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### Snohomish Health District TB Control Program

Subject: Protocol and Standing Orders for Evaluation and Management of Tuberculosis Infection and Disease	Effective date: July 1, 2006
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Purpose: To provide SHD clinical staff with medical guidelines for evaluating and managing patients who present for tuberculosis (TB) screening or who present with a clinical presentation suspicious for active TB. This document is intended to complement pursuit of consultation from the TB medical consultant/control officer where appropriate.

*Administrative Note: Eligibility for clinical TB services through SHD is limited to Snohomish County residents. Exceptions may be granted for disease control purposes at the discretion of the Health Officer, the TB Control Officer, or the TB Control Program Manager.*

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## I. TB Skin Testing

### A. Candidates for TB Screening through SHD

1. Recent close contacts of active cases (i.e., within the past 24 months)
2. Persons known to have radiographic evidence suggestive of old, healed TB
3. Persons identified by immigration screening to have abnormal chest films suggestive of old or active TB (Class A/B)
4. Refugees
5. Other immigrants who have resided in the US for 5 years (i.e. 60 months) or less
6. Persons who have traveled to high-prevalence regions for  $\geq 6$  months during the preceding 5 years
7. Homeless persons
8. Persons who have injected illicit drugs
9. Persons seeking treatment for substance abuse
10. HIV infected persons
11. Organ transplant recipients
12. Persons with medical conditions that predispose to developing active disease if infected
  - a. Diabetes mellitus (especially insulin dependent or poorly controlled)
  - b. Chronic steroid therapy (e.g., equivalent of prednisone 15-20 mg per day for greater than one month)
  - c. Other immunosuppression (congenital immunodeficiency syndromes, HIV infection, or medically induced)
  - d. Cancer of the head/neck, lung, hematologic system (e.g., leukemia) or reticuloendothelial system (e.g., lymphoma)
  - e. End-stage renal disease (i.e., chronic hemodialysis and transplant candidates)
  - f. Malabsorptive states (e.g., small bowel resection, intestinal bypass, inflammatory bowel disease)
  - g. Less than 90% ideal body weight-for-height
  - h. Silicosis
13. Residents and employees of high-risk congregate settings (e.g., correctional facilities, homeless shelters, inpatient facilities)

*Note: Employees of high-risk congregate settings who do not meet any of the other risk criteria set forth above should be triaged to their employer's occupational health care provider or to primary care.*

14. Patients who are clinically well and are neither recent contacts to active TB, nor HIV-infected, nor refugees, nor class A/B immigrants may have TB screening deferred until arrival in their anticipated community of residence if they do not plan to reside in this jurisdiction for a period adequate to complete screening and treatment. More specifically...

For persons with disabilities, this document is available on request in other formats. To submit a request, please call 1-800-525-0127 (TDD/TTY 1-800-833-6388).

- a. Such clients planning to move out of the United States should be screened only if their current stay in the United States will exceed nine months.
- b. Such clients planning to move out of Washington (but to remain in the United States) should be screened only if their current stay in Washington will exceed six months.
- c. Such clients planning to move out of Snohomish County (but remain in Washington) should be screened only if their current stay in Snohomish County will exceed three months.

## B. TB Screening in Pregnancy

1. Pregnant women should not be screened unless the managing health care provider plans to treat them during pregnancy, if they are indeed found to have latent TB. Consequently, screening during pregnancy should generally be limited to women who meet one or more of the following criteria:

- a. Contact with a pulmonary TB case within the preceding 24 months
- b. HIV infection
- c. Other medical conditions (listed above) that increase the risk for developing active TB
- d. Known radiographic abnormalities consistent with prior active TB (including class A/B immigrants)
- e. Refugees and immigrants who have arrived within the preceding 24 months from high-risk regions of the globe
- f. Tuberculin skin-test converters

If PPD positive, pregnant women in this group (these groups?) should undergo a PA chest radiograph with abdominal shielding, regardless of the stage of pregnancy.

2. Pregnant women who lack all of the factors described immediately above may have skin testing deferred until the post-partum medical evaluation.

3. In the event such screening does occur in such a “lower-priority” pregnant woman who is asymptomatic and she is found to have a positive skin test (e.g.,  $\geq 10$ mm), a posteroanterior chest radiograph (with abdominal shield) should be obtained *after the first trimester* to assess for evidence of active pulmonary disease. If the radiograph is normal or shows only calcified granulomata, treatment should be deferred until 4-6 weeks after delivery. At that time a repeat chest radiograph should be obtained and reviewed prior to starting treatment for latent TB.

## C. Standing Orders for Administration and Interpretation of TB Skin Tests:

1. Administer Purified Protein Derivative (PPD) 5 units (0.1 ml) intradermally in the left lateral forearm.

2. Alternative sites include the right lateral forearm or the posterior aspect of either trapezius muscle.

3. Skin tests should not be administered on a day that will cause the 48-72 hour reading date to fall on a weekend or holiday unless a specific plan has been established to permit a reliable reading.

