Attachment 4

National Surveillance for Severe Adverse Events Associated with Treatment of Latent Tuberculosis Infection

0920-05AJ

Guidelines to Investigate Reports of Severe Adverse Events to LTBI Treatment

Form Approved
OMB No. 0920-XXXX
Expiration Date XX/XX/20XX

Guidelines to Investigate Reports of Severe Adverse Events to LTBI Treatment
To be used by Local, State, and CDC Investigators

These are suggestions to conduct an investigation of a suspected severe adverse event to an LTBI medication. Modify each investigation protocol as is appropriate to the situation, keeping in mind that medical staff and the patient involved may be reticent to speak if litigation is pending, or if they believe litigation will result from this investigation.

Prior to visit

- Formal invitation received by state for CDC to investigate suspected adverse medication reaction.
- Request and arrange site visit to county and city/town where adverse event occurred. Must have state, county and town agreement before going on investigation.
- Have state or county arrange for investigation team to meet with public health and other medical staff involved in patient's care.
- Have state or county arrange for investigation team to meet with patient
- Get names and titles of contact persons prior to visit.
- Make travel arrangements/travel orders and rental car.
- Bring at least one additional copy of the complete study protocol to share.

Site visit

Meet with TB program staff at all levels involved.

- First day: Meet with state-level TB Controller and/or TB Program Manager, county-level, city and/or town TB staff involved in case. Establish rapport with local staff. Explain reason for investigation and what we hope to learn from the study.
- Exchange contact information and who will be point-of-contact at each level. Bring business cards to exchange.
- Review case with available staff before review medical records (if possible). Meet with all public health staff involved in the care of the patient; listen and document their stories. Ensure that staff members understand that the CDC team is there to learn, not to assign blame.

Review all medical records and meet with any public health or other medical staff involved in this patient's care who agree to be interviewed.

If the patient has received a liver transplant, try to incorporate an interview

with the transplant coordinator, surgeon, or other transplant team member knowledgeable about the patient's case. If the patient died, in addition to interviewing healthcare providers who cared for this patient while he was alive, interviewing the pathologist who performed the autopsy (if done) might also be valuable. If the patient died, try to arrange an interview with the family. Endeavor to have interviews scheduled prior to traveling to the state.

- Review all medical records from all patient visits to all public health clinics, ER's, private providers and hospitals involved. Visit each site. Review the radiographs and other imaging studies performed. If radiologist available to review radiographs, review with radiologist.
- Review and document all labs (pre-TB medicines as well as while patient was on medicines).
- Complete all forms in Appendix A of study protocol.
- **Specific information needed:**

  Past Medical History-
  - Any past history of TB or LTBI treatment
  - History of hepatic injury, chronic diseases (Diabetes Mellitus, alpha1-antitrypsin deficiency, chronic renal insufficiency, hepatitis A, B, C; HIV status; cardiac disease; immunosuppression or cancer)
  - Medication allergies
  - Medication history prior to- and during the time the patient was taking anti-TB medication (prescription and non-prescription; include vitamins, herbs, over-the-counter medicines)

  Social history
  - Tobacco use, drug use (intravenous drug use and non-intravenous drug use), alcohol use/abuse and try to **quantify** drug and alcohol use
  - Educational level; country of origin; if foreign-born, when came to U.S.; travel history primary language spoken; living situation (married with kids living in a home, homeless, institutionalized/incarcerated, etc); occupation and any known occupational exposure to TB; exposure to unpasteurized milk products or animal exposure or hunting history, if appropriate

  Family History
  - History of liver disease
  - Have other relatives taken medication for TB? If so, did they have any problems?

  History of Present Illness
  - Document how and why patient came to be on TB medication
  - Document medication(s) taken, dosage and frequency
  - Document start and stop dates, lapses in treatment (if any), reason for lapses (if known)
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- Document any patient symptoms associated with TB medication and timing of symptoms with respect to taking TB medication
- Document any "baseline" laboratory testing and subsequent laboratory testing (Document symptoms, if any, at time of lab testing)
- Document actions taken and treatments provided to patient when patient became symptomatic.
- Document all clinic and hospital visits
- Document outcome

Interview patient (and family if patient wants family involved). *If the patient has died, try to arrange an interview with the family so that information from the chart can be verified and/or additional information from the family's perspective can be gathered.*

Verify patient's past medical history, social history, and family history:

-Acute and /or chronic illnesses

-Tobacco use, drug use (IDU and non-IDU), alcohol use/abuse and **quantify** drug and alcohol use

-Educational level; country of origin; if foreign-born, when came to U.S.; travel history primary language spoken; living situation (married with kids living in a home, homeless, institutionalized/incarcerated, etc); occupation and any known occupational exposure to TB; exposure to unpasteurized milk products or animal exposure or hunting history, if appropriate

-Family history of liver/GI disease

Have other relatives taken medication for TB? If so, did they have any problems?

Patient's story:

- From the patient's standpoint, what happened?
- How and why patient came to be on TB medication
- What medication(s) was taken, dosage and frequency
- Any known medication allergies or sensitivities
- Self-reported compliance with medication
- Document start and stop dates, lapses in treatment (if any), reason for lapses (if known)
- Ask patient to discuss symptoms associated with TB medication and timing of symptoms with respect to taking TB medication
- Did patient know what to do in case symptoms developed?
- What actions did patient and/or family take when patient became symptomatic?
- Did patient try other medications, herbs, etc to help alleviate the symptoms?
- How does patient feel now?
- How did this impact him?

Leaving site--Thank hosts in state

Return to CDC

- Send thank you letter to all persons met
- Complete forms in LTBI Adverse event protocol and assign classification to case (i.e. definite, probable, possible…).
- Record any specific difficulties encountered during this investigation (i.e. litigation preventing you from viewing records or interviewing the patient, family, or healthcare providers, etc.).
- Meet with CDC Medical Board to present findings, discuss case, and assign final disposition.
- Final report put through clearance and sent to persons designated by the state to see the report