Centers for Disease Control and Prevention Performance Evaluation Program for *Mycobacterium tuberculosis*/Non-Tuberculous Mycobacteria (NTM) Drug Susceptibility Testing

A. Justification

1. Circumstances Making the Collection of Information Necessary

This study is authorized under the Public Health Service Act, (42 USC 241) Section 301. A copy is included in the attachments. (Attachment #1)

As part of the continuing effort to assess the quality and effectiveness of laboratory testing systems that support public health objectives of tuberculosis treatment programs, the Centers for Disease Control and Prevention (CDC) seeks to assess the performance of domestic public health laboratories and international laboratories which have public health responsibilities for drug susceptibility testing of *Mycobacterium tuberculosis* (*M. tuberculosis)* and other selected non-tuberculous mycobacteria (NTM), and have the approval of their National Tuberculosis Program. This voluntary performance evaluation program will assess the reproducibility of test results and practices reported by clinical and public health laboratories twice annually through the use of a specialized reporting form and a set of clinical mycobacterial culture strains.

Tuberculosis (TB) is a continuing public health problem despite the declining number of cases in the United States (U.S) over the past few years. Although there has been an overall decrease in the number of cases in the U.S, rates still remain high among foreign-born persons, prisoners, the homeless populations, and individuals infected with HIV in major metropolitan areas.

From 1985 to 1992, the increase in the number of tuberculosis (TB) cases was accompanied by increasing numbers of *M. tuberculosis* found to be resistant to one or more of the primary drugs used for treatment. This pattern of resistance added significantly to the cost and duration of treatment while reducing the efficacy of therapy. Although recent public health efforts have brought multi-drug resistant tuberculosis (MDRTB) under control in the U.S., the potential for MDRTB to be a major public health problem still remains. These concerns continue to challenge TB control programs in the U. S. In the U. S.., adequate TB control depends on rapid isolation and identification of the etiologic agent, *M. tuberculosis*, and confirmation of the appropriate therapeutic regimen by anti-tuberculosis drug susceptibility testing. With this information the necessary infection control procedures and contact tracing can be initiated, and informed decisions can be made regarding therapy. Mycobacteriology laboratories have a key role in breaking the chain of tuberculosis transmission. Competent staff, adequate test procedures, and facilities for thorough evaluations of clinical specimens are crucial.

In 1998, CDC commissioned the Institute of Medicine (IOM) to conduct a study to determine if TB elimination is still feasible as a goal based on an earlier strategic plan published in 1989. The 2002 report by the IOM indicated that the goal of eliminating TB in the United States is indeed feasible with “aggressive and decisive action beyond what is now in effect.” Among the several recommendations listed for eliminating TB, it was suggested that the United States implement aggressive strategies to help fight the global TB epidemic. Although the incidence of TB in the U.S. has decreased, the rate of TB cases in foreign born persons was almost 9 times higher than the rate among the U.S.

born population. Elimination of TB will be virtually impossible without considerable reduction of the heavy disease burden in other countries. CDC is actively involved in strengthening TB laboratory services in developing countries by providing equipment and consultation services to improve the detection and diagnosis of TB. Because of the high prevalence of TB and HIV, organizations such as the World Health Organization (WHO) and the International Union against Tuberculosis and Lung Disease (IUATLD) have developed standards to assist national programs with the management of tuberculosis. Both fiscal and professional resources are limited in high burden international settings such that TB susceptibility testing is performed only at the national or regional laboratories. When treatment problems are detected or observed, resistance in one or more drugs is not uncommon. The CDC has maintained an active role in quality laboratory testing and assisting in developing the infrastructure through the Global AIDS Program (GAP). The CDC Performance Evaluation Program for *M. tuberculosis*/NTM susceptibility testing will assist in this goal by monitoring the level of performance and practices among both domestic and international laboratories. As an example in 2006, this program assisted 133 domestic and 32 international laboratories in this effort.

