SUPPORTING STATEMENT A FOR:

THE DRUG ACCOUNTABILITY RECORD (NCI)

SUBMITTED BY:
PHARMACEUTICAL MANAGEMENT BRANCH, CTEP, DCTD
NATIONAL CANCER INSTITUTE

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A. Justification

A.1 Circumstances making the collection of information necessary.

The National Cancer Institute (NCI) fosters drug development to benefit cancer patients and as an Investigational New Drug (IND) sponsor makes investigational drugs available to patients through investigators registered with the sponsor and, in turn, registered with the U.S. Food and Drug Administration (FDA). The FDA has numerous requirements for IND's specified in 21 CFR 312.1. FDA regulations require investigators: To maintain adequate records of the disposition of all investigational drugs received from the sponsor; to prepare and maintain adequate case histories of treated patients and controls; and to furnish reports to the drug sponsor who is responsible for evaluating the results of the investigation. Similarly, 21 CFR 312.1 includes requirements for sponsors to maintain adequate records on the shipment of drugs to investigators; to make individual patient records available to the FDA for inspection; and to submit accurate progress reports of the drug investigation to the FDA. The information collection implemented through these forms is authorized under sections 413(b)(1) of the Public Health Service Act 42 USC 285a-2). The NCI, as an IND sponsor has developed the "Drug Accountability Record" form (DARF) (Attachment 1) to help investigators using NCI sponsored drugs under NCI protocols to meet FDA requirements.

These requirements include the responsibility to "maintain adequate records of the disposition of all receipts of the drug, including dates, quantity and use by subjects" (21 CFR 312.1). For the NCI, the DAR form (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. This request is for an extension of OMB 0925-0240 that expires on 11/30/07. The DARF is used by the NCI in the management of approximately 160 NCI sponsored INDs.

A.2 Purpose and Use of the Information Collection

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 uses the data from the DARF to ensure compliance with NCI's responsibilities as an IND sponsor. NCI Management 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 PMB-DARTS 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 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 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.

A.3 Use of Information Technology and Burden Reduction

Consideration of the use of improved information technology has been addressed. As indicated in this supporting statement (see Section A.8), a committee of seven representative investigators and institutions were selected to field-test the accountability procedure. In so doing, one institution, St. Jude

Children's Research Hospital voluntarily programmed the accountability form into a microcomputer. This approach using automated technology worked well and provided NCI with the drug dispensing data required. According to St. Jude, it also gave the institution greater flexibility in utilizing data available at the institution to better manage patient drug treatment. It was the consensus of the committee that Automated Data Processing (ADP) technology could be applied to the accountability record by any institution if they chose to do so. Since the original report, additional clinical sites and organizations (including the NCI) have or will be automating this process.

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

The committee, mentioned in A.3, at that time, was unable to identify any duplication of efforts regarding the Drug Accountability Record.

A.5 Impact on Small Business or Other Small Entities

Data collection for Drug Accountability mostly involves Hospitals, Universities and Cancer Centers, which are not small businesses. In some instances it involves physicians in private practice who receive investigational drugs. Private practice physicians do not receive vast amounts of drugs, and therefore the burden of data collection is minimal.

A.6 Consequence of Less Frequent Collection

Drug accountability data record keeping is timely; it changes and must be recorded every time a drug is received, administered, dispensed, or returned which can be several times each day. The IND sponsor reviews the Drug Accountability data at triennial site visits. Between site visits, there may also be an institutional effort made 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

No special circumstances inconsistent with the guidelines in 5CFR 1320.5 are known.

