SUPPORTING STATEMENT A For:

Drug Accountability Report Form and Investigator Registration Procedure in the Conduct of Investigational Trials for the Treatment of Cancer (NCI)

OMB No. 0925-0613

February 5, 2013

Yellow text identifies revisions.

This is a revision of:

Investigator Registration and Financial Disclosure for Investigational Trials in Cancer Treatment (NCI) (OMB No. 0925-0613, Expires 2/28/2013)

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*Indicates a form/instrument.

[1] NCI/DCTD/CTEP refers to the National Cancer Institute's, Division of Cancer Treatment and Diagnosis, Cancer Therapy Evaluation Program.
[2] DCP refers to the National Cancer Institute's, Division of Cancer Prevention.

The U.S. Food and Drug Administration (FDA) holds the National Cancer Institute (NCI), Division of Cancer Treatment and Diagnosis/Cancer Therapy Evaluation Program (NCI/DCTD/CTEP) and the Division of Cancer Prevention (DCP) responsible, as a sponsor of investigational drug trials, for the collection of information about the clinical investigators who participate in these trials and to assure the FDA that systems for accountability are being maintained by investigators in its clinical trials program. The information collected is used to identify qualified investigators and to facilitate the submission and distribution of important information relative to the investigational drug and the response of the patient to that drug. Investigators are physicians who specialize in the treatment of patients with cancer. Data obtained from the Drug Accountability Record is used to track the dispensing of investigational anticancer agents from receipt from the NCI to dispensing or administration to patients. NCI and/or its auditors use this information for compliance purposes.

A. JUSTIFICATION

A.1. Circumstances Making the Collection of Information Necessary

The National Cancer Institute, Division of Cancer Treatment and Diagnosis/Cancer Therapy Evaluation Program (NCI/DCTD/CTEP) and the Division of Cancer Prevention (DCP) is requesting OMB approval under the Paperwork Reduction Act (44 U.S.C. 3501 et seq.) for the reporting and record keeping requirements contained in the Food and Drug Administration (FDA) regulation "Investigational New Drug Application" (Title 21 Code Federal Regulations (CFR) Part 312) specifically as it pertains to the registration of investigators who participate in NCI/DCTD/CTEP and DCP sponsored protocols and requirements for Investigational New Drug (IND)'s sponsors. The NCI/DCTD/CTEP fosters drug development to benefit cancer patients and as an IND sponsor is:

1) required to select only investigators qualified by training and experience as appropriate experts to investigate the drug, and
2) to assure the FDA that systems for accountability are being maintained by investigators in its clinical trials program.

This request is for a revision of OMB No. 0925-0613 that expires on February 28, 2013. This revision includes the combination of both the Investigator Registration and the Drug

Accountability Forms (OMB No. 0925-0240), which prior to now, existed as separate OMB submissions. As well as the expansion of the Division of Cancer Prevention's use of investigator registration forms. Additionally, it is planned that some of these forms will be collected electronically (see Section A.3 for further discussion).

Investigator Registration Procedure in the Conduct of Investigational Trials for the Treatment of Cancer

The U.S. Food and Drug Administration (FDA) have numerous requirements for sponsors specified in 21 CFR Part 312.53. These regulations require sponsors to obtain information from the investigator. Before permitting an investigator to begin participation in an investigation the sponsor shall obtain the following:

(1) a signed investigator statement (Form FDA 1572)
(2) Curriculum vitae, and
(3) Financial disclosure information

The information collected on the NCI/DCTD/CTEP *Modified* FDA Form 1572[3] is similar to that collected by the FDA. However, the NCI/DCTD/CTEP version provides guidance to the investigator to facilitate the completion of the form. The FDA has allowed NCI/DCTD/CTEP to use a different process for collection and revision of the data due to the unique manner in which the NCI conducts studies compared to other sponsors.

The Cancer Therapy Evaluation Program (CTEP) collaborates with other programs within the NCI to collect registration data for their trials. This joint process reduces duplication and provides a consistent procedure within those programs of the National Cancer Institute. A

[3] The FDA Form 1572 has been used at NCI/DCTD/CTEP for several decades with this title, or is also known as, Investigator Registration Form. It is recommended that the current name remain as is since a change in the name of the form would cause confusion and compromise the process, ultimately effecting the timely treatment and care for patients.

small subset of trials conducted by the Division of Cancer Prevention (DCP) uses an *unmodified* Form FDA 1572, however the information collected is similar in both Divisions.

