Supporting Statement A For:

The Clinical Trials Reporting Program **(CTRP)** Database (NCI)

OMB #0925-0600

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Reinstatement with Change –
Extending the current program for another three (3) years

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List of Attachments

The Clinical Trials Reporting Program (CTRP) is an electronic resource that serves as a single, definitive source of information about all NCI-supported clinical research. This resource allows the NCI to consolidate reporting, aggregate information and reduce redundant submissions. Information is submitted by clinical research administrators as designees of clinical investigators who conduct NCI-supported clinical research. The designees can electronically access the CTRP website to complete the initial trial registration for each protocol. Subsequent to registration, up to four amendments and four study subject accrual updates occur per protocol annually.

A. Justification

A.1 Circumstances Making the Collection of Information Necessary

This is a request for OMB to approval a reinstatement with change for the NIH NCI Clinical Trials Reporting Program (CTRP) Database for an additional three (3) years. This submission includes no changes to the data collected from the 2010 submission; the only changes have been to improve the user interface, system performance, and reporting capability to support NCI information needs.

The National Cancer Institute (NCI) developed the Clinical Trials Reporting Program (CTRP) Database (http://www.cancer.gov/clinicaltrials/ctrp/page2) to serve as a single, definitive source of information about all NCI-supported clinical research, thereby enabling the NCI to execute its mission to reduce the burden of cancer and to ensure an optimal return on the nation's investment in cancer clinical research. Deployment and extension of the CTRP Database is an infrastructure development project that was enabled by public funds expended pursuant to the American Recovery and Reinvestment Act of 2009. In addition, deployment of this resource has allowed the NCI to consolidate reporting, aggregate information and reduce redundant submissions. Information is submitted by clinical research administrators as designees of clinical investigators who conduct NCI-supported clinical research.

In 2005, the National Cancer Advisory Board (NCAB) (see **Attachment 1**), the federal advisory committee that advises the National Cancer Institute (NCI) on the national cancer

program, approved the recommendation of its Clinical Trials Working Group (CTWG) to consolidate reporting, aggregate information and reduce redundant submissions (see **Attachment 2**) The NCAB also charged NCI program staff with implementing this recommendation. Subsequent reports to the NCI Clinical Trials Operating Committee (CTROC), the group within NCI responsible for implementing the CTWG recommendations, indicate that the agency's current approach to clinical trials reporting prevents NCI from fully executing its mission. In effect, advances in information technology have rendered obsolete NCI's current framework for complying with its statutory data collection and dissemination obligations.

NCI is charged by the National Cancer Act, 42 USC § 285, with managing the Nation's cancer program. Specifically, NCI is required to:

- ***Collect, analyze and disseminate all data useful in the prevention, diagnosis, and treatment of cancer, including the establishment of an international cancer research data bank*** to collect, catalog, store, and disseminate insofar as feasible the results of cancer research undertaken in any country for the use of any person involved in cancer research in any country. *Stated in Section 407(a)(4) of the Public Health Service Act (codified at 42 USC § 285a-2(a)(2)(D); expanded in National Cancer Amendments of 1974 and the Health Research Extension Act of 1985 consolidated cancer communication activities and highlighted the International Cancer Research Data Bank.*

- Take necessary action to ensure that all channels for the dissemination and exchange of scientific knowledge and information are maintained between the National Cancer Institute and the other scientific, medical and biomedical disciplines and organizations nationally and internationally. *Stated in Section 410(8) of the Public Health Service Act, codified at 42 USC § 285a-2(a)(1).*

- Prepare in consultation with the National Cancer Advisory Board and submit to the President for transmittal to the Congress a report on the activities, progress, and accomplishments under the National Cancer Program during the preceding calendar year and a plan for the Program during the next five years. *Stated in Section 410A(b) of the Public Health Service Act, codified at 42 USC § 285a-4(b).*

NCI's role as the sponsor of a large number of cancer clinical trials implemented across a wide range of venues uniquely positions the Institute to take a global view of emerging knowledge about the effectiveness of cancer therapies, and to identify and disseminate important

patterns and insights in a timely way. Furthermore, these patterns and insights can be fed quickly back into NCI's program planning and prioritization activities to better identify global patterns in cancer trials as well as other diseases occurring in these large populations and avoid the inefficiency that results from duplication of clinical trials (e.g., two trials on broadly the same agent and condition being conducted simultaneously) and/or clinical trials conducted out of sequence (e.g., a Phase II trial being initiated after a Phase III trial of the same agent/condition has already begun).