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 August 13, 2007, Vol. 72, No. 55, Page 45251. No public comments were received on the proposed information collection**.** The 30-Day Federal Register Notice of the proposed data collection was published on November 1, 2007, Vol. 72, No. 211, Page 61889. When the NCI 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. 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 represent 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. Although the work of this task force was done many years ago, it is still representative of the current drug accountability procedure.

a) The Consultants were as follows:

Investigator: Stephen Schimpff, M.D.
Pharmacist: Mr. William Grove
University of Maryland Cancer Center
22 S. Greene Street
Baltimore, Maryland 21201
(410) 328-7606

Investigator: Robert Warren, M.D.
Nurse: Ms. Faith Jodoin
5226 Dawes Avenue
Alexandria, Virginia 22311
(703) 379-9111

Investigator: James Holland, M.D.
Pharmacist: Mr. Robert Frank
Mt. Sinai Hospital
1 Gustave L. Levy Place
New York, New York 10029
(212) 41-6361

Investigator: Emil Frei, M.D.
Pharmacist: Dr. Steve Steckel
Dana Farber Cancer Center
44 Binney Street
Boston, Massachusetts 02115
(617) 632-3555

Investigator: Joseph Simone, M.D.
Pharmacist: Mr. Raymond Mueller
Memorial Sloan-Kettering Cancer Center
1275 New York Ave
New York, NY 10021
(212) 639-5842

Investigator: Ray Warrell, M.D.
Pharmacist: Mr. Raymond Mueller
Memorial Sloan-Kettering Cancer Center
1275 York Avenue
New York, New York 10021
(212) 794-7615

Investigator: Philip Schein, M.D.
U.S. Bioscience, Inc.
One Tower Bridge, Ste 400
West Conshohockem, PA 19428
(215) 832-4501

b) Methods: In September 1982, each participant received the proposed Drug Accountability Record form and instructions and were asked to apply it to the dispensing of investigational anticancer drugs in their practice setting. In November 1982, each consultant 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.

c) Results: 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. The Privacy Act would not apply to the Drug Accountability Record since there is no direct linkage of patient information. This protects the patient confidentiality during the study.

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

a. Investigators or their designees are the record keepers of drug accountability information. The information is made available to the IND sponsor and to FDA upon request to verify the legal use of investigational drugs. Investigators are made aware of their legal requirements when they complete a FDA-1572 form and the Investigator Supplemental Data form by which they become eligible to use investigational new drugs. 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.

b. Patient Names: Individual patient names are not required on accountability forms, only patient initials and hospital numbers are requested to allow comparisons with patient protocol flow sheets (in compliance with HIPPA rules). Without this reference, drug accountability would be impossible.

c. The records in this data system are covered by NIH Privacy Act system of records, 09-25-0200, "Clinical, Epidemiologic and Biometric Studies of the National Institutes of Health (NIH) HHS/NIH/OD."

A. 11 Justification for Sensitive Questions

No sensitive questions are involved.

A. 12 Estimate of Hour Burden Including Annualized Cost Estimate

The annualized respondent's burden for record keeping is estimated to require 6,240 hours for the DARF. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.

A.12-1 Estimates of Annual Burden

Type of Respondents	Number of Respondents	Frequency of Response	Average Time per Response	Total Hour Burden
Investigators, or Designees	3,900	16	0.1 (6 minutes)	6,240

The annualized cost burden to the respondents is estimated at $156,000. The record-keeping burden represents an average time required for entries (6 minutes) on the DARF, the average number of forms maintained by each record keeper and the number of record keepers. These estimates are based on the number of investigators supported by PMB. Cost estimates are based upon burden hours at an average cost of $25.00 per hour.

A.12-2 Annualized Cost to Respondents			
Type of Respondents	Total Hour Burden	Wage Rate per Hour	Respondent Cost
Investigators, or Designees	6,240	$25	$156,000

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

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

A. 14 Annualized Cost to the Federal Government

There is no annualized cost to the Federal government for printing. The annualized cost to the Federal government for distributing the forms is estimated at $500.

A. 15 Explanation of program Changes or Adjustments

The change in burden from the previous request is partially a reflection of an increase in the number of IND's, protocols, investigators and drug shipments. The other factor that has increased the burden is driven by a reduction in manufacturing levels by our industrial partners. This practice has resulted in lower stock levels and the need for the investigators to order more frequently.

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 Exception to Certification of Paperwork Reduction Act Submissions

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