2. Purpose and Use of Information Collection

Over the past 3 years, despite the fact that the number of cases of TB has slightly declined for the U.S. population, the number of domestic laboratories participating in the *Mycobacterium Tuberculosis* (TB)/non-tuberculosis Mycobacteria (NTM) Drug Susceptibility Testing Program (TPEP) have remained stable. However, enrollment has increased for foreign laboratories. Information collected from both domestic and

international laboratories will be compiled, analyzed, and distributed in aggregate form for use as a self-assessment tool to aid in maximizing skills of laboratory participants in susceptibility testing of TB and other selected mycobacteria. The challenge culture strains are sent to the laboratories twice yearly. If this data are not collected and analyzed, laboratories may not have the ability to detect susceptibility testing and quality control problems, and therefore not correct them. Data from this program will be used by CDC and other public health organizations to measure reproducibility of susceptibility test results performed with various test procedures in the U.S. and other countries. These results will be used to determine areas of need for training while monitoring reagents and test methodologies to improve the quality of susceptibility testing of *M. tuberculosis* and other mycobacteria.

Because of the importance of accurate and timely test results for the success of TB surveillance, prevention, and treatment programs, the CDC has maintained an active role in the assurance of high quality laboratory testing. The *M. tuberculosis*/NTM program fulfills part of this role by monitoring the level of performance and practices among public health and private sector laboratories within the U.S., as well as internationally. Information obtained on susceptibility testing practices and procedures will assist with determining variables related to good performance, with assessing areas for training and with developing practice standards. By providing a performance evaluation program to assess the ability of the laboratories to test for drug resistant *M. tuberculosis* and selected strains of NTM, laboratories will also have a self-assessment tool to aid in maximizing their skills in susceptibility testing.

3. Use of Improved Information Technology and Burden Reduction

To reduce the burden on each laboratory participant, CDC has provided on-line access to the enrollment and Results Form Booklet through the CDC internet webpage at (http://www.phppo.cdc.gov/mpep/enrollment.asp). Submission of forms may be done electronically; however, other methods of data submission will be acceptable which include mail, fax, and e-mail. A toll-free phone number will be available to provide technical assistance to program participants during the data entry periods.

4. Efforts to Identify Duplication and Use of Similar Information

CDC has taken steps to ensure that the information collected on laboratory susceptibility testing practices and challenge strains are not duplicated or otherwise accessible from any other source. To do so, CDC communicates with Association of Public Health Laboratories (APHL), and American Public Health Association (APHA), and maintains a panel of external experts to ensure that there is no duplication of information requested in this program. Any information collection that is currently conducted either internally or externally in the area of mycobacteriology does not specifically survey the same technical personnel or provide similar testing and feedback on *M. tuberculosis*/NTM susceptibility testing.

5. Impact on Small Businesses or Other Small Entities

Some laboratories can be classified as small business entities. To reduce the burden on these entities two different shipment panels are offered. A limited panel of strains will be shipped to laboratories that only perform primary drug testing on *M. tuberculosis* and a panel of non-tuberculous mycobacteria will be shipped for testing upon request. Laboratories are only expected to report information for the level of testing they perform routinely. Therefore, each laboratory's voluntary participation imposes no additional record keeping.

6. Consequences of Collecting the Information Less Frequently

Laboratories will receive test and record data on select *M. tuberculosis* strains twice per year. This semi-annual shipment and data collection system allows laboratories the opportunity to maintain proficiency in detecting drug resistance while providing the necessary feedback to ensure a period of time sufficient for resolving any proficiency issues in the laboratory. Semi-annual shipments and data collection allows laboratories entering the program to participate at least once during their entry year. There are no legal obstacles to reduce the burden.

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

The information collection activity fully complies with Guidelines 5 CFR 1320.5. No special circumstances are planned or intended for the respondents.

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

A. This study was published in the Federal Register on Tuesday, May 9, 2006, Volume 71, Number 89, Pages 26968 - 26969. A copy of the Notice is attached to this request (Attachment # 2). No public responses to this notice were received.

B. In development of the survey questions, CDC solicited the expertise of the following personnel in reviewing the Results Form Booklet within the past year:

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None of the members submitted comments on the Results Form Form.

9. Explanation of Any Payment or Gifts to Respondents

There will be no compensation offered for participation in the program.

