

A Multilaboratory, Multicountry Study to Determine MIC Quality Control Ranges for Phenotypic Drug Susceptibility Testing of Selected First-Line Antituberculosis Drugs, Second-Line Injectables, Fluoroquinolones, Clofazimine and Linezolid

Koné Kaniga^{a*}, Daniela M. Cirillo^b, Sven Hoffner^c, Nazir A. Ismail^{d,e}, Devinder Kaur^f, Nacer Lounis^g, Beverly Metchock^h, Gaby E. Pfyfferⁱ and Amour Venter^j

^a*Janssen Research & Development, LLC, Titusville, NJ, USA;*

^b*IRCCS, San Raffaele Scientific Institute, Milan, Italy;*

^c*TB Supranational Reference Laboratory, The Public Health Agency of Sweden, Solna, Sweden;*

^d*National TB Reference Laboratory, Center for Tuberculosis, National Institute of Communicable Diseases, Johannesburg, South Africa;*

^e*Department of Medical Microbiology, University of Pretoria, Pretoria, South Africa;*

^f*University of Massachusetts Medical School, Massachusetts Supranational TB Reference Laboratory, Boston, MA, USA*

^g*Janssen Infectious Diseases BVBA, Beerse, Belgium;*

^h*Reference Laboratory, Division of TB Elimination, United States Centers for Disease Control and Prevention, Atlanta, GA, USA;*

ⁱ*Department of Medical Microbiology, Center of Laboratory Medicine, Luzerner Kantonsspital LUKS, Luzern, Switzerland;*

^j*TASK Applied Science, SA MRC Centre for TB Research, DST/NRF Center of Excellence for Biomedical TB Research, Division of Molecular Biology and Human Genetics, Faculty of Medicine and Health Sciences, Stellenbosch University, Tygerberg, South Africa*

*Corresponding author. Tel: +1-609-647-3519; Fax: +1-609-730-7566;

E-mail: kkaniga@its.jnj.com

Abstract

Objectives: Our objective was to establish reference minimal inhibitory concentration (MIC) quality control (QC) ranges for drug susceptibility testing of antimycobacterials, including first-line agents, second-line injectables, fluoroquinolones and World Health Organization Category 5 drugs for multidrug-resistant tuberculosis, using a 7H9 broth microdilution MIC method.

Methods: A Tier-2 reproducibility study was conducted in eight participating laboratories using Clinical Laboratory and Standards Institute (CLSI) guidelines. Three lots of custom-made frozen 96-well polystyrene micro titer plates were used and pre-prepared with 2X pre-diluted drugs in 7H9 broth/oleic acid albumin dextrose catalase. The QC reference strain was *Mycobacterium tuberculosis* (MTB) H37Rv. MIC frequency, mode and geometric mean were calculated for each drug. QC ranges were derived, based on predefined, strict CLSI criteria. Any data lying outside CLSI criteria resulted in exclusion of the entire laboratory dataset.

Results: Data from one laboratory were excluded due to higher MIC values than for other laboratories. QC ranges were established for eleven drugs: isoniazid (0.03–0.12 µg/ml), rifampin (0.03–0.25 µg/ml), ethambutol (0.25–2 µg/ml), levofloxacin (0.12–1 µg/ml), moxifloxacin (0.06–0.5 µg/ml), ofloxacin (0.25–2 µg/ml), amikacin (0.25–2 µg/ml), kanamycin (0.25–2 µg/ml), capreomycin (0.5–4 µg/ml), linezolid (0.25–2 µg/ml) and clofazimine (0.03–0.25 µg/ml). QC ranges could not be established for nicotinamide (pyrazinamide surrogate), prothionamide or ethionamide, which were assay non-performers.

Conclusions: Using strict CLSI criteria, QC ranges against the MTB H37Rv reference strain were established for the majority of commonly used antituberculosis drugs, with a convenient 7H9 broth microdilution MIC method suitable for use in resource-limited settings.

Keywords: *Mycobacterium tuberculosis*; MIC; QC; validation; antimycobacterials

Introduction

Managing an estimated global annual incidence of 9.6 million *Mycobacterium tuberculosis* (MTB) cases requires an arsenal of effective antituberculosis (anti-TB) drugs that are active against both susceptible and multidrug-resistant strains (1). Furthermore, maximizing the effectiveness of treatment and minimizing the risk of development of further resistance requires accurate drug susceptibility testing (DST) for MTB clinical isolates (2,3). To improve reliability of DST for MTB, regulators have introduced a requirement to establish QC ranges for new and repurposed anti-TB drugs (4).

Two approaches to MTB DST are currently employed; critical concentration (CC)-based agar proportion assay (APA) or minimal inhibitory concentration (MIC)-based methodology. CC is well established and used widely for classifying the sensitivity of MTB to anti-TB drugs. The CC, also known as the antimicrobial susceptibility testing breakpoint, is defined by international convention as the lowest concentration of a drug that inhibits growth of 95% (90% for pyrazinamide) of wild-type MTB strains, while at the same time does not inhibit strains that are considered to be clinically 'resistant' (i.e., isolated from patients unresponsive to therapy) (3). However, several disadvantages are associated with using CC values in DST. Firstly, up to 5% of wild-type MTB strains (10% for pyrazinamide) are effectively classified as drug resistant and secondly, clinical outcome data for individual drugs are often not available because combination therapy is the norm for TB treatment (5). In addition, the CCs for many older anti-TB drugs, including some examined in this study, were established many years ago and have not since been re-validated; hence, any genetic variation over time, as well as the development of resistance will not have been accounted for (3). For example, one analysis has reported that regional variability of MTB susceptibility to ofloxacin would result in different CC values from isolates in different settings (6,7). As a result of these factors, together with the common occurrence that the CC is close to the MIC, there is a high probability of misclassification of MTB strains as 'susceptible' or 'resistant' when using a CC-based APA method (5).

The second approach used in MTB DST is based on the MIC, defined as the lowest concentration of a drug (in µg/ml) that results in complete inhibition of visual growth *in vitro* (8). In DST, a susceptible reference isolate is tested alongside the clinical isolates to act as a quality control. H37Rv is an established MTB reference strain, being well-documented as a 'pansusceptible' wild-type isolate, and used in laboratories worldwide for routine monitoring of assay performance (3). Ongoing quality control and quality assurance of DST requires QC ranges to be established by MIC testing of such a reference isolate.

Our objective was therefore to establish, by means of a Tier-2 study, DST QC MIC ranges against the H37Rv reference strain for a broad panel of anti-TB drugs using a 7H9 broth microdilution MIC method recognized by the Clinical Laboratory and Standards Institute (CLSI). Our choice of a broth microdilution MIC method that could be commercially available in the future was influenced by the advantage it offers over agar dilution MIC methods in that DST results are produced in half the time (incubation period of 10 days or less compared with 21 days or more for agar media) as required with current methodologies (9). Drugs were selected for the study on the basis of having an important role in MTB treatment, as well as having no established QC range for MTB H37Rv using a broth microdilution MIC method. The 14 anti-TB drugs tested included first-line agents, second-line injectables, fluoroquinolones, and World Health Organization (WHO) Category 5 drugs (linezolid and clofazimine).

Materials and methods

Study design

This Tier-2 reproducibility study (TMC207-PMR-1988-004), was designed according to CLSI criteria (10), with the appropriate modifications required for MTB as described in the companion paper on bedaquiline (9). As such, the results were generated in eight different laboratories based in eight separate and distinct institutions (Tier-2 criteria specify a minimum of seven laboratories). Furthermore, each laboratory was instructed to perform 10 replicate tests on

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separate days using the internationally recognized MTB reference strain H37Rv and separate lots of custom-made frozen 96-well polystyrene micro titer plates (Thermo Fisher Sensititre For Research Use Only, Thermo Fisher Scientific Inc, Waltham, Massachusetts). For the purpose of the analysis, each lot was assigned a number from 1 to 3. The study protocol was developed through a consensus approach, based on feedback from the participating investigators. The study was performed in a blinded fashion as none of the laboratories had access to any results from other laboratories.

The broth microdilution MIC method employed was adapted from that described in CLSI Document M07-A9, section 10.4 (8). Modifications included the preparation of the drug stock concentration, the QC reference strain, and the preparation of the inoculum. The reproducibility of the DST methods was evaluated within each participating laboratory, between different laboratories and between reagent lots.

Participating laboratories

The eight participating laboratories were spread across the world, located on three different continents. The investigators and their laboratories included CLSI members or advisors, the WHO Supranational Reference Laboratory Network (SRLN), the US Centers for Disease Control and Prevention (CDC) and other internationally recognized TB laboratories.

Materials

The reference strain used was MTB H37Rv originating from the American Type Culture Collection (ATCC 27294). Each laboratory used its own H37Rv strain, rather than it being provided centrally, as well as its own standard media for its culture.

Other materials provided centrally included 12.5 ml sterile deionized water tubes and saline Tween broth to reconstitute the mycobacterial inoculum. Middlebrook 7H9 broth base and

oleic acid albumin dextrose catalase (OADC) (7H9-S) were obtained from Becton Dickinson (Franklin Lakes, New Jersey).

A total of 14 anti-TB drugs were evaluated, comprising first line drugs (isoniazid, rifampin, ethambutol), fluoroquinolones (levofloxacin, moxifloxacin and ofloxacin), second-line injectable agents (amikacin, kanamycin and capreomycin), oral bacteriostatic drugs (prothionamide and ethionamide), and WHO Category 5 drugs (linezolid and clofazimine). Given that pyrazinamide DST is problematic due to a low pH requirement, nicotinamide was evaluated as a potential surrogate (11). The frozen 96-well polystyrene micro titer plates contained pre-diluted drugs at 2X the final concentration made in 2X 7H9-S (Thermo Fisher Sensititre For Research Use Only). The concentration ranges in the MIC frozen panels for the drugs tested are summarized in Table 1.

