

# QFT NEWS

July 2009

“Changing the way  
the world looks at TB”

## Highlights

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## In Focus Putting IGRAs Into Practice

A glimmer of hope.

That's what the latest World Health Organization (WHO) report offers the global TB community. Over the past year, the rates of both new and existing cases of TB have fallen. These declines are not only numerically significant, considering the StopTB Partnership's goal of reducing incidence and halving prevalence and death rates by 2015, but also regionally significant. All six WHO-defined regions had diminishing prevalence and death rates, and five have slashed incidence rates.

While not trivial, these successes do not yet eclipse concern. Although the overall rate of new TB cases fell, the decline tallied to less than 1% per year, and the absolute number of cases is still rising alongside population. Furthermore, the TB case detection rate reached 63% in 2007—a great effort, but one that failed to meet the expected 70%. European results are particularly concerning: Europe was the one WHO region that did not achieve an incidence rate drop (the rate was virtually unchanged) and joins Africa as the second of three regions projected to miss the target reduction rates for

prevalence and mortality by 2015. Perhaps most alarming are the figures for TB-HIV co-infection (see [May QFT News](#) for full story). Collectively, these signal that we, as a TB community, have a long way to go.

The WHO's StopTB strategies to enhance TB diagnosis and treatment (from implementation of TB control in the primary health care setting to promotion and participation in developing diagnostic pathways) were echoed by several international key opinion leaders at the recent Global Symposium on Interferon-Gamma Release Assays (IGRAs). The IGRA meeting, adjunct to the Fifth European meeting of the IUATLD, took place in Dubrovnik, Croatia from May 30 to June 1. The theme of the meeting was “putting IGRAs into practice,” and the program was designed to examine both the current evidence for using IGRAs in place of the tuberculin skin test (TST) and the obstacles limiting change. Several of the key points of discussion and presentation voiced by the 240 symposium attendees are reported below. ►

## Predictive Value

Much evidence now demonstrates that QFT is more specific than the TST and has equal or better sensitivity for detecting both active and latent TB. Despite this, some clinicians have been reluctant to adopt QFT, and indeed IGRAs, without data from prospective studies that demonstrate the IGRAs' ability to detect those who will progress to active TB infection. An important presentation in Dubrovnik by Dr Roland Diel reviewed currently available data on this topic and concluded that people who are IGRA-positive have a higher rate of progression to active TB than those who are TST-positive. Additionally, Dr Diel presented that contacts who are TST-positive *and* IGRA-negative have little chance of progressing. He concluded that "all current evidence is supportive of IGRAs being better predictors of progression" and that "IGRAs should be preferentially used in place of the TST in almost all situations" (view [presentation](#)).

A presentation from Dr Maximilian Aichelburg (view [presentation](#)) revealed that from a cohort of 822 HIV-positive patients in Austria, 37 were QFT-positive and the three subjects who progressed to active TB over a two-year follow-up period all came from this subset. A further presentation reported on the predictive value of QFT in a highly endemic setting in Cape Town. Dr Hassan Mahomed and colleagues' data suggested that in this setting, a recently converted QFT (similar to the TST) may represent a higher risk of progression. They further suggested that the magnitude of a positive QFT result may be related to risk of progression to TB disease (view [presentation](#)).

## Putting IGRAs into Practice

Changing medical practice generally involves overcoming a number of logistic and cost hurdles. This is especially the case with the move to IGRAs because TST use is so entrenched, making the change to updated technology difficult for some. Dr L. Masae Kawamura, Director of the TB Control Section, San Francisco Department of Public Health, gave a key presentation highlighting how her Health Department overcame several obstacles to implement extensive QFT use (view [presentation](#)). Moving to QFT has resulted in a greater than 60% decline in the number of people testing positive for TB and, thus, reducing the number of follow-up visits. Despite this lower number, no cases of TB have been missed from the more than 45,000 people screened in San Francisco since QFT was adopted. Dr Kawamura listed the critical elements of QFT implementation: obtaining political commitment, having leadership and advocacy driving the change, sourcing initial start-up funding, and in some cases overcoming the passive TB control culture in some areas.