The rapid pace of scientific progress has created an ever-increasing number of novel therapies to test. Only through an open, collaborative prioritization system involving all the critical stakeholders can the best decisions be made as to which agents and disease targets warrant an investment of taxpayer dollars in clinical trials.

Building a national clinical trials enterprise founded on the best science requires a new level of coordination and cooperation by ensuring that comprehensive information on cancer clinical trials is readily available for all stakeholders. This in turn will enhance scientific quality and prioritization so that NCI supports the best-designed trials, addressing the most important questions, leveraging the most significant scientific advances. It will also enhance standardization of tools and procedures for trial design, data capture, data sharing, and administrative functions to decrease effort and minimize duplication.

Routine review of safety, efficacy, and administrative data reported from ongoing NCI-funded clinical trials is essential to the timely recognition and appropriate dissemination of emerging insights on the safety and efficacy of new treatments, while also assuring that NCI's resources are invested productively, and that its program planning and prioritization activities are based on the best and most recent available data.

Fundamental to the success of this strengthened clinical trials prioritization process is access to comprehensive, up-to-date information about the status of cancer clinical trials. Accordingly, one of the CTWG report's recommendations was the creation of an electronic database that would afford the following benefits:

- When preparing new trial concepts and proposals, investigators can take into account other trials already completed or underway addressing similar questions, and thus eliminate unnecessary duplication of effort.
- Clinical trial prioritization is enhanced by having available a full picture of the cancer clinical trials enterprise.
- Patient accrual to trials is enhanced because physicians and patients are aware of relevant opportunities for participation in clinical trials.
- Potential patient harm is reduced because toxicity and adverse events that are recognized in active trials can be rapidly disseminated to other investigators and practicing clinicians.
- Patients benefit because patterns of favorable outcomes that are recognized in active trials can be rapidly disseminated to the clinical trials community.

The CTRP provides these benefits. The approval of this information collection will allow NCI to improve the user interface and functionality of this system.

A.2 Purpose and Use of the Information

The CTRP Database provides a comprehensive real-time view of the state of NCI-funded cancer clinical trials, which enables NCI to make informed prioritization decisions via disease-specific steering committees. Accordingly, this resource allows the NCI to:

- Manage its portfolio of cancer clinical research investments effectively;
- Consolidate and streamline existing reporting to individual programs within the NCI by aggregating the information already collected and eliminating the need for redundant submissions to the NCI;
- Comply with regulatory reporting requirements when acting as the sponsor of FDA-regulated clinical investigations;

- Prepare the detailed performance, financial management and administrative accountability reports required of Executive Branch agencies, including those required by Executive Orders or OMB Circulars, Memoranda and Guidelines; and

- Provide appropriate public access to cancer research information.

Additional benefits include:

- The reporting burden for grantees will become increasingly streamlined.
- Investigators will be aware of trials addressing similar questions that are already completed or in process to avoid duplication of efforts.
- Researchers will have a comprehensive view of the clinical research enterprise that will support the cancer research community's ability to prioritize efforts.

In order to achieve these objectives, the resource must contain information that is structured to facilitate comparison across trials and that complies with Federal guidelines related to health information standards. The information must be detailed enough to fully describe the rich portfolio of clinical research supported by NCI and updated in a regular, timely fashion so that effective, real-time decision making can be made. Further, in order to assess the performance of the NCI's research portfolio, the resource needs up-to-date information on accrual and outcomes, collected at an individual level with most identifiers removed as described below. For effective decision-making, the database will need to contain information for every clinical research activity supported either directly through awards for a specific project, or indirectly through funding support for technical or administrative infrastructure. More specifically, the resource will need to contain complete, standards-based, structured information on development phase, type of intervention or treatment, study design, and program through which funding is provided. The database must contain information concerning all clinical interventional and observational research conducted at institutions that receive NCI funding,

including NCI Cooperative Group trials, externally peer-reviewed trials, institutionally supported investigator-initiated trials, and industry-sponsored studies.

