

1 **SUPPLEMENTAL MATERIAL**

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3 **Comparing QuantiFERON-TB Gold Plus with other tests to diagnose**

4 ***Mycobacterium tuberculosis* infection**

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9 **REFERENCE**

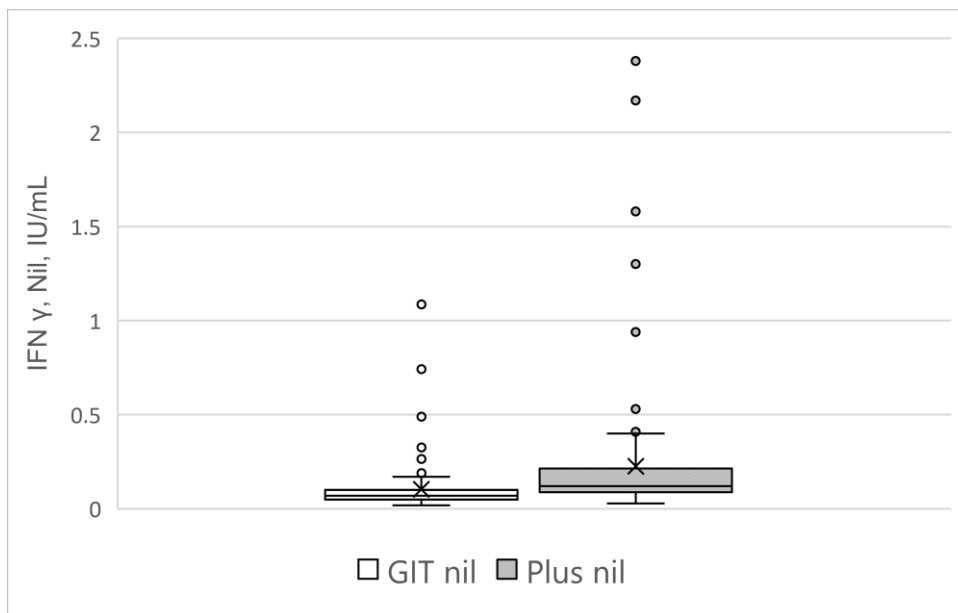
10 **S1.** Cain KP, Benoit SR, Winston CA, Mac Kenzie WR. Tuberculosis among foreign-
11 born persons in the United States. JAMA. 2008; 300 (4):405-12.

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18 **FIG S1** Box and whisker plot showing the nil distribution for samples that used
19 separate nil tubes (P=0.001). For 102 samples nil tubes were either from GIT
20 (QuantiFERON-TB Gold In-Tube) or Plus (QuantiFERON-TB Gold Plus) sets for
21 respective tests.

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23 **TABLE S1 Countries by risk level**
 24 (Based on TB case rates of foreign-born persons in the United States^{S1})