The Drug Accountability Record (Form NIH 2564) (NCI/DCTD/CTEP)

For the Drug Accountability Form (Form NIH 2564), the FDA has numerous requirements for IND's for both the investigators and the sponsors. These regulations require investigators to:

- "…maintain adequate records of the disposition of the drug, including dates, quantity and use by subjects…" (312.62);
- "……. upon request from any properly authorized officer or employee of FDA, at reasonable times, permit such officer or employee to have access to, and copy and verify any records or reports made by the investigator pursuant to 312.62. The investigator is not required to divulge subject names unless the records of particular individuals require a more detailed study of the cases, or unless there is reason to believe that the records do not represent actual case studies, or do not represent actual results obtained." (312.68)
- "…furnish all reports to the sponsor of the drug who is responsible for collecting and evaluating the results obtained [in the investigation.]" (312.64).

Similarly, 21 Code of Federal Regulations includes requirements for sponsors to:

- "…maintain adequate records showing the receipt, shipment or other disposition of the investigational drug [to investigators]" (312.57);
- "…submit the records or reports (or copies of them) to the FDA [for inspection] (312.58);
- "…discontinue shipments of the investigational new drug to the investigator and end the investigator's participation in the investigation [if this] investigator is not complying with the signed agreement (Form FDA-1572), the general investigational plan, or the requirements of this part or other applicable parts…" (312.56); and
- "…make such reports to FDA regarding information relevant to the safety of the drugs..." (312.56).

The information collection implemented through these forms is authorized under sections 413(b)(1) of the Public Health Service Act (42 USC 285a-2). NCI/DCTD/CTEP, as an IND

sponsor, “shall establish or support the large-scale production or distribution of specialized biological materials and other therapeutic substances for cancer research and set standards of safety and care for persons using such materials.” To support this, NCI/DCTD/CTEP developed the "Drug Accountability Record" form (DARF) **(Attachment 1)** to help investigators using NCI sponsored drugs under NCI protocols to meet FDA requirements. For the NCI, the DARF serves as the missing link between NCI's record of drug distribution to an investigator and NCI's review of the clinical data on research patients; it ensures that investigational drugs are not diverted for inappropriate protocol or patient use.

Further, in response to change in the practice wherein the medication that was developed in the past was produced almost exclusively for intravenous administration, more investigational agents have been developed for oral administration because it is more convenient for the patient. The sponsor of the investigational trial is required to assure the proper distribution of the agent, but is also required to ensure the proper disposition of investigational agent. Whereas intravenous formulations of medications are administered at the medical facility, oral medications are commonly dispensed to patients for administration at home. Often these medications must be returned to the dispensing institution when the patient does not use them, for any number of reasons (withdraw from study, change in dose etc). In order to meet the regulatory requirements for the medications dispensed to the patient, NCI/DCTD/CTEP developed the Drug Accountability Report Form for Oral agents (DARF-Oral), (**Attachment 2**), to document the return of medication to the dispensing facility for final disposition.

A.2. Purpose and Use of the Information

Investigator Registration Procedure in the Conduct of Investigational Trials for the Treatment of Cancer

Various Programs within the NCI use different forms to collect data:

- NCI/DCTD/CTEP Modified FDA Form 1572 for annual submission (**Attachment 3A**)
- DCP unmodified Form FDA 1572 submitted on a protocol by protocol basis (**Attachment 3B**)
- NCI/DCTD/CTEP Supplemental Investigator Data Form (**Attachment 4**)
- NCI/DCTD/CTEP Financial Disclosure Form (**Attachment 5A**)
- DCP Financial Disclosure Form per protocol submission (**Attachment 5B**)
- Optional electronic form for Investigator Registration (Online Credentialing Repository aka. OCR, formerly referred to as Firebird) (**Attachment 10)**
- Curriculum vitae (**Attachment 11**)