Broth microdilution MIC method

The 7H9 broth microdilution MIC method was conducted as described in the companion paper (9). In brief, MTB H37Rv was grown in 7H11 medium or Lowenstein-Jensen and re-suspended into saline Tween with glass beads. The turbidity of the resulting suspension was adjusted with sterile deionized water to match that of a McFarland standard 1 suspension, corresponding to $\sim 5 \times 10^7$ colony forming units (CFU)/ml. There is good concordance between the McFarland Scale and CFU/ml for MTB (12). A 2X inoculum was to be prepared by inoculating 12.5 ml sterile de-ionized water tubes with 300 μ l of the 1 McFarland suspension to give a 50-fold dilution from 1 McFarland ($\sim 1 \times 10^6$ CFU/ml). The 2X MTB H37Rv suspension was then poured into a disposable inoculum reservoir, and then 100 μ l transferred to the micro titer plate wells using an 8 or 12 channel micro-pipette and sterile tips with filters. The final inoculum size in each well was $\sim 5 \times 10^5$ CFU/ml. The growth control well, but not the well containing the negative control, was also inoculated with MTB H37Rv. After inoculation, the plates were sealed in plastic

Table 1. Summary of 7H9 broth microdilution MIC QC ranges against MTB H37Rv strain for anti-TB drugs

Drug	Dilution range used in the study (µg/ml)	MIC QC range (µg/ml)
Isoniazid ^a	0.03–1	0.03–0.12
Rifampin	0.06–1	0.03–0.25
Ethambutol	0.25–8	0.25–2
Nicotinamide ^b	16–512	NA
<i>Fluoroquinolones</i>		
Levofloxacin	0.12–4	0.12–1
Moxifloxacin	0.06–2	0.06–0.5
Ofloxacin	0.12–4	0.25–2
<i>Second-line injectables</i>		
Amikacin	0.12–8	0.25–2
Kanamycin ^c	0.12–8	0.25–2
Capreomycin	0.12–4	0.5–4
<i>Oral bacteriostatic drugs</i>		
Prothionamide	0.06–2	NA
Ethionamide	0.12–4	NA
<i>WHO category 5 drugs</i>		
Linezolid	0.12–4	0.25–2
Clofazimine ^d	0.06–1	0.03–0.25

^aQC range derived from micro titer plate Lot-1 and Lot-2 only.

^bNicotinamide was included as a potential surrogate for pyrazinamide.

^cQC range derived from Lot 2 and Lot 3 only.

^dThe modal concentration of clofazimine, 0.06 µg/ml, was the lowest concentration tested.

NA, not applicable as QC ranges that included at least 95% of the observed values could not be set.

bags (10 plates per bag) and incubated at 35–37°C. Each drug was tested over a 5–7-fold range, taking into consideration the CLSI guidance that whenever possible, the low end of the QC range for dilution testing should only include concentrations that can be accurately prepared and that dilutions should extend to no more than five dilutions below a drug’s susceptibility breakpoint (10). The final drug concentration ranges in the wells following inoculation are given in Table 1; e.g. for isoniazid the concentrations were: 1, 0.5, 0.25, 0.12, 0.06 and 0.03 µg/ml.

Data collection and statistical methods

Microtiter plates were read by visual inspection at days 7, 10 and 14 after inoculation to establish MICs for each drug. MIC was defined as the lowest concentration of the drug (in µg/ml) that prevented visual growth. Growth and negative control wells were checked to ensure adequate growth and no contamination, respectively. Any negative control well with a turbid appearance was suspected of contamination; the results were discounted as invalid and the procedures and reagents checked.

Standardized forms for data capture and reporting were provided to all principal investigators ahead of study start to ensure consistency (9). Quality control was conducted on datasets from each laboratory, and data quality was monitored, with any data inconsistencies queried to the providing investigator.

The MIC distribution, mode and geometric mean were calculated for each drug. Initial QC ranges were determined by centering on the MIC mode ± 1 dilution and doubling dilution over a 3-dilution QC range (10). However, if the mode occurred at the end of the proposed dilution range, the geometric mean was used instead. The proposed QC range was required to encompass at least 95% of the observed MIC values. In the event that a QC range over 3-dilutions could not be established, a 4-dilution QC range was analyzed. In such cases, the initial proposed range was adjusted: 1) to include at least 95% of the observed MIC values to accommodate variability expected in routine testing; 2) if the frequency distribution showed a

'shoulder' off the modal value that included $\geq 60\%$ of the data points; or 3) if a bimodal distribution was observed. If these criteria were not met, it was concluded that the QC range could not be set.

Upon observation of outlying ranges for any given drug tested, the entire dataset (all three micro titer plate lots) from the laboratory providing the outlying data for that drug was excluded. The analyses for that drug were then repeated using the data from the remaining laboratories. Also in accordance with CLSI recommendations, any non-performing lot was excluded from the analyses (10). Therefore, as explained in the companion paper (9), the number of planned observations (240; 8 laboratories x 30 tests) was not always achieved.

Results

Overall findings

Using the CLSI M23-A3 guidelines, QC ranges were established for 11 anti-TB drugs using the 7H9 broth microdilution MIC (Table 1). The three remaining drugs (nicotinamide, prothionamide and ethionamide) were deemed to be non-performers in the assay as QC ranges that included at least 95% of the observed MIC values could not be established. Details are given below of how MIC QC ranges were established for four of the most commonly used drugs (rifampin, isoniazid, levofloxacin and amikacin). A summary of observations, including geometric mean and mode, for all of the drugs tested is provided in the online supplement (Table S1). For most of the drugs tested, no significant differences were reported between results for the three different micro titer plate lots. Data from one laboratory (Lab-1) were excluded due to potential contamination during shipment as some plates were thawed upon arrival at the laboratory. The raw data from all laboratories are shown in the Supplementary data (Table S2). Day 10 MICs were used in the analyses, except for Lab-1 and Lab-8, which recorded data at day 7 and day 14, respectively.

Setting the QC range for rifampin

A 3-dilution QC range which was centered on the mode value of 0.12 µg/ml for the rifampin MIC distribution was found to include 208/212 (98.1%) of the observations (Figure 1a). However, a shoulder was observed at 0.06 µg/ml with observations at this concentration representing 96.4% (80/83) of the mode value. Since this was well above the 60% defined threshold, the QC range was extended to a 4-dilution range in accordance with the recommendation of CLSI document M23-A3. As a result, the MIC QC range for rifampin broth microdilution MIC was set at 0.03–0.25 µg/ml.