Afghanistan (High)	Equatorial Guinea (High)	Macedonia (Medium)	Seychelles (High)
Albania (Medium)	Eritrea (High)	Madagascar (High)	Sierra Leone (High)
Algeria (Medium)	Estonia (Medium)	Malawi (High)	Singapore (High)
Angola (High)	Ethiopia (High)	Malaysia (Medium)	Slovakia (Medium)
Argentina (Medium)	Federated States of Micronesia (High)	Maldives (High)	Slovenia (Medium)
Armenia (Medium)	French Guiana (Medium)	Mali (High)	Solomon Islands (High)
Azerbaijan (High)	French Polynesia (Medium)	Marshall Islands (High)	Somalia (High)
Bahrain (Medium)	Gabon (High)	Mauritania (High)	South Africa (Medium)
Bangladesh(High)	Gambia (High)	Mauritius (High)	South Korea (Medium)
Belarus (Medium)	Georgia (High)	Mexico (Medium)	South Sudan (Medium)
Belize (Medium)	Ghana (Medium)	Moldova (Medium)	Sri Lanka (High)
Benin (High)	Guam (Medium)	Mongolia (High)	Sudan (Medium)
Bhutan (High)	Guatemala (High)	Morocco (Medium)	Suriname (Medium)
Bolivia (High)	Guinea (High)	Mozambique (High)	Swaziland (High)
Bosnia and Herzegovina (Medium)	Guinea-Bissau (High)	Myanmar (Burma) (High)	Syria (Medium)
Botswana (High)	Guyana (Medium)	Namibia (High)	Taiwan (Medium)
Brazil (Medium)	Haiti (High)	Nepal (High)	Tajikistan (Medium)
Brunei (High)	Honduras (High)	New Caledonia (Medium)	Tanzania (High)
Bulgaria (Medium)	Hong Kong (Medium)	Nicaragua (Medium)	Thailand (Medium)
Burkina Faso (High)	Hungary (Medium)	Niger (High)	Tibet (High)
Burundi (High)	India (High)	Nigeria (Medium)	Togo (High)
Cambodia (High)	Indonesia (High)	North Korea (Medium)	Tonga (Medium)
Cameroon (High)	Iran (Medium)	Northern Mariana Islands (Medium)	Tunisia (High)
Cape Verde (High)	Iraq (Medium)	Oman (Medium)	Turkey (Medium)
Central African Republic (High)	Ivory Coast (High)	Pakistan (High)	Turkmenistan (Medium)
Chad (High)	Japan (Medium)	Palau (Medium)	Tuvalu (High)
Chile (Medium)	Jordan (Medium)	Palestine (Medium)	Uganda (High)
China (High)	Kazakhstan (Medium)	Panama (Medium)	Ukraine (Medium)
Colombia (Medium)	Kenya (High)	Papua New Guinea (High)	Uruguay (Medium)
Comoros (High)	Kiribati (High)	Peru (High)	Uzbekistan (Medium)
Congo (High)	Kuwait (Medium)	Philippines (High)	Vanuatu (Medium)
Cook Islands (Medium)	Kyrgyzstan (Medium)	Poland (Medium)	Venezuela (Medium)
Costa Rica (Medium)	Laos (High)	Portugal (Medium)	Vietnam (High)
Croatia (Medium)	Latvia (Medium)	Qatar (Medium)	Western Sahara (Medium)
Democratic Republic of Congo (High)	Lebanon (Medium)	Romania (Medium)	Yemen (High)
Djibouti (High)	Lesotho (High)	Russia (Medium)	Zambia (High)
Dominican Republic (High)	Liberia (High)	Rwanda (High)	Zimbabwe (High)
East Timor (High)	Libya (High)	Sao Tome and Principe (High)	
Ecuador (High)	Lithuania (Medium)	Saudi Arabia (Medium)	
Egypt (Medium)	Hong Kong (Medium)	Senegal (High)	
El Salvador (Medium)	Macao (Medium)	Serbia and Montenegro (Medium)	

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28 **TABLE S2** Comparing QFT-Plus for 77 children^a <15 years old with QFT-GIT, T-SPOT and
 29 TST results

QFT-Plus	Total, <i>n</i>	<u>QFT-GIT</u>		<u>T-SPOT</u>		<u>TST</u>	
		Positive <i>n</i> (%)	Negative <i>n</i> (%)	Positive <i>n</i> (%)	Negative <i>n</i> (%)	Positive <i>n</i> (%)	Negative <i>n</i> (%)
Positive	1	1 (100)	0(0)	1(100)	0 (0)	1(100)	0(0)
Negative	76 ^b	0(0)	76(100)	0(0)	75(97)	14(18)	62(81)

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31 ^aThe 77 children included 15 U.S.-born and 12 close contacts to an infectious TB case.

32 QFT-GIT=QuantiFERON-TB Gold In-Tube; QFT-Plus=QuantiFERON-TB Gold Plus;

33 TST=Tuberculin skin test; T-SPOT= T-SPOT. *TB*; ^bOne participant had a borderline

34 T-SPOT result

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37 **TABLE S3a** Test agreement between QFT-GIT and QFT-Plus TB1 and TB2 antigens
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Category	Total, <i>n</i>	QFT-Plus antigens	QFT-GIT/TB1 and TB2 results, <i>n</i> (%)				Kappa
			+/+	-/-	+/-	-/+	
All ^a	506	TB1	92 (18)	389 (77)	9 (2)	16 (3)	0.85
		TB2	93 (18)	385 (76)	8 (2)	20 (4)	0.83
Non-U.S.-born ^b	434	TB1	86(20)	324 (75)	9 (2)	15(3)	0.84
		TB2	87(20)	320 (74)	8 (2)	19 (4)	0.83
Class B1 immigrant	49	TB1	19 (39)	26 (53)	0 (0)	4 (8)	0.83
		TB2	18 (37)	27 (55)	1 (2)	3 (6)	0.83
U.S.-born ^c	71	TB1	6 (9)	64 (90)	0 (0)	1 (1)	0.92
		TB2	6 (9)	64 (90)	0 (0)	1 (1)	0.92
Close Contact	48	TB1	3 (6)	44 (92)	0 (0)	1 (2)	0.85
		TB2	3 (6)	44 (92)	0 (0)	1 (2)	0.85