These data forms ensure compliance with NCI/DCTD/CTEP and DCP's responsibilities as an IND sponsor. The FDA can request copies of these forms at any time for audit and review. Record keeping of investigator registration and financial disclosure data in a standard format is required to track compliance and to allow an investigator to receive, and continue to receive NCI-sponsored drugs. NCI/DCTD/CTEP does not establish a standardized format for submission of the Curriculum vitae (CV) but allows the investigator to submit the information in the any configuration they chose. This requirement is an essential part of investigator accountability process and motivates them maintain accurate, appropriate records. The NCI Online Credentialing Repository (OCR) allows for capture of structured CV information through the use of web forms. Implementation of this information collection mechanism is being explored and is included in this application for approval. The record keeping retention period is specified by FDA regulation, and the NCIdoes not deviate from that requirement. As noted

above, the FDA requires IND sponsors to maintain adequate records on the shipment and disposition of drugs to investigators.

The Drug Accountability Record (Form NIH 2564)

In September 1982, each participant received the proposed Drug Accountability Record form and instructions and was asked to apply it to the dispensing of investigational anticancer drugs in their practice setting. In November 1982, each participant submitted his or her records to NCI. A meeting was then arranged at NIH to discuss their experiences. All participants felt that the procedure could be implemented without undue burden. The committee decided that recording of patient's "informed consent" each time a drug was dispensed would be difficult. Since obtaining Informed Consents from patients is a legal requirement for all clinical investigation, it was decided that the recording of the date of each patient's consent was unnecessary and deleted from the original form.

The DARF is used by NCI/DCTD/CTEP in the management of approximately 100, NCI/DCTD/CTEP sponsored INDs. Pharmacists, nurses and investigators or their designee at medical institutions use the information entered onto the DARF to keep track of the dispensing of investigational anticancer drugs to patients. NCI/DCTD/CTEP uses the data from the DARF to ensure compliance with our responsibilities as an IND sponsor. The requested information is retained exclusively at the institution and examined on a triennial basis or as needed more frequently if investigational medication cannot be accounted for. It is not collected or sent anywhere else. NCI/DCTD/CTEP Management can request copies of the DARF at any time for audit and review and DARFs are reviewed at least once every 3 years during site audits.

The information contained in the DARF is compared to already existing information in the Pharmaceutical Management Branch-Drug Authorization Review and Tracking System (PMB-DARTS)[4] module histories for each investigator and clinical site to ensure no diversion of investigational drug supplies to inappropriate protocol or patient use. The accountability information is also compared to patient flow sheets (protocol reporting forms) during site visits conducted for each institution. All comparisons are completed with the intention of ensuring protocol integrity, patient safety, and compliance with FDA regulations. Record keeping of drug accountability information in a standard format is required to allow an investigator to receive, and continue to receive NCI-sponsored drugs. This information is reviewed at the time of site visit audits, which currently occur at least once every 3 years. The IND sponsor may also request copies of the DARF at any time. This requirement is an essential part of investigational agent accountability process and motivates the investigator to maintain accurate, appropriate records. The record keeping retention period is specified by FDA regulation, and the NCI/DCTD/CTEP does not deviate from that requirement. As noted above, the FDA requires IND sponsors to maintain adequate records on the shipment and disposition of drugs to investigators.

During the past 20+ years, the Drug Accountability Record Form has been in continuous use; there have been no significant problems expressed concerning the use of the form and site visit audit team leaders have not made any suggested changes in the form or procedures. In May of 2012, the Pharmaceutical Management Branch worked with members of the investigational community to address the issue of accountability of for oral medication that had been dispensed to the patient, but had to be returned when it was no longer required. This effort resulted in the

[4] PMB-DARTS is part of the CTEP Enterprise computer database discussed further in Section A.3.

modification of the existing DARF to develop the DARF-Oral so that the returned medication could be documented more clearly and comply with regulatory requirements.

A.3. Use of Information Technology and Burden Reduction

Investigator Registration Procedure in the Conduct of Investigational Trials for the Treatment of Cancer

The use of improved information technology techniques has been considered. One element of the NCI Online Credentialing Repository (OCR) initiative, previously known as FIREBIRD, is the incorporation of this information into an electronic database that integrates the submissions of the public and private sectors. This project is currently under development by NCI, however is not currently in use for this information collection. The NCI OCR system is being included for approval in this application as an information collection mechanism for investigator registration. NCI OCR will allow investigators to maintain their registration and optionally their CV data electronically in an online profile, which is anticipated to lower the overall burden of information collection as the information provided in the first registration will be available for reuse on subsequent registrations.