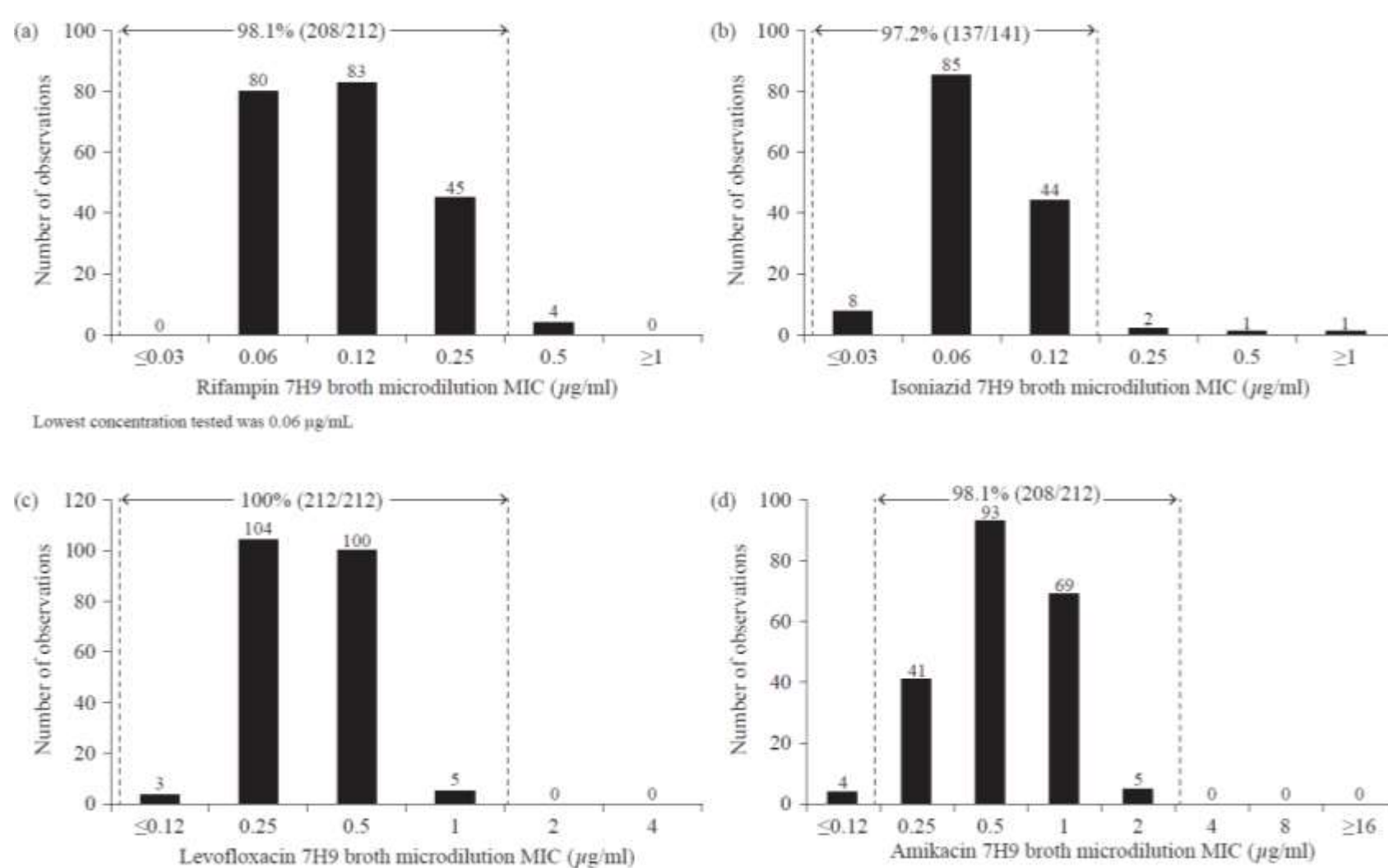
Setting the QC range for isoniazid

Preliminary testing was performed at a TB laboratory not participating in the current study on the frozen plates prior to initiating the study. The results indicated that INH MICs for Lot-3 were an order of magnitude higher than those for Lot-1 and Lot-2. Therefore, Lot-3 data for INH only was excluded from the analyses (Figure S1). Therefore Lot-3 was excluded from the analysis and the total number of included observations was 141. The mode was 0.06 µg/ml and geometric mean was 0.076 µg/ml (Figure 1b). A 3-dilution QC range of 0.03–0.12 µg/ml, centered on the mode was found to include 97.2% (137/141) of the observations.

Setting the QC range for levofloxacin

The 3-dilution QC range for the levofloxacin MIC distribution centered on the mode included 207/212 (97.6%) of observations, with a mode value of 0.25 µg/ml and a geometric mean of 0.355 µg/ml (Figure 1c). However, since the shoulder at 0.5 µg/ml was 96.1% of the mode value, the QC range was extended to a 4-dilution range. The MIC QC range for levofloxacin was therefore set at 0.12–1 µg/ml.

Figure 1. 7H9 broth MIC distribution against MTB H37Rv and quality control range for (a) rifampin, (b) isoniazid, (c) levofloxacin and (d) amikacin.



Setting the QC range for amikacin

A 3-dilution QC range which was centered on the mode value of 0.5 µg/ml for the amikacin MIC distribution was found to include 203/212 (95.8%) of the observations (Figure 1 d). However, since the shoulder at 1 µg/ml was 74.2% of the mode value, the QC range was extended to a 4-dilution range. The MIC QC range for amikacin was therefore set at 0.25–2 µg/ml.

Discussion

This multicenter reproducibility study has defined 7H9 broth microdilution MIC QC ranges for commonly used anti-TB drugs, using the MTB reference strain H37Rv. The study employed a consensus methodology devised by experienced MTB investigators from various geographically separate laboratories, in accordance with CLSI guidance (8,10).

To our knowledge, MIC ranges for TB drugs have not previously been established for the MTB reference strain H37Rv in a Tier-2 study. One study assessed 7H9 broth microdilution for DST of common anti-TB drugs but did not report the actual MIC values (13). However, similar MIC distributions have been reported for the same reference strain between different liquid culture systems, with MIC variability of a two-fold dilution or less (5). Studies using 7H10 agar or BACTEC MGIT 960 and BACTEC 460 determined MICs against H37Rv of 0.5 µg/ml for ofloxacin, 0.125 µg/ml for moxifloxacin, 0.25 µg/ml for levofloxacin, 2 µg/ml for ethambutol, 0.5 µg/ml for amikacin, and 1–2 µg/ml for both kanamycin and capreomycin (14–16); all these values lie within the MIC QC ranges we report for these drugs. For isoniazid, a microdilution method using 7H10 agar or BACTEC460 yielded an MIC range of 0.064–0.125 µg/ml for H37Rv, which is essentially within the MIC QC range of 0.03–0.12 µg/ml determined in this study (16). So, while MIC distributions will vary according to the particular DST method used, our results are in line with existing data generated using other liquid culture methods.

The microbiological method described here is standardized, reliable and convenient. Such methods represent the most practical DST approach for existing anti-TB drugs. While it would

be ideal to establish clinical breakpoints for each TB drug, such an approach would be prohibitively expensive as it would require new clinical trials, and would still be complicated by the fact that a combination of drugs is used to treat MTB. Although MIC data alone will not always be sufficient to make informed clinical decisions in the field, such data can often be supplemented by knowledge of PK/PD data for the drugs in question when available. Thus, PK/PD cut-offs can be applied to the MIC distributions to set breakpoints that can be used to select the appropriate drugs for the patient, optimizing therapy (16,17). One important consideration in this regard is that PK/PD data determined in serum cannot always be used to predict susceptibility of an intracellular mycobacterium. For example, reduced moxifloxacin and ethambutol efficacy within macrophages has been shown against *Staphylococcus aureus* and *Mycobacterium avium* (18–21).

Strengths of the study include a design that followed strict CLSI criteria (10). Furthermore, the methodology was developed by consensus by participating laboratories that were highly experienced in MTB DST. Given that the eight participating laboratories were located in geographically diverse countries, the study findings are likely to be representative of a Tier-2 study. While the study did not include any laboratories in resource-limited settings, future data generated in those settings using the H37Rv strain will help further refine the Tier-3 quality control ranges.

The study experienced a logistical challenge in that it was not practical for all participating laboratories to use the same batch of MTB H37Rv strain; hence each used its own stock. A second study limitation was that some data had to be excluded from the analysis, however, this was conducted according to CLSI guidance (10). Excluded data were from Lab-1 which reported that some plates were thawed upon arrival. These factors may have contributed to inconsistencies of MICs from Lab-1. Therefore, it was not surprising that the MICs for all drugs tested in Lab-1 were somewhat impacted. Also, Lot-3 data for INH were excluded from the analysis. Indeed, preliminary DST performed on all lots indicated that INH MICs for Lot-3 were

an order of magnitude higher than those for Lot-1 and Lot-2. Therefore, Lot-3 data for INH were excluded without significant impact on the remaining data since two other lots were tested by eight laboratories ten times each. Finally, we were unable to establish QC ranges for nicotinamide, prothionamide or ethionamide as no range of tested concentrations encompassed at least 95% of the observed MIC values. The inclusion of nicotinamide was experimental in nature, and yielded an alternative and simple substitute for pyrazinamide (which requires acidic conditions for DST) (11). Since ethionamide and prothionamide are bacteriostatic rather than bactericidal against MTB, the rules for antifungal DST had to be applied, with the lowest concentration that resulted in 80% inhibition of growth determined. Such endpoints are expected to lead to inconsistent readings that will vary between personnel in the same laboratory, and consequently, among laboratories.

Using the convenient 7H9 broth microdilution method, which is suitable for use in resource-limited settings, we were able to establish QC ranges against the MTB H37Rv reference strain for the majority of commonly-used anti-TB drugs, including both first- and second-line agents, as well as WHO category 5 drugs.

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Transparency declarations

K.K. and N.L. are full-time employees of Janssen. The authors declare no additional financial conflicts of interest. The findings and conclusions in this report are those of the author(s) and do not necessarily represent the views of the CDC.

This study was done in part to satisfy FDA post marketing requirements.

Author contributions

All authors substantially contributed to the study's design and protocol and execution of the work described. All authors were involved in the development of the primary manuscript, interpretation of the data, have read and approved the final version, and have met the criteria for authorship as established by the ICMJE.

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Supplementary Material

Table S1. 7H9 broth microdilution MIC dilution ranges, QC ranges and geometric mean and mode for all of the anti-TB drugs tested against MTB H37Rv strain.

Anti-TB drug ^a	N	Dilution range (drug concentration in µg/ml) n (%) for each dilution							Mode (µg/ml)	Geometric mean (µg/ml)	QC range (µg/ml)
		≤0.03	0.06	0.12	0.25	0.5	1	≥2			
Isoniazid ^b	141	≤0.03	0.06	0.12	0.25	0.5	1	≥2	0.06	0.076	0.03–0.12
		8 (5.7)	85 (60.3)	44 (31.2)	2 (1.4)	1 (0.7)	1 (0.7)	0			
Rifampin	212	≤0.03	0.06 ^c	0.12	0.25	0.5	1	≥2	0.12	0.111	0.03–0.25
		N/A	80 (37.7)	83 (39.2)	45 (21.2)	4 (1.9)	0	0			
Ethambutol	212	≤0.25	0.5	1	2	4	8	≥16	1	0.819	0.25–2
		3 (1.4)	79 (37.3)	112 (52.8)	14 (6.6)	3 (1.4)	0	1 (0.5)			
Fluoroquinolones											
Levofloxacin	212	≤0.12	0.25	0.5	1	2	4	≥8	0.25	0.355	0.12–1
		3 (1.4)	104 (49.1)	100 (47.2)	5 (2.4)	0	0	0			
Moxifloxacin	212	≤0.06	0.12	0.25	0.5	1	2	≥4	0.25	0.167	0.06–0.5
		27 (12.7)	74 (34.9)	100 (47.2)	11 (5.2)	0	0	0			
Ofloxacin	211	≤0.12	0.25	0.5	1	2	4	≥8	1	0.73	0.25–2
		0	0	98 (46.4)	111 (52.6)	2 (0.9)	0	0			
Second-line injectables											

Amikacin	212	≤0.12	0.25	0.5	1	2	4	≥8	0.5	0.551	0.25–2
		4 (1.9)	41 (19.3)	93 (43.9)	69 (32.5)	5 (2.4)	0	0			
Kanamycin ^b	142	≤0.12	0.25	0.5	1	2	4	≥8	1	0.771	0.25–2
		3 (2.1)	21 (14.8)	29 (20.4)	65 (45.8)	21 (14.8)	3 (2.1)	0			
Capreomycin	212	≤0.12	0.25	0.5	1	2	4	≥8	1	1.178	0.5–4
		0	1 (0.5)	40 (18.9)	84 (39.6)	82 (38.7)	5 (2.4)	0			
WHO Category 5 drugs											
Linezolid	211	≤0.12	0.25	0.5	1	2	4	≥8	0.5	0.657	0.25–2
		0	2 (0.9)	131 (62.1)	71 (33.6)	7 (3.3)	0	0			
Clofazimine	212	≤0.03	0.06^c	0.12	0.25	0.5	1	≥2	0.06	0.085	0.03–0.25
		N/A	124 (58.5)	72 (34.0)	14 (6.6)	2 (0.9)	0	0			

^aData not shown for nicotinamide, prothionamide and ethionamide as QC ranges that included at least 95% of the observed MIC values could not be established, and these drugs were therefore classed as non-performers in this assay.