Expectedly, for IGRAs to be put into practice there has to be proof that the tests provide an accurate means of detecting TB infection. Separate sessions in Dubrovnik covered the application of IGRAs (generally in comparison with the TST) for contact investigations, healthcare worker screening, testing for vulnerable populations such as those with HIV infection and immunosuppression, and also in children. These presentations, most of which are available at the conference website; <http://www.igrasymposium.com/agenda.html>, have highlighted QFT's enhanced specificity over the TST and IGRAs' enhanced sensitivity for the detection of TB infection. These findings are reflected in the overall sentiment of the symposium: there is enough evidence to adopt IGRAs without delay because routine IGRA use will further elucidate any concerns regarding test performance.

## Practicality and Cost-Effectiveness

Practicality and cost benefits of IGRAs were discussed in detail in Dubrovnik, with superior ease-of-use and performance of QFT In-Tube over the TST highlighted in several presentations. Conversely, the *impracticality* of the TST was a talking point. It was reported that anywhere between 10 and 74%, depending on the population ►

Dr Deborah Lewinsohn, Associate Professor at the Oregon Health and Science University, takes the podium in Croatia to discuss IGRA use in children.



studied, of TSTs initiated give “indeterminate” results. That is, between 10 and 74% of people who had the TST placed do not return for test reading.

Two presentations directly looked at the cost-effectiveness of QFT in comparison with the TST. Dr Akiko Kowada presented that using QFT alone for screening TB contacts in Japan was more cost-effective than either TST alone or TST followed by QFT (view [presentation](#)). Similarly, QFT alone was the most cost-effective method for screening healthcare workers. A second presentation by Dr Kawamura discussed the cost implications of QFT having replaced the TST for Public Health testing and healthcare worker screening in San Francisco (view [presentation](#)). She noted that implementing QFT instead of TST for healthcare worker screening saved San Francisco’s TB control program US\$101,648 over one year. For Public Health use, Dr Kawamura reported that QFT “pays for itself AND is likely cost-saving” based on her team’s estimated *savings* of between \$328,068 to \$460,265 per annum as a direct result of switching to QFT from the TST.

Longitudinal performance of IGRAs is another practical issue noted at the symposium. Presenting preliminary results from routine screening of 1200 US health care workers, Dr Charles Daley from National Jewish Hospital in Denver, compared QFT and T-SPOT®.TB’s reproducibility and repeatability (i.e. conversions and reversions) when used for serial screening. While no difference existed between QFT and T-SPOT®.TB in terms of repeatability over 6 months, QFT demonstrated better reproducibility (QFT: 4% discordant results vs. T-SPOT®.TB: 12%). Furthermore, positive TST results reverted to negative more frequently over a half-yearly follow-up period than IGRA results (TST: 16/35 or 46%; QFT: 22/67 or 33%), creating more confusion about the interpretation of TST results. Another interesting finding was that TST may “boost” a subsequent IGRA result (view [presentation](#)). This has significant implications for countries that may consider using an IGRA to confirm a positive TST, as this may lead to falsely-positive IGRA responses.

## Regulatory Synopsis

A presentation given by Dr Madhukar Pai provided a succinct summary of current guidelines worldwide (view [presentation](#)). Overall, 16 countries have at least one guideline or statement, but QFT is used in many more that do not have guidelines. Generally, these guidelines indicate one of three testing strategies: TST followed by IGRA, IGRA only, or an option of either IGRA or TST alone.