Submissions should include the trial protocol document, the template informed consent document, and IRB approval documentation, if available. In addition, information about the protocol registration (including lead organization, principal investigator, responsible party, trial type and purpose, etc.) and study subject accrual elements (date of birth, race/ethnicity, gender, and zip code) are collected (see **Attachment 3**).

The NCI Clinical Trials Reporting Office (CTRO), a unit in the Office of the NCI Director, supports the NCI's CTRP, extracts additional information from submitted documents, including information describing any limitations on data use or limitations that may affect the submission or affect re-disclosures. Awardees are responsible for reviewing any documents governing the conduct of study or use or disclosure of information collected during the study (e.g., informed consent documents, clinical trial agreements, material transfer agreements, and other sponsored funding or resource sharing agreements) and notifying NCI of any restrictions that could affect NCI's use or disclosure of the submitted information. With respect to trials subject to proprietary restrictions, awardees are only be expected to submit the protocol title, the name of the principal investigator, the sponsor, and the accrual data listed above though additional information may be submitted voluntarily. In some instances, certain entities funded by NCI may be expected to submit additional information as compared to previous reporting patterns.

The portions of the NCI CTRP Database that pertain to the description of clinical research projects and summarized information on accrual will be publicly accessible. This availability will facilitate the cancer community's development of research proposals by

providing up-to-date information on the existing portfolio of research activities, thereby reducing duplication of effort by accessing a full picture of the cancer clinical research enterprise. Patient accrual and recruitment will be enhanced through better physician/patient access to clinical research data. All nonpublic parts of the resource will be maintained confidentially in accordance with appropriate security access controls pursuant to applicable policies.

While no additional information is being collected beyond that which was submitted in the previous application, over the past two years, significant effort has been made by the NCI to further improve the reporting process within CTRP, via backend system enhancements to improve system response times, streamlined user interfaces based on analysis of user interactions and feedback from the user community, and extensive communications and training efforts with the user community.

A.3 Use of Improved Information Technology and Burden Reduction

Development of the NCI CTRP Database is managed by the NCI Center for Biomedical Informatics and Information Technology (CBIIT); it is built on a state-of-the-art information technology platform using a shareable, common semantic services-oriented architecture and compliant with current biomedical data standards such as HL7® Version 3 and CDISC®. A current Privacy Impact Assessment (PIA) is in place and the IT system name is, "NIH NCI Enterprise Services and Clinical Trials Reporting Program" (see **Attachment 4**).

The CTRP Database receives electronic data feeds from existing NCI systems to the extent available, thereby reducing the reporting burden. The data received from these systems represent the vast majority of trial registrations and accruals in the NCI-supported clinical research enterprise. For the remaining trials, the CTRP Database will support three methods for registration, study subject accrual reporting, and ongoing reporting:

- Online registration, update, and amendment of individual trials and submission of study subject accrual information via the CTRP web portal (see **Attachment 3**)

- Batch registration, update, and amendment of multiple trials, and batch submission of study subject accrual information, uploadable directly to the CTRP Database via a Microsoft Excel file

- Direct connection of site systems to NCI Enterprise Services for seamless near-real-time update of the CTRP Database

NCI's statutory collection obligations under the National Cancer Act, as well as its objective to consolidate existing reporting to individual programs within the NCI, aggregate the information already collected by these programs and eliminate the need for redundant submissions to the NCI, were major considerations in establishing this system. The CTRP Database has been designed so that as much as possible of the burden is shouldered by the staff of the NCI CTRO rather than by the respondent. In brief, the registration process is as follows:

1. The respondent registers the trial with the NCI Clinical Trials Portal (see **Attachment 3**) by entering the data elements identified above in Section A.2 and uploading the protocol document file. The system sends an electronic notification to staff at the CTRO that the protocol has been registered.

