Yukon
Health and Social Services

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# APPENDIX D
# GUIDELINES FOR THE USE OF INTERFERON GAMMA RELEASE ASSAYS (IGRA)
# SEPT, 2013

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Guideline for the Use of IGRA
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September 2013

# Guidelines for the Use of Interferon Gamma Release Assays (IGRA)

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## Guidelines for the Use of Interferon Gamma Release Assays (IGRA)

### 1.0 Background

Interferon Gamma Release Assay's (IGRA) are blood tests created to assist with the diagnosis of latent TB infection (LTBI). IGRA tests are similar to the tuberculin skin test (TST). Neither IGRA tests nor TST can distinguish between latent and active TB infection and neither of them is able to diagnose active TB disease. The TST remains the preferred test for diagnosis of LTBI in Canada.

IGRAs are immunological tests that are *predominantly* used to diagnose TB infection. Unlike TSTs they are not influenced by prior BCG vaccine or by most nontuberculous mycobacteria. As such, IGRA can aid in LTBI diagnosis in those with prior BCG vaccine and in those who have been exposed to nontuberculous mycobacteria.

In Yukon, IGRA testing **does not** replace the TST but is used in **specific populations** who require additional information to better determine LTBI status (see Table 2).

IGRAs and TSTs are imperfect tests which must be interpreted within the context of the risks the individual faces of TB infection and the risks for progression to active TB disease.

IGRA's currently licensed for use in Canada:

- Quantiferon-Gold (QFT) (Enzyme-linked Immunosorbent Assay (ELISA) on whole blood)
- T-Spot (Enzyme-linked Immunospot Assay on peripheral blood mononuclear cells)

Both tests are performed at the BC CDC PHSA lab. Due to logistical constraints, only the Quantiferon Gold In-Tube is available in Yukon.

### 2.0 Sensitivity & Specificity

The sensitivity and specificity of testing varies depending upon the population being tested.

***Table 1: Comparison of Sensitivity and Specificity of TST, QFT and T-Spot***

| | Population | TST | IGRA | |
|---|---|---|---|---|
| | | | QFT | T-spot |
| Sensitivity | General | 75-89% | 75-83% | ~90% |
| Specificity | General | 85-95% | >95% | 88-95% |
| Specificity | Low Prevalence, Non-BCG vaccinated | 97% | >95% | 88% |
| Specificity | BCG vaccinated | 60% | 96% | 93% |

**3.0 Advantages of IGRA**

- No repeat visit is required to read the test
- Has higher specificity than TST in BCG vaccinated individuals
- Has higher sensitivity in immunocompromised individuals. In the context of IGRA, the definition of immunocompromised includes individuals of any age with: HIV, AIDS, transplant or cancer patient on immunosuppressive treatment, silicosis, chronic renal failure requiring hemodialysis, or clients taking prednisone 15mg/day or more for more than 4 weeks
- Less between-clinician variability in interpreting test

**4.0 Disadvantages of IGRA**

- Costly and requires more sensitive lab processing
- Specific blood drawing techniques and short time frame for laboratory testing limit where test can be offered
- Sensitivity and specificity are similar to TST in healthy, non BCG vaccinated groups
- Serial test results may vary in an individual so IGRAs are not preferred for serial testing for employment or other screening activities
- Does not confirm or rule out active TB disease.
- Clinical significance in predicting active disease has yet to be ascertained

**5.0 Do not consider IGRA if**

- Client is already on treatment or has been treated for LTBI in the past
- A patient is a contact or a suspected contact and has converted from a negative to a positive TST
- There are no plans/indications for LTBI treatment
- Active TB is suspected or confirmed in the past
- Serial testing for employment or mass screening of individuals who have a very low risk of exposure to TB e.g. immigrants from low incidence countries
- Returning travelers unless specifically indicated

**6.0 Authority**

All referrals for IGRA will be facilitated by the TB nurses at Yukon Communicable Disease Control. Ultimately, final decisions related to IGRA testing eligibility rest with the Clinical Manager at Yukon Communicable Disease Control. When considering eligibility, the Yukon Communicable Disease Control may take into consideration recommendations from BC TB Control, Yukon TB program, Yukon's CMOH, references such as the *Canadian Tuberculosis Committee Recommendations on Interferon Gamma Release Assays for the Diagnosis of Latent Tuberculosis Infection-2010 Update,* and available funding.

