

QuantiFERON-TB Gold in-tube

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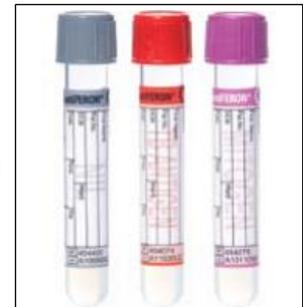
Texas Department of State Health Services, Austin, TX

What is Quantiferon-TB?

- A whole blood interferon-gamma (IFN- γ) release assay (IGRA)
- Detects *M. tuberculosis* infection, but does not differentiate latent infection from disease
- Can be used in place of tuberculin skin test (TST) in all situations in which CDC recommends TST as an aid in diagnosing *M. tuberculosis* infection (CDC Guidelines, MMWR, June 25, 2010)

History of QFT-TB

- QFT, 1st generation FDA approved Nov 28, 2001
 - Uses PPD, test response similar to TST
- QFT-Gold (QFT-G), 2nd generation FDA approved Dec 2, 2004
 - Detects response to 2 TB specific proteins (ESAT-6 & CFP-10)
- QFT-Gold In-Tube (QFT-GIT), 3rd generation FDA approved Oct 10, 2007
 - Improved by addition of another TB-specific antigen, TB 7.7
 - Detects response to 3 TB specific proteins (ESAT-6, CFP-10, & TB 7.7)
 - Uses specialized blood collection tubes coated w/ TB-specific Ag & control
 - “In-tube” test easier even in remote locations
- **QFT-Gold In-Tube (QFT-GIT), 4th generation with addition of 4th tube for antigen, TB1 green and TB2 yellow ???**