2. CTRO staff members perform quality control (QC) on the registration submission and then abstract the remaining protocol elements used by the CTRP Database. Other CTRO staff members perform quality assurance (QA) on a sample of abstracted data.

3. The system generates a "trial summary report", detailing the data that have been abstracted, and sends it via e-mail to the respondent for review. The coding letter e-mail message includes a "verification link" on which the respondent can click to either:

    a. approve the data as correct, or
    b. query, or request change, to abstracted data.

The NCI has worked with the user community to develop study subject accrual reporting mechanisms which are similar to those already in place for reporting on NCI sponsored clinical trials to the NCI, reporting on these trials is done separately via established mechanisms and that information is supplied to CTRP electronically within the NCI to reduce reporting burden. The

primary mechanism used for accrual reporting is a series of excel templates (see **Attachments 5a-5e**) though a web interface is provided for trials/sites with minimal study subject accrual (see **Attachment 3**).

There is also a CTRP Registration Site User's Guide (see **Attachment 6**) and CTRP Accrual User's Guide (**Attachment 7**) which provides the users reference material should they need assistance during the registration or amendments of the clinical trials and submission of study subject accrual information.

A.4 Efforts to Identify Duplication and Use of Similar Information

The Clinical Trials Working Group conducted a comprehensive review of current systems managing protocol information at the NCI. Due to initial scope, purpose, and data structure, it was determined that a new comprehensive system was necessary to accommodate the evolving NCI clinical trials enterprise. Existing systems were determined to be inappropriate for the purpose of pan-NCI trial prioritization, management and monitoring. Accordingly, the NCAB approved the establishment of an electronic resource to address these needs.

The CTRP Database, which serves to modernize the existing cancer clinical trials reporting infrastructure previously instantiated through the NCI's PDQ/Cancer.gov clinical trials submission portal, is also designed as an operational database for active, efficient and ongoing prioritization and management of cancer clinical trials. For example, in terms of data elements, several key concepts, such as objectives and structured eligibility criteria, are embedded in the CTRP Database specifications. In addition, the CTRP Database allows the specification of data elements of interest within conditions (e.g., in cancer clinical stage, histological type, grade of tumor), or qualifiers (e.g., "unresectable", "localized", "recurrent"). With respect to timing of collection, the CTRP Database enables investigators to update current data elements quarterly in

real-time. Real-time submission by NCI awardees of accrual, outcome and adverse event data directly into the CTRP Database is critical if NCI is to be able to perform this kind of portfolio management. Further, as the data elements relating to outcomes are finalized, NCI expects the scope of information to be solicited to be much broader and more detailed, given the role of the CTRP Database in terms of facilitating NCI's portfolio management responsibilities.

A.5 Impact on Small Businesses or Other Small Entities

The vast majority of data collection for clinical trials will involve NCI-designated Cancer Centers or other major medical centers. A small number of physicians in small practices conduct trials within the context of NCI Cooperative Groups.

A.6 Consequences of Collecting the Information Less Frequently

The initial registration occurs once per protocol and it is estimated that there will be up to 5,500 protocol registrations per year.

For each protocol, consistent with regulatory and reporting requirements, respondents must supply an update to protocol/study information every time there is an amendment or a change in recruitment status. After analysis of the number of amendments over the past couple of years, amendments occurred up to four (4) times per protocol per year for some protocols. Not collecting updates and amendments will greatly compromise NCI’s ability to prioritize and monitor the system.

For accrual information reporting, the CTRP Database is designed to accept data submissions on a quarterly basis, consistent with the schedule for NCI-sponsored trials in fulfillment of NCI’s reporting obligations to the Food and Drug Administration. This synchronization is intended to minimize the burden of accrual reporting. Indeed, collecting

accrual information less frequently could even increase the burden on NCI awardees as they might have to keep to two distinct schedules for different kinds of trials.

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

No special circumstances are anticipated.

