Author's response to reviews

Title: Validation of the GenoType(R) MTBDRplus assay for detection of MDR-TB in a public health laboratory in Thailand

Authors:

Rapeepun Anek-vorapong (rapeepan.anek@gmail.com)
Chalinthorn Sinthuwattanawibool (chalinthornS@th.cdc.gov)
Laura Jean Podewils (lpp8@cdc.gov)
Kimberly McCarthy (dxu8@cdc.gov)
Keerataya Ngamlert (supatcharan@yahoo.com)
Busakorn Promsarin (busa_kornp@hotmail.com)
Jay K Varma (jcv9@cdc.gov)

Version: 2 Date: 7 January 2010

Author's response to reviews: see over
January 7, 2010

Dr. Melissa Norton
Editor-in-Chief
BMC Infectious Diseases

Dear Dr. Norton:

Please find attached our revised manuscript entitled, “Validation of the GenoType® MTBDRprofile assay for detection of MDR-TB in a public health laboratory in Thailand” for consideration for publication in BMC Infectious Diseases. We have reviewed and addressed the reviewer’s comments (please see attached) and made revisions to the manuscript.

This manuscript has not been submitted or accepted elsewhere for publication. All authors have contributed to, seen, and approved the final, submitted version of the manuscript. The signed copyright form was also included as an attachment with our initial online manuscript submission. In addition, the authors declare that they have no competing interests.

Thank you in advance for your time and consideration. Please address all correspondence to Laura Jean Podewils, 1600 Clifton Road NE, MS E-10, Atlanta, Georgia 30333 lpp8@cdc.gov.

Sincerely,

Laura Jean Podewils, PhD, MS
Epidemiologist
Division of Tuberculosis Elimination
National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention Centers for Disease Control and Prevention 1600 Clifton Road NE, MS E-10 Atlanta, GA 30333
office: (404) 639-5346
fax: (404) 639-1566
e-mail: lpp8@cdc.gov
Reviewer #1:

Title: Validation of the GenoType(R) MTBDRplus assay for detection of MDR-TB in a public health laboratory in Thailand

Version: 1 Date: 13 October 2009

Reviewer: Yasuhiko Suzuki

Reviewer's report:

The manuscript entitled "Validation of the GenoType® MTBDRplus assay for detection of MDR-TB in a public health laboratory in Thailand" by Rapeepun Anek-vorapong et al is showing the comparison of GenoType® MTBDRplus assay to Mycobacterial Growth Indicator Tube for Antimycobacterial Susceptibility Testing (MGIT AST) for detection INH resistance, RIF resistance, and MDR-TB in stored acid-fast bacilli (AFB)-positive sputum specimens and isolates. Although their data are secure, there are a few issues to be clarified.

Major issues

1. As authors know that there are several publications on the evaluation of GenoType® MTBDRplus assay. More samples for both INH and RFP resistant tuberculosis should be analyzed to conclude the applicability of this assay. The current sample size was based on previous publications that have demonstrated the performance of this assay, and is considered an adequate sample size to establish laboratory proficiency and assay performance. The investigators are currently conducting a 1-year demonstration project to evaluate the performance and public health impact, in terms of translation to patient management, of implementing the GenoType® MTBDRplus assay as part of the routine National TB program. Information from this prospective analysis will help to evaluate the applicability and utility of the assay.

2. As this manuscript is for the validation of GenoType® MTBDRplus assay, authors should add the sequence results to table 1a & b. Sequencing was only performed on specimens that were discordant – those with INH resistance detected by conventional testing but not molecular testing. Of these 2 specimens, we were only able to obtain interpretable sequence dating for one of the two specimens. This isolate was identified as wild type. We have stated this in the results section of the manuscript.

Minor issues

1. As authors know, the ratio of correlation between mutations and drug resistance are different from country to country. For example, katG and/or inhA mutation correlate with less than 70% of INH resistance. Explanation on correlation between mutations and drug resistance in Thailand should be added to "Discussion", if authors intend to say the applicability of GenoType® MTBDR assay in this country.

We have added to the discussion citing a recent publication that looked at specific mutations conferring INH and Ethionamide resistance in Thailand. Please see the added revisions in the third paragraph of the Discussion section.
2. There is no explanation on the correlation between RFP susceptibility and GenoType® MTBDR assay result in the text. Though reader can see it in tables, authors should kindly add this to the text. 

Thank you for your suggestion. The information on sensitivity and specificity of the GenoType MTBDR assay compared to the conventional DST testing for INH-resistance, RIF(RFP)-resistance, and MDR-TB is in the second sentence of the first paragraph in the results section. For RIF-resistance, the specificity was 100% for both specimens tested directly from sputum and isolates.

Reviewer #2:
Title: Validation of the GenoType(R) MTBDRplus assay for detection of MDR-TB in a public health laboratory in Thailand
Version: 1 Date: 10 November 2009
Reviewer: Saad Al Alghamdi
Reviewer's report:
The paper is very well structured and I have no suggestions to improve the outline. The contents are descriptive enough to be accepted for publication.