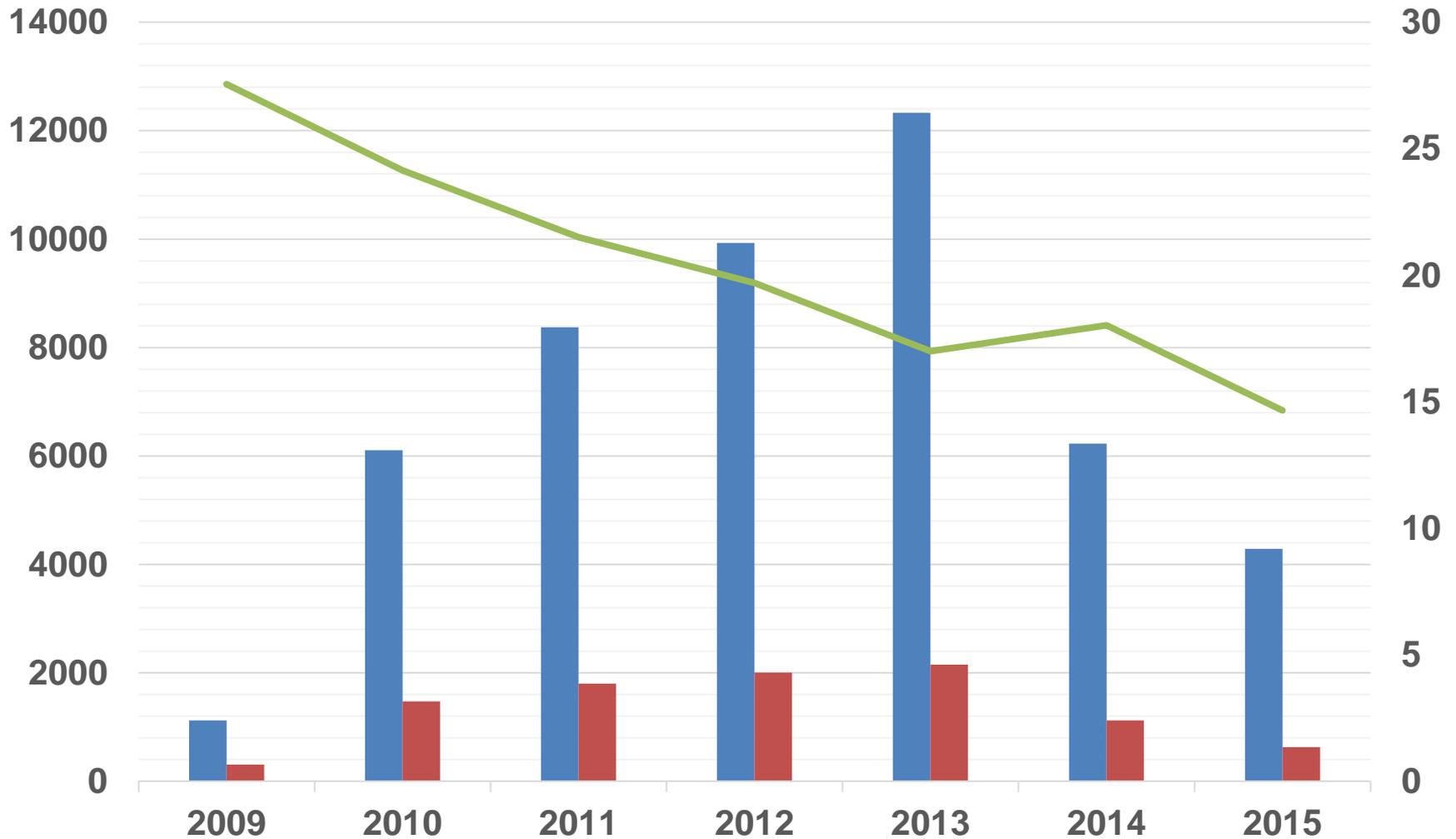


QuantiFERON-TB Gold In-Tube



QFT #s Tested & % Positivity

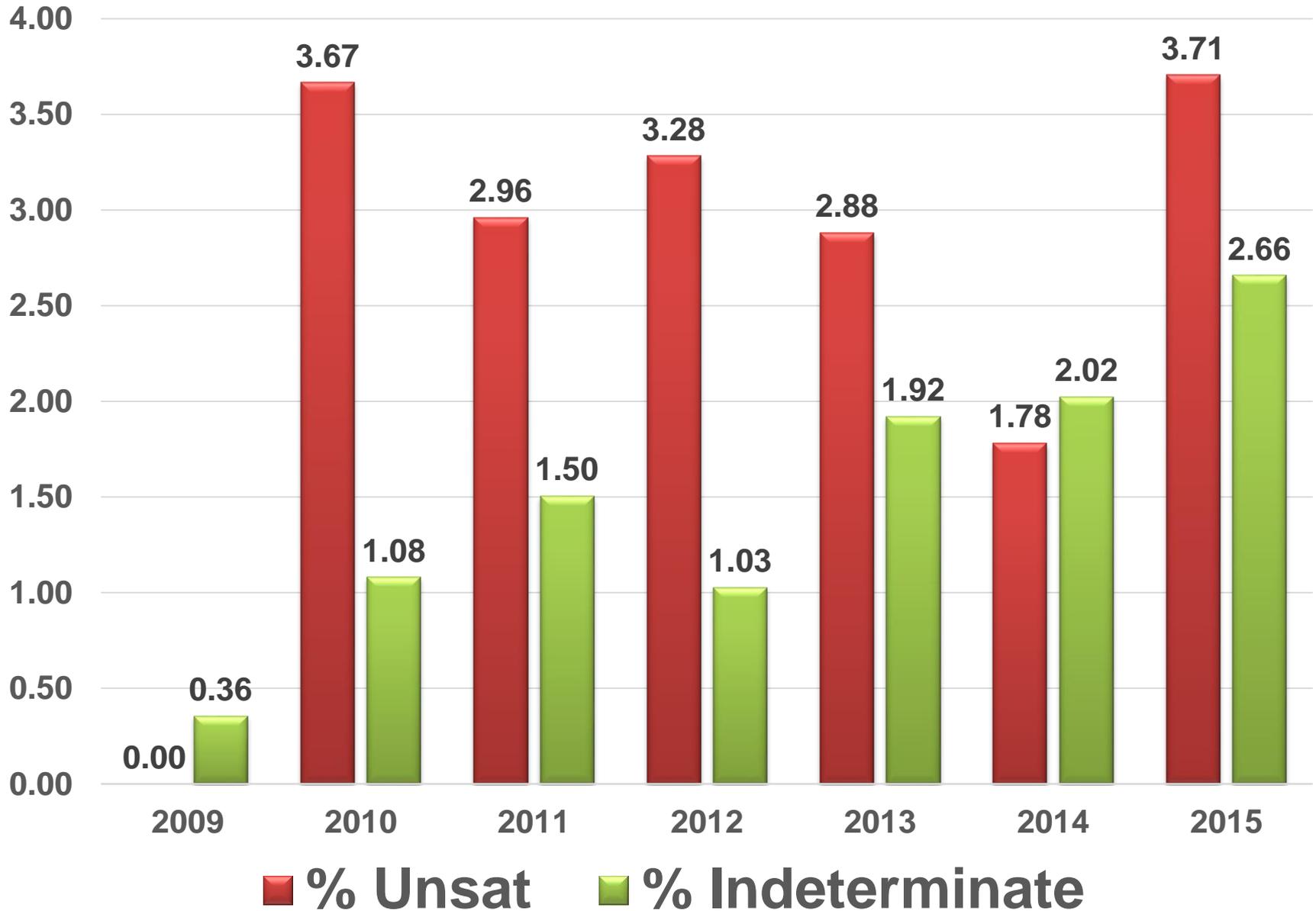
■ Total ■ Positive — % Positivity



Indeterminate results & causes

- National average of indeterminate QFT-GIT results ~ 1-10%
 - Immunosuppression
 - Shaking tubes for thorough mixing
 - Incorrect transport / handling of specimens
 - Lab – deviation for SOP, washing, incubation, pipetting errors
- Dallas ~ 8-12%
- DSHS lab average $\leq 1.5\%$ (0.36 – 1.5%)
 - Strict acceptance criteria
 - Blood collection training thru Cellestis
 - Good quality of specimens

Indeterminate and Unsat



Changes implemented effective Jul, 2012

- Reporting values with interpretation criteria
- Discontinued repeat testing of initial positive / indeterminate results
 - Automation thru DYNEX instrumentation
 - Decreased TAT, results are reported in a day
- Currently QFT testing 388 samples / day thru automation

QFT Report Format

QuantiFERON-TB Gold IT	TB-Antigen Responsiveness Detected
Nil Control	0.19
TB Antigen - Nil	0.61
Mitogen Control - Nil	>10

QuantiFERON-TB Gold IT results are interpreted using the following criteria:

Nil [IU/mL]	TB Antigen minus Nil [IU/mL]	Mitogen minus Nil [IU/mL]	QuantiFERON®-TB Gold IT Result	Report/Interpretation
≤ 8.0	≥ 0.35 and ≥ 25% of Nil value	Any	Positive	<i>M. tuberculosis</i> infection likely
	< 0.35 OR ≥ 0.35 and < 25% of Nil value	≥ 0.5	Negative	<i>M. tuberculosis</i> infection NOT likely
		< 0.5		
> 8.0	Any	Any	Indeterminate	Results are indeterminate for TB-Antigen responsiveness

Note: *M. tuberculosis* infection likely.

QFT-GIT is an indirect test for *M. tuberculosis* infection (including disease). Diagnosing or excluding tuberculosis disease, and assessing the probability of LTBI, requires a combination of epidemiological, historical, medical, and diagnostic findings that should be taken into account when interpreting QFT results. See general guidance on the diagnosis and treatment of TB disease and LTBI (<http://www.cdc.gov/nchstp/tb/>).

Where *M. tuberculosis* infection is not suspected, please resubmit another sample.

