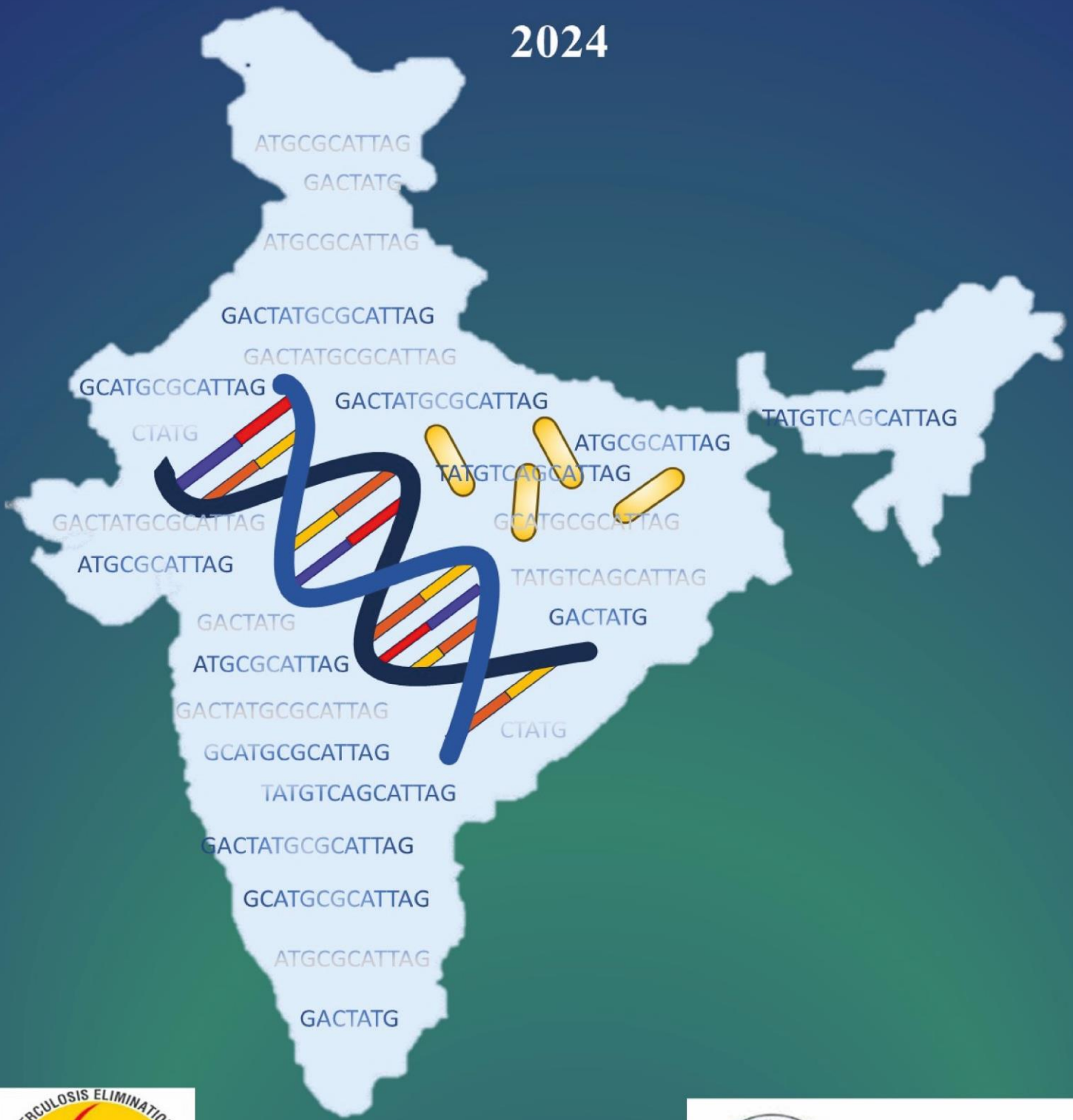
Indian Catalogue of *Mycobacterium tuberculosis* Mutations and their Association with Drug Resistance