4. Interpretation:

Skin tests should be read by a SHD clinician at 48-72 hours after administration with the result recorded in double digits (e.g., 07 mm).

a. Skin tests may be read up to 96 hours under the following limited circumstances

b. Reasonable efforts to read by 72 hours have failed.

c. The observed result is clearly 00 mm induration without any erythema or is clearly 10 mm induration or greater.

d. Classification of the skin-test result is pursuant to CDC guidelines as set forth in *Appendix A*.

e. A skin test conversion is defined as the following: a documented increase of 10 mm induration (or greater) over the preceding 24 months (e.g., 08--- $\geq$ 18 mm or 00---- $\geq$ 10 mm). Such persons should be considered “PPD-positive,” regardless of their placement in the risk matrix cited above.

f. Persons entering a serial TB skin testing program should undergo two-step testing at baseline. Specifically, if the initial result is negative AND no documented result from the preceding 12 months is available, a second PPD should be applied 1-3 weeks after the first. This second step should be interpreted using the same criteria as the first. For instance, if the first step is 08 mm and the second step is 16 mm, the second test is interpreted as “positive” (even though it is not a 10 mm increase).

## **II. Interferon-gamma assays for detecting tuberculosis infection**

An FDA-licensed assay (Quantiferon Gold--QFG) exists which measures in vitro production of gamma-interferon production by patient lymphocytes when incubated with synthetic peptides (ESAT-6 and CFP-10). These two antigens are relatively specific for *M. tuberculosis* complex and carry great potential for increasing the specificity and positive predictive value of testing for latent tuberculosis, particularly among BCG-vaccinated populations and in serial testing programs. Specimen collection involves obtaining at least 5 ml of whole blood in a heparinized tube. Handling requirements are somewhat rigorous in that the specimen must be delivered to the laboratory and processed within 12 hours from the time of collection. This assay is considered interchangeable with the tuberculin skin test; it can be used in all circumstances cited above as indications for PPD skin testing. QFG cannot be used to confirm a tuberculin skin test, however, and recent tuberculin skin-testing may produce a falsely positive QFG result.

QFG is not currently available for clinical use in the setting of SHD TB Control clinical operations. Should it become available, guidelines for the interpretation of results are set forth in Appendix E.

## **III. Standing Orders for Obtaining Radiographic Studies of the Chest**

### **A. Indications**

1. New positive skin test
2. Past positive skin test with no chest radiograph since skin-test positivity was first documented
3. Skin test negative household contacts of pulmonary cases, if the contact is:
  - a. under 15 years of age, or
  - b. HIV infected, or
  - c. immunosuppressed
4. Reports of any abnormality on immigration chest radiographs
5. Persons seeking treatment for latent TB infection whose last chest radiograph is >3 months old or unavailable
6. Persons with a productive cough greater than 3 weeks in duration
7. End-of-therapy for active TB that included a pulmonary, pleural, or other intrathoracic component (e.g., hilar or mediastinal lymphadenopathy).
8. As otherwise directed by TB medical consultant

Note: Patients undergoing administrative screening (e.g., for health care work) who have a history of both a previous positive skin test AND a subsequent normal chest radiograph should be referred to the provider who conducted these examinations for the appropriate documentation to provide to their employer. These patients may be invited to return with this documentation for consideration of treatment of latent infection if they are interested in treatment and do not have access to a primary care

provider. If such documentation is not recoverable, the skin test and/or chest radiograph may be repeated when program and client resources permit.

B. Chest-radiography should include both a posteroanterior and lateral view in the following settings:

- 1.. Persons less than 10 years of age
  2. HIV infection
  3. Suspected or reported pleural effusion or hilar adenopathy
  4. TB medical consultant direction
- Otherwise, chest radiography should be limited to a single, PA view.

C. Interpretation

1. The TB medical consultant should review radiographs if a patient will be treated or is being treated directly by SHD, regardless of whether the radiograph has been previously reviewed by another health care provider. When time, distance, or access considerations provide a substantial barrier to obtaining the radiograph for viewing in a timely fashion (e.g.,  $\leq 2$  weeks), a copy of the radiologist's report may be submitted to the TB medical consultant for review.

2. SHD nursing staff may accept the readings of outside health care providers for the purposes of making recommendations on treatment to community-based providers, provided that they make it clear to the consulting provider that SHD has not directly reviewed the image but has only seen the report.

## **IV. Standing Orders for Sputum Evaluation**

### **A. Indications for Sputum Collection for Acid-fast Bacilli Smear and Culture**

1. As part of screening for HIV-infected patients who are potential candidates for treatment of latent TB infection.
2. Among suspected and confirmed cases of active pulmonary TB:
  - a. Three baseline specimens, then
  - b. One-to-two specimens weekly until AFB smears are negative on three or more consecutive occasions, then
  - c. Two specimens monthly until AFB cultures are negative on three or more occasions, then
  - d. Two specimens every three months until the end of therapy
3. Class B immigrants whose documentation of overseas screening indicates findings suggestive of active or inactive TB (e.g., “infiltrate”, “fibrosis”, “previous treatment”).
4. As otherwise ordered by the TB medical consultant

### **B. General procedure for collection of sputum specimens**

1. Attempt to collect three specimens, unless otherwise directed by medical consultant
2. Five milliliters (5 ml) of sputum (not saliva) is the desired specimen.
3. In general, specimens should be collected upon rising in the morning, before the first meal. However, for expediting management among ill suspects and unreliable patients, it is recommended that the first specimen be collected while the patient is in the clinic (or in the presence of an SHD clinician in the field).
4. If the patient has a productive cough, attempt to collect the first specimen while s/he is still in the clinic. Use the isolation room.
5. If the patient is unable to raise early morning sputum, suggest that s/he take a hot shower in a steamy room first. If that still fails, notify the medical consultant.