The performance of the USA format of QuantiFERON-TB Gold IT has not been extensively evaluated with specimens from the following individuals:

1. Individuals who have impaired or altered immune function such as those who have HIV infection or AIDS, those who have transplantation managed with immunosuppressive treatment or others who receive immunosuppressive drugs (e.g. corticosteroids, methotrexate, azathioprine, cancer chemotherapy), and those who have other clinical conditions: diabetes, silicosis, chronic renal failure, hematological disorders (e.g. leukemia and lymphoma), and other specific malignancies (e.g. carcinoma of the head or neck and lung).
2. Individuals younger than age 17 years.
3. Pregnant women.

DSHS Lab Automation Capacity

1. DYNEX Agility Instrument

a. 12 plate

b. Total specimen can be tested = $12 \times 24 = 288$

2. DYNEX DSX Instrument

a. 4 plate

b. Total specimen can be tested = $4 \times 24 = 48$

- Total specimen can be tested = 336
- **Instruments are interfaced with LIMS and results with values are transferred after review**
- **There are no subjective steps. All measurements and interpretations are performed automatically.**

QFT-GIT Use in tb contact investigations

Place	# Tested	Date Started	Date Ended	Region
Del Rio	245/248	Jan 18, 2012	Ongoing	HSR 8
Ellis	250	Sep, 2011	Ongoing	HSR 2/3
ATCHD (50)	1,820	During 2011	completed	HSR 7
Caldwell	50	Sep, 2011	Ongoing	HRR 7
Bell Co.	59	Jul, 2011	Ongoing	HRR 7
Brazos	18	Sep, 2011	Ongoing	HRR 7
Coryell	51	May, 2011	Ongoing	HRR 7
Hays (24 investigations)	272	Jul '09 – Jan 2012	Closed, ongoing	HRR 7
Hill	20	Dec, 2011	Ongoing	HRR 7
Leon	21	Feb, 2011	Ongoing	HRR 7
McLennan	73	Jul, 2011	Ongoing	HRR 7
Williamson	36	Aug, 2011	Ongoing	HRR 7
Bastrop, Burnet, Grimes, Llano, Washington	1 - 7	Feb-Jul, 2011	Ongoing	HRR 7