There is an IT system associated with the Investigator Registration (IR) process. Data is extracted into a Registration Module in the CTEP Enterprise computer system and a pilot program is underway. The pilot program involves scanning some already collected IR documents into a database. It is hoped that this pilot program will facilitate the implementation of either an online registration process or a 100% electronic storage for documents. A Privacy Impact Assessment (PIA) was approved by HHS on May 23, 2012. The IT system is titled, "NIH NCI Investigator Registration Filing Process" (**Attachment 9A**). In addition, the IT System name for OCR is "NIH NCI Clinical Research Information Exchange Federal Investigator Registry (CRIX FIREBIRD)" (**Attachment 9B**).

The Drug Accountability Record (Form NIH 2564)

At this time, use of improved and additional information technology has not been considered. The system continues to make the electronic version of the forms available on the CTEP web site. Sites download and print the form as it is needed.

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

Investigator Registration Procedure in the Conduct of Investigational Trials for the Treatment of Cancer

Though NCI/DCTD/CTEP's procedure is to collect the investigator registration on an annual basis compared to the FDA and DCP process, which is to collect this information on a per protocol basis, the NCI is requesting approval in the same document. The FDA utilizes a similar form and mechanism to collect this information from other sponsors of investigational trials. The FDA and DCP process is significantly different in that the investigator registration portion is a very small part of the Investigational New Drug Application process. The information and method utilized by the FDA requires significantly greater burden to the investigators who complete the forms and the government who review and retain the forms. More than 30 years ago the FDA and the NCI established a modified submission and retention procedure for investigator registration and financial disclosure information. Whereas the FDA requires other sponsors to submit this information on a protocol by protocol basis, the NCI/DCTD/CTEP collects this data annually. This was done to reduce the administrative burden on the individual NCI/DCTD/CTEP registered investigators since they often participate in numerous trials simultaneously.

Additionally, though the questions between the FDA version of the FDA Form 1572 and the NCI/DCTD/CTEP versions are the same, CTEP has pre-populated two responses in Blocks 6 (see **Attachment 3A**):

> *N/A-The Cancer Therapy Evaluation Program, National Cancer Institute requires each investigator to submit a separate FDA Form 1572, CV, Supplemental Data Form, and Financial Disclosure Form. The information entered in this section will NOT be entered in the CTEP NCI database.*

and Block 7 of the Form FDA 1572 to account for the annual submission of data.

> *I am participating in Cancer Therapy Evaluation Program (CTEP), National Cancer Institute-sponsored clinical trials. I understand that this single FDA Form 1572 will cover my participation in all (one or more) clinical trials under CTEP sponsorship (IND and/or funding). I also understand that I am responsible for meeting all the requirements for clinical trials specified by this signed FDA Form 1572 for EACH CTEP clinical trial in which I participate.*

Regarding the NCI/DCTD/CTEP Supplemental Investigator Data Form (see **Attachment 4**) and NCI/DCTD/CTEP Financial Disclosure Form (see **Attachment 5A**) the FDA does not specify a specific form for collection of this essential data. These forms were developed to fill the void created by the FDA requirement. The exact contents of the financial disclosure document are under review by higher authority based on conflicting requirements of regulatory entities. When the dispute is resolved changes to the documents may be required. Until that time, NCI/DCTD/CTEP continues to utilize the current document. The NCI/DCTD/CTEP procedure has been in place and met all of the regulatory requirements for more than 30 years. CTEP has built an extensive submission and tracking process around the annual submission procedure because it provides NCI/DCTD/CTEP with the most current data. Any changes to the existing process will require a major change in the form retention and retrieval mechanism as

well as the business processes at NCI/DCTD/CTEP. A change will increase the burden to both the investigator and the government.