WGH lab will only accept samples to be sent for IGRA testing that are authorized by Yukon Communicable Disease Clinical Manager.

**7.0 Eligibility**

YCDC will recommend IGRA, based on the following criteria:

1. Client does not have a current or past history of active TB disease
2. Client has not been treated for LTBI or active TB disease in the past
3. Clint meets specific indications outlined in Table 2
4. At the discretion of the YCDC Clinical Manager and/or designate

*Table 2: Indications for IGRA Testing*

| Indications for IGRA | Explanation | Examples of appropriate testing include | Test |
|---|---|---|---|
| **History of BCG Vaccine** | | | |
| **TST positive AND BCG vaccinated AND *Low* risk TB exposure[1]** | To avoid unnecessary LTBI therapy or serial radiographs in those who had a BCG and are at low risk of developing active TB i.e. to exclude diagnosis | Student or healthcare worker with BCG<br><br>Returned traveller with BCG | QFT |
| **TST positive AND BCG vaccinated AND *High* risk TB exposure[2]** | To provide additional information to those who likely have LTBI (based on history and TST) and are questioning LTBI treatment **yet are willing to accept LTBI therapy if IGRA is positive.**[3] | Contact in BCG vaccinated individual who does not believe TST result | QFT |
| **Regardless of History of BCG Vaccine** | | | |
| **TST negative AND Immuno-compromised[4] AND *High* risk of TB exposure[2]** | To provide additional information to help diagnose LTBI in specific individuals in whom TST is negative but there is strong clinical suspicion of LTBI with increased risk for morbidity/mortality | Select contacts if IGRA result changes clinical management eg. Some children <5yr or individual with HIV or immunosuppression | QFT[5] |
| **Specific medical conditions** | High likelihood of progression to active TB disease and poor predictive value of TST in these populations | New dialysis clients<br><br>Before renal or bone-marrow transplants<br><br>Client for TNF inhibitors | QFT |
| **Previous indeterminate IGRA** | To confirm an indeterminate IGRA test if a change in clinical management will result | | QFT |
| **At discretion of BC CDC TB Physician** | Complex medical circumstances that do not fit into general guidelines | | QFT |

[1] E.g. From low TB incidence country or never been a contact of someone with active pulmonary TB. See http://www.stoptb.org/countries/tbdata.asp for most recent TB incidence rates by country.

[2] E.g Type 1 or 2 contact of active pulmonary TB case or from high TB incidence country. See http://www.stoptb.org/countries/tbdata.asp for most recent TB incidence rates by country.

[3] Patients who are TST positive, at high risk of TB exposure and ***not*** BCG vaccinated should be treated for LTBI irrespective of IGRA result. **In these patients IGRA should not be offered.**

[4] HIV, AIDs, transplant or cancer patient on immunosuppressive treatment, silicosis, chronic renal failure requiring hemodialysis, or patient taking prednisone 15mg/day or more for more than 4 weeks

[5] Although T-Spot is a more sensitive test in immunosuppressed individuals, if unavailable, use QFT.

**8.0 Precaution**

As with TST, live virus vaccines may affect IGRA test results. IGRA testing should be done either on the same day as administration of live-virus vaccines or 4-6 weeks following administration of live-virus vaccine.

**9.0 Yukon Process**

- Blood must be drawn by a nurse or phlebotomist familiar with QuantiFERON TB Gold or T-Spot blood collection.
- A fully completed requisition must accompany all samples
- Blood must be received at the WGH lab on a Monday or Tuesday AND within 16 hours of collection. Do not refrigerate or freeze blood samples, maintain the tubes at room temperature (22 degrees Celsius plus/minus 5 degrees). Whitehorse hospital lab will incubate, harvest plasma and ship to PHSA in BC.