10. Assurance of Confidentiality Provided to Respondents

The CDC Privacy Act Officer has reviewed this OMB application and has determined that the Privacy Act is not applicable. Respondents are domestic and international laboratories that perform *M. tuberculosis* susceptibility testing. Although data collection forms request the name of the individual who completes the form on behalf of the respondent laboratory, the individual is speaking in their role as an official contact for the laboratory, and does not provide personal information. The Privacy Act does not apply to organizations.

The contractor is responsible for processing registration forms for the TPEP. Domestic sites that wish to enroll do so through a web-based enrollment interface (see Attachment #4). However, because the web-based enrollment option is unavailable to foreign sites, the contractor assists foreign sites by entering their enrollment data into the TPEP database. For all participating sites (respondents), the contractor is responsible for

conducting a quality assurance review of the enrollment information, assigning a unique identification number to the respondent, and maintaining records that link the unique TPEP ID Number to the respondent organization's name. The contractor's Statement of Work specifies its obligations to safeguard the privacy and identity of respondents. Similarly, the contractor is also responsible for processing the Results Form data. Respondent sites that wish to submit data on-line are assigned a unique log-in ID for this purpose by the contractor. Respondent sites that prefer to submit paper forms mail them to the contractor, which performs data entry and quality assurance tasks prior to uploading the data to the secure CDC IT site.

Both the contractor and CDC IT staff have access to respondent names and the information that links a respondent's name to the corresponding TPEP Number. However, only CDC's Division of Laboratory Systems (DLS) staff has routine access to response information that is coded by the TPEP Number. This system safeguards respondent privacy and allows DLS staff to conduct primary analyses only on de-identified data. The contractor provides for anonymity of laboratories enrolled in the TPEP by isolating the Laboratory TPEP number (TPEPNUM) from all other data pertaining to the laboratory identification. Thus, the Laboratory TPEP Number is associated with laboratory performance records only. The Laboratory TPEP Number link to the Master Laboratory Identification Number link is stored in a separate data set, accessible only by the contractor, allowing only the contractor to connect the Laboratory TPEP Number to laboratory identity. The contractor uses this Master Laboratory Identification Number to link the Laboratory TPEP number to the laboratory address for

the purpose of connecting files and creating reports for the TPEP as needed. No software has been or will be written which produces an output linking the Master Laboratory Identification Number to the Laboratory TPEP Number or linking the Master Laboratory Identification Number to any laboratory performance information. All report generation which requires the use of the laboratory identity is the responsibility of the contractor. CDC program staff must send a written request to the contractor or the CDC IT personnel should it become necessary to identify the laboratory.

Response data is primarily filed and retrieved by the *M. tuberculosis* susceptibility testing identification number. All data provided by the contractor contains no laboratory identifiers. The master copy of the data base to be maintained by the contractor resides on the CDC mainframe computer, an IBM 3090 running the MVS operating system. The facilities of the TOP SECRET mainframe security package will be used to restrict access to the data to designated DLS personnel and the contractor. The contractor is responsible for ensuring that adequate backup and recovery procedures are in place to ensure that accidental or natural occurrences will not result in loss of project data. These procedures, as a minimum, include regular generation of two (2) backup copies of the data base, with one copy transferred to a secure, off-site facility. In addition, backups are made after major updates to the data base are performed.

The data collection procedures allow CDC to conduct primary analyses on the data. However, since CDC is offering consultation for the participant laboratories, we maintain the capability to ask the contractors to re-link identification information if an individual

laboratory seeks CDC's help in elucidating testing problems. While we do not anticipate the need for re-linking identifiers to be a regular occurrence, no one can be sure exactly how certain tests will perform in laboratories. We envision that the re-linking function will persist only for the brief length of time needed to address the performance issues of high public health impact associated with any given survey. The name and address of the participating testing sites appear on a cover page for *M. tuberculosis* susceptibility testing result booklet. The cover page is removed by the contractor prior to forwarding any result forms to the CDC. Hard copies of the *M. tuberculosis* susceptibility testing result booklet with identifiers removed are secured in locked, fire-proof file and storage cabinets whose access is strictly limited. Thus data is treated in a secure manner, and is not disclosed unless compelled by law. Individual laboratories are not identified in any way in the published national reports.