A small portion of the NCI's portfolio, managed by the Division of Cancer Prevention (DCP), relies on the protocol by protocol registration process and uses the exact same forms as cleared by FDA, forms are available in **Attachments 3B and 5B**. As noted, DCP is required to capture this information under the Code of Federal Regulations. This registration process has also been in place for decades and while the NCI is working to streamline investigator registration through the implementation of an electronic information collection mechanism, NCI OCR, the NCI needs to continue to capture information via the two different sets of forms (annual and per protocol) due to the nature of NCI's clinical research and regulatory requirements.

In addition, it may be that respondents who complete the NCI/DCTD/CTEP Modified FDA Form 1572 may or may not fill out the FDA Form 1572 for other organizations (e.g. pharmaceutical companies) who also sponsor investigational trials. FDA holds the sponsor (i.e., NCI/DCTD/CTEP in this case) responsible for the conduct of the clinical trial and the collection and review of the NCI/DCTD/CTEP Modified Form 1572 to provide to the FDA upon demand.

The Drug Accountability Record (Form NIH 2564)

When NCI/DCTD/CTEP proposed development of the DARF in 1982, seven investigators who received investigational anticancer drugs from NCI were asked to form a task force to pilot the proposed drug accountability procedure **(Attachment 6)**. These investigators were selected from hospitals, universities, adult and pediatric cancer centers, clinical cooperative study groups and private practice settings. They were chosen because they accurately

represented the community of investigators receiving investigational drugs from the NCI. These investigators recruited the support of pharmacists and nurses who were familiar with the availability of the data, the frequency of collection and the clarity of instructions and record keeping.

The task force, at that time, was unable to identify any duplication of efforts regarding the Drug Accountability Record. When it became necessary to further document the return of oral medication, NCI worked with pharmacists at the institutional level who are responsible for accounting for medication disposition and those who monitor and audit the conduct of trials. This collaboration resulted in the identification of the essential elements for the form DARF-Oral. The DARF-Oral (**Attachment 2**) contains the information similar to that developed and implemented by the National Cancer Institute of Canada (NCIC) in collaboration with the NCI/DCTD/CTEP in the United States in 2010.

A.5. Impact on Small Businesses or Other Small Entities

Data collection for investigator registration involves primarily Hospitals, Universities and Cancer Centers, which are not small businesses. In some instances it involves physicians in private practice who participate in NCI sponsored investigational studies or receive investigational drugs but the number is very small. Private practice physicians do not receive vast amounts of drugs, and therefore the burden of data collection is minimal.

A.6. Consequence of Collecting the Information Less Frequently

Investigator Registration Procedure in the Conduct of Investigational Trials for the Treatment of Cancer

NCI/DCTD/CTEP collects the investigator registration and financial disclosure information annually. DCP collects this information on a per protocol basis where the one time

registration typically lasts for a number of years, depending on the length of the study. This frequency has been acceptable to the NCI and the FDA for 30 or more years with the justification that it adequately reflects changes in the investigator status, financial changes and shipping requirements. Investigators notify NCI/DCTD/CTEP when there are significant changes within the one year period, or over the course of a study.

The Drug Accountability Record (Form NIH 2564)

Drug accountability data record must be recorded every time a drug is received, administered, dispensed, or returned. The IND sponsor reviews the drug accountability data at triennial site visits. Between site visits, the institution should validate the data to maintain the quality of the drug accountability data. If drug accountability information were reviewed less often than once every 3 years, its accuracy and usefulness during site visits would be questionable. Since accountability data is cumulative by protocol, any error made would be compounded. Compounded errors are more difficult to detect and correct, thus limiting the effectiveness of the drug accountability procedure as an auditing tool.

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

For the investigator registration process, there are no special circumstances inconsistent with the guidelines in 5CFR 1320.5. However for the drug accountability record forms, it is estimated that the investigator or their designee would make 16 entries on this form annually, based upon the number of patients participating in the investigational study.

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

The 60-Day Federal Register Notice of the proposed data collection was published on September 20, 2012, Vol. 77, p. 58401. No public comments were received.

For the investigator registration process, there have been no recent collaborations with the FDA to work on the development of an electronic submission platform (refer to Section A.3 for a discussion about NCI OCR). FDA was consulted to ensure the electronic mechanism for investigator registration met regulatory requirements.