### **C. Nucleic acid amplification testing**

Testing for amplification and direct detection of TB nucleic acid (e.g., MTD) should be requested on two of the initial three sputum specimens from all new suspected cases of active pulmonary TB.

**V. Assignment of TB Diagnosis Classification and General Approaches to Treatment**

- Class 0: Not recently exposed, not infected (or exposed >8-10 weeks ago and infection ruled out with follow-up skin testing)
- Class 1: Recently exposed, not infected (should become reclassified within 3 months)
- Class 2: Latent infection (without disease)
- Class 3: Confirmed active disease
- Class 4: Old, inactive disease
- Class 5 High: Suspected active disease, with intention of empiric treatment
- Class 5 Low: Suspected active disease, empiric treatment not intended

A. The TB medical consultant will assign disease classification.

B. The TB medical consultant will order all treatment.

C. Management of class 1, 3, and 5 patients will be individualized but typically will reflect guidelines set forth by the American Thoracic Society and CDC.

## **VI. General Standing Orders for TB Therapy:**

### **A. Indications for directly observed therapy of LTBI**

In the context of treatment for latent infection or inactive disease (i.e., class 2 or 4 TB), the choice of daily self-administered vs. twice weekly observed is delegated to the nursing staff, unless otherwise ordered by the TB Medical Consultant. The following patients should be prioritized for twice-weekly observed therapy over patients who lack these characteristics:

1. Recent close contacts of pulmonary cases
2. HIV infection
3. Old, inactive TB (class 4)
4. Previous history of non-adherence to treatment
5. Homelessness
6. Chemical dependency
7. Severe mental health disorders (e.g., poorly controlled psychotic illnesses)
8. Frequent or recent incarceration
9. Patients with complex medical problems or taking multiple medications
10. Patients with considerable language and cultural barriers to adherence
11. Other patients whose social, medical, or behavioral circumstances raise reasonable concern about adherence.

B. Release of “packets” of DOPT medication for self-administration to class 1, 2, and 4 patients on DOPT should be used sparingly and should never exceed 15% of the total dose count. Holiday packets should not be provided unless otherwise ordered by the TB Medical Consultant. In general, the SHD TB Control Program policy is that for patients on DOPT, a missed dose is preferred to an unobserved one. In adherent cases with no medical or psychosocial barriers to tolerance and compliance, consider changing to daily self-administered therapy instead of making frequent use of packets. Packet usage by patients should be reviewed periodically (e.g., at least every 3 months) with the TB Control Program Supervising Nurse.

### **C. Suspected (Class 5) and confirmed (Class 3) active TB**

1. Treatment regimen will be individualized and ordered by the TB medical consultant
2. As a local standard of medical and public health management, all active cases should receive treatment under direct observation. At nurse discretion, this may include use of videophone or analogous technology. Exceptions will be permitted only rarely. In cases where this is not the method of supervision, the alternative method of supervision (e.g., monthly or weekly pill counts, use of DOT extenders) and circumstances leading to its choice (e.g., provider refusal, schedule conflicts) should be clearly documented in the chart and reviewed with the TB medical consultant.

3. For patients on “daily DOT”, administration of medication should occur five times weekly, Monday-Friday (holidays excepted). Unless otherwise specified by the medical consultant, medications will not be administered or released to patients on weekends or holidays.

4. Release of “packets” of DOT medications for self-administration by active TB cases (class 3 and 5-High) must be approved and guided by the case’s assigned PHN or the TB Control Program Supervising Nurse *prior* to release. Again, in general, the SHD TB Control Program policy is that a missed dose is preferred to an unobserved one.

D. Pyridoxine (50 mg po daily or twice weekly) should be routinely administered to the following patients receiving isoniazid, regardless of whether or not the TB medical consultant has specifically ordered it:

1. Underlying peripheral neuropathy
2. Regimen includes other agents in addition to isoniazid
3. Diabetes mellitus
4. HIV infection
5. Seizure disorder, anti-seizure medication, anti-psychotic medication, or other conditions associated with lowered seizure threshold
6. Conditions associated with chronic malabsorption (e.g., inflammatory bowel disease, resections of small intestine)
7. Chronic renal failure
8. Alcoholism
9. Pregnancy
10. Body mass index <20 (calculate @ <http://nhlbisupport.com/bmi/>)
11. Age >65

The TB Medical Consultant will order specific pyridoxine dosing for children whose state of (mal-)nutrition or whose underlying medical conditions warrant its use.

