

		<b>Tuberculin Purified Protein Derivative (PPD) (Mantoux) Biological Page</b>	
<b>Section 7:</b>	<b>Biological Product Information</b>		<b>Standard #: 07.330</b>
<b>Created by:</b>	Tuberculosis Program		
<b>Approved by:</b>	Tuberculosis Program		
<b>Approval Date:</b>	February 12, 2013	<b>Revised:</b>	May 3, 2024

	<b>Tubersol®</b>
<b>Manufacturer</b>	Sanofi Pasteur Ltd.
<b>Indications for Provincially Funded PPD</b>	<p><b>NOTE:</b>  ** A Tuberculin Skin Test (TST) should <b>NOT</b> be performed to diagnose <b>active TB disease</b>. Please consult TB Services before performing a TST on individuals with <b>abnormal chest radiograph consistent with, or symptoms of, active TB disease</b>.</p> <p>The following are the indications for a provincially funded Tuberculin Skin Test:</p> <ul style="list-style-type: none"> <li>• <b>Recent contacts</b> of a known infectious tuberculosis case (determined in consultation with TB Services).</li> <li>• Individuals with <b>immune compromising medical conditions</b> and those receiving (or soon to receive) <b>immunosuppressive medical therapy</b> (e.g. for malignancy or inflammatory diseases). <ul style="list-style-type: none"> <li>○ HIV infection / AIDS</li> <li>○ Transplantation (donor and recipient)</li> <li>○ Chronic renal failure / Chronic Kidney Disease</li> <li>○ Silicosis</li> <li>○ Carcinoma of head &amp; neck</li> <li>○ Lung Cancer</li> <li>○ Hemolytic malignancies</li> <li>○ Uveitis</li> <li>○ Radiologic changes of inactive TB – i.e. fibronodular scarring or other changes suggestive of <b>prior</b> TB disease.</li> <li>○ Individuals referred for TST with any chronic inflammatory condition, or because they are receiving immune suppressive medical therapy, or because they may require immune suppressive therapy in the future, are eligible for publicly funded TST (ideally, TST is completed prior to commencing immunosuppressive treatment). Examples of immunosuppressive medication classes that warrant Latent TB Infection (LTBI) screening include: <ul style="list-style-type: none"> <li>▪ Corticosteroids (equivalent of ≥15mg/day of prednisone (or equivalent) for ≥ 1 month)</li> <li>▪ Cytotoxic chemotherapy</li> <li>▪ Anti-rejection medications (mTOR inhibitors, calcineurin inhibitors, mycophenolate)</li> <li>▪ TNF-inhibitors</li> <li>▪ Interleukin signal inhibitors</li> <li>▪ Kinase signal-transduction inhibitors</li> <li>▪ Integrin inhibitors</li> <li>▪ Immune check-point inhibitors</li> <li>▪ B-cell depleting agents</li> <li>▪ Patients on non-specific immune modulating drugs (e.g. methotrexate, azathioprine, leflunomide) may be candidates for biological therapy and would reasonably undergo LTBI screening in anticipation of this.</li> </ul> </li> </ul> </li> </ul>

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	<ul style="list-style-type: none"> <li>All foreign-born people less than 65 years of age who have originated from a <b>country with TB incidence &gt; 200 per 100,000, and who have arrived</b> within the past five years. For TB incidence in individual countries see the World Health Organization TB country, regional and global profiles <a href="https://worldhealthorg.shinyapps.io/tb_profiles/">https://worldhealthorg.shinyapps.io/tb_profiles/</a></li> <li>All <b>refugees and evacuees aged less than 65 years</b> originating from countries with TB incidence ≥50 per 100,000 <b>AND</b> have arrived in Canada within the past two years. For TB incidence in individual countries see the World Health Organization TB country, regional and global profiles <a href="https://worldhealthorg.shinyapps.io/tb_profiles/">https://worldhealthorg.shinyapps.io/tb_profiles/</a></li> <li>Foreign-born individuals, immigrants, refugees and evacuees of all ages who are referred for medical surveillance</li> <li>Individuals at risk for <b>potential occupational exposure</b> to infectious TB: <ul style="list-style-type: none"> <li>Health care workers (HCW). See Notes Section for definition of health care worker and Standard for Immunization of Health Care Workers #08.301</li> <li>Post-secondary health care students. See Notes Section and Standard for Immunization of Post-Secondary Health Care Students #08.302</li> <li>Other individuals who work in programs, facilities or institutions that provide services <i>to populations at increased risk for TB disease</i>: <ul style="list-style-type: none"> <li>the homeless/under-housed (i.e., individuals who access homeless shelters)</li> <li>people who reside in congregate living settings such as correctional facilities, substance abuse rehabilitation centres, or continuing care facilities</li> <li>foreign-born individuals from countries with high TB incidence</li> <li>Canadian Indigenous Peoples from communities with high rates of TB</li> </ul> </li> </ul> </li> <li>Volunteers who work regularly with populations at increased risk for TB who will be volunteering for 150 or more hours in a year (i.e., approximately one-half day per week)</li> <li>Long term (&gt;3 months) residents of <b>substance rehabilitation centres</b> <b>AND</b> have a risk factor for progression from LTBI to active TB disease</li> <li><b>Travelers to high incidence TB countries</b> who meet the following guidelines should undergo a single post-trip TST, performed two-months after return <div style="border: 1px solid black; padding: 10px; margin: 10px 0;"> <p><b>For post-travel TST</b></p> <p>≥1 month of travel with very high risk contact</p> <ul style="list-style-type: none"> <li>particularly direct patient contact in a hospital or indoor setting</li> <li>possibly including work in prisons, homeless shelters, refugee camps or innercity slums.</li> </ul> <p>Travel to TB incidence countries:</p> <ul style="list-style-type: none"> <li>≥400 / 100,000 population - ≥3 months</li> <li>200-399 / 100,000 population - ≥6 months</li> <li>100-199 / 100,000 population - ≥12 months</li> </ul> </div> </li> <li><b>Inmates at Provincial Correctional Institutions</b> (not including Remand Centres)</li> <li><b>Inmates at Federal Correction Institutions</b></li> </ul>
<b>Schedule</b>	<p><b>Timeframe for Tuberculin Skin Test (TST) reading</b></p> <ul style="list-style-type: none"> <li><b>48 to 72 hours</b> after administration. If the TST is not read within 72 hours, the test needs to be repeated at a different site. Self-reading of TSTs is not an acceptable practice under <b>ANY</b> circumstances. If the TST is not read within 72 hours, the result is not valid and must be repeated, unless there is 10 mm or more of induration present. The repeat test can be done immediately. Use opposite forearm, or the same forearm, at least 5 cm from the site of the previous TST.</li> </ul>

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	Interpretation								
	<table><tr><th>TST reaction size (mm of induration)</th><th>Situation in which reaction necessitates referral to the AHS TB Program</th></tr><tr><td>0 to 4 mm</td><td><ul style="list-style-type: none"><li>Person with HIV <b>AND</b> the expected likelihood of TB infection is high (e.g., the client is from a population with a high incidence of TB infection, is a close contact of an active infectious case, or has an abnormal x-ray)</li><li>Child under 5 years of age and recent contact of infectious TB case</li></ul></td></tr><tr><td>5 mm and greater</td><td><ul style="list-style-type: none"><li>People with HIV</li><li>Known contact of an active infectious case within 2 years</li><li>Bone marrow or solid-organ transplantation (related to immune suppressant therapy)</li><li>Stage 4 or 5 Chronic Kidney Disease, with or without dialysis</li><li>History of abnormal chest x-ray with fibronodular disease (suggestive of prior TB disease not previously treated)</li><li>Immunosuppressed</li></ul></td></tr><tr><td>10 mm and greater</td><td><p>All others meeting indication criteria for TST, including individuals with:</p><ul style="list-style-type: none"><li>TST conversion</li><li>Silicosis, carcinoma of head or neck, lung cancer, hematologic malignancies (leukemia, lymphoma)</li><li>Prior to receipt of biologic drugs such as TNF-inhibitor</li><li>Prior to Receipt of other immune suppressive drugs such as corticosteroids</li></ul></td></tr></table>	TST reaction size (mm of induration)	Situation in which reaction necessitates referral to the AHS TB Program	0 to 4 mm	<ul style="list-style-type: none"><li>Person with HIV <b>AND</b> the expected likelihood of TB infection is high (e.g., the client is from a population with a high incidence of TB infection, is a close contact of an active infectious case, or has an abnormal x-ray)</li><li>Child under 5 years of age and recent contact of infectious TB case</li></ul>	