^bData derive from two lots of media for isoniazid and kanamycin, all other data are for findings with three lots of media.

^cLowest concentration tested.

Table S2. 7H9 broth microdilution raw data from all laboratories for all of the anti-TB drugs tested against MTB H37Rv strain.

DST, drug susceptibility test; INH, Isoniazid; RMP, Rifampin; NIC, Nicotinamide; LZD, Linezolid; CFZ, Clofazimine; LVX, Levofloxacin; OFX, Ofloxacin; MXF, Moxifloxacin; PTH, Prothionamide; ETH, Ethionamide; CAP, Capreomycin; KAN, Kanamycin; AMI, Amikacin; EMB, Ethambutol

Media Lot No	Supplier's Lot No	DST No	Date of DST	INH	RMP	NIC	LZD	CFZ	LVX	OFX	MXF	PTH	ETH	CAP	KAN	AMI	EMB	Day Read	Lab ID
Lot 1	14181	1	7/1/2014	0.06	0.06	128	2	0.25	0.5	1	0.5	0.5	2	1	2	2	1	7	Lab-1
Lot 1	14181	2	7/2/2014	1	0.06	256	2	0.25	1	1	0.5	0.5	2	1	2	4	2	7	Lab-1
Lot 1	14181	3	7/7/2014	>1	0.06	256	2	0.12	0.5	2	0.25	2	4	4	4	1	2	7	Lab-1
Lot 1	14181	4	7/9/2014	0.06	0.06	128	2	0.06	0.5	1	0.12	2	4	0.25	4	2	2	7	Lab-1
Lot 1	14181	5	7/14/2014	0.06	0.06	512	1	0.12	0.5	0.5	0.25	0.5	4	2	2	0.5	1	7	Lab-1
Lot 1	14181	6	7/16/2014	0.5	0.06	128	1	0.12	0.5	1	0.12	0.5	2	2	4	1	1	7	Lab-1
Lot 1	14181	7	7/17/2014	1	0.06	128	2	>1	0.5	0.5	0.25	>2	2	4	8	2	2	7	Lab-1
Lot 1	14181	8	7/23/2014	0.12	0.06	128	1	0.06	0.5	1	0.25	0.25	1	4	4	2	2	7	Lab-1
Lot 1	14181	9	7/24/2014	0.25	0.06	256	1	1	0.5	1	0.25	1	2	4	4	2	1	7	Lab-1
Lot 1	14181	10	7/25/2014	0.12	0.06	64	1	>1	0.5	1	0.25	0.5	>4	4	2	2	1	7	Lab-1
Lot 1	14181	11	7/29/2014	0.5	0.06	256	2	0.06	0.5	1	0.25	0.5	4	4	4	1	1	7	Lab-1
Lot 1	14181	12	7/30/2014	0.12	0.06	128	1	0.06	0.5	1	0.12	0.5	4	4	2	2	1	7	Lab-1
Lot 2	14202	1	7/1/2014	0.06	0.12	>512	2	0.25	1	1	0.25	0.5	4	1	1	1	2	7	Lab-1
Lot 2	14202	2	7/2/2014	0.25	0.25	>512	2	0.12	0.5	1	0.25	1	4	4	2	2	2	7	Lab-1
Lot 2	14202	3	7/7/2014	0.06	0.06	>512	4	0.5	0.5	1	0.25	0.25	1	1	1	0.5	4	7	Lab-1
Lot 2	14202	4	7/9/2014	0.12	0.06	>512	2	1	0.5	1	0.12	0.25	1	2	0.5	0.5	0.5	7	Lab-1
Lot 2	14202	5	7/14/2014	0.25	0.06	>512	2	0.12	0.5	1	0.12	0.25	1	1	1	0.25	0.5	7	Lab-1

Media Lot No	Supplier's Lot No	DST No	Date of DST	INH	RMP	NIC	LZD	CFZ	LVX	OFX	MXF	PTH	ETH	CAP	KAN	AMI	EMB	Day Read	Lab ID
Lot 2	14202	6	7/16/2014	0.12	0.06	>512	2	0.06	0.5	2	0.12	0.25	1	1	0.5	0.25	0.5	7	Lab-1
Lot 2	14202	7	7/17/2014	0.06	0.06	>512	2	0.5	0.5	1	0.12	0.5	2	1	1	0.5	1	7	Lab-1
Lot 2	14202	8	7/23/2014	0.5	0.12	>512	4	0.12	0.5	1	0.25	2	4	2	2	1	1	7	Lab-1
Lot 2	14202	9	7/24/2014	0.06	0.06	>512	2	0.5	0.5	1	0.25	2	4	2	2	0.5	1	7	Lab-1
Lot 2	14202	10	7/25/2014	0.5	0.12	>512	2	0.25	0.5	1	0.25	>2	4	>4	1	1	1	7	Lab-1
Lot 2	14202	11	7/29/2014	0.12	0.12	>512	2	0.25	0.5	1	0.12	0.12	1	2	1	0.25	0.5	7	Lab-1
Lot 2	14202	12	7/30/2014	0.5	0.12	>512	2	0.12	0.5	1	0.25	1	4	2	1	0.5	0.5	7	Lab-1
Lot 3	14203	1	7/1/2014	0.5	0.06	>512	1	0.12	0.25	1	0.25	0.25	2	0.5	2	1	1	7	Lab-1
Lot 3	14203	2	7/2/2014	0.5	0.12	>512	2	0.25	0.5	1	0.5	0.5	4	4	2	1	8	7	Lab-1
Lot 3	14203	3	7/7/2014	0.5	0.06	>512	2	0.12	0.25	1	0.12	0.5	4	1	1	0.5	0.5	7	Lab-1
Lot 3	14203	4	7/9/2014	0.5	0.06	>512	2	0.5	0.25	1	0.25	1	>4	2	2	1	1	7	Lab-1
Lot 3	14203	5	7/14/2014	0.5	0.06	>512	1	1	0.25	1	0.12	0.5	4	1	2	0.5	0.5	7	Lab-1
Lot 3	14203	6	7/16/2014	0.5	0.06	128	2	0.06	0.5	1	0.25	0.5	4	1	1	1	4	7	Lab-1
Lot 3	14203	7	7/17/2014	0.5	0.06	>512	2	0.06	0.25	1	0.12	2	>4	1	2	0.5	0.5	7	Lab-1
Lot 3	14203	8	7/23/2014	0.5	0.06	>512	2	0.06	0.25	0.5	0.12	2	>4	1	2	1	8	7	Lab-1
Lot 3	14203	9	7/24/2014	0.5	0.06	>512	2	0.06	0.5	1	0.25	1	>4	1	2	0.5	1	7	Lab-1
Lot 3	14203	10	7/25/2014	0.5	0.12	>512	1	0.5	0.5	1	0.25	1	>4	4	1	0.5	0.5	7	Lab-1
Lot 3	14203	11	7/29/2014	0.5	0.06	>512	2	0.06	0.5	2	0.25	1	>4	1	1	0.5	0.5	7	Lab-1
Lot 3	14203	12	7/30/2014	0.5	0.06	>512	2	0.06	0.5	1	0.25	>2	>4	2	2	1	0.5	7	Lab-1
Lot 1	14181	1	8/5/2014	0.06	0.5	128	1	0.12	0.5	1	0.25	0.5	4	2	2	1	1	10	Lab-2
Lot 1	14181	2	8/5/2014	0.06	0.12	64	0.5	0.12	0.5	0.5	0.12	1	>4	1	2	0.5	1	10	Lab-2