#### E. Completion of Therapy for Active Disease

1. Appendix B shows, under typical circumstances, when the medical consultant will consider a patient’s therapy complete.
2. Duration of treatment may be extended by the medical consultant in the following circumstances:
  - a. Cavitory or otherwise extensive disease
  - b. Culture conversion delayed beyond two months into therapy
  - c. Other clinical judgment that extended therapy is warranted
3. Some patients are eligible for once-weekly treatment with isoniazid and rifapentine during the continuation phase (see Appendix B). Inclusion criteria are:
  - a. Pulmonary disease only
  - b. Age  $\geq$ 18 years
  - c. Non-pregnant
  - d. Unilateral, non-cavitory disease OR minimal bilateral non-cavitory disease

- e. Smear negative at or before 8 weeks into therapy
- f. HIV negative
- 4. Alert the medical consultant prior to the 8-week milestone when such patients are recognized.
- 5. Duration of alternative regimens not listed in Appendix B will be individualized and follow ATS/CDC and other national TB expert-generated guidelines and recommendations.
- 6. Each case's completion of therapy should be reviewed and approved by the medical consultant before discontinuation of treatment occurs.

F. Lapses in Treatment and Completion of Therapy for Latent or Inactive TB:

- 1. Appendix C shows when clinical staff can consider a patient's therapy complete
- 2. Continue current therapy in dose and frequency as previously ordered and seek TB medical consultant consultation if
  - a. lapses in therapy of greater than 3 weeks (cumulatively) occurred during the first three months of therapy, OR
  - b. other factors lead to a desire for medical consultation regarding adequacy of therapy

G. Indications for repeat chest radiograph in patients who have lapsed or failed to start treatment

- 1. Under treatment for active pulmonary TB and lapse >3 weeks
- 2. Symptoms of TB
- 3. Intercurrent illness with productive cough lasting  $\geq 2$  weeks
- 4. Lapse greater than three months (since last dose or, if never started, since last chest radiograph)
- 5. Intercurrent delivery of an infant

## **VII. Standing Orders for Drug Dosing:**

A. When the TB medical consultant orders drugs to be dosed “per standing orders,” use the tables in Appendix D to administer correct doses of medications. Verbal or written orders from the TB medical consultant always supersede these standing orders.

B. Weigh all active cases and children <13 years on a monthly basis. Other patients should be weighed every three months. Adjust dose per tables, if necessary. However, if a *reduction* in weight would result in a decreased dose, hold the dose at its current level and refer the chart to the TB medical consultant.

C. Seek TB medical consultant consultation if standing order doses conflict with nursing judgment in the case at hand or if patient weight falls outside parameters set forth in tables.

## **VIII. Standing Orders for HIV Counseling and Testing**

A. All suspected and confirmed active cases should be strongly encouraged to undergo HIV counseling and testing, unless the patient is already known to be HIV infected. Highest priority should be placed on persons who:

1. are aged 25-54 years, OR
2. homeless, OR
3. have a history of drug injection

B. Patients undergoing screening or treatment for LTBI should be briefly assessed for risk of HIV infection, with highest priority for this assessment being directed to homeless persons and close contacts of HIV-infected cases. In addition to active cases, contacts of HIV-infected TB cases should, whenever feasible, be tested by the TB Control Program.

C. The following are guidelines for referral of other patients:

1. Individuals with risk factors for HIV infection... (for example
2. drug injection
3. male-male sexual contact
4. partner HIV infected
5. partner injecting drugs
6. multiple partners in preceding 3 months
7. sexually transmitted disease in preceding year

D. . individuals who have not been tested in the preceding 12 months should be encouraged to undergo HIV testing.

E. Other persons without risk factors undergoing LTBI screening may be offered HIV testing at the TB nurse's discretion.

**IX. Standing Orders for Monitoring Adverse Effects to and Tolerance of Treatment:**

A. Patients should be clinically evaluated for adherence, tolerance, and adverse effects on the following schedule:

Regimen	Clinical Evaluation	Laboratory Evaluation
INH or RIF for Class 2 or 4	Baseline, monthly and prn <ul style="list-style-type: none"> <li>▪ Anorexia</li> <li>▪ Nausea</li> <li>▪ Vomiting</li> <li>▪ Abdominal pain</li> <li>▪ Jaundice</li> <li>▪ Fever</li> <li>▪ Headache</li> <li>▪ Fatigue</li> <li>▪ Joint pains</li> <li>▪ Paraesthesiae</li> <li>▪ Rash</li> <li>▪ Dizziness</li> </ul>	Hepatic function panel (HFP) at baseline if: History of drug injection Ongoing alcohol use $\geq 10$ drinks per week Chronic hepatitis Other liver disease Multiple medications Pregnancy Clinical suspicion of underlying liver disease Otherwise ordered by medical consultant  In these patients, the plan for follow-up biochemical and viral serology testing, if any, will be individualized through TB medical consultant orders.  Otherwise, HFP should only be conducted as ordered by TB medical consultant or as clinically indicated by patient report of symptoms of hepatitis
Class 3 or 5 High	Baseline, monthly and prn <ul style="list-style-type: none"> <li>▪ Same content as above, plus:</li> <li>▪ visual acuity</li> <li>▪ color discrimination</li> <li>▪ Vision assessments need only be repeated prn or if EMB is extended beyond two months.</li> </ul>	Comprehensive metabolic panel (CMP) and complete blood count with platelets and differential (CBC) at baseline. <i>The plan for follow-up laboratory testing, if any, will be individualized through TB medical consultant orders.</i>