Turnaround time for reporting QFT Results

Large contact investigation completed = 250 specimens

Turnaround Time for results = 48 hours

Result spreadsheet provided to Regional Medical Director with

- Patient demographic info

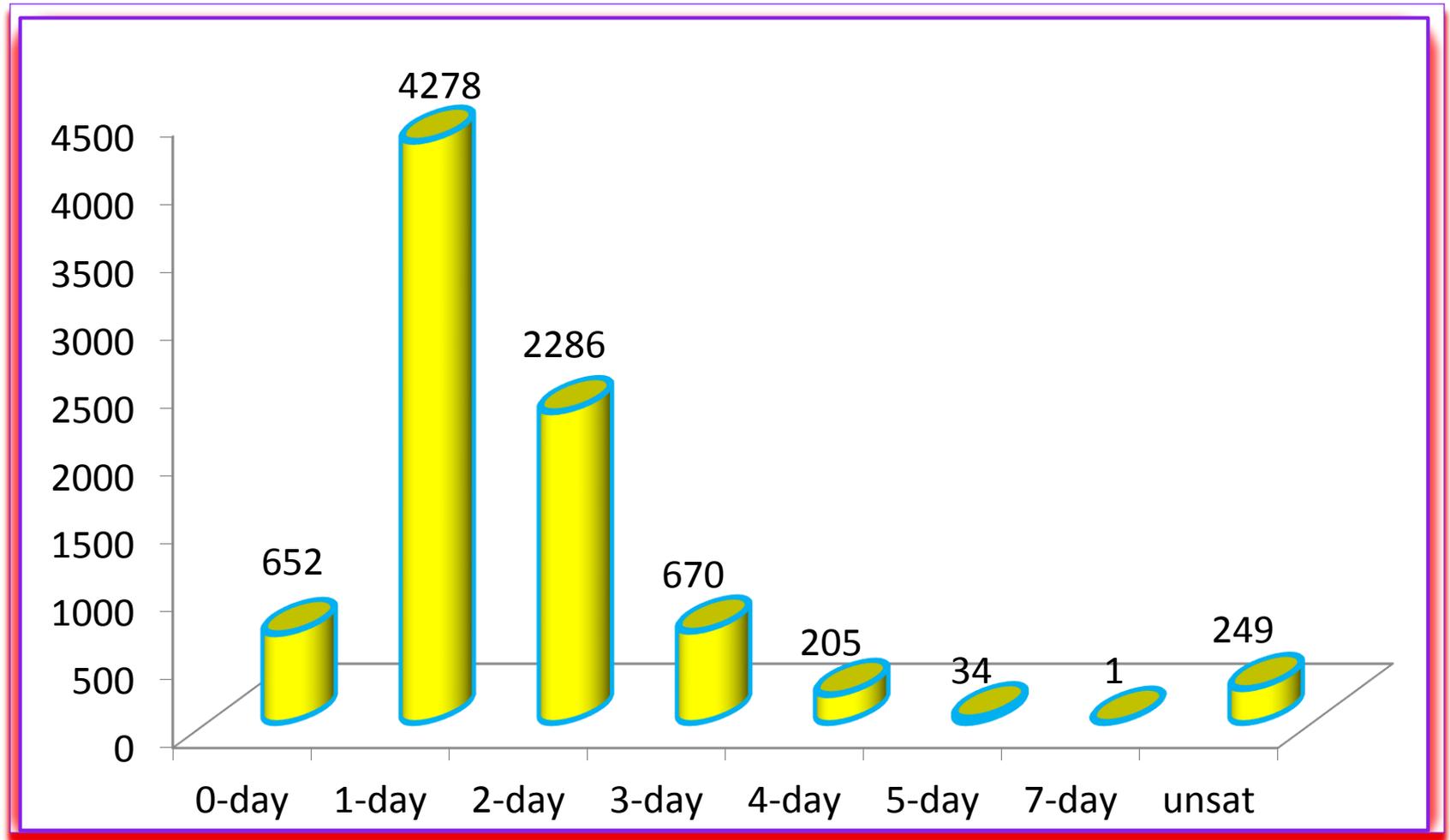
- QFT result interpretation and values for

