

# NOTICE

Our file number: 06-116801-306

## **To Clinical Trial Sponsors : Requirements for Tuberculosis Screening of Healthy Volunteers in Phase I Clinical Trials involving Immunosuppressant Drugs or Drugs with Immunosuppressant Properties**

This notice provides information on the Therapeutic Products Directorate's (TPD) and Biologics and Genetic Therapies Directorate's (BGTD) requirements related to the screening for tuberculosis (TB) of healthy volunteers involved in Phase I clinical trials involving immunosuppressant drugs or drugs with immunosuppressant properties.

Proposed clinical trial participants must have a normal physical exam and laboratory results within the normal laboratory limits. Protocols should contain criteria to exclude patients with latent or active TB, history or possible exposure to endemic areas, current or recent infections. To ensure such persons are excluded from participation in the trial, the sponsor must undertake the following prior to the commencement of the clinical trial:

### **1. Symptom screening for TB:**

Administer a standard TB Medical History screening questionnaire to each proposed clinical trial participant (see Appendix 1 for additional information).

### **2. Tuberculin Skin Test (TST):**

When the half-life ( $t_{1/2}$ ) is known and the clinical trial involves the administration of a single or multiple doses of an immunosuppressant drugs or drugs with immunosuppressant properties, administer a TST to each clinical trial participant with a negative TB Medical History if the  $t_{1/2}$  is greater than 24 hours. If  $t_{1/2}$  is not known, TST is required for all participants, unless justified by a rationale that is supported by the appropriate scientific evidence.

Repeat TST testing prior to each dosing period is not required for clinical trials involving more than one period of exposure (e.g., QTc study).

The TST positive threshold limit for the purposes of these screening requirements is 5mm induration. If the first TST is negative (defined as 0-4mm induration), further testing is not required. If the first TST test is positive (defined as 5+mm induration), exclude person from participation in the trial and refer to a specialist with expertise in TB for further investigation. Prior BCG vaccination should not be taken into account when interpreting the TST result.

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## Appendix 1:

### Sample TB Medical History Screening Questionnaire

- a) Have you ever had active TB? (If yes, exclude from trial)
- b) Have you previously had a TB skin test? This is also called a Mantoux or tuberculin skin test. (If yes, ask for documented result. If 5+mm, exclude from trial)
- c) Do you have any of these unexplained symptoms? Fever, cough/sputum (more than 3 weeks), coughing blood, weight loss, chest pains, persistent hoarse voice, fatigue (unusual), loss of appetite, night sweats (unrelated to menopause) or persistent cough for which an antibiotic has been taken. (If yes to any symptom, exclude from trial until a medical exam rules out TB disease and a tuberculin skin test (TST) is less than 5mm induration)
- d) Do you have any of the following medical conditions which may influence the development of TB disease? HIV/AIDS, transplant, injection drug use, kidney disease requiring hemodialysis, treatment with immunosuppressant drugs, underweight, oral steroid use, diabetes, silicosis, lymphoma or leukemia or contact with an active TB case within the past 2 years (If yes to any condition, exclude from trial)
- e) List each country (other than Canada) where you have lived or visited during the last eight (8) weeks\*.

\* If a participant has lived in or visited a country with high TB incidence, defined as one with a WHO estimated sputum smear positive pulmonary TB rate (3 year average) of 15 per 100,000 or higher (see: [http://www.phac-aspc.gc.ca/tbpc-latb/itir\\_e.html](http://www.phac-aspc.gc.ca/tbpc-latb/itir_e.html) for rates), then there is a possibility that they were infected while there and it is too early for the TST to turn positive. Such participants should be excluded until at least eight (8) weeks have passed since they have left such a country and then a TB skin test is to be administered. If the TST is 5+mm induration, the participant is to be excluded from the trial)

(Source: Public Health Agency of Canada)

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