Despite the understandably conservative nature of national guidelines, many nations seem to be shifting quickly toward universal IGRA adoption with a number of countries now promoting IGRAs as the ‘preferred’ test for latent TB diagnosis. However, in most guidelines the use of IGRAs in place of the TST is not yet recommended for children under

five years of age, largely due to the limited number of IGRA studies in very young children

The Director of the CDC’s Division of Tuberculosis Elimination, Dr Kenneth Castro, via video link to Dubrovnik, presented the provisional update of the CDC’s US guideline, which will include IGRAs as the ‘preferred’ test in BCG-vaccinated and other populations. Some countries, like Japan, have accounted for the high predictive value and cost-effectiveness of QFT and adopted it as the preferred screening test for public health outbreak investigations and healthcare worker screening.

In summary, the 2nd Global Symposium on IGRAs highlighted the large body of evidence now available on the enhanced accuracy of IGRAs over the TST and discussed what is needed for putting IGRAs into practice. The discussions in Dubrovnik highlighted the need for an accurate, practical, and highly cost-effective method for TB testing. Based on the evidence presented at the symposium, IGRAs, and QFT in particular, are tools that can greatly improve TB diagnosis and offer hope to patients and clinicians who are fighting TB disease.

The 2nd Global Symposium on IGRAs was sponsored by Cellestis and the Foundation for Innovative Diagnostics (FIND). Symposium presentations and posters are available online at [www.igrasymposium.com/agenda.html](http://www.igrasymposium.com/agenda.html) ■



Dr Anja Schablon presents data on the value of IGRAs in contact tracing

## Latest News

### Publications and Guidelines Update

#### New TB testing recommendations for autoimmune disease (Germany)

The German Central Committee for the Fight Against Tuberculosis (TB) released updated guidelines in June regarding TB screening of patients with autoimmune disease prior to therapy with tumor necrosis factor-alpha (TNF- $\alpha$ ) inhibitors. To be published in the September issue of the journal *Zeitschrift für Rheumatologie*, the updated German guidelines recommend exclusion of active TB and screening for latent TB infection using interferon-gamma-release assays (IGRAs) before commencing a patient with autoimmune disease on TNF- $\alpha$  inhibitor therapy. The guidelines also state that the tuberculin skin test "is recommended only in exceptional situations" because many false-positive or false-negative results can be expected.

▷ View the full abstract in English [here](#).

### New European Authorized Representative

Medical Device Safety Service (MDSS) is Cellestis' newly appointed Authorized Representative in Europe. MDSS will assist Cellestis with regulatory and product vigilance responsibilities and is a correspondent member of EUCOMED.

### Product Updates

#### New Package Insert translations on web

With a growing customer base throughout the world, Cellestis now provides the Package Insert in 25 different languages. Individual translations can be accessed by clicking on the "Package Insert Translations" button on Cellestis' [homepage](#) (see image below) and selecting the flag corresponding to the particular language you wish to read. Languages include:

Bulgarian	Italian	Slovakian
Croatia	Latvian	Slovenian
Danish	Lithuanian	Spanish
Estonian	Dutch	Swedish
Finnish	Norwegian	Turkish
French	Polish	English (Non-US)
German	Portuguese	English (US)
Greek	Romanian	
Hungarian	Russian	



Participants of the 2nd Global Symposium on IGRAs.

## Upcoming events list

### North America/South America

Force Health Protection (FHP)

August 19–20

Albuquerque, NM

Interscience Conference on Antimicrobial Agents and Chemotherapy (ICCAC)

September 12–14

San Francisco, CA

Association of Occupational Health Professionals (AOHP)

September 16–19

Portland, OR

### Europe/Middle East/Africa

Tuberkulosefortbildung

September 2–3

Coswig, Germany

European Respiratory Society (ERS) Annual Congress

September 12–16

Vienna, Austria

Health Protection Agency (HPA)

September 14–17

Warwick University, UK

Najaarsdagen Reumatologie

September 17–19

Ede, Netherlands

61st Annual Meeting of the German Society for Hygiene and Microbiology (DGHM)

September 20–24

Göttingen, Germany

More information about Cellestis events is available [here](#).

If you have any questions or comments about QFT-News, contact us at [news@cellestis.com](mailto:news@cellestis.com)

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