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

The 60-Day Federal Register notice soliciting comments regarding the revision of the existing information collection and expansion to include new data elements prior to submission to OMB was published on February 1, 2013 (Volume 78, page 7437). No public comments were received.

In the past, NCI has solicited and received public input from many sources, including direct input from NCI Advisory Boards and research organizations supported by the NCI, both of which include patient advocates (See **Attachments 1 and 8**). In addition, the informational website for the NCI Clinical Trials Reporting Program provides a mechanism for ongoing and routine electronic communications with the public (http://www.cancer.gov/clinicaltrials/ctrp/page9.) In 2010, the Clinical Trials Reporting Program (CTRP) Strategic Subcommittee, co-chaired by Dr. Kevin Cullen, Director, University of Maryland Greenebaum Cancer Center, and Dr. Sheila Prindiville, Director, Coordinating Center for Clinical Trials, NCI, was formed in collaboration with members of the NCI cancer research community, leadership of NCI designated Cancer Centers and the AACI. The charge of the subcommittee was to identify current and estimated future workload and timeframe to meet CTRP information requirements for: 1) registration; 2) accrual (summary, patient level with demographics, disease coding); and 3) outcomes (**see Attachment 11**).

A.9 Explanation of Any Payment or Gift to Respondents

No gifts will be given to respondents, nor any such expectations set. However, in order to mitigate the burden associated with adjusting to this new reporting mechanism, the NCI has offered participating NCI-designated Cancer Centers administrative grant supplements. Other awardees are not expected to have significant costs during the first year of operation and therefore will be encouraged to estimate reporting costs in connection with submission of grant and contract proposals to the NCI.

A.10 Assurance of Confidentiality Provided to Respondents

Personally identifiable information (PII) will be collected in the form of individual level study subject accrual information to the CTRP Database on a quarterly basis. Patient birth date, patient zip code, patient gender and race/ethnicity are considered PII. However, as none of the data elements for individual level study subject data request individually identifying information, e.g., names, addresses, or phone numbers, NCI does not collect any individual information through CTRP that can be retrieved using personal identifiers.

"Study subject ID" refers to a code assigned by an individual trial site where a research subject or patient is accrued on a study. The code is unique to the study subject within the context of the specific protocol but does not replace any individual identifiers and cannot be derived from any information related to the individual. Further, any key associated with such code is not provided to NCI. Therefore, NCI has no mechanism by which it can link information provided pursuant to this data element with an individual subject's identity. In other words, NCI does not receive any information from submitters which it could use with the PII to re-identify research subjects or patients. This information collection has also been reviewed by NIH Office of Human Subjects Research (see **Attachment9**).

The NIH Privacy Act Officer has determined that the Privacy Act does not apply to this information collection (see **Attachment 10**).

A.11 Justification for Sensitive Questions

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

A.12 Estimates of Annualized Burden Hours and Costs

The annualized burden for CTRP registration and amendments is estimated to require 33,000 hours, which amounts to 99,000 burden hours over the three year clearance period (see Table A.12-1). In the 2009 and 2010 OMB submissions initial registration was estimated to take respondents up to 2 hours to complete. However after several years of analysis, it is apparent that the average time to complete the initial registration ranges from 45 to 60 minutes, rarely exceeding 1 hour to complete. Thus the time to complete the instrument has been decreased to account for this adjustment.

A total number of 570 small, medium and large institutions are anticipated to complete the initial registration, updates, amendments and accrual process during the year. At these institutions, a varying number of clinical investigator designees will submit this information. As a result of the difficulty in estimating the number of designees submitting information per institution, it is more reasonable to account for the burden based on a per-trial basis. It is estimated that there will approximately 500 trials submitted from small entities and 5000 trials submitted from the medium to large institutions; this amounts to a total of 5,500 trials annually.

This burden estimate is very conservative because it assumes that no respondent will take advantage of the electronic batch upload features of the CTRP Database. As the NCI gains more experience with the program, it will be able to revise the burden estimate to reflect more accurately the actual time required for record-keeping.