Media Lot No	Supplier's Lot No	DST No	Date of DST	INH	RMP	NIC	LZD	CFZ	LVX	OFX	MXF	PTH	ETH	CAP	KAN	AMI	EMB	Day Read	Lab ID
Lot 1	14181	3	8/5/2014	0.06	0.12	64	0.5	0.12	0.5	0.5	0.25	1	>4	2	2	1	1	10	Lab-2
Lot 1	14181	4	8/5/2014	0.06	0.12	64	1	0.12	0.5	1	0.25	2	>4	2	2	0.5	1	10	Lab-2
Lot 1	14181	5	8/7/2014	0.06	0.12	128	1	0.25	0.5	0.5	0.25	>2	>4	2	2	1	1	10	Lab-2
Lot 1	14181	6	8/7/2014	0.12	0.12	128	1	0.25	0.5	1	0.25	2	>4	2	2	1	1	10	Lab-2
Lot 1	14181	7	8/7/2014	0.12	0.12	256	1	0.25	0.5	1	0.25	1	4	2	2	1	1	10	Lab-2
Lot 1	14181	8	8/18/2014	0.06	0.12	128	1	0.12	0.5	1	0.25	2	>4	1	2	1	1	10	Lab-2
Lot 1	14181	9	8/18/2014	0.06	0.12	128	0.5	0.12	0.5	1	0.25	2	>4	2	2	1	1	10	Lab-2
Lot 1	14181	10	8/18/2014	0.06	0.12	128	0.5	0.12	0.5	1	0.25	2	>4	2	2	0.5	1	10	Lab-2
Lot 2	14202	1	8/5/2014	0.12	0.12	256	1	0.12	0.5	1	0.25	1	2	1	1	0.5	1	10	Lab-2
Lot 2	14202	2	8/5/2014	0.12	0.25	512	1	0.12	0.5	1	0.25	1	4	1	0.5	0.5	1	10	Lab-2
Lot 2	14202	3	8/5/2014	0.12	0.25	256	0.5	0.12	0.5	1	0.12	1	4	1	0.5	0.5	1	10	Lab-2
Lot 2	14202	4	8/5/2014	0.12	0.12	128	0.5	0.12	0.5	1	0.25	1	4	1	0.5	0.5	1	10	Lab-2
Lot 2	14202	5	8/7/2014	0.25	0.12	128	1	0.25	0.5	1	0.25	1	4	1	1	1	1	10	Lab-2
Lot 2	14202	6	8/7/2014	0.12	0.25	256	1	0.25	0.5	1	0.25	2	4	1	1	0.5	1	10	Lab-2
Lot 2	14202	7	8/7/2014	0.12	0.25	512	1	0.25	0.5	1	0.25	2	2	1	1	0.5	1	10	Lab-2
Lot 2	14202	8	8/18/2014	0.12	0.12	256	1	0.12	0.5	1	0.25	1	4	1	1	0.5	1	10	Lab-2
Lot 2	14202	9	8/18/2014	0.12	0.12	256	0.5	0.12	0.5	1	0.25	2	4	1	1	0.5	1	10	Lab-2
Lot 2	14202	10	8/18/2014	0.12	0.12	256	1	0.12	0.5	1	0.25	2	4	1	1	0.5	1	10	Lab-2
Lot 3	14203	1	8/5/2014	1	0.25	256	0.5	0.12	0.5	0.5	0.12	>2	>4	0.5	1	0.5	0.5	10	Lab-2
Lot 3	14203	2	8/5/2014	0.5	0.12	128	0.5	0.12	0.25	0.5	0.25	2	>4	0.5	0.5	0.5	0.5	10	Lab-2
Lot 3	14203	3	8/5/2014	1	0.12	256	0.5	0.12	0.25	1	0.25	>2	>4	0.5	1	0.5	1	10	Lab-2

Media Lot No	Supplier's Lot No	DST No	Date of DST	INH	RMP	NIC	LZD	CFZ	LVX	OFX	MXF	PTH	ETH	CAP	KAN	AMI	EMB	Day Read	Lab ID
Lot 3	14203	4	8/5/2014	1	0.12	256	0.5	0.12	0.5	0.5	0.25	>2	>4	1	1	0.5	1	10	Lab-2
Lot 3	14203	5	8/7/2014	0.5	0.12	256	1	0.25	0.5	1	0.25	2	>4	1	1	1	1	10	Lab-2
Lot 3	14203	6	8/7/2014	0.5	0.12	512	0.5	0.25	0.5	1	0.25	2	>4	1	1	0.5	0.5	10	Lab-2
Lot 3	14203	7	8/7/2014	1	0.12	>512	0.5	0.12	0.25	0.5	0.25	1	4	1	2	0.5	0.5	10	Lab-2
Lot 3	14203	8	8/18/2014	0.5	0.12	512	0.5	0.12	0.5	0.5	0.25	>2	>4	2	1	0.5	0.5	10	Lab-2
Lot 3	14203	9	8/18/2014	0.5	0.12	128	0.5	0.12	0.5	1	0.12	2	>4	1	1	0.5	0.5	10	Lab-2
Lot 3	14203	10	8/18/2014	0.5	0.12	256	0.5	0.12	0.5	0.5	0.25	2	4	1	1	0.5	1	10	Lab-2
Lot 1	14181	1	9/2/2014	0.06	0.12	64	0.5	0.12	0.25	0.5	0.12	0.5	2	1	4	1	1	10	Lab-3
Lot 1	14181	2	9/2/2014	0.06	0.06	128	0.5	0.06	0.25	0.5	0.12	1	4	1	4	1	1	10	Lab-3
Lot 1	14181	3	9/2/2014	0.06	0.06	64	0.5	0.06	0.25	0.5	0.12	1	4	1	2	1	1	10	Lab-3
Lot 1	14181	4	9/2/2014	0.06	0.06	128	0.5	0.06	0.25	0.5	0.12	1	4	1	2	1	1	10	Lab-3
Lot 1	14181	5	9/2/2014	0.06	0.06	128	0.5	0.06	0.25	0.5	0.12	1	4	1	2	1	1	10	Lab-3
Lot 1	14181	6	9/2/2014	0.06	0.06	128	0.5	0.06	0.25	0.5	0.12	1	4	1	2	1	1	10	Lab-3
Lot 1	14181	7	9/2/2014	0.06	0.12	128	0.5	0.06	0.25	0.5	0.12	1	4	2	2	1	1	10	Lab-3
Lot 1	14181	8	9/2/2014	0.06	0.06	64	0.5	0.06	0.25	0.5	0.12	1	2	1	2	1	1	10	Lab-3
Lot 1	14181	9	9/2/2014	0.06	0.06	128	0.5	0.06	0.25	0.5	0.12	1	4	1	2	1	1	10	Lab-3
Lot 1	14181	10	9/2/2014	0.06	0.06	128	0.5	0.06	0.25	0.5	0.12	0.5	2	1	2	1	1	10	Lab-3
Lot 2	14202	1	9/4/2014	0.12	0.06	>512	0.5	0.06	0.25	0.5	0.12	0.5	1	1	1	0.5	0.5	10	Lab-3
Lot 2	14202	2	9/4/2014	0.12	0.12	128	0.5	0.06	0.25	0.5	0.12	0.5	2	0.5	1	0.5	0.5	10	Lab-3
Lot 2	14202	3	9/4/2014	0.12	0.12	>512	0.5	0.12	0.25	0.5	0.12	0.5	2	0.5	1	0.5	0.5	10	Lab-3
Lot 2	14202	4	9/4/2014	0.12	0.12	>512	0.5	0.12	0.25	0.5	0.12	0.5	1	1	1	0.5	0.5	10	Lab-3

Media Lot No	Supplier's Lot No	DST No	Date of DST	INH	RMP	NIC	LZD	CFZ	LVX	OFX	MXF	PTH	ETH	CAP	KAN	AMI	EMB	Day Read	Lab ID
Lot 2	14202	5	9/4/2014	0.12	0.06	>512	0.5	0.06	0.25	0.5	0.12	0.5	2	0.5	1	0.5	0.5	10	Lab-3
Lot 2	14202	6	9/9/2014	0.12	0.25	256	0.5	0.12	0.5	0.5	0.25	0.5	2	1	1	0.5	1	10	Lab-3
Lot 2	14202	7	9/9/2014	0.12	0.12	256	0.5	0.12	0.25	0.5	0.12	0.25	2	1	1	0.5	0.5	10	Lab-3
Lot 2	14202	8	9/9/2014	0.12	0.25	512	0.5	0.12	0.25	0.5	0.12	0.5	2	1	1	0.5	0.5	10	Lab-3
Lot 2	14202	9	9/9/2014	0.12	0.12	256	0.5	0.06	0.25	0.5	0.12	0.25	1	1	1	0.5	0.5	10	Lab-3
Lot 2	14202	10	9/9/2014	0.12	0.25	512	0.5	0.06	0.25	0.5	0.25	0.5	1	1	1	0.5	0.5	10	Lab-3
Lot 3	14203	1	9/4/2014	0.12	0.12	512	0.5	0.12	0.25	0.5	0.12	0.5	2	0.5	2	0.5	0.5	10	Lab-3
Lot 3	14203	2	9/4/2014	0.12	0.12	512	0.5	0.12	0.25	0.5	0.12	0.5	2	1	2	0.5	0.5	10	Lab-3
Lot 3	14203	3	9/4/2014	0.12	0.06	512	0.5	0.06	0.25	0.5	0.12	0.5	2	0.5	1	0.5	0.5	10	Lab-3
Lot 3	14203	4	9/4/2014	0.12	0.06	512	0.5	0.06	0.25	0.5	0.12	1	2	0.5	1	0.5	0.5	10	Lab-3
Lot 3	14203	5	9/4/2014	0.12	0.06	512	0.5	0.06	0.25	0.5	0.12	0.5	2	0.5	1	0.5	0.5	10	Lab-3
Lot 3	14203	6	9/4/2014	0.12	0.06	256	0.25	0.06	0.25	0.5	0.12	0.5	2	0.5	1	0.25	0.5	10	Lab-3
Lot 3	14203	7	9/4/2014	0.12	0.06	512	0.5	0.06	0.25	0.5	0.12	0.5	2	0.5	1	0.5	0.5	10	Lab-3
Lot 3	14203	8	9/4/2014	0.12	0.12	256	0.5	0.06	0.25	0.5	0.12	0.5	2	0.5	1	0.5	0.5	10	Lab-3
Lot 3	14203	9	9/4/2014	0.12	0.12	512	0.5	0.06	0.25	0.5	0.12	0.5	2	0.5	1	0.5	0.5	10	Lab-3
Lot 3	14203	10	9/4/2014	0.12	0.06	512	0.5	0.06	0.25	0.5	0.12	0.5	0.5	0.5	1	0.5	0.5	10	Lab-3
Lot 1	14181	1	8/29/2014	<0.03	0.12	>512	1	0.12	0.5	1	0.5	2	>4	2	2	1	1	10	Lab-4
Lot 1	14181	2	8/29/2014	0.06	0.25	>512	0.5	0.25	0.5	0.5	0.25	1	>4	1	2	0.5	1	10	Lab-4
Lot 1	14181	3	8/29/2014	<0.03	0.12	>512	2	0.12	0.5	1	0.5	1	4	4	2	0.5	2	10	Lab-4
Lot 1	14181	4	9/1/2014	0.06	0.12	>512	2	0.12	1	1	0.5	>2	>4	2	2	1	2	10	Lab-4
Lot 1	14181	5	9/1/2014	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	10	Lab-4

