several topics, including the scope of trials for which mandatory reporting will be necessary and the types of information to be provided. Implementation of this regulation could therefore entail additional collections of information. Appropriate steps will be taken to provide public notice of such changes at the proper time.

17. Reason(s) Display of OMB Expiration Date is Inappropriate

No exemption is requested.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

No exceptions are requested.