5 mm and greater	<ul style="list-style-type: none"><li>People with HIV</li><li>Known contact of an active infectious case within 2 years</li><li>Bone marrow or solid-organ transplantation (related to immune suppressant therapy)</li><li>Stage 4 or 5 Chronic Kidney Disease, with or without dialysis</li><li>History of abnormal chest x-ray with fibronodular disease (suggestive of prior TB disease not previously treated)</li><li>Immunosuppressed</li></ul>	10 mm and greater	<p>All others meeting indication criteria for TST, including individuals with:</p> <ul style="list-style-type: none"><li>TST conversion</li><li>Silicosis, carcinoma of head or neck, lung cancer, hematologic malignancies (leukemia, lymphoma)</li><li>Prior to receipt of biologic drugs such as TNF-inhibitor</li><li>Prior to Receipt of other immune suppressive drugs such as corticosteroids</li></ul>
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Single-step TST									
<ul style="list-style-type: none"><li>Single-step (one TST only) is recommended for most persons, including post-secondary students at risk for potential occupational exposure to infectious TB.</li></ul>									
Two-step TST									
<ul style="list-style-type: none"><li>Indication for baseline two-step testing (meet one or more of the following criteria):<ul style="list-style-type: none"><li>It is anticipated that the individual will undergo repeated screening with TSTs at regular intervals<ul style="list-style-type: none"><li>HCW involved in high-risk activities<ul style="list-style-type: none"><li>cough-inducing procedures (this does not include throat and or nasal swabs)</li><li>autopsy</li><li>morbidity anatomy and pathology examination</li><li>bronchoscopy</li><li>designated mycobacteriology laboratory procedures especially handling cultures of <i>M. tuberculosis</i>.</li></ul></li><li>HCW who work on high-risk units to which patients with active TB are admitted<ul style="list-style-type: none"><li>High-risk units are determined in collaboration by Infection Control, Workplace Health and Safety, and TB Services based on the Canadian Tuberculosis Standards risk classification of health care facilities</li></ul></li><li>Other employees or volunteers at facilities that require TST screening at regular intervals due to high risk of TB exposure, such as homeless shelters, correctional facilities, and inner-city agencies</li></ul></li></ul></li><li>Administration of two-step TST<ul style="list-style-type: none"><li>The first TST of a two-step TST is administered in the same manner as a single-step TST.</li></ul></li></ul>									

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	<ul style="list-style-type: none"> <li>○ <b>If the initial TST is positive, the second TST should <u>not</u> be done.</b></li> <li>○ If the initial TST result is negative, a second TST should be administered at a different site.</li> <li>○ The second TST should be given 7-28 days after the first TST (<b>no sooner than 7 days and no later than 28 days</b>).</li> </ul> <p><b>Note:</b> A two-step protocol needs to be performed ONCE only if properly performed and documented. It never needs to be repeated. Any subsequent test can be one step, regardless of how long it has been since the last TST.</p> <p><b>TSTs for Contact Investigation</b></p> <ul style="list-style-type: none"> <li>• In a contact investigation, a baseline TST should be performed on close contacts as soon as possible after the source case diagnosis has been made (In consultation with TB program)</li> <li>• If this first TST is negative and it was performed less than 8 weeks after contact with the source case was broken, then a second TST should be performed between 8-12 weeks after the contact was broken. <u>Note:</u> that this second TST is considered a repeat TST, and thus does not follow the criteria, nor parameters, for a 2 step.</li> <li>• This is done to detect very recent infection that occurred just before contact was broken. It takes anywhere from 3-8 weeks for a TST to become positive after new infection.</li> <li>• Some contacts with less significant exposure a single TST, performed 8 weeks after last contact may be all that is advised (In consultation with TB program)</li> </ul>
<b>Preferred Use</b>	At this time Tubersol® is the only product licensed for tuberculin skin testing in Canada.