Version 2.0

2024



NATIONAL TUBERCULOSIS ELIMINATION PROGRAMME
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NATIONAL INSTITUTE FOR RESEARCH IN TUBERCULOSIS

Contents

Abbreviations

CC	Critical Concentration
CI	Confidence Interval
CTAB	Cetyl TrimethylAmmonium Bromide
CRyPTIC	Comprehensive Resistance Prediction for Tuberculosis: an International Consortium
DNA	Deoxyribo Nucleic Acid
DST	Drug Susceptibility Testing
FDR	False Discovery Rate
FMR	The Foundation for Medical Research
gDST	Genotypic Drug Susceptibility Testing
indel	Insertion/ Deletion
lb	Lower Bound
MDR-TB	Multi-Drug Resistant TB
MGIT	Mycobacteria Growth Indicator Tube
MICs	Minimum Inhibitory Concentrations
MTB	*Mycobacterium tuberculosis*
MTBC	*Mycobacterium Tuberculosis* Complex
NA	Not Available
NGS	Next Generation Sequencing
NTEP	National Tuberculosis Elimination Program
OR	Odds Ratio
OR SOLO	Odds Ratio of SOLO Mutation
pDST	phenotypic Drug Susceptibility Testing
PPV	Positive Predictive Value
RRDR	Rifampicin Resistance-Determining Region
TB	Tuberculosis
ub	Upper Bound
WGS	Whole Genome Sequencing
WHO	World Health Organization

Drugs

AMK	Amikacin
CAP	Capreomycin
EMB	Ethambutol
ETO	Ethionamide
INH	Isoniazid
KAN	Kanamycin
LFX	Levofloxacin
LZD	Linezolid
MFX	Moxifloxacin
OFX	Ofloxacin
PAS	para-amino salicylic acid
PZA	Pyrazinamide
RIF	Rifampicin
STM	Streptomycin

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ICMR-NIRT

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NTEP: National Tuberculosis Elimination Program

Introduction

Tuberculosis remains a significant global public health concern, profoundly impacting morbidity and mortality. According to the World Health Organization (WHO), in 2020, an estimated 10 million people worldwide contracted tuberculosis, with 1.4 million succumbing to the disease. Although substantial progress has been achieved in recent years, challenges such as drug-resistant tuberculosis and the repercussions of the COVID-19 pandemic have impeded disease control efforts. India, in particular, bears a substantial burden of tuberculosis cases, representing approximately 26% of the global incidence (1).

As indicated by TB surveillance efforts in India, the year 2022 marked a high record of 2.42 million cases, a 13% upsurge compared to 2021. This translates to a notification rate of approximately 172 cases per lakh population. In 2022, a total of 63,801 cases were diagnosed with MDR/RR in India. Furthermore, the presumptive TB examination rate (PTBER) for the country in 2022 increased to 1,281 per lakh population, a 68% increase from 763 in 2021 (2).

In 2021, the World Health Organization released the "Catalogue of Mutations in *Mycobacterium tuberculosis* Complex and Their Association with Drug Resistance" (WHO Mutation Catalogue). This catalogue synthesized and analyzed resistance profiles from a global collection of isolates, utilizing complementary whole-genome sequencing (WGS) and phenotypic drug susceptibility testing (DST) data (3, 4). The catalogue facilitates standardized interpretation of genotypic data for all currently recommended anti-tuberculosis drugs. However, it's worth noting that as the sources of data and *Mycobacterium tuberculosis* (MTB) strains in the WHO Mutation Catalogue are not evenly distributed globally, cataloged mutations may predominate regionally rather than globally or exhibit varying levels of association with drug-resistant tuberculosis (DR-TB). In 2022, following the WHO Mutation Catalogue, an Indian Mutation Catalogue was introduced, marking the first country-specific catalogue of its kind for *M. tuberculosis* (5). The study employed a quota sampling technique to obtain *M. tuberculosis* isolates from 25 states and four union territories. Subsequently, next-generation WGS and WHO-approved phenotypic DST were applied to these isolates. Employing a setting-adapted categorization scheme based on the WHO Mutation Catalogue and a validated bioinformatics workflow, genomic and phenotypic drug resistance profiles were compared and evaluated. This catalogue represents the first national Indian Catalogue of Mutations for drug-resistant tuberculosis (DR-TB). Currently, we have formulated another catalogue based on the CRyPTIC

consortium data representing the Indian region, which encompasses both drug-resistant and sensitive strains.