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40 ^a2 Indeterminate QFT-Plus results excluded; ^bIncludes 49 Class B1 immigrants and 31
 41 close contacts; ^cIncludes close contacts; Definitions: Class B1 immigrant=immigrant with
 42 abnormal chest radiograph but negative sputum smears and cultures in overseas
 43 examinations; Close contact= ≥8h/week exposure to TB case; QFT-GIT= QuantiFERON-
 44 TB Gold In-Tube; QFT-Plus= QuantiFERON-TB Gold Plus;

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47 **TABLE S3b** Agreement between QFT-Plus antigens TB1 and TB2
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Category	Total, <i>n</i>	QFT-Plus TB1/TB2, <i>n</i> (%)				Kappa
		+/+	-/-	+/-	-/+	
All ^a	506	102 (20)	387(77)	6 (1)	11 (2)	0.90
Non-U.S.-born ^{a,b}	434	96 (22)	323 (74)	5 (1)	10 (2)	0.90
Class B1 immigrant	49	20 (41)	25 (51)	3 (6)	1 (2)	0.84
U.S.-born ^c	71	6 (8)	63 (89)	1 (1)	1 (1)	0.84
Close contact	48	4 (8)	44 (92)	0 (0)	0 (0)	1.0

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 50 ^a2 Indeterminate QFT plus results excluded; ^bIncludes 49 Class B1 immigrants and 31
 51 close contacts; ^cIncludes close contacts; Definitions: Class B1 immigrant=immigrant
 52 with abnormal chest radiograph but negative sputum smears and cultures in overseas
 53 examinations; Close contact= \geq 8h/week exposure to TB case; to TB case; QFT-Plus=
 54 QuantiFERON-TB Gold Plus;

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71 **TABLE S4a** Combined QFT-GIT, T-SPOT, and TST results among positive or negative
 72 QFT-Plus results

QFT-Plus result	Total, <i>n</i>	Triple positive <i>n</i> (%)	Triple negative <i>n</i> (%)	IGRA(+)/ TST(-) <i>n</i> (%)	IGRA(-)/ TST(+) <i>n</i> (%)
Positive	119	51 (43)	10 (8)	10 (8)	6 (5)
Negative	387	2 (0.5)	288 (74)	0 (0)	77 (20)
Indeterminate	2	1 (50)	0 (0)	0 (0)	0 (0)

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 74 Definitions: Triple positive= Positive by QFT-GIT, T-SPOT, and TST; Triple negative:
 75 Negative by QFT-GIT, T-SPOT, and TST; IGRA= Interferon gamma release assay;
 76 IGRA(+)= Results positive for both QFT-GIT and T-SPOT; IGRA(-)= Results negative for
 77 both QFT-GIT and T-SPOT; QFT-GIT= QuantiFERON-TB Gold In-Tube; QFT-Plus=
 78 QuantiFERON-TB Gold Plus; TST=Tuberculin skin test; T-SPOT= T-SPOT. *TB*

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81 **TABLE S4b** Distribution of QFT-GIT, T-SPOT and TST results among positive or
 82 negative QFT-Plus results

QFT-Plus	QFTGIT			TSPOT				TST	
	Total, <i>n</i>	Positive <i>n</i> (%)	Negative <i>n</i> (%)	Positive <i>n</i> (%)	Negative <i>n</i> (%)	Borderline <i>n</i> (%)	Invalid <i>n</i> (%)	Positive <i>n</i> (%)	Negative <i>n</i> (%)
Positive	119	94(79)	25(21)	68(57)	37(31)	10(8)	4(3)	91(76)	28(24)
Negative	387	7 (2)	380(98)	6(2)	369(95)	11(3)	1(0)	87(22)	300(78)
Indeterminate ^a	2	2(100)	0	1 (0.5)	1(0.5)	0(0)	0(0)	2 (100)	0(0)
Total	508	103(20)	405(80)	75(15)	407(80)	21(4)	5(1)	180(35)	328(65)

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84 QFT-GIT=QuantiFERON-TB Gold In-Tube; QFT-Plus=QuantiFERON-TB Gold Plus;

85 TST=Tuberculin skin test; T-SPOT= T-SPOT. *TB*. ^aThe 2 indeterminate QFT-Plus were

86 either due to high nil, >8.0 IU/mL, or low mitogen, 0.5 IU/mL.