**Whitehorse Process**

- Fax the requisitions to the lab so the lab has them on the file. If the patient brings a copy that is fine too.
- Mondays & Tuesdays are the only day the lab will collect the blood due to shipping constraints. Anytime between 7 am and 2 pm; ideally between 10 am and 2 pm to miss the crowd. No appointment is necessary. No fasting required.
- If there are going to be more than 5 clients per Monday, let both the lab in Whitehorse and PHSA lab in BC know.
- Advise clients to present to the admitting desk to process their Yukon Health Insurance. The admitting desk will then send the person to the lab. They should either bring their requisition with them or let the lab tech know the requisition is on file.

**Results**

- All IGRA test results will be forwarded to YCDC. BC TB control in collaboration with YCDC TB control will interpret the results and provide recommendations regarding treatment for LTBI and appropriate follow-up for TB screening in the future.

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## PHSA Laboratories

Public Health Microbiology & Reference Laboratory

BC Centre for Disease Control, 655 West 12th Avenue, Vancouver, BC V5Z 4R4 www.phsa.ca/bccdcpublichealthlab

### Zoonotics & Emerging Pathogens Requisition

**FOR TB CONTROL USE ONLY**

**Section 1 - Patient Information**

| | | |
|---|---|---|
| PERSONAL HEALTH NUMBER (or out of province Health Number and province) | DOB (DD/MM/YYYY) | GENDER ☐ M ☐ F ☐ UNK |
| PATIENT SURNAME | PATIENT FIRST AND MIDDLE NAME | |
| ADDRESS | CITY | POSTAL CODE |

DATE RECEIVED

PHSA LABORATORIES USE ONLY

OUTBREAK ID

**Section 2 - Healthcare Provider Information**

ORDERING PHYSICIAN (Provide MSC#)
Name and address of report delivery

☐ I do not require a copy of the report

CLINIC OR HOSPITAL
Name and address of report delivery

PHSA CLIENT NO.

ADDITIONAL COPIES TO: (Address / MSC#)

1.

2.

3.

SAMPLE REF. NO.

DATE COLLECTED (DD/MM/YYYY)

TIME COLLECTED (HH:MM)

**Section 3 - Test(s) Requested**

**VIRUSES**

☐ Arbovirus Panel
Eastern Equine Encephalitis, Western Equine Encephalitis, Powassan, St. Louis Encephalitis
☐ Dengue Virus Antibody
☐ Hanta Virus Antibody
☐ West Nile Virus Antibody
☐ Other, specify: _____

**Travel / Clinical History Required for Above Tests:**

_____

_____

**Signs / Symptoms**

☐ Asymptomatic
☐ Insect bite ☐ Skin rash
Type/Location _____
☐ Neurological ☐ Other, specify _____

**BACTERIA**

☐ Anti-Streptolysin O (ASO) / Anti-DNase B
☐ *Bartonella henselae* Antibody
☐ *Borrelia burgdorferi* (Lyme disease) Antibody
☐ *Borrelia hermsii* Antibody
☐ *Brucella abortus* Antibody
☐ *Coxiella burnetii* (Q-fever) Antibody
☐ *Francisella tularensis* Antibody
☐ *Helicobacter pylori* Antigen (Feces)
☐ *Legionella* species Urine Antigen
☐ *Leptospira* Antibody
☐ *Rickettsia rickettsii* Antibody
(Rocky Mountain Spotted Fever)
☐ **TB Interferon Gamma Release Assay***
☐ **QFT Gold in Tube** ☐ **T Spot**
☐ Other, specify: _____

**PARASITES**

☐ *Echinococcus* Antibody
☐ *Entamoeba histolytica* (Amoebiasis) Antibody
☐ *Schistosoma* Antibody
☐ *Strongyloides* Antibody

**Travel History Required for Above Tests:**

☐ Travel within past 12 months, specify:

_____

_____

☐ *Leishmania* Antibody
☐ *Toxoplasma gondii* Antibody
☐ *Trichinella* Antibody
☐ *Trypanosoma cruzi* (American trypanosomiasis) Antibody
☐ Other, specify: _____