Outline of Indian Mutation Catalogue Version 2

In 2022, Indian Mutation Catalogue Version 1 was released by the honorable Minister of Health and Family Welfare and Chemicals and Fertilizers of India, Dr. Mansukh Mandaviya. This catalogue utilized a quota-based sampling frame for the collection of 3,167 isolates of the *M. tuberculosis* complex (MTBC) obtained from patients living in 25 States and 4 Union Territories. The sample collection mainly focused on MDR strains, with cultures obtained from processed sputum and directly from collection sites totaling 448 and 1,635, respectively, while 28 cultures had unavailable processing history, and one sample was of extrapulmonary origin. After quality filtering, matching WGS data were obtained for 2,112 isolates, which were then included for further analysis. This catalogue comprises descriptions of more than 8,000 mutations.

In 2023, a dataset of 6,782 isolates of the *M. tuberculosis* complex (MTBC) obtained from The Foundation for Medical Research (FMR), mumbai, India was further collated and included in the catalogue (Version 2.0). Among these 6,782 isolates, 50% were MDR and 30% were pan-sensitive isolates. In addition to the earlier catalogue (Version 1.0), descriptions of 3,033 mutations were obtained from the FMR data.

Thus, Version 2.0 is obtained by merging Version 1.0 with FMR data. This current version comprises 8,894 isolates, among which 2,444 (27%) were drug-sensitive TB isolates, with overall descriptions of 10,673 mutations. For a more detailed description of the collating process, please refer to the Methodology section of this catalogue.

Catalogue Disclaimer Statement

Next generation WGS is yet to be endorsed by the WHO or the Indian NTEP as a diagnostic or drug susceptibility testing method for clinical use. Hence, Indian Mutation Catalogue version 2.0 data shall not serve as a guide for clinical care of patients in India or elsewhere in the world. It should be noted that this catalogue is mainly collated and presented in order to support the DR-TB surveillance and disease control efforts in India.

Phenotypic and Genotypic Drug Susceptibility Testing Results

The current catalogue (Version 2.0) comprises 8,894 isolates, featuring mutations pertaining to 14 drugs. Among these 14 drugs, Phenotypic Drug Susceptibility Testing (pDST) data were available for all isolates only for 9 drugs. In the case of PAS, pDST data were available for 4,443 isolates. For the remaining drugs such as CAP, PZA, OFX, and STM, pDST data were available for only 2,112 isolates.

Genotypic Drug Susceptibility Testing (gDST) data were available for all 8,894 isolates studied. The total numbers and percentages of collected samples with pDST and gDST resistance results for each drug are outlined in **Table 1**. The prevalence of phenotypic resistance to first-line drugs INH and RIF was found to span 65.44% and 54.15% among the tested isolates, respectively. In the case of EMB and PZA, it was observed to be 34.46% and 42.61%, respectively. The prevalence of phenotypic resistance to AMK, KAN, CAP, LZD, and PAS ranged between 7–15% (**Table 1**). In the case of gDST, resistance to the first-line drugs RIF and INH was observed to be >=60% of isolates tested, whereas resistance to EMB was 57.71% (23% higher than reported using pDST) and PZA was observed in 36.77% of the isolates. Resistance to the fluoroquinolones (LFX, MFX, and OFX) was observed for 48.28% of isolates, while resistance to the second-line drugs AMK, KAN, CAP, LZD, and PAS ranged from 2.0 to 20.0%. Finally, the percentage of resistance detected to STM was observed to be high for both pDST and gDST, at 50.38% and 51.24%, respectively.