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88 **TABLE S5** Demographics of 12 participants with QFT-Plus positive and TST/T-
 89 SPOT/QFT-GIT negative results, and QFT-Plus negative and TST/T-SPOT/QFT-GIT
 90 positive results

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#	Gender	Age	Birth country	TST (mm)	T-SPOT ^b	IFN γ (IU/mL)		
						QFT-GIT	QFT-Plus	
							TB1	TB2
1	Male	43	Bhutan	7	2	0.2	0.55	0.45
2	Female	27	Mongolia	0	1	-0.06	0.5	0.38
3	Male	31	Iraq	0	2	0.19	0.52	0.07
4	Male ^a	47	United States	0	3	0.08	0.36	0.31
5	Male	39	Bhutan	7	2	0.18	0.32	0.36
6	Female	40	Myanmar	0	0	0.06	0.26	0.4
7	Female	28	Bhutan	9	1	0.17	0.16	0.45
8	Male	42	Congo (DRC)	5	2	0.34	0.27	0.46
9	Male	26	Somalia	0	0	0.01	0.14	0.43
10	Male ^a	49	United States	0	1	0.02	0	2.21
11	Female	24	El Salvador	17	33	1.33	0.29	0.25
12	Female	18	Philippines	14	44	0.46	0.27	0.32

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93 ^aHomeless shelter residents with local LTBI prevalence $\geq 25\%$, ^bNumber of spots,
 94 greater of Panel A or B minus nil. #1-10 QFT-Plus positive/QFT-GIT, T-SPOT, TST
 95 negative; # 11 & 12 QFT-Plus negative and QFT-GIT, T-SPOT, TST positive; QFT-
 96 GIT=QuantiFERON-TB Gold In-Tube, antigen minus nil values are presented; QFT-

97 Plus=QuantiFERON-TB Gold Plus, antigen minus nil values are presented for TB1 and
 98 TB2; TST=Tuberculin skin test; T-SPOT= T-SPOT. *TB*

99 **TABLE S6** Sample collection and laboratory methods for discordant and all samples
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Procedure/Methods	<u>Discordant, n=34</u>		<u>All, n=508</u>	
	QFT-GIT <i>n</i> (%)	QFT-Plus <i>n</i> (%)	QFT-GIT <i>n</i> (%)	QFT-Plus <i>n</i> (%)
Blood draw				
Directly into QFT tubes	29 (85)	27 (79)	414 (81)	364 (72)
Heparin tube first, transferred	5 (15)	7 (21)	94 (19)	144 (28)
Number of blood collection tubes				
5 tubes/Common nil and mitogen	30 (88)	30 (88)	406 (80)	406 (80)
7 tubes/Separate nil and mitogen	4 (12)	4 (12)	102 (20)	102 (20)
Source of Nil/Mitogen for 5 tubes ^a				
From QFT-GIT set	21 (70)	21 (70)	278 (69)	278 (69)
From QFT-Plus set	8 (27)	8 (27)	115 (28)	115 (28)
Plates				
Common plate ^b	12 (35)	12 (35)	144 (28)	144 (28)
Separate plates ^c	22 (65)	22 (65)	364 (72)	364 (72)
Standard curve				
4 point	5 (15)	34 (100)	92 (18)	508 (100)
8 point	29 (85)	0 (0)	416 (82)	0 (0)
Samples storage before run				
Run directly after 37°C incubation	2 (6)	0 (0)	50 (10)	0 (0)

Stored at 4°C before running	32 (94)	32 (100)	458 (90)	508 (100)
ELISA run				
Automated	16 (47)	14 (41)	204 (40)	154 (30)
Manual	18 (53)	20 (58)	304 (60)	354 (70)

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102 ^aMissing information for samples on the source of nil and mitogen tubes, denominator
103 for discordant sample, n=30 and for 'All' samples, n= 406; QFT-GIT=QuantiFERON-TB
104 Gold In-Tube; QFT-Plus=QuantiFERON-TB Gold Plus; ^bBoth QFT-GIT and QFT-Plus
105 samples run on the same plate with one set of nil and mitogen, ^cBoth QFT-GIT and
106 QFT-Plus samples run on separate plates, each with its own nil and mitogen