Media Lot No	Supplier's Lot No	DST No	Date of DST	INH	RMP	NIC	LZD	CFZ	LVX	OFX	MXF	PTH	ETH	CAP	KAN	AMI	EMB	Day Read	Lab ID
Lot 1	14181	6	9/1/2014	0.06	0.12	>512	1	0.12	0.5	1	0.5	1	4	1	1	1	2	10	Lab-4
Lot 1	14181	7	9/5/2014	0.06	0.12	256	1	0.12	0.25	1	0.5	2	4	2	1	1	1	10	Lab-4
Lot 1	14181	8	9/5/2014	<0.03	0.12	64	1	0.12	0.5	1	0.25	1	2	2	1	0.5	1	10	Lab-4
Lot 1	14181	9	9/5/2014	0.06	0.12	>512	1	0.12	0.5	1	0.25	2	4	2	1	1	1	10	Lab-4
Lot 1	14181	10	9/5/2014	0.06	0.12	>512	1	0.12	0.5	1	0.25	2	4	1	2	1	>8	10	Lab-4
Lot 2	14202	1	8/29/2014	0.06	0.25	512	0.5	0.25	0.5	0.5	0.25	2	4	0.5	<0.12	0.5	0.5	10	Lab-4
Lot 2	14202	2	8/29/2014	0.06	0.25	>512	0.5	0.12	0.5	1	0.25	1	4	2	1	1	0.5	10	Lab-4
Lot 2	14202	3	8/29/2014	0.06	0.25	>512	0.5	0.12	0.5	1	0.25	1	2	2	0.25	0.25	1	10	Lab-4
Lot 2	14202	4	9/1/2014	0.06	0.25	>512	0.5	0.25	0.5	0.5	0.5	1	4	1	0.5	0.5	4	10	Lab-4
Lot 2	14202	5	9/1/2014	0.06	0.25	>512	1	0.5	0.5	1	0.5	1	4	2	1	0.5	1	10	Lab-4
Lot 2	14202	6	9/1/2014	0.06	0.25	>512	2	0.12	0.5	1	0.5	2	4	2	1	0.5	1	10	Lab-4
Lot 2	14202	7	9/5/2014	0.06	0.12	256	0.5	0.12	0.5	1	0.25	0.5	0.5	1	0.25	<0.12	0.5	10	Lab-4
Lot 2	14202	8	9/5/2014	0.06	0.12	>512	0.5	0.12	0.5	1	0.5	1	2	1	0.25	0.25	0.5	10	Lab-4
Lot 2	14202	9	9/5/2014	0.06	0.12	512	1	0.12	0.5	1	0.25	1	1	1	0.5	0.5	1	10	Lab-4
Lot 2	14202	10	9/5/2014	0.06	0.25	512	2	0.12	0.5	1	0.5	1	4	2	1	1	1	10	Lab-4
Lot 3	14203	1	8/29/2014	0.5	0.25	>512	1	0.5	0.25	1	0.12	2	>4	1	0.5	0.25	1	10	Lab-4
Lot 3	14203	2	8/29/2014	0.5	0.25	>512	0.5	0.25	0.25	1	0.12	2	>4	0.5	0.5	0.25	1	10	Lab-4
Lot 3	14203	3	8/29/2014	0.5	0.12	>512	0.5	<0.06	0.25	1	0.25	2	>4	2	1	0.25	1	10	Lab-4
Lot 3	14203	4	9/1/2014	0.5	0.25	>512	1	0.12	0.25	1	0.25	2	>4	2	1	0.5	1	10	Lab-4
Lot 3	14203	5	9/1/2014	0.5	0.25	>512	1	0.12	0.5	1	0.25	>2	>4	2	1	0.5	2	10	Lab-4
Lot 3	14203	6	9/1/2014	0.5	0.12	>512	1	0.12	0.25	1	0.25	2	4	2	1	0.5	1	10	Lab-4

Media Lot No	Supplier's Lot No	DST No	Date of DST	INH	RMP	NIC	LZD	CFZ	LVX	OFX	MXF	PTH	ETH	CAP	KAN	AMI	EMB	Day Read	Lab ID
Lot 3	14203	7	9/5/2014	0.5	0.12	>512	0.5	0.06	0.25	0.5	0.25	1	4	4	0.25	0.25	2	10	Lab-4
Lot 3	14203	8	9/5/2014	0.5	0.12	>512	0.25	<0.06	0.25	1	0.25	1	>4	1	1	0.25	0.5	10	Lab-4
Lot 3	14203	9	9/5/2014	0.5	0.12	>512	0.5	0.12	0.25	1	0.25	2	4	2	0.25	0.5	0.5	10	Lab-4
Lot 3	14203	10	9/5/2014	0.5	0.12	>512	1	0.12	0.25	1	0.25	1	4	1	1	0.5	1	10	Lab-4
Lot 1	14181	1	8/20/2014	0.06	0.06	512	1	0.06	0.25	1	0.25	0.5	2	1	2	0.25	1	10	Lab-5
Lot 1	14181	2	8/20/2014	0.25	0.12	512	0.5	0.06	0.12	2	0.12	0.5	0.5	1	2	0.12	0.25	10	Lab-5
Lot 1	14181	3	8/20/2014	0.06	0.06	512	0.5	0.12	0.5	1	0.25	0.25	2	0.5	2	1	1	10	Lab-5
Lot 1	14181	4	8/20/2014	0.12	0.25	512	0.5	0.12	0.5	1	0.25	1	4	1	2	1	1	10	Lab-5
Lot 1	14181	5	8/20/2014	0.12	0.12	512	0.5	0.06	0.5	1	0.25	0.5	2	1	2	0.5	1	10	Lab-5
Lot 1	14181	6	8/20/2014	0.06	0.12	256	0.5	0.06	0.25	0.5	0.12	0.25	2	1	2	0.5	2	10	Lab-5
Lot 1	14181	7	8/20/2014	0.06	0.12	>512	0.5	0.06	0.5	1	0.25	0.5	4	1	2	1	1	10	Lab-5
Lot 1	14181	8	8/20/2014	0.06	0.12	>512	0.5	0.12	0.5	0.5	0.25	0.5	2	1	2	0.5	1	10	Lab-5
Lot 1	14181	9	8/20/2014	0.06	0.12	512	0.5	0.06	0.5	1	0.25	1	2	1	2	0.5	0.5	10	Lab-5
Lot 1	14181	10	8/20/2014	0.06	0.25	512	0.5	0.06	0.5	1	0.25	0.25	4	1	2	0.5	1	10	Lab-5
Lot 2	14202	1	8/22/2014	0.06	0.25	>512	0.5	0.06	0.25	0.5	0.25	0.5	1	0.25	0.25	0.12	0.5	10	Lab-5
Lot 2	14202	2	8/22/2014	0.06	0.25	512	0.5	0.06	0.25	0.5	0.25	0.25	1	0.5	0.25	0.12	0.5	10	Lab-5
Lot 2	14202	3	8/22/2014	0.06	0.25	512	0.5	0.06	0.5	1	0.25	0.25	0.5	0.5	0.25	0.25	0.5	10	Lab-5
Lot 2	14202	4	8/22/2014	0.12	0.12	>512	0.5	0.06	0.5	1	0.25	0.25	1	0.5	0.25	0.25	0.5	10	Lab-5
Lot 2	14202	5	8/22/2014	0.06	0.12	512	0.5	0.12	0.25	0.5	0.25	0.25	1	0.5	0.25	0.25	0.5	10	Lab-5
Lot 2	14202	6	8/22/2014	0.12	0.25	>512	0.5	0.12	0.5	1	0.25	0.25	1	0.5	0.25	0.25	0.5	10	Lab-5
Lot 2	14202	7	8/22/2014	0.12	0.25	256	0.5	0.12	0.5	1	0.25	0.5	1	0.5	0.25	0.25	0.5	10	Lab-5