<b>Dose</b>	0.1 mL
<b>Route</b>	Intradermal
<b>Contraindications/Precautions</b>	<p><b>Contraindications:</b></p> <ul style="list-style-type: none"> <li>• Anaphylactic or other allergic reaction to previous tuberculin PPD</li> <li>• Known hypersensitivity to any component of TUBERSOL®</li> <li>• History of past active tuberculosis or treatment for LTBI</li> <li>• History of blistering TST reaction</li> <li>• Well documented history of a positive TST reaction <ul style="list-style-type: none"> <li>○ Individuals with a history of <b>undocumented</b> positive TST reaction (other than blistering) <b>can</b> receive a TST; if these individuals decline to have baseline TST they do require baseline chest X-ray through their family physician</li> </ul> </li> <li>• Inflammatory skin condition at the site of injection (i.e., burns or eczema)</li> <li>• Have received a live virus vaccine within the past 28 days/4 weeks</li> <li>• Major viral infections</li> </ul> <p><b>Precautions:</b></p> <ul style="list-style-type: none"> <li>• Do not inject subcutaneously, intramuscularly or intravenously.</li> <li>• False positive reaction may occur in individuals who have been: <ul style="list-style-type: none"> <li>○ infected with non-tuberculous mycobacterium (NTM)</li> <li>○ vaccinated with BCG (Bacille Calmette-Guerin) for tuberculosis</li> </ul> </li> <li>• False negative reactions may occur due to: <ul style="list-style-type: none"> <li>○ immune suppression due to HIV, advanced age, treatment with immune suppressive drugs or therapies</li> <li>○ severe illness (which may include active TB disease)</li> <li>○ major viral illness (e.g., mononucleosis, mumps, measles but <b>NOT</b> the common cold)</li> <li>○ immunization with MMR, varicella, or yellow fever vaccine within the previous four weeks</li> <li>○ very young age (less than six months) – validity of TST is unknown, thus TST in this group is not generally recommended</li> </ul> </li> </ul>

	<b>Tubersol®</b>
<b>Possible Reactions</b>	<p><b>Common</b></p> <ul style="list-style-type: none"> <li>Local pain, itchiness and discomfort at the test site may occur.</li> </ul> <p><b>Rare</b></p> <ul style="list-style-type: none"> <li>2 to 3% will have localized redness or rash without induration within 12 hours of testing (does not indicate TB infection)</li> </ul> <p><b>Very Rare</b></p> <ul style="list-style-type: none"> <li>Ulceration or necrosis at the test site in highly sensitive persons</li> <li>Acute allergic reactions including anaphylaxis, angioedema, urticaria and/or dyspnea</li> </ul>
<b>Pregnancy</b>	Can be administered to eligible pregnant women. While pregnancy is not a contraindication, administration of TST in the absence of HIV infection or recent contact with a confirmed TB case is usually deferred until after delivery.
<b>Lactation</b>	Can be administered to eligible breastfeeding women.
<b>Composition</b>	<p>Tubersol® contains:</p> <ul style="list-style-type: none"> <li>Purified protein derivative of M tuberculosis – 5 TU per 0.1 mL</li> <li>Polysorbate 80 – 0.0006%</li> <li>Phenol – 0.22% to 0.35%</li> </ul> <p>in sterile isotonic phosphate buffered saline.</p>
<b>Blood/Blood Products</b>	Does not contain blood/blood products
<b>Bovine/Porcine Products</b>	No Bovine/Porcine products are in Tubersol
<b>Latex</b>	There is no latex in product or the stopper of the vial.
<b>Interchangeability</b>	N/A
<b>Administration with Other Products</b>	<ul style="list-style-type: none"> <li>Timing of TST and live virus vaccines: <ul style="list-style-type: none"> <li>TST can be administered either: <ul style="list-style-type: none"> <li>Before, on the same day as live virus vaccines, or</li> <li>delayed for 4 weeks following the live virus vaccine.</li> </ul> </li> </ul> </li> <li>Specifically, for <u>COVID vaccines</u>: <ul style="list-style-type: none"> <li>Currently there is no data on the impact of the COVID-19 mRNA vaccines on tuberculin skin testing or IGRA (QFT) test results. There is a theoretical risk that COVID-19 vaccines may temporarily affect cell-mediated immunity, resulting in false-negative tuberculin skin testing or IGRA (QFT) test results. <ul style="list-style-type: none"> <li>In the absence of data and acknowledging the importance of both timely tuberculosis testing and immunization, immunization with COVID-19 vaccines can take place at any time before, after or at the same visit as the TST or IGRA test.</li> <li>However, re-testing (at least 28 days after a dose of COVID-19 vaccine) of individuals with negative results for whom there is high suspicion of TB infection may be prudent in order to avoid missing cases due to potentially false-negative results.</li> </ul> </li> </ul> </li> <li>There is <b>no spacing required</b> between Tuberculin Skin Testing (TST) and quadrivalent live attenuated influenza vaccine (QLAIV). TST may be given at any time before or after QLAIV.</li> </ul>