**SYPHILIS**

☐ VDRL (CSF sample only)
Submit 1 mL CSF in sterile leak-proof tube
☐ *Treponema pallidum* Nucleic Acid Testing*
Submit exudate, tissue or body fluid
☐ Darkfield (DF) Microscopy
Source of sample: _____
☐ Direct Fluorescent Assay (DFA) Microscopy
Source of sample: _____

**Signs / Symptoms**

☐ Asymptomatic ☐ Rash
☐ Other, specify: _____

**FUNGI**

☐ *Blastomyces dermatitidis* Antibody
☐ *Coccidioides* species Antibody
☐ *Cryptococcus neoformans* Antigen
☐ *Histoplasma* Antibody
☐ Other, specify: _____

**Travel History Required for Above Tests:**

☐ Travel within past 12 months, specify:

_____

_____

*** TB IGRA TESTING CRITERIA**

☐ 1. TST negative, immunocompromised
☐ 2. TST positive, BCG positive
☐ 3. TST positive, Aboriginal / Foreign born

For other available tests and additional information, consult the Public Health Microbiology & Reference Laboratory's *Guide to Programs and Services* at

www.phsa.ca/bccdcpublichealthlab

For information on sample collection, please call Zoonotic & Emerging Pathogens Lab at (604) 707-2628

Form DCZP_100_1001F Version 1.0 09/2009

ZEP ZEP

## QuantiFERON®-TB Gold
**Blood Collection Tubes**

cellestis

**Catalogue No.: T0590-0301 (300 tubes)**
(100 x Nil Antigen (Grey cap) tubes, 100 x TB Antigen (Red cap) tubes & 100 x Mitogen (Purple cap) tubes)

**Catalogue No.: T0590-0201 (200 tubes)**
(100 x Nil Antigen (Grey cap) tubes & 100 x TB Antigen (Red cap) tubes)

**Catalogue No.: T0593-0201 (100 tubes)**
(100 x Mitogen (Purple cap) tubes)

Note: 'High Altiitude' tubes should be used if blood collection is performed at altitudes above 1020 metres.

The blood collection tubes supplied are for use only with the QuantiFERON®-TB Gold (QFT®) system. The following instructions relate solely to the use of QFT blood collection tubes. Instructions for the entire QFT system incorporating the use of the blood collection tubes can be found in the Package Insert for the QFT ELISA kit (Catalogue No.: 0594-0201 or 0594-0501).

Antigens have been dried onto the inner wall of the blood collection tubes so it is essential that the contents of the tubes be thoroughly mixed with the blood. The tubes must be transferred to a 37°C incubator as soon as possible and within 16 hours of collection.

The following procedures should be followed for optimal results:

**1. Blood Collection:**

1.1 For each subject collect 1mL of blood by venipuncture directly into each of the QFT blood collection tubes. This procedure should be performed by a trained phlebotomist.

- As 1mL tubes draw blood relatively slowly, keep the tube on the needle for 2-3 seconds once the tube appears to have completed filling, to ensure that the correct volume is drawn.

  *The black mark on the side of the tubes indicates the 1mL fill volume. QFT blood collection tubes have been validated for volumes ranging from 0.8mL – 1.2mL. If the level of blood in any tube is not close to the indicator line, it is recommended to obtain another blood sample.*

- If a "butterfly needle" is being used to collect blood, a "purge" tube should be used to ensure that the tubing is filled with blood prior to the QFT tubes being used.

1.2 Immediately after filling tubes, shake them ten (10) times just firmly enough to ensure the entire inner surface of the tube is coated with blood, to solubilise antigens on tube walls.

- Tubes should be between 17- 25°C (63-77°F) at the time of filling.
- Over-energetic shaking may cause gel disruption and could lead to aberrant results.

1.3. Label tubes appropriately.

1.4 The tubes must be transferred to a 37°C ± 1°C incubator as soon as possible, and within 16 hours of collection. Prior to incubation, maintain the tubes at room temperature (22°C ± 5°C) (72° F± 9°C). Do not refrigerate or freeze the blood samples.