Media Lot No	Supplier's Lot No	DST No	Date of DST	INH	RMP	NIC	LZD	CFZ	LVX	OFX	MXF	PTH	ETH	CAP	KAN	AMI	EMB	Day Read	Lab ID
Lot 2	14202	8	8/22/2014	0.12	0.25	512	0.5	0.06	0.5	1	0.25	0.25	1	0.5	0.25	0.25	0.5	10	Lab-5
Lot 2	14202	9	8/22/2014	0.12	0.25	>512	0.5	0.12	0.5	0.5	0.25	0.25	1	0.5	0.25	0.25	0.5	10	Lab-5
Lot 2	14202	10	8/22/2014	0.12	0.25	>512	0.5	0.12	0.5	1	0.25	0.25	1	0.5	0.5	0.25	0.5	10	Lab-5
Lot 3	14203	1	8/22/2014	0.5	0.12	>512	0.5	0.06	0.25	0.5	0.12	0.25	2	0.5	0.25	0.25	0.5	10	Lab-5
Lot 3	14203	2	8/22/2014	0.5	0.06	512	0.5	0.12	0.25	0.5	0.12	0.5	2	0.5	0.25	0.25	0.5	10	Lab-5
Lot 3	14203	3	8/22/2014	0.5	0.12	512	0.5	0.06	0.25	0.5	0.12	0.5	2	0.5	0.25	0.25	0.5	10	Lab-5
Lot 3	14203	4	8/22/2014	0.5	0.12	512	0.5	0.12	0.25	1	0.12	0.5	2	0.5	0.25	0.25	0.5	10	Lab-5
Lot 3	14203	5	8/22/2014	0.5	0.12	512	0.5	0.12	0.25	0.5	0.12	0.5	2	0.5	0.5	0.25	0.5	10	Lab-5
Lot 3	14203	6	8/22/2014	0.5	0.12	512	0.5	0.06	0.25	0.5	0.12	0.5	2	0.5	0.25	0.25	0.5	10	Lab-5
Lot 3	14203	7	8/22/2014	0.5	0.12	>512	0.5	0.12	0.25	1	0.25	0.5	2	1	0.5	0.25	0.5	10	Lab-5
Lot 3	14203	8	8/22/2014	0.5	0.12	>512	0.5	0.12	0.25	0.5	0.12	0.5	2	0.5	0.5	0.25	0.5	10	Lab-5
Lot 3	14203	9	8/22/2014	0.5	0.12	256	0.5	0.12	0.25	1	0.25	0.5	2	1	0.25	0.25	0.5	10	Lab-5
Lot 3	14203	10	8/22/2014	0.5	0.12	>512	0.5	0.12	0.25	0.5	0.12	0.5	2	0.5	0.25	0.25	0.5	10	Lab-5
Lot 1	14181	1	9/26/2014	0.06	0.12	256	1	≤ 0.06	0.5	0.5	0.25	> 2	> 4	2	2	1	1	10	Lab-6
Lot 1	14181	2	9/26/2014	0.06	0.25	128	1	≤ 0.06	0.5	1	0.25	> 2	> 4	2	2	1	1	10	Lab-6
Lot 1	14181	3	9/26/2014	0.06	0.25	256	1	≤ 0.06	0.5	1	0.25	> 2	> 4	2	2	1	1	10	Lab-6
Lot 1	14181	4	9/26/2014	≤ 0.03	0.25	128	0.5	≤ 0.06	0.25	1	0.12	1	> 4	2	2	1	1	10	Lab-6
Lot 1	14181	5	9/26/2014	0.06	0.12	256	1	≤ 0.06	0.5	1	0.25	2	4	2	2	1	1	10	Lab-6

Media Lot No	Supplier's Lot No	DST No	Date of DST	INH	RMP	NIC	LZD	CFZ	LVX	OFX	MXF	PTH	ETH	CAP	KAN	AMI	EMB	Day Read	Lab ID
Lot 1	14181	6	9/26/2014	0.06	0.12	256	1	≤ 0.06	0.5	1	0.25	> 2	> 4	2	2	1	2	10	Lab-6
Lot 1	14181	7	9/26/2014	≤ 0.03	0.12	64	0.5	≤ 0.06	0.5	1	0.25	> 2	> 4	2	2	0.5	2	10	Lab-6
Lot 1	14181	8	9/26/2014	0.06	0.12	64	1	≤ 0.06	0.5	1	0.12	> 2	> 4	2	1	0.5	1	10	Lab-6
Lot 1	14181	9	9/26/2014	0.06	0.12	64	1	≤ 0.06	0.5	1	0.25	> 2	> 4	2	2	1	1	10	Lab-6
Lot 1	14181	10	9/26/2014	0.06	0.25	128	1	≤ 0.06	0.5	2	0.25	> 2	> 4	2	2	1	4	10	Lab-6
Lot 2	14202	1	9/22/2014	0.06	0.25	> 512	1	0.12	1	1	0.25	1	4	2	1	0.5	1	10	Lab-6
Lot 2	14202	2	9/22/2014	0.06	0.12	> 512	0.5	≤ 0.06	0.5	1	0.25	1	4	2	0.5	0.5	1	10	Lab-6
Lot 2	14202	3	9/22/2014	0.06	0.25	512	0.5	≤ 0.06	0.5	1	0.25	1	4	2	0.5	0.5	1	10	Lab-6
Lot 2	14202	4	9/22/2014	0.06	0.25	> 512	1	≤ 0.06	0.5	1	0.25	1	4	2	0.5	1	1	10	Lab-6
Lot 2	14202	5	9/22/2014	0.06	0.12	> 512	0.5	≤ 0.06	0.5	1	0.25	1	4	1	1	0.5	1	10	Lab-6
Lot 2	14202	6	9/22/2014	0.12	0.25	256	1	0.12	0.5	1	0.25	2	> 4	2	1	1	2	10	Lab-6
Lot 2	14202	7	9/22/2014	0.12	0.25	128	0.5	0.06	0.5	1	0.25	2	> 4	2	1	0.5	1	10	Lab-6
Lot 2	14202	8	9/22/2014	0.12	0.25	128	2	≤ 0.06	1	1	0.5	> 2	> 4	2	1	0.5	1	10	Lab-6
Lot 2	14202	9	9/22/2014	0.06	0.5	256	1	0.06	0.5	1	0.25	2	> 4	2	1	0.5	2	10	Lab-6
Lot 2	14202	10	9/22/2014	0.06	0.5	128	2	0.06	0.5	1	0.25	> 2	> 4	2	1	2	1	10	Lab-6

Media Lot No	Supplier's Lot No	DST No	Date of DST	INH	RMP	NIC	LZD	CFZ	LVX	OFX	MXF	PTH	ETH	CAP	KAN	AMI	EMB	Day Read	Lab ID
Lot 3	14203	1	9/29/2014	0.5	0.25	> 512	0.5	≤ 0.06	0.25	0.5	0.12	> 2	> 4	2	1	0.5	1	10	Lab-6
Lot 3	14203	2	9/29/2014	0.5	0.25	256	0.5	≤ 0.06	0.25	1	0.12	> 2	> 4	2	1	0.5	0.5	10	Lab-6
Lot 3	14203	3	9/29/2014	0.5	0.25	512	0.5	0.12	0.25	0.5	0.12	> 2	> 4	2	1	0.5	1	10	Lab-6
Lot 3	14203	4	9/29/2014	0.5	0.25	> 512	0.5	0.12	0.25	0.5	0.12	> 2	> 4	1	1	0.5	0.5	10	Lab-6
Lot 3	14203	5	9/29/2014	0.5	0.25	> 512	0.5	≤ 0.06	0.25	0.5	0.12	> 2	> 4	1	1	0.5	0.5	10	Lab-6
Lot 3	14203	6	9/29/2014	0.5	0.12	128	0.5	≤ 0.06	0.5	1	0.25	> 2	> 4	2	1	0.25	1	10	Lab-6
Lot 3	14203	7	9/29/2014	0.5	0.12	64		≤ 0.06	0.25		0.12	> 2	> 4	2	1	0.5	1	10	Lab-6
Lot 3	14203	8	9/29/2014	0.5	0.12	128	0.5	≤ 0.06	0.5	1	0.25	> 2	> 4	2	1	1	1	10	Lab-6
Lot 3	14203	9	9/29/2014	0.5	0.12	128	0.5	≤ 0.06	1	1	0.25	> 2	> 4	1	1	0.5	0.5	10	Lab-6
Lot 3	14203	10	9/29/2014	0.5	0.12	256	0.5	≤ 0.06	0.5	1	0.25	> 2	> 4	1	0.5	0.25	0.5	10	Lab-6
Lot 1	14181	1	9/29/2014	0.12	0.06	512	0.5	0.06	0.25	0.5	0.06	1	4	2	1	1	0.5	10	Lab-7
Lot 1	14181	2	9/29/2014	0.03	0.06	512	0.5	0.06	0.25	0.5	0.06	2	4	2	4	2	1	10	Lab-7
Lot 1	14181	3	9/29/2014	0.03	0.06	512	2	0.06	0.5	0.5	0.06	2	4	4	4	1	1	10	Lab-7
Lot 1	14181	4	9/29/2014	0.06	0.06	512	0.5	0.06	0.25	1	0.12	2	4	2	4	1	1	10	Lab-7
Lot 1	14181	5	9/29/2014	0.06	0.06	64	0.5	0.06	0.5	1	0.06	2	4	2	2	1	2	10	Lab-7
Lot 1	14181	6	9/30/2014	0.06	0.06	512	1	0.06	0.5	0.5	0.12	2	4	1	2	1	2	10	Lab-7