11. Justification for Sensitive Questions

Some laboratories may view their laboratory performance data as sensitive. The data de-identification procedures (described above) were instituted to encourage laboratories to participate in voluntary self-assessment.

12. Estimates of Annualized Burden Hours and Costs

A. One hundred sixty-five (165) laboratories (respondents) will receive the 13-question Results Form Booklets twice per year. The estimated annualized burden hours will be 30/60 or hours to enter data and answer the questions in the Results Form Booklet. Initially, all laboratories in the program complete the enrollment or the form

was completed by the contractor (Attachment #4). This is a one-time event. If there is a change in the information on the form, i.e. director, phone number, or addresschange of staff performing the tests, then, the Change of Information Form (Attachment #7) is filled out and returned to the contractor. In the past, this occurs about 1-2 times a year. [The annualized response burden of the survey, including the occasional enrollment, the change of information, the Results Form is 165.334 hours.] The variables on response burden and burden hours will depend on the extent of procedures performed by each laboratory. In cases where some procedures are not performed, the questions will prompt the respondent to skip to the next question(s).

A. 12.1: ESTIMATE OF ANNUALIZED BURDEN HOURS AND COST

Type of Respondents	Form Name	No. of Respondents	No. of responses per Respondent	Average Burden per Response (in hours)	Total Burden (in hours)*
Laboratories (U.S. and foreign)	Enrollment	2	1	(5/60) 0.083	(10/60) 0.167
	Information change	2	1	(5/60) 0.083	(10/60) 0.167
	Results Form	165	2	(30/60) 0.5	165
				Total	165.334

B. The average hourly wage shown below in Table 12 B-1 for respondents is based on salary ranges for laboratory staff and the contractor-reported wages in U.S. dollars. Also, the educational classification and salary scale for respondent who may fill in the Results

Form Booklet may vary from certificate level, Bachelor's degree level or higher is considered.

12 B-1: Estimated Annualized Burden Cost

Type of Respondents	No. of Respondents	No. of Responses per Respondent	Average Burden per Response (in hours)	Total Burden Hour	Hourly Wage Rate	Total Respondent Costs
Laboratory	165 Reporting results	2	0.5	165	$32.50	$5,362.5
Laboratory	2 (enrollees)	1	0.0833	0.167	$32.50	$5.42
Laboratory	2 (change of information)	1	0.0833	0.167	$32.50	$5.42
					Total	**$5,373.34**

The average hourly wage rate for respondents participating in this survey was obtained from the resources listed below:

Website on www.bls.gov/news.release/empsit.t16.htm

Website on Salary expert.com/SE Report

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

None.

14. Annualized Cost to the Government

The estimated cost to the government by the contractor will be $1,153 per respondent (laboratory). This cost includes wages for staff hours involved in sample preparation of culture slants, shipping, electronic data collection/management and overhead expenses

for the performance evaluation program. All of the work mentioned above is performed by the contractor with a cost plus fixed-fee contract.

Type of RESPONDENTS	Number of Laboratories	COST TO FEDERAL GOVERNMENT
Domestic Laboratories	133	$153,349.00
International Laboratories	32	$36,896.00
Total amount of Contract		$190,245.00

15. Explanation for Program Changes or Adjustments

This is a request for an extension of an ongoing data collection program.

16. Plans for Tabulation and Publication and Project Time Schedule

Laboratories will be surveyed twice annually using the Results Report Form Booklet. Data will be analyzed by tabulating and comparing results from various test methodologies and associated practice variables. Analysis will also include compiling and collating a variety of methods and drug concentrations. The data will be published as an aggregate report and distributed to participation laboratories in hard copy, pdf files and/or posted on the CDC TPEP website at http://www.phppo.cdc.gov/mpep/mtbds.aspx This information will assist in determining guidelines to improve *M. tuberculosis* susceptibility testing.

A. 16.1 PROJECT TIME SCHEDULE

Letters to Respondents	Results Form Booklet Delivery	Preliminary Reports to Respondents	Analysis of Aggregate Data	Final Report to Respondents
June and December	January and July	March and September	April and October	May and November

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

Approval is not requested to not display OMB expiration date.