	<b>Tubersol®</b>
	<ul style="list-style-type: none"> <li>When tuberculin screening is required at the same time as a live virus vaccine, administration of the Tuberculin skin test and the vaccine at separate anatomic sites is preferred.</li> <li>Do not use EMLA cream (or similar local anesthetic cream), as application of this cream has been reported to cause localized edema, which could easily be confused with a positive TST result.</li> </ul>
<b>Appearance</b>	Clear, colorless liquid
<b>Storage</b>	<ul style="list-style-type: none"> <li>Store product between +2°C and +8°C at all times.</li> <li>Do not freeze</li> <li>Label product with the day opened on the vial (using yyyy=4 digit year, mon=3 letter month, dd=2 digit date) once opened and discard any unused solution after <b>30 days</b> of first puncture of the vial</li> <li>Store in original packaging to protect from light</li> </ul>
<b>Vaccine Code</b>	PPD
<b>Antigen Code</b>	PPD
<b>Licensed for</b>	All individuals as based on indications
<p><b>Notes:</b></p> <ul style="list-style-type: none"> <li>Draw up solution with tuberculin syringe just prior to giving, do not pre-load syringe, <b>do not inject air into vial.</b></li> <li>If wheal does not appear, repeat TST immediately in opposite arm.</li> <li>Do not massage or cover the site with a bandage after injection.</li> <li>Measure only the transverse diameter of induration; redness is to be ignored.</li> <li>Record the result in millimeters. Do not round off the diameter of the induration to the nearest 5 mm, as this can interfere with determining whether TST conversion has occurred in the event of a future TST. If the measurement falls between demarcations on the ruler, the smaller of the two numbers should be recorded.</li> <li>If a TST cannot be performed in the preferred site of the inner forearm (i.e. double mastectomy), alternate site is the upper back intradermal within the skin overlying the scapula.</li> </ul> <p><b>Health care worker (HCW) (adapted from Alberta Health (AH):</b></p> <ul style="list-style-type: none"> <li>Includes all hospital employees, other staff who work or study in hospitals (e.g., <b>students in health care disciplines</b> and contract workers) physicians, volunteers and other health care personnel (e.g., those working in clinical laboratories, long term care facilities, home care agencies and community settings), who are at risk of exposure to infectious TB because of their contact with individuals or material from individuals with infectious TB both diagnosed and undiagnosed.</li> <li>Students in dental programs would not be included routinely as an eligible group for baseline TST unless they are working with high risk clients or in high risk settings.</li> </ul> <p><b>All individuals with symptoms of active TB should be referred immediately to TB Services. Call TB Services for direction before the client leaves your site. A TST is not appropriate for these clients.</b></p> <p><b>Referral to TB Services</b></p> <ul style="list-style-type: none"> <li>Instructions for referral are found on the Immunization Program Standards Manual webpage on Insite: <a href="https://insite.albertahealthservices.ca/cdc/Page11322.aspx">https://insite.albertahealthservices.ca/cdc/Page11322.aspx</a> (under Tuberculin PPD),</li> <li>For all positive reactors, please either: <ul style="list-style-type: none"> <li>follow the local zone referral process to TB Services (for Calgary and Edmonton TB Clinics and for TB Central Services) or</li> <li>return patient and results to the specialty program/specialist (e.g. oncology, rheumatology, dermatology, transplant, etc.) requesting the TST.</li> </ul> </li> </ul>	

	<b>Tubersol®</b>
<b>Related Documents:</b> Referral process for Calgary TB Clinic Referral process for Central TB Services Referral process for Edmonton TB Clinic Tuberculin Skin Test for Healthcare Workers and Post-Secondary Students	
<b>References:</b> <ol style="list-style-type: none"><li>1. Alberta Health (2022). <i>Tuberculosis Prevention and Control Guidelines for Alberta</i>. Edmonton AB.</li><li>2. <i>Canadian Tuberculosis Standards 8<sup>th</sup> ed</i>). Ottawa ON: Tuberculosis Prevention and Control, Public Health Agency of Canada, The Canadian Lung Association. Editor: Richard Menzies. Canadian <a href="#">Journal of Respiratory, Critical Care, and Sleep Medicine</a> Volume 6, 2022 - Issue sup1: <a href="#">Canadian Tuberculosis Standards - 8th Edition</a></li><li>3. Sanofi Pasteur Limited. (2016, February 11). TUBERSOL® Tuberculin Purified Derivative (Mantoux). <i>Product Monograph</i></li></ol>	