A.12 - 1 Estimates of Annual Burden Hours					
Type of Respondents	Instrument	Number of Respondents	Number of Responses per Respondent	Average Time per Response (in hours)	Annual Burden Hours
Clinical Trials	Initial Registration	5,500	1	1	5,500
	Amendment	5,500	4*	1	22,000
	Accrual Updates	5,500	4	15/60	5,500
Total					33,000

* It is estimated that amendments (major scientific change requiring IRB approval) will occur up to four (4) times per year. However, some protocols have no changes and others change more frequently.

Cost estimates are based upon burden hours at an average cost of $35.00 per hour for clinical research administrators to complete the information. The annualized cost to the respondents is estimated at $1,155,000 (see Table A.12-2). This amounts to a total cost of approximately $3.5 million over the three year clearance period. The record-keeping burden represents an average time required for the initial registration and amendments to the records.

A.12 - 2 Annualized Cost to Respondents				
Type of Respondents	Survey Instrument	Annual Burden Hours	Hourly Wage Rate	Respondent Cost
Clinical Trials	Initial Registration	5,500	$35	$192,500
	Amendments	22,000	$35	$770,000
	Accrual Updates	5,500	$35	$192,500
Totals		33,000		$1,155,000

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

There is no additional cost burden to the respondents and record-keepers.

A.14 Annualized Cost to the Federal Government

The operating budget for the CTRP Database in FY2012 was approximately $4.5 million, which includes NCI staff salaries, overheads and equipment. It is anticipated that these costs will decrease over the next three years as the system and program is in an Operations and Maintenance state.

Costs (in millions)	FY2013	FY2014	FY2015	Estimated Annualized Cost over next 3 years
NCI staff salaries, overheads and equipment	4.0	3.5	3.5	3.67

A.15 Explanation for Program Changes or Adjustments

This application seeks a reinstatement with change for an additional 3 more years. Changes to the program have focused on improving system performance, reporting capability to support NCI information needs, and user interface enhancements. There are no changes to the information collected and no new data elements have been added. A decrease in the burden hours is being requested compared to the previous submission. In the previous submission, initial registration was estimated to take respondents up to 2 hours to complete. However after several years of analysis, it is apparent that the average time to complete the initial registration ranges from 45 to 60 minutes, rarely exceeding 1 hour to complete. Thus the estimated time to complete the initial registration has been decreased from 11,000 hours to 5,500 hours/year, which has decreased the total burden being requested from 38,500 to 33,000 hours/year.

A.16 Plans for Tabulation and Publication and Project Time Schedule

NCI deployed CTRP while minimizing disruption to the active conduct of clinical trials within the NCI-supported clinical research enterprise. CTRP is fully deployed and reporting happens according to the described schedule.

Table A.16-1: Implementation Time Schedule

Activity	Start Date after OMB Approval	Completion Date after OMB Approval
Production Deployment of CTRP Database		
Registration of New Trials	Immediately	Ongoing
Registration of Existing Trials	Immediately	12 months
Submission of Study Subject Accrual Information	Immediately	Ongoing

Access to data in the NCI CTRP Database is provided as follows:

Access for NCI program and administrative staff (in order to provide reports as needed for NCI's prioritization infrastructure): Full access to the data within the CTRP Database is provided to designated, appropriate NCI employee and contractor staff for purposes of portfolio management and compliance with regulatory and administrative reporting obligations. Access is limited to those with a direct need to access the data. Access is granted to non-Federal staff under a non-disclosure agreement and staff are given mandatory privacy and security training.

Public access: Appropriate open access to protocol registration information and summary level patient accrual and outcomes information will be provided to all persons not described above, including NCI intramural researchers.

Access for submitters: Individual submitters have full access to information they have submitted; institutions of individual submitters have access to tools that gather and present the accumulated data submitted by their individual investigators. Some cancer centers have

indicated to NCI that the CTRP Database will be useful to them in order for them to manage their own clinical research portfolios.

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

All instruments display the OMB expiration date.

A.18 Exceptions to Certification for Paperwork Reduction Act Submissions

No exceptions to the Certification for Paperwork Reduction Act Submissions are requested.