Media Lot No	Supplier's Lot No	DST No	Date of DST	INH	RMP	NIC	LZD	CFZ	LVX	OFX	MXF	PTH	ETH	CAP	KAN	AMI	EMB	Day Read	Lab ID
Lot 1	14181	7	9/30/2014	0.06	0.06	512	1	0.06	0.5	1	0.06	2	4	4	4	2	4	10	Lab-7
Lot 1	14181	8	9/30/2014	0.06	0.06	512	0.5	0.06	0.25	0.5	0.06	1	4	2	1	1	0.5	10	Lab-7
Lot 1	14181	9	9/30/2014	0.03	0.06	512	1	0.06	0.25	1	0.12	2	4	2	4	1	2	10	Lab-7
Lot 1	14181	10	9/30/2014	0.06	0.06	512	0.5	0.06	0.25	0.5	0.06	2	4	2	2	1	1	10	Lab-7
Lot 2	14202	1	9/29/2014	0.06	0.06	512	0.5	0.06	0.25	1	0.06	1	4	2	1	0.5	0.5	10	Lab-7
Lot 2	14202	2	9/29/2014	0.12	0.06	512	0.5	0.06	0.25	0.5	0.06	2	4	2	2	1	0.5	10	Lab-7
Lot 2	14202	3	9/29/2014	0.06	0.06	512	1	0.06	0.5	1	0.06	2	4	2	4	1	1	10	Lab-7
Lot 2	14202	4	9/29/2014	0.06	0.06	512	1	0.06	0.5	1	0.06	1	4	1	2	1	0.5	10	Lab-7
Lot 2	14202	5	9/29/2014	0.06	0.06	512	1	0.06	0.25	0.5	0.06	1	4	1	2	0.5	0.5	10	Lab-7
Lot 2	14202	6	9/30/2014	0.06	0.06	512	1	0.06	0.5	1	0.12	2	4	2	2	1	1	10	Lab-7
Lot 2	14202	7	9/30/2014	0.06	0.06	512	0.5	0.06	0.25	1	0.06	2	4	2	2	0.5	0.5	10	Lab-7
Lot 2	14202	8	9/30/2014	0.06	0.06	512	1	0.06	0.25	1	0.06	1	2	2	4	1	0.25	10	Lab-7
Lot 2	14202	9	9/30/2014	0.06	0.06	512	1	0.06	0.25	1	0.06	1	4	1	2	2	1	10	Lab-7
Lot 2	14202	10	9/30/2014	0.06	0.06	512	0.5	0.06	0.25	1	0.06	1	4	2	2	0.5	1	10	Lab-7
Lot 3	14203	1	9/29/2014	0.25	0.06	512	1	0.06	0.25	1	0.06	2	2	1	2	0.5	1	10	Lab-7
Lot 3	14203	2	9/29/2014	0.12	0.06	512	0.5	0.06	0.25	0.5	0.06	2	4	2	2	2	1	10	Lab-7
Lot 3	14203	3	9/29/2014	0.12	0.06	512	0.5	0.06	0.25	1	0.06	2	4	1	2	0.5	1	10	Lab-7
Lot 3	14203	4	9/29/2014	0.25	0.06	512	1	0.06	1	0.5	0.06	2	4	2	2	1	2	10	Lab-7
Lot 3	14203	5	9/29/2014	0.25	0.06	512	1	0.06	0.25	1	0.12	2	4	2	2	0.5	1	10	Lab-7
Lot 3	14203	6	9/30/2014	0.25	0.06	512	1	0.06	0.25	1	0.06	4	2	0.5	2	1	1	10	Lab-7
Lot 3	14203	7	9/30/2014	0.06	0.06	512	0.5	0.06	0.25	1	0.06	2	4	2	2	0.5	0.5	10	Lab-7

Media Lot No	Supplier's Lot No	DST No	Date of DST	INH	RMP	NIC	LZD	CFZ	LVX	OFX	MXF	PTH	ETH	CAP	KAN	AMI	EMB	Day Read	Lab ID
Lot 3	14203	8	9/30/2014	0.12	0.06	512	0.5	0.06	0.25	0.5	0.06	1	1	2	2	1	0.5	10	Lab-7
Lot 3	14203	9	9/30/2014	0.25	0.06	512	1	0.06	0.25	1	0.06	2	4	2	2	1	1	10	Lab-7
Lot 3	14203	10	9/30/2014	0.25	0.06	512	1	0.06	0.12	0.5	0.06	2	4	0.5	4	0.5	0.5	10	Lab-7
Lot 1	14181	1	8/13/2014	0.06	<0.06	128	0.5	<0.06	0.5	0.5	0.25	1	4	2	2	0.5	1	14	Lab-8
Lot 1	14181	2	8/20/2014	0.06	<0.06	>512	1	<0.06	0.5	0.5	0.25	0.5	2	2	2	1	1	14	Lab-8
Lot 1	14181	3	8/27/2014	0.06	<0.06	>512	1	<0.06	0.25	0.5	0.12	0.5	>4	2	2	1	1	14	Lab-8
Lot 1	14181	4	9/3/2014	0.06	<0.06	128	1	<0.06	0.5	0.5	0.25	0.5	>4	2	2	1	1	14	Lab-8
Lot 1	14181	5	9/4/2014	0.12	<0.06	>512	1	0.25	0.5	1	<0.06	1	>4	2	2	1	1	14	Lab-8
Lot 1	14181	6	9/11/2014	0.06	<0.06	>512	0.5	<0.06	0.5	0.5	0.25	0.5	2	2	2	1	1	14	Lab-8
Lot 1	14181	7	9/15/2014	0.06	<0.06	128	1	<0.06	0.5	0.5	0.25	0.5	>4	2	2	1	1	14	Lab-8
Lot 1	14181	8	9/24/2014	0.06	<0.06	128	0.5	<0.06	0.25	0.5	0.12	1	4	2	1	1	1	14	Lab-8
Lot 1	14181	9	10/2/2014	0.06	<0.06	>512	0.5	<0.06	0.25	0.5	0.12	1	>4	2	2	1	1	14	Lab-8
Lot 1	14181	10	10/9/2014	0.06	<0.06	128	1	<0.06	0.5	0.5	0.12	0.5	4	2	2	1	1	14	Lab-8
Lot 1	14181	11	10/12/2014	0.5	<0.06	>512	0.5	<0.06	<0.12	0.5	<0.06	1	2	0.5	1	0.25	0.5	14	Lab-8
Lot 2	14202	1	8/13/2014	0.12	<0.06	256	0.5	<0.06	0.25	0.5	0.12	1	4	2	2	1	1	14	Lab-8
Lot 2	14202	2	8/20/2014	0.06	<0.06	>512	0.5	<0.06	0.25	0.5	0.12	1	2	1	0.5	0.25	0.5	14	Lab-8
Lot 2	14202	3	8/27/2014	0.12	0.5	>512	1	<0.06	0.5	0.5	0.25	0.25	1	1	0.5	0.5	1	14	Lab-8
Lot 2	14202	4	9/3/2014	0.12	<0.06	>512	1	<0.06	0.25	1	0.12	0.5	1	1	<0.12	0.25	1	14	Lab-8
Lot 2	14202	5	9/4/2014	0.12	<0.06	512	1	0.12	0.5	1	0.25	1	1	1	1	0.5	1	14	Lab-8
Lot 2	14202	6	9/11/2014	0.12	<0.06	>512	1	0.25	0.5	1	0.25	0.5	1	2	0.5	0.5	1	14	Lab-8
Lot 2	14202	7	9/15/2014	0.12	<0.06	>512	1	0.12	0.5	1	0.25	0.5	1	1	0.5	0.25	1	14	Lab-8

Media Lot No	Supplier's Lot No	DST No	Date of DST	INH	RMP	NIC	LZD	CFZ	LVX	OFX	MXF	PTH	ETH	CAP	KAN	AMI	EMB	Day Read	Lab ID
Lot 2	14202	8	9/24/2014	0.12	<0.06	512	1	<0.06	0.5	1	0.25	1	2	1	0.5	0.5	1	14	Lab-8
Lot 2	14202	9	10/2/2014	0.12	<0.06	>512	1	<0.06	0.25	1	0.25	0.5		1	0.5	0.25	0.5	14	Lab-8
Lot 2	14202	10	10/9/2014	0.12	<0.06	>512	0.5	<0.06	0.25	0.5	0.12	0.25	1	1	0.5	0.5	0.5	14	Lab-8
Lot 2	14202	11	10/12/2014	1	0.12	>512	0.5	<0.06	0.25	0.5	0.12	0.5	0.25	1	0.5	0.25	0.5	14	Lab-8
Lot 3	14203	1	8/13/2014	0.12	<0.06	512	1	<0.06	0.5	1	0.25	0.5	2	1	<0.12	0.5	1	14	Lab-8
Lot 3	14203	2	8/20/2014	0.12	<0.06	>512	1	<0.06	0.25	0.5	0.25	0.5	1	1	0.5	0.5	1	14	Lab-8
Lot 3	14203	3	8/27/2014	0.5	<0.06	>512	0.5	<0.06	0.25	0.5	0.12	1	>4	1	1	0.5	0.5	14	Lab-8
Lot 3	14203	4	9/3/2014	0.5	<0.06	>512	0.5	<0.06	0.25	0.5	0.12	0.5	2	4	1	1	<0.25	14	Lab-8
Lot 3	14203	5	9/4/2014	1	<0.06	>512	1	<0.06	0.25	0.5	0.12	1	>4	0.5	1	0.25	0.5	14	Lab-8
Lot 3	14203	6	9/11/2014	1	<0.06	>512	0.5	<0.06	0.25	0.5	0.25	1	2	1	0.5	0.25	0.5	14	Lab-8
Lot 3	14203	7	9/15/2014	1	<0.06	>512	0.5	0.12	0.25	0.5	0.12	1	4	1	1	0.5	1	14	Lab-8
Lot 3	14203	8	9/24/2014	1	<0.06	>512	0.5	<0.06	0.25	0.5	0.12	0.5	2	1	0.5	0.25	0.5	14	Lab-8
Lot 3	14203	9	10/2/2014	1	<0.06	>512	0.5	<0.06	0.25	0.5	0.12	0.5	2	1	0.5	0.25	0.5	14	Lab-8
Lot 3	14203	10	10/9/2014	1	<0.06	>512	0.5	<0.06	0.25	0.5	0.12	1	2	0.5	0.5	0.25	0.5	14	Lab-8
Lot 3	14203	11	10/12/2014	1	<0.06	>512	0.5	<0.06	0.25	0.5	0.12	>2	>4	1	2	0.25	0.5	14	Lab-8

Figure S1. Isoniazid 7H9 broth MIC distribution against MTB H37Rv, by 96-well micro titer plate lot.

