

Tubersol®

Tuberculin Purified Protein Derivative (Mantoux) Diagnostic Antigen

DESCRIPTION

Tuberculin Purified Protein Derivative (Mantoux) for intradermal tuberculin testing is prepared by the Sanofi Pasteur Laboratories Limited from a large Master Batch Connaught Tuberculin (CT68) which has been obtained from a human strain of *Mycobacterium tuberculosis* grown on a protein-free synthetic medium. The use of a standard preparation derived from a single batch (CT68) has been recommended in order to eliminate batch to batch variation by the same manufacturer.

It is estimated that this batch is large enough to provide solutions for many years. From this batch, Tuberculin PPD at three concentrations is available in sterile isotonic phosphate buffered saline containing polysorbate 80 (0.0006%) as a stabiliser. Phenol 0.28% is added as a preservative.

Independent studies conducted by the US Public Health Service in humans have determined the amount of CT68 in stabilised solution necessary to produce bio-equivalency with Tuberculin PPD-S (in phosphate buffer without polysorbate 80) using 5 US units (TU) Tuberculin PPD-S as the standard.

Prior to release, each successive lot is tested for potency in sensitised guinea pigs in comparison with a reference standard.

Tuberculin PPD (Mantoux) - Tubersol® bioequivalent to 5 US units (TU) PPD-S per test dose (0.1 mL) is available in 1 mL and 5 mL vials. Tuberculin PPD (Mantoux) - Tubersol® solutions are ready for immediate use without further dilution.

INDICATIONS

Tuberculin PPD is indicated as an aid in the detection of infection with *Mycobacterium tuberculosis*.

DOSAGE AND ADMINISTRATION

The Mantoux test is performed by injection intradermally, with a syringe and needle, 0.1mL of Tuberculin PPD. For the intradermal (Mantoux) tuberculin test, the dose is 5 TU per test dose of 0.1mL.

Method of Administration:

1. The site of the test is the flexor surface of the forearm about 4 inches below the bend of the elbow.
2. The skin of the forearm is first cleansed with alcohol and allowed to dry.
3. The test dose (0.1 mL) of Tuberculin PPD is administered with a 1 mL syringe calibrated in tenths and fitted with a short, one-half inch 26 or 27 gauge needle.
4. Disposable sterile syringes and needles may be used.
5. Wipe the rubber cap of the vial with an alcohol swab. The needle is then inserted gently through the cap and 0.1 mL of Tuberculin PPD is drawn into the syringe.
6. The point of the needle is inserted into the most superficial layers of the skin with the needle bevel pointing upward. If the intradermal injection is performed properly, a definite pale bleb will rise at the needle point, about 10 mm (3/8") in diameter. This will disappear within minutes. No dressing is required.

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7. A separate sterile syringe and needle must be used for each individual injection to prevent the possibility of transmission of viral hepatitis or other infectious agents from one person to another. In particular, the same needle and/or syringe must never be used to re-enter a multi-dose vial to withdraw product even when it is to be used for testing of the same patient. This may lead to contamination of the vial contents and infection of patient who subsequently receive product from the vial.

Failure to store and handle Tuberculin PPD as recommended will result in a loss of potency and inaccurate test results.

Interpretation of the Test:

Intradermal tuberculin testing is an accepted aid in the diagnosis of tuberculosis. A positive reaction indicates sensitivity to tuberculin, which may be the result of a previous infection with mycobacteria. This infection, likely due to *Mycobacterium tuberculosis*, may have occurred years ago or may be of recent origin.

The test should be read 48 to 72 hours after administration of the tuberculin. Sensitivity is indicated by induration only; redness should not be measured. The diameter of induration should be measured transversely to the long axis of the forearm and recorded in millimetres (mm). Presence of oedema or necrosis should also be recorded, although it is not used in the interpretation of the test.

Any palpable induration measuring 10 mm or more is considered a positive reaction. Induration measuring 5-9 mm indicates a doubtful reaction. Induration of less than 5 mm is considered a negative reaction.