 - Nil Control

 - TB Antigen – Nil

 - Mitogen - Nil

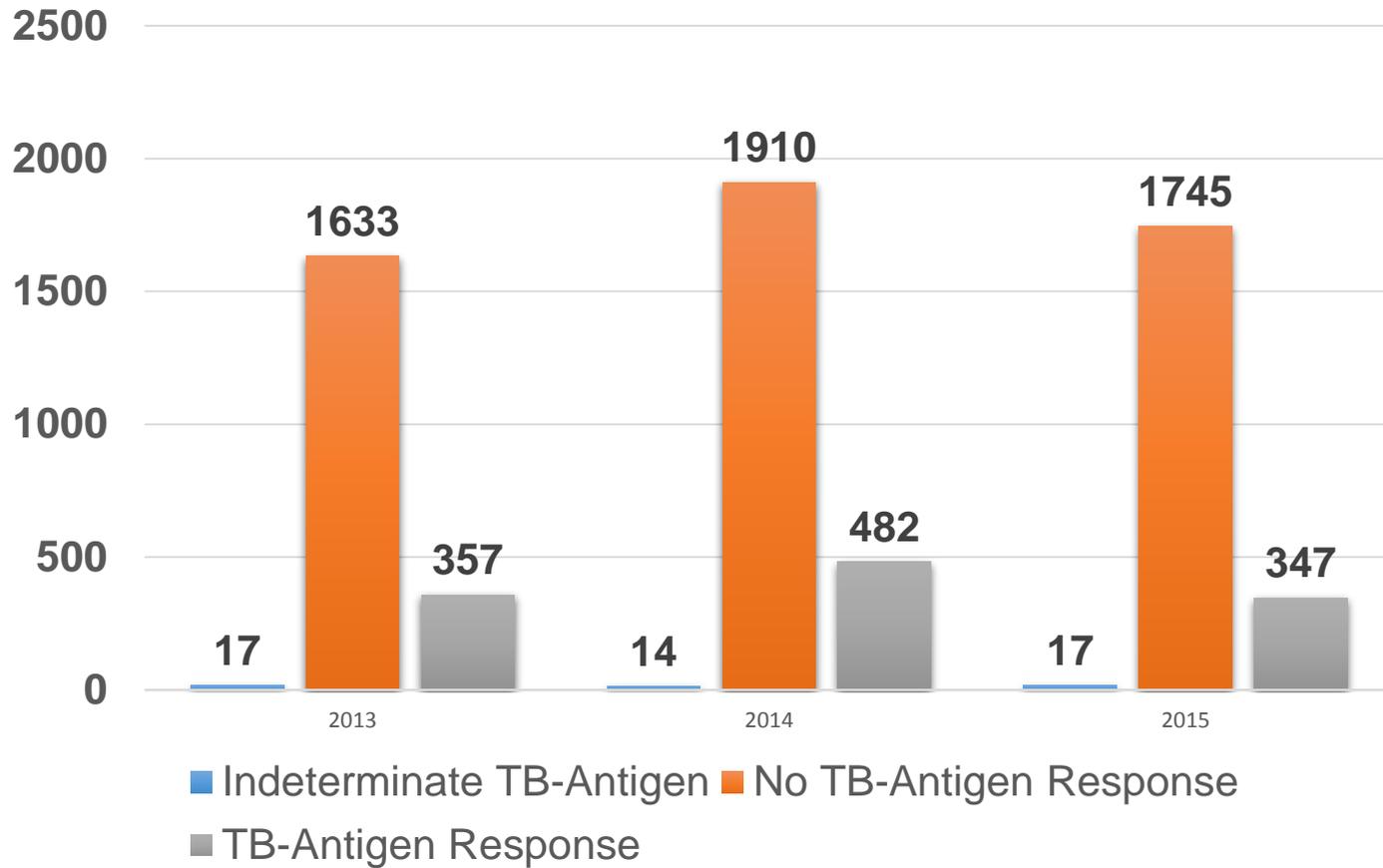
TAT for QFT results - 2011



**DSHS Laboratory serves as the Texas site
for**

**Multicenter study at the 10 Tuberculosis
Epidemiologic Studies Consortium
(TBESC) sites within the United States**

TBESC Site-Tarrant County



Laboratory challenges

- Shipping cost of specimens to the DSHS lab?
- Capacity for QuantiFERON testing
 - How can we better utilize the excess capacity?
 - Need ↑ volume of testing to bring the cost ↓
- Unsatisfactory rate
 - How can we help in reduction of unsat rate?
 - QFT blood collection training thru QIAGEN vendor
- Unsatisfactory specimens
 - Under fill or overfill blood volume
 - Improper storage conditions
- Cost savings - Wastage of reagents, blood collection tubes
 - Blood collection sets expire before use
 - Fixes – dispenser sets, individual color tube



Take-home points

- QFT-GIT is *In vitro* test, detects TB-specific antigens, unaffected by BCG, and no boosting affects
- QuantiFERON-TB results available **within 24-48 hours** after received in the lab
- Single patient visit for blood collection for QFT-GIT
- QFT-GIT results are reliable, not subject to biases & errors as with TST
 - Except error in collecting, labeling, incubating, and transporting blood specimens
- Cost-effectiveness?
- Can be shipped from remote locations within 72 hours with the availability of QFT-GIT blood collection sets (incubated specimens)
- **QFT-GIT meets all criteria for screening large # of MTB latent infections in a public health setting**

How to enroll in QFT-GIT testing?

- Site must be approved by the TB Control Program
 - Offered to all City, County, & Health Services Regions in TX
- Contact DSHS lab
- Serological Analysis Group
 - Pushker Raj, Manager 512-776-7760 pushker.raj@dshs.state.tx.us
- Diagnostic Serology Team
 - Karen Teague, Team Lead 512-776-7514 karen.teague@dshs.state.tx.us
- Set up G-2A form & Web Portal access for results and blood collection training thru QIAGEN vendor
- Ship supplies—blood collection tubes & incubators as needed
 - Begin submissions for QFT testing.....