18. Exceptions to Certification for Paperwork Reduction Act Submissions

No exceptions are identified.

B. Collections of Information Employing Statistical Methods

This data collection will assess the ability of laboratories to detect *M. tuberculosis* drug resistance using various drug concentrations in different test methods, and the interpretation of susceptibility test results. Responses to questions in the Results Form Booklet will complement mycobacteria susceptibility test data. Respondents will be laboratories that perform *M. tuberculosis* susceptibility testing on at least primary drugs used which are used to treat patients with tuberculosis. Based on reporting from previous years, the response rate is anticipated to be greater than 95%. It is expected that some laboratories may have technical or staff issues which may delay the reporting of results. Laboratories may request to not receive a shipment if they feel they will not be able to complete testing and return the Results Form Booklet on the scheduled shipment dates given in pre-shipment letters.

1. Respondent Universe and Sampling Methods

Statistical methods are not employed to select (respondents) laboratories for the program. Laboratories will volunteer for this program as a means of assessing their testing proficiency with that of other laboratories domestically and internationally as well as evaluating various testing methods used by other laboratories.

2. Procedures for the Collection of Information

Advance letters will be sent to laboratories (respondents) to inform them of the expected date for receiving the culture shipment (Attachment #6). Cultures are sent to the laboratories along with instructions for handling the cultures and reporting testing results for the shipment. The laboratories are assigned a login number for electronic data entry. Data is collected from respondents who return either the hard copy of the *M. tuberculosis* susceptibility testing result form booklet or respondents who submits their data via electronic web site. Data collected will be stored as SAS data sets and imported into Excel files with a unique identifier which provides anonymity. This anonymity is accomplished by de-linking the provided program identification numbers from the facility classification information for data sets which will reside at the CDC mainframe computer. Hard copy the result booklets are returned to the contractor through mail in a postage-paid envelope. Hard copies of the Result Form Booklet are secured in locked, fire-proof files and storage cabinets whose access is strictly limited to approved personnel. The contractor will download the online data from the electronic website and combine it with the data resulting from laboratories submitting the hard copy data. All data is treated in a

secure manner and will not be released in identifiable form, unless compelled by law, or unless CDC requests re-linking in order to facilitate communication with a site that is experiencing a high rate of inaccurate results.

3. Methods to Maximize Response Rates and Deal with Nonresponse

Non-respondents receive one follow-up call from the contractor three weeks after the initial surveys are mailed, as a reminder. During this call they ask the participant to respond by submitting their forms. The data will be treated in a confidential manner, unless otherwise required by law. Results will be reported as aggregate data.

Other methods used to maximize the response rate include a FAX or phone/answering machine message to the laboratories which do not respond by the deadline for submission of results. The contractor will confirm that the shipment was received, ensure that Results Form Booklet or responses are entered into the web based data entry form and provide a toll free number for the laboratory to call, if they have questions. Over the past five years, the response rate has been 92-96%. Because of the introduction of on-line data entry, the response rate of the 165 laboratories is expected to be greater than 95%. Laboratories that do not submit data on the shipped strains two days past the results deadline will be contacted by phone or e-mail to confirm their continued participation in the program. Laboratories which do submit test results or have an acceptable reason for not submitting susceptibility results will be removed from the program. The option to request deferment from a specified shipment panel is available to laboratories when needed.

4. Tests of Procedures or Methods to be Undertaken

The Results Form Booklet and the strains to be sent to laboratories will be selected by CDC in collaboration with a team of clinical scientists with experience in mycobacteriology susceptibility testing and test question survey development skills. The Results Form Booklet was reviewed by scientists in both domestic and international laboratories and feed-back was provided on the format, relevance and clarity of questions.

5. Individuals Consulted on Statistical Aspects and Individuals Collecting and/or Analyzing Data

Statistical consultation on the collection and analysis of data will be performed by Mr. Jim Handsfield (404-718-1040) JHandsfield@cdc.gov- Division of Laboratory Systems, NCID, CCID, CDC. The Results Form Booklet was designed by:

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