For the drug accountability record, in May 2012 at the request of investigators and pharmacists, the NCI/DCTD/CTEP cooperatively revised the DARF to provide additional information to document the return or oral medication to the institution when it is no longer required by or not appropriate for the study recipient to use. This revision was also consistent with the regulatory requirements of the sponsor.

A.9. Explanation of Any Payment or Gift to Respondents

Respondents will not receive any payment or gift for answering the questions.

A.10. Assurance of Confidentiality Provided to Respondents

For Investigator Registration, the release of information submitted to the NCI as part of the Investigator Registration/Financial Disclosure process is compliant with current regulatory requirements. For the Drug Accountability Record, the investigators or their designees are the record keepers of drug accountability information. The information submitted to NCI is made available to the IND sponsor and to FDA upon request to meet regulatory requirements 21 CFR Part 312.64(d) (for Investigator Registration) and to verify the legal use of investigational drugs (for DARF). Investigators are made aware of their legal requirements when they complete a FDA-1572 form and the NCI/DCTD/CTEP Investigator Supplemental Data form by which they

become eligible to use investigational new drugs (OMB # 0925-0613, Expiry Date 2/28/2013). The investigators or their designees retain the forms for a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated and closure of the NCI IND. However, if no application is to be filed or if the application is not approved for such indications, the records must be retained until 2 years after the NCI IND closure and FDA is notified.

The Office of Human Subjects Protection (OHSR) does not need to review this submission since this is an administrative collection of information in which generalization of findings is not conducted, and thus it does not meet the definition of "research" under regulations 45 CFR 46 (**Attachment 7**).

Individual patient names are not required on the DARF and DARF-Oral, only patient initials or institutional assigned patient specific code numbers to allow comparisons with patient protocol flow sheets (in compliance with HIPPA rules). These codes could be compared with patient protocol flow sheets and which if linked, could identify the patient. Without this reference, drug accountability would be impossible. The NIH Privacy Act Officer has reviewed this submission and has determined that the Privacy Act would apply to this data collection. This data collection for the Investigator Registration and the DARF is covered by NIH Privacy Act Systems of Record, 09-25-0200, "Clinical, Basic and Population-based Research Studies of the National Institutes of Health (NIH) HHS/NIH/OD," published in the Federal Register on 9/26/2002 (67 FR 60776) (**Attachment 8**).

A.11. Justification for Sensitive Questions

No sensitive questions are involved for either the Investigator Registration or DARF. However, personally identifiable information (PII) is being collected for both information collections.

Investigator Registration Procedure in the Conduct of Investigational Trials for the Treatment of Cancer

PII is being collected in the form of education, date of birth and UPIN of the investigator, and financial disclosure information. This information is necessary to meet regulatory requirements established by the FDA and to clearly establish the identity of investigators where there are similar or identical names. It also ensures that the investigator has completed required training, is licensed and practicing in the field of expertise in which the research is conducted. The collection and evaluation of this information by the NCI is required by the FDA of NCI as sponsor and protects the health and safety of patients who participate in investigational trials.

The Drug Accountability Record (Form NIH 2564)

PII is collected in the form of patient's initial, patient ID, NCI protocol number and title, NCI investigator number and information pertaining to the drug and its dose form and strength. As mentioned in A.10, alone this information may not be PII, however when linked it could identify a patient.

A.12. Estimates of Hour Burden Including Annualized Hourly Costs

A total number of 20,200 investigators are anticipated to complete the three Investigator Registration forms; this is an increase in about 3,000 respondents/annually since last submission. Due to the nature of DCP protocol registration, and additional 600 respondents are anticipated to complete the Financial Disclosure Form for DCP. The annualized burden for record keeping is

estimated to require 14,328 (see Table A.12-1). Over a three-year time frame, the burden is estimated to be 42,983 hours.

Including the DARF is estimated to add 3,907 investigators and 4,167 hours to the annual burden; this represents a slight decrease from the previous submission that estimated 4,196 investigators and 6,714 burden hours. Altogether, for both the Investigator Registration process and the DARF the annualized burden for record keeping is estimated to require 14,223 hours or approximately 42,670 hours for the three-year approval period. Additionally, provisions for the incremental implementation of electronic capture of structured curriculum vitae (CV) information has been added, a limited number of respondents are estimated to complete the electronic CV. The NCI will evaluate wide-scale implementation of the electronic CV over the next three years and reassess whether it impacted burden at that time.