**B. Medication Education for Patients**

1. Patients should be educated about the adverse effects of TB medications and told to hold their medications and call the clinic immediately if such effects develop.
  - a. Hepatotoxicity (isoniazid, rifampin, pyrazinamide, ethionamide): nausea, vomiting, right upper quadrant pain, anorexia, jaundice, bilirubinuria, acholic stools
  - b. Gastritis (pyrazinamide, rifampin, fluoroquinolones, para-amino salicylate): severe epigastric pain, nausea, vomiting
  - c. Hypersensitivity (any): rash, fever
  - d. Neurologic (isoniazid, fluoroquinolones, cycloserine, ethionamide): headache (severe, persistent), paraesthesiae, restlessness, tremor, agitation, insomnia, seizures, psychosis
  - e. Visual (ethambutol, isoniazid, ethionamide): visual changes (loss of acuity, loss of color discrimination)

- f. Vestibular (aminoglycosides and capreomycin): tinnitus, loss of hearing, vertigo, loss of balance
- g. Joints (pyrazinamide, fluoroquinolones, isoniazid): gout, arthralgias
- h. Muscles (fluoroquinolones): tendon pain or rupture
- i. Hematologic (rifampin): easy bruising, bleeding gums, blood in stools or urine

C. Among women of potentially childbearing age (13-54 years), assess last menstrual period and perceived pregnancy status monthly. If pregnancy is suspected (e.g., menses overdue), perform urine HCG. Call TB medical consultant for direction if HCG-positive or pregnancy otherwise reported.

D. Subject to nurse discretion, monthly monitoring of persons undergoing treatment for latent infection may be done by telephone, unless clients require specimen collection for laboratory evaluation or unless other elements in the patient's social, medical, or behavioral circumstances make such history-taking reasonably unlikely to be reliable.

E. All patients with active disease must be seen in person at least monthly by SHD nursing staff or the community-based provider who is managing their TB disease.

F. Administration or dispensing of medication should cease for any patient who is more than one month overdue for monitoring.

1. If the patient has active TB, the chart should be referred to the TB Control Officer for remedy.

2. If the patient has latent or inactive TB, then the chart should be held open for up to one additional month (two months total) before dismissing the case and closing the file.

3. Prior to such closure, at least two telephone attempts and one written (certified mail) attempt to engage the patient should be conducted and documented in the chart.

**X. Standing Orders for Notification of TB Medical Consultant:**

A. Immediate—hold medications (if applicable) and immediately contact TB medical consultant by telephone:

1. Icterus
2. Severe nausea and vomiting (e.g.,  $\geq 4$  times in any 48 hour period)
3. Other overt clinical evidence of hepatitis
4. Transaminases  $> 5$  times upper limit of normal (e.g.,  $> 200$  IU/ml)
5. Transaminases  $> 2$  times upper limit of normal (e.g.,  $> 80$  IU/ML) and symptoms consistent with hepatitis
6. Other critical laboratory abnormalities (e.g., platelets  $< 50K/mcl$ , WBC  $< 2500/mcl$ , neutrophils  $< 1000/mcl$ )
7. Gout
8. Tendon pain or rupture (if on fluoroquinolones)
9. Overt bleeding manifestations (e.g., purpura, petechiae, bleeding gums, hemorrhage)
10. Anaphylactic or anaphylactoid reaction reported
11. Hospitalization due to TB medications in latent infection
12. Hospitalization for any reason among active cases

B. Priority—hold medications (if applicable) and refer chart (or fax key contents) to TB medical consultant for review and feedback within 48 hours:

1. New suspected case (send radiographs and key chart contents)
2. Persistent, severe headache
3. Persistent nausea and vomiting to a degree less than set forth above under “Immediate”
4. Paraesthesiae
5. Non-urticarial rash
6. Visual changes
7. Vestibular changes
8. Other adverse effect symptoms not of an emergent nature which still merit prompt attention
9. Hospitalization for reasons unrelated to TB or TB treatment among persons with latent infection

C. Routine—continue medications and refer chart (or fax key contents) to TB medical consultant for review and feedback within 96 hours

1. Transaminases  $>$  upper limit of normal (e.g.,  $> 50$  IU/ml), but not meeting more urgent criteria set forth above
2. Other (non-critical) laboratory abnormalities
3. Pruritus without rash
4. Other adverse effect symptoms not of an urgent nature

D. Other—hold for next on-site visit by (or courier shipment to) TB medical consultant

1. Charts and radiographs of asymptomatic persons with positive skin tests and radiographs completed.
2. Charts and radiographs of patients awaiting diagnostic classification whose sputum cultures are negative and final .

