"National Surveillance for Severe Adverse Events Among Persons on Treatment of Latent Tuberculosis Infection"

OMB No. 0920-0773
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Supporting Statement Part B

Reinstatement without Change

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LIST OF ATTACHMENTS

Supporting Statement B

1. Respondent Universe and Sampling Methods

The Division of Tuberculosis Elimination (DTBE), National Center for HIV, Viral Hepatitis, STD, and TB Prevention, Centers for Disease Control and Prevention requests approval for a 3-year reinstatement of the previously approved National Surveillance for Severe Adverse Events Among Persons on Treatment of Latent Tuberculosis Infection (NSSAE) —(OMB No. 0920–0773, expires 01/31/2018). This project will continue the passive reporting system for severe adverse events (SAEs) among persons on LTBI treatment. The system will rely on medical chart review and/or onsite investigations by tuberculosis (TB) control staff.

NSSAE will investigate the patients' clinical characteristics and other factors that may play a role in the occurrence of SAEs to recommended therapy. Persons who will be included in this study will be already diagnosed with latent TB infection (LTBI) and started a course of therapy. The majority of the patients will tolerate the anti-TB drug with little or no ill-effect. A small number will have SAEs requiring hospitalization or resulting in death. An SAE may be metabolic acidosis, anaphylaxis, seizure, severe dermatitis, liver injury, or other symptoms leading to hospitalization or death of a person receiving treatment for LTBI. These persons will be the focus of this investigation.

DTBE will continue to solicit reports of SAEs that occurred on or after January 1, 2004 from healthcare providers and health departments (local/state/territorial) from any of the 60 reporting areas for the National TB Surveillance System (NTSS). During 2004−2016, CDC received 66 reports of SAEs among recipients of isoniazid (INH)-only (n=44), INH-rifapentine (RPT) (n=20), rifampin (RIF) (n=1) and INH/Levofloxacin

(n=1) for LTBI. Among INH-only recipients, seven died; five, including one child, underwent liver transplantation. Among INH-RPT, RIF, and INH/Levofloxacin recipients, length of hospitalization ranged 1–20 (median: 3) days; no liver transplants or deaths were reported. The RIF recipient had an acute kidney injury but recovered after three hemodialysis treatments.

2. Procedures for the Collection of Information

Persons who are diagnosed with LTBI are prescribed anti-TB medication as seen appropriate by their physicians. A few develop mild reactions that may be managed in the outpatient clinic. Rarely, the reactions can be life-threatening or lethal. Persons who develop an SAE that resulted in an admission to a hospital or death as a result of taking at least one dose of drug therapy for the treatment of LTBI will be evaluated by the patient's physician at the hospital. The physician or health care staff at the hospital will report the case to the local health department, who in turn will report it to their state health department. When the presumptive diagnosis is made, the *Source of Report, Basic Patient and Illness Description*- Part 1 section of the NSSAE form (**Attachment 4**) will be completed by the medical clerk. Part 2 of the NSSAE form that includes *LTBI Diagnosis and Treatment* (**Attachment 5**) will be filled out by the nurse and Part 3 includes *Monitoring during Therapy and Hepatitis/Liver Injury Diagnosis* (**Attachment 6**) will be filled out by the physician. The procedures and case definitions to be used in the investigations of the SAEs are described in the "Guidelines to Investigate Reports of Severe Adverse Events to LTBI Treatment" (**Attachment 3**).

Three different respondents (physicians, nurses, medical clerks) will be involved in collecting the information from each case; a physician, a nurse, and a medical clerk.

The physician completes Part 3 of NSSAE form with the help of the medical clerk or nurse as needed. The information from the physician provides a history of the clinical events and the laboratory findings applicable to the diagnosis of the SAE associated with one or more anti-TB medications. If the patient has been treated or admitted to the hospital previously, the medical clerk will be able to provide the history from the medical records at this hospital. The medical clerk completes Part 1 of the NSSAE form and may provide information to the physician to complete Parts 3. The medical clerk assembles the patient's hospital records from the hospital of current admission and hospitals where he/she was admitted previously to complete Part 1.

The nurse completes Part 2 of the NSSAE form. If the patient routinely uses other clinics or hospitals, the nurse will locate all clinical and laboratory information from these sources and supplements the information available at the admitting hospital and accessed by the medical clerk. The nurse completes the collating of all clinical, laboratory, and treatment protocols used in the history of the case. The nurse also collates socio-demographic and risk factor information from the TB surveillance reports that are available at the health department.

State health departments may invite CDC to join their investigation team at their location. When CDC is invited to help with the investigation, CDC team will join the local investigators at the site.

3. Methods to Maximize Response Rates and Deal with No Response

This section is inapplicable to this surveillance activity because the proposed investigation starts only when a person on TB treatment has been admitted to a hospital or died and has been suspected to be a result of an abnormal reaction to prescribed TB

antibiotics. Nevertheless, towards assuaging any concerns of the patient, we will use a patient consent procedure whereby the patient will be informed of the condition and the need for the interview. The consent form is **Attachment 8**.

4. Test of Procedures or Methods to be Undertaken

No tests of procedures or methods are being proposed.

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

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