Table A.12-1 Estimates of Annual Burden

Type of Respondents	Form	Number of Respondents	Frequency of Response	Average Time per Response (in Hours)	Total Hour Burden
Investigators and Designee for Investigator Registration and DARF	Statement of Investigator (Attachments 3A, 3B or 10)	20,200	1	15/60	5,050
	NCI/DCTD/CTEP Supplemental Investigator (Attachment 4)	20,112	1	10/60	3,352
	Financial Disclosure Forms (Attachment 5A or 5B)	20,800	1	5/60	1,733
	Electronic Curriculum Vitae (Attachment 11)	100	1	15/60	25
	NCI/DCTD/CTEP Drug Accountability Record Form (DARF and DARF-Oral) (Attachments 1 & 2)	3,907	16	4/60	4,168

Totals			14,328

The annualized cost burden to the respondents is estimated at $713,806.67 (see Table A.12-2).

The total cost is estimated at $2,141,420 over the course of the three-year information collection.

These estimates are based on the number of investigators supported by Pharmaceutical Management Branch. Cost estimates are based upon burden hours at an average cost of $60.00 per hour for Investigator Registration and $25.00 per hour for Drug Accountability Record. This estimate reflects the routine practice by the investigators to have administrative personnel complete the form followed by verification and signature by the investigator. The estimate is also based on FDA estimates of an industry average for preparing and submitting collected information. For re-registration the NCI sends forms pre-populated with the current data for the investigator to review, modify if required and sign. This practice dramatically reduces the burden to the investigator.

Table A.12-2 Annualized Cost to Respondents

Type of Respondents	Form	Total Hour Burden	Wage Rate per Hour	Respondent Cost
Investigators and Designee	NCI/DCTD/CTEP Statement of Investigator	5,050	$60	$303,000
	NCI/DCTD/ CTEPSupplemental Investigator	3,352	$60	$201,120
	Financial Disclosure	1,733	$60	$104,000
	Curriculum Vitae	25	$60	$1,500
	NCI/DCTD/ CTEPDrug Accountability Record Form	4,168	$25	$104,187
Total				$713,806.67

A.13. Estimate of Other Total Annual Cost Burden to Respondents or Record Keepers

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

A.14. Annualized Cost to the Federal Government

For both collections of information, the annualized cost to the Federal Government is estimated to be $812,500. Development of the NCI OCR system is projected to incur a one-time capital expense of $2.7 million. For the Investigator Registration process, the annualized cost to the Federal government for collecting, evaluation, sorting, entering into a tracking database, storing and coordinating annual renewal requires 9 FTEs at an estimated $795,000[5]. For the Drug Accountability Record, the total estimated cost to the Federal government is approximately $17,500. The annualized cost to audit the contents of the DARF at the institution is estimated to be approximately $17,500. This is based on one auditor spending 30 minutes (0.5 hours) reviewing the contents of the DARF files. Typically the auditors spend three (3) days auditing patient records of which one auditor spends 30 minutes auditing the DARF records. There is no additional cost for printing or distribution of the DARF since the form is available exclusively in electronic format and posted on the CTEP web site. Forms are downloaded at the institutional level and printed locally as needed.

A.15. Explanation for Program Changes or Adjustments

This is a request for a program change, considered a revision, which includes the logical combination of previously two OMB submissions into one. The U.S. Food and Drug Administration (FDA) holds the National Cancer Institute (NCI) responsible, as a sponsor of investigational drug trials, for the collection of information about clinical investigators who participate in trials and to assure the FDA that systems for accountability are being maintained by investigators in its clinical trials program. The increase in burden is primarily a reflection of the

[5] . There has been no increase in the costs since the last submission.

combination of these two submissions. This submission also includes the addition of the DCP information collection for investigator registration and the electronic mechanism for investigator registration information collection, NCI OCR. Additionally, the burden has increased as a result of actively accruing investigational studies and a greater number of patients participating in studies.

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

There are no plans to publish this data for statistical use.

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

The date will appear on all forms and information.

A.18. Exceptions to Certification for Paperwork Reduction Act Submissions

No exceptions to the certification statement are required by this information collection.