## **XI. Isolation Guidelines**

A. Active pulmonary TB suspects (Class 5—High) and cases (Class 3) should be isolated when they meet any of the following criteria:

1. Completion of <2 weeks of effective therapy
2. Smear positive
3. Lapse in treatment greater than one month and sputum smear status unknown

B. Conversely, isolation may be discontinued when sputum smears are negative on three separate appropriately spaced specimens (i.e.,  $\geq 8$ -24 hours apart) AND  $\geq 2$  weeks of effective therapy have been completed.

C. The medical consultant may, on a case-by-case basis, direct isolation more or less stringently than defined here, taking into account characteristics of the case, potentially exposed persons, and the environment being entered.

D. Whenever an active pulmonary case under SHD jurisdiction is hospitalized or placed in another high-risk congregate setting, review the situation with the medical consultant to confirm isolation parameters.

E. Patients being isolated in the community for infectious TB should be advised of the following:

1. The need to stay in the place of residence approved by SHD.
2. Obligation to not change their place of residence without obtaining approval from SHD.
3. While in isolation, agreeing to see only persons who have been cleared by SHD.
4. To see anyone who has not been cleared by SHD, such meeting must occur out of doors.
5. They should not visit homes of others, churches, school, work place, or other public or private places where they would be in contact with other persons.
6. They also should not use public transportation or taxis.

**APPENDIX A**  
**INTERPRETATION OF TB SKIN TEST AS “POSITIVE”**  
**SNOHOMISH HEALTH DISTRICT**

<b>≥05 mm</b>	<b>≥10 mm</b>	<b>≥15 mm</b>
Clinical suspicion of active TB	Children <4 years	Persons with none of the risk factors to the left. Includes: <ul style="list-style-type: none"> <li>◆ Recent immigrants from nations not listed in footnote below (e.g., Canada, Western Europe, Russia, Ukraine, Belarus, Australia, New Zealand, and some <del>Carribbean</del><u>Caribbean</u> and Pacific Islands)</li> <li>◆ Persons entering treatment for alcohol and other non-injection drug use</li> </ul>
Radiographic evidence of currently active or old-inactive TB	Other children <18 years regularly exposed to high risk adults	
Immunosuppressed states <ul style="list-style-type: none"> <li>◆ HIV infection</li> <li>◆ Solid organ or bone marrow transplant</li> <li>◆ Other (e.g., ≥15-20 mg prednisone equivalents per day for ≥3 weeks, cancer chemotherapy, etc.)</li> </ul>	Medical conditions predisposing to reactivation: <ul style="list-style-type: none"> <li>• Diabetes mellitus</li> <li>• End stage renal disease</li> <li>• Hematologic and reticuloendothelial malignancies</li> <li>• Lung, head, or neck cancers</li> <li>• Malabsorptive states (e.g., partial/total gastrectomy, intestinal bypass, inflammatory bowel disease)</li> <li>• ≤90% of ideal body weight</li> <li>• Other evidence of malnutrition</li> <li>• History of drug injection</li> </ul>	
Close contacts of active pulmonary TB	Staff, volunteers, or residents in <ul style="list-style-type: none"> <li>◆ Acute or long-term care facilities</li> <li>◆ Adult correctional facilities</li> <li>◆ Homeless shelters</li> </ul> Foreign born persons from the following high risk countries*	

\*Includes any countries in Africa, Asia, Central or South America, most of the Carribbean and Pacific Islands, as well as Afghanistan, Albania, Armenia, Azerbaijan, Bosnia & Herzegovina, Bulgaria, Croatia, Djibouti, Estonia, Georgia, Hungary, Kazakhstan, Kyrgyzstan, Latvia, Lebanon, Lituania, Poland,

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Portugal, Mexico, Moldova, Qatar, Romania, Slovakia, Slovenia, Spain, Syria, Tajikstan, Macedonia, Turkey, Turkmenistan, Uzbekistan, West Bank and Gaza, Yemen, Yugoslavia (i.e., most countries where rates exceed 20/100K)

## APPENDIX B

### STANDARD REGIMENS FOR TREATMENT OF ACTIVE TB

REGIMEN	INITIAL PHASE		CONTINUATION PHASE		COMMENT
	Agents	Duration	Agents	Duration	
<b>I. A</b>	INH RIF PZA EMB*	40 doses (5d/wk for 8 weeks)	INH RIF	36 doses (BIW for 18 weeks)	<ul style="list-style-type: none"> <li>• Extend continuation phase from 36 to 62 BIW doses if cavitation was present at baseline and culture is positive @ ≥8 weeks into therapy***</li> <li>• BIW therapy contraindicated in HIV infection—QD or TIW only</li> </ul>
<b>B</b>	INH RIF PZA EMB*	40 doses (5d/wk for 8 weeks)	INH Rifapentine	18 doses (QW for 18 weeks)	<ul style="list-style-type: none"> <li>◆ Use limited to               <ul style="list-style-type: none"> <li>◆ HIV-negative adults</li> <li>◆ Non-cavitating pulmonary disease only (no EPTB, no cavities)</li> <li>◆ Smears must be negative by 2 months into therapy</li> </ul> </li> <li>◆ If smear negative specimen turns out to be culture positive @≥8 weeks, extend continuation phase to 31 QW doses</li> </ul>
<b>C</b>	RIF PZA EMB +/- INH**	130 doses (5d/wk for 26 weeks)			<ul style="list-style-type: none"> <li>◆ Treatment should be administered daily when drug resistance is present or when either INH or a rifamycin are missing from the regimen</li> </ul>
<b>D</b>	INH RIF EMB	40 doses (5d/wk for 8 weeks)	INH RIF	62 doses (BIW for 31 weeks)	<ul style="list-style-type: none"> <li>◆ Generally reserved for patients who are PZA intolerant or pregnant and who have minimal risk of drug resistance</li> </ul>