Booster Effect - Infection of an individual with tubercle bacilli or other mycobacteria results in a delayed hypersensitivity response to tuberculin which is demonstrated by the skin test. The delayed hypersensitivity response may gradually wane over a period of years. If a person received a tuberculin test at this time (after several years) the response may be a reaction that is not significant. However, the stimulus of the test may boost or increase the size of the reaction to a second test, sometimes causing an apparent conversion or development of sensitivity.

Two-step testing – Two-step testing is performed when there is a need to establish a true baseline tuberculin reaction. Two-step testing is done to distinguish boosting from conversion in people who are having serial tuberculin testing for instance health-care workers. If the first test showed either no reaction or small reaction, the second test should be performed one week after the first test.

In the case of doubtful tuberculin reactions (5-9 mm) to 5 TU, the possibility should be considered that the skin sensitivity is due to previous contact with atypical mycobacteria or previous BCG vaccination.

Since tuberculin reactivity may not necessarily indicate the presence of active tuberculous disease, individuals showing a tuberculin reaction should be further evaluated with other diagnostic procedures.

Those individuals giving a positive tuberculin reaction may or may not show evidence of tuberculous disease. Chest X-ray examination and microbiological examination of the sputum in these cases is recommended as a means of determining the presence or absence of pulmonary tuberculosis.

CONTRAINDICATIONS

Previous hyper-sensitivity to PPD antigen.

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PRECAUTIONS FOR USE

Do not inject intravenously or intramuscularly.

Do not inject subcutaneously. If this occurs, the test cannot be interpreted.

Reactivity to the test may be depressed or suppressed for as long as 4 to 6 weeks in individuals who have had viral infections (rubella, influenza, mumps and probably others) or in those who are receiving corticosteroids or immunosuppressive agents. Reactivity to PPD may be temporarily depressed by certain live virus vaccines (measles, mumps, rubella). Therefore, if a tuberculin test is to be performed it should be administered either before or simultaneously with the injection of measles, mumps and rubella vaccines.

Adrenaline injection (1:1000) and other appropriate agents should be readily available for use in case an anaphylactic or acute hypersensitivity reaction occurs. The possibility of allergic reactions in persons sensitive to components of Tubersol® should be evaluated. Allergic reactions may occur following the use of Tubersol® even in persons with no prior history of hypersensitivity to the product components.

In those who are elderly or being tested for the first time, reactions may develop slowly and may not peak until after 72 hours.

ADVERSE REACTIONS

Local

Very rarely, vesiculation, ulceration or necrosis may appear at the test site in highly sensitive persons.

Pain, pruritus and discomfort at the test site may also occur.

Strongly positive reactions may result in scarring at the test site.

Immediate erythematous or other reactions may occur at the injection site. The reason(s) for these infrequent occurrences are presently unknown.

Two to three percent of tested persons will have localised redness or rash (without induration) occurring within 12 hours of testing. These reactions do not indicate TB infection.

Injection site bleeding after the needle is withdrawn and haematoma and bruising up to three days after the administration of the test have been seen.

Systemic

There have been rare severe systemic hypersensitivity reactions (anaphylactic/anaphylactoid reactions) following Tubersol® administration that were manifested by angioedema, upper respiratory stridor, dyspnea, skin rash, generalised rash and/or urticaria reported within 24 hours. These were treated with epinephrine, diphenhydramine and/or steroids. Some of these events were reported in patients who had no prior exposure to Tubersol®. No cause and effect was able to be established with a specific component of the skin test.

OVERDOSAGE

There are no reports of overdosage.

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STORAGE

Tuberculin PPD (Mantoux) - Tubersol[®] should be stored between 2° and 8°C (35°-48°F).

Tuberculin PPD solutions can be adversely affected by exposure to light. The product should be stored in the dark except when doses are actually being withdrawn from the vial.

A vial of Tuberculin PPD which has been opened and in use for one month should be discarded because oxidation and degradation may have reduced the potency.

MEDICINE CLASSIFICATION

Prescription Medicine

MANUFACTURER

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DISTRIBUTOR

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1 November 2007