\* In Regimens A and B, EMB may be discontinued as soon as susceptibility to INH and RIF is demonstrated

\*\* When Regimen C is used for INH-resistant TB, INH may be continued if resistance to INH is only partial. Typically INH is administered BIW in this setting, to provide a high serum level for overcoming partial resistance.

\*\*\* Treatment may be likewise extended if disease was cavitary OR culture positive @ >8 wks if clinically indicated (e.g., HIV infection, BMI <20, extensive disease). Even without cavities or other risk factors for relapse, therapy should continue for at least 4 months (18 weeks) beyond sputum culture conversion.

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## APPENDIX C

### STANDARD REGIMENS FOR TREATMENT OF LATENT OR INACTIVE TB

REGIMEN	Agents	No. of Doses	COMMENT
<b>INH DAILY 9 MONTHS</b>	INH	270 QD	<ul style="list-style-type: none"> <li>• Must be completed over the course of 12 months</li> <li>• Notify MD before discontinuing if lapses greater than three week-equivalents of dosing during the first three months of therapy</li> <li>• Patients whose therapy is interrupted after 26 week-equivalents of dosing for non-compliance, refusal, loss-to-follow-up, or adverse effects may be considered adequately treated for program reporting purposes</li> </ul>
<b>INH BIW 9 MONTHS</b>	INH	78 BIW	
<b>INH/RIF DAILY 4 MONTHS</b>	INH & RIF	120 QD	<ul style="list-style-type: none"> <li>◆ Generally reserved for inactive (class 4 TB)</li> <li>◆ Must be completed over the course of six months</li> <li>◆ Notify MD if lapses greater than three week-equivalents occur during any portion of therapy</li> </ul>
<b>INH/RIF BIW 4 MONTHS</b>	INH & RIF	36 BIW	
<b>RIF DAILY 4 MONTHS</b>	RIF	120 QD	<ul style="list-style-type: none"> <li>◆ Intermittent dosing not permitted for rifampin monotherapy</li> <li>• 4 month regimen must be completed over the course of 6 months</li> <li>• Notify MD if lapses greater than three week-equivalents occur during any portion of therapy</li> </ul>

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## Appendix D

### II. TB Drug Dosing Tables

#### Definitions:

- ◆ Adults: Persons of ages 18 years or greater.
- ◆ Children: Persons of ages 17 years or less.
- ◆ Twice weekly: To be administered on a Monday/Thursday or Tuesday/Friday schedule
- ◆ Thrice weekly: To be administered Monday/Wednesday/Friday or Tuesday/Thursday/Saturday

<b>Contents</b>	
<b>Agent</b>	<b>Page</b>
Isoniazid	2
Rifapentine	4
Rifampin	5
Pyrazinamide	6
Ethambutol	7
Pyridoxine	8

## A. ISONIAZID

### **Isoniazid:**

**Pediatric daily dosing (10-20 mg/kg po [up to 300 mg] daily)**

Scored tablets: 100mg and 300mg

Syrup: 10mg/mL (may cause diarrhea due to sorbitol. Shake well)

<b>Kg</b>	<b>lbs.</b>	<b>Dosage (mg qd)</b>
3.3 – 5	7.3-12	50
5-7.5	13-17	75
7.5-10	18-22	100
10-15	23-33	150
15-20	34-44	200
20-25	45-55	250
≥25kg	≥56	300

### **Isoniazid:**

**Pediatric twice weekly dosing (20-40 mg/kg po [up to 900 mg] twice weekly)**

Children: **INH** twice a week dosage (20-30 mg/kg)

<b>Kg</b>	<b>lbs</b>	<b>Dosage (mg biw)</b>
3.3 -5	5.5-12	100
5-7.5	13-17	150
5-10	18-22	200
10-15	23-33	300
15-22.5	34-50	450
22.5-30	51-66	600
30-37.5	67-83	750
≥37.5	≥84	900

### **Isoniazid:**

**Adult daily dosing (5 mg/kg po [up to 300 mg] daily)**

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<b>Wt range (kg)</b>	<b>Wt range (lb)</b>	<b>Daily Dose (mg)</b>
<48	<105	consult physician
≥49	≥106	300

**Isoniazid:**

**Adult twice and thrice weekly dosing (15 mg/kg po [up to 900 mg] twice weekly)**

<b>kg</b>	<b>Lbs</b>	<b>No. Tablets (300mg)</b>	<b>Dosage (mg biw)</b>
45 or less	100 or less	2	600mg
45-55	101-121	2 1/2	750mg
55-	122-	3	900mg

**Isoniazid:**

**Adult once-weekly dosing (15 mg/kg po [up to 900 mg] weekly)**

<b>Kg</b>	<b>Lbs</b>	<b>No. Tablets (300mg)</b>	<b>Dosage (mg biw)</b>
45 or less	100 or less	2	600mg
45-55	101-121	2 1/2	750mg
55-	122-	3	900mg

## RIFAPENTINE

### Rifapentine:

Adult weekly dosing (10 mg/kg po [up to 600 mg] weekly)

Wt range (kg)	Wt range (lb)	Daily or Twice-weekly Dose (mg)
<45	100	consult physician
≥45	>100	600

## RIFAMPIN

### **Rifampin:**

**Pediatric daily and twice- or thrice-weekly dosing (10-20 mg/kg po [up to 600 mg] daily or twice weekly)**

Capsules: 150mg and 300mg

Syrup: formulated in syrup from capsules (stability is very questionable—generally not recommended). When syrup is used, keep refrigerated and shake well; limit supply to 7 days at a time.

<b>Kg</b>	<b>lbs.</b>	<b>Daily or Twice-weekly Dose (mg)</b>
2.5 – 5	5.5-12	50
5-7	13-16	100
8-15	17-33	150
15-25	34-55	300
25-45	55-100	450
45 kg or over	100-	600

### **Rifampin:**

**Adult daily and twice- or thrice-weekly dosing (10 mg/kg po [up to 600 mg] daily or twice weekly)**

<b>Wt range (kg)</b>	<b>Wt range (lb)</b>	<b>Daily or Twice-weekly Dose (mg)</b>
<40	<88	consult physician
40-48	88-105	450
>48	>105	600

## PYRAZINAMIDE

**Children: PZA daily dosage (15-30 mg/kg)**

Scored tablets: 500mg

kg	Lbs	Dosage (mg qd)
9-17	20-38	250
18-33	39-73	500
34-44	74-97	750
45-50	98-110	1000
50-62	111 - 137	1250
63-75	138 - 165	1500
76-87	166 - 192	1750
88 kg or over	193 -	2000

**PZA: Twice or thrice weekly for children: call physician**

**Adult: PZA daily dosage (15 – 30mg/kg; Max 2 gm)**

Weight (kg)	lbs	No. Tablets	dosage (mg qd)
40-55	88-122	2	1000
56-75	123-165	3	1500
76-90	167-198	4	2000

**Adult: PZA thrice-weekly (TIW--MWF) dosage**

Weight (kg)	lbs	No. Tablets	dosage (mg qd)
40-55	88-122	2	1500
56-75	123-165	3	2500
76-90	167-198	4	3000

**Adult: PZA (BIW--M/F or T/Th) twice-weekly dosage**

Weight (kg)	lbs	No. Tablets	dosage (mg qd)
40-55	88-122	2	2000
56-75	123-165	3	3000
76-90	167-198	4	4000

## ETHAMBUTOL

### Children Ethambutol daily dosage (15-20 mg/kg)

Tablets: 100 mg and 400 mg

Kg	lbs.	Dosage (mg qd)
5-6.7	11-15	100
6.8-10	16-22	150
10-13.3	22-30	200
13.4- 15	31-33	250
15-20	34-44	300
20-26	45-57	400
27-33	58-73	600
34-40	74-88	800
40 or over	89 or over	Consult physician

**Ethambutol twice or thrice weekly for children: call physician**

### Adult Ethambutol daily dosage (15 – 25 mg/kg)

Weight (kg)	lbs	No. Tablets	dosage (mg qd)
40-55	88-122	2	800
56-75	123-165	3	1200
76-90	167-198	4	1600

### Adult Ethambutol thrice-weekly dosage

Weight (kg)	lbs	No. Tablets	dosage (mg qd)
40-55	88-122	2	1200
56-75	123-165	3	2000
76-90	167-198	4	2400

### Adult Ethambutol twice-weekly dosage

Weight (kg)	Lbs	No. Tablets	dosage (mg qd)
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40-55	88-122	2	2000
56-75	123-165	3	2800
76-90	167-198	4	4000

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## PYRIDOXINE

### **Pyridoxine:**

#### **Dosing in concert with daily isoniazid**

<b>Age group</b>	<b>Dose (mg po)</b>
Children <25 kg	12.5 mg every other day
Children 25-50 kg	25 mg every other day
Children >50 kg and adults	50 mg daily

### **Pyridoxine:**

#### **Dosing in concert with twice weekly isoniazid**

<b>Age group</b>	<b>Dose (mg po twice weekly)</b>
Children <25 kg	12.5 mg
Children 25-50 kg	25 mg
Children >50 kg and adults	50 mg

# Appendix E: Interpretation of QF-Gold Results

ESAT6 CFP10	Nil	Mitogen -Nil	Result	Interpre tation
>0.35* and 50% above Nil	Any	Any	Positive	Positive
<0.35	≤0.7	≥0.5	Negative	Negative
<0.35	Any	<0.5	Indeterminate	Cannot interpret; low mitogen response
<50% above Nil	Any	>0.7	Any	Cannot interpret; high background response

\*units=IU/ml