Table 1. Phenotypic and genotypic drug susceptibility testing results

Drug	Number of resistant isolates by pDST (n=8894)	Percentage (95% CI)	Number of resistant isolates by gDST (n=8894)	Percentage (95% CI)
RIF	4816	54.15(53.11-55.19)	5304	59.64(58.61-60.66)
INH	5820	65.44(64.44-66.43)	5783	65.02(64.02-66.01)
EMB	3065	34.46(33.47-35.46)	5133	57.71(56.68-58.74)
LFX	4307	48.43(47.38-49.47)	4294	48.28(47.24-49.32)
MFX	5298	59.57(58.54-60.59)	4294	48.28(47.24-49.32)
LZD	881	9.91(9.29-10.55)	189	2.13(1.84-2.45)
AMK	707	7.95(7.40-8.53)	775	8.71(8.14-9.32)
CAP	*163	7.72(6.62-8.94)	1766	19.97(19.14-20.81)
KAN	1326	14.91(14.18-15.67)	1144	12.86(12.17-13.58)
ETO	2444	27.48(26.55-28.42)	1590	17.88(17.09-18.69)
PAS	$623	14.02(13.00-15.04)	470	5.28(4.83-5.77)

PZA	**900	42.61(40.49-44.76)	3270	36.77(35.76-37.78)
OFX	***1223	57.91(55.77-60.02)	4294	48.28(47.24-49.32)
STM	#1064	50.38(48.22-52.53)	4557	51.24(50.19-52.28)

* CAP – pDST available for only 2112 isolates
$ PAS – pDST available for only 4443 isolates
**PZA – pDST available for only 2112 isolates
***OFX – pDST available for only 2112 isolates
#STM – pDST available for only 2112 isolates

Diagnostic Testing of confidence-graded mutations for predicting phenotypic drug susceptibility

Table 2. Numerical Split of grading of mutations based on analysis

Drug	1) Associated with Resistance	2) Associated withInterim Resistance	3) Uncertain Significance	4) Not Associated with Interim	5) Not Associated with Resistance
RIF	4	84	1652	1	392
Sensitivity (95% CI), Specificity (95% CI), PPV (95% CI)	96.12%(95.57%-96.67%) 86.2 %(85.2%-87.3%) 89.2%(88.37%-90.5%)	59.57%(58.96%-60.18%) 22.90%(21.70%-24.28%) 82.70%(82.15%-83.25%)			
INH	4	55	1730	0	107
Sensitivity (95% CI), Specificity (95% CI), PPV (95% CI)	96.12%(95.57%-96.67%) 86.2 %(85.2%-87.3%) 89.2%(88.37%-90.5%)	59.57%(58.96%-60.18%) 22.90%(21.70%-24.28%) 82.70%(82.15%-83.25%)			
EMB	4	13	432	0	822
Sensitivity (95% CI), Specificity (95% CI), PPV (95% CI)	79.60%(78.17%-81.03%) 78.03%(76.97%-79.09%) 65.56%(64.03%-67.09%)	33.10%(31.43%-34.77%) 91.58%(90.87%-92.29%) 67.38%(65.01%-69.75%)			
LFX	7	14	385	0	176
Sensitivity (95% CI), Specificity (95% CI), PPV (95% CI)	81.61%(80.45%-82.77%) 81.67%(80.55%-82.79%) 80.69%(79.52%-81.86%)	5.18%(4.52%-5.84%) 98.32%(97.95%-98.69%) 74.33%(69.39%-79.27%)			
MOX	6	16	398	0	159
Sensitivity (95% CI), Specificity (95% CI), PPV (95% CI)	63.82%(62.53%-65.11%) 74.46%(73.03%-75.89%) 78.65%(77.43%-79.87%)	19.83%(18.76%-20.90%) 79.61%(78.29%-80.93%) 58.91%(56.63%-61.19%)			
OFX	6	10	186	0	165
Sensitivity (95% CI), Specificity (95% CI), PPV (95% CI)	98.19%(97.46%-98.92%) 97.07%(95.96%-98.18%) 97.96%(97.18%-98.74%)	6.53%(5.15%-7.91%) 98.76%(98.03%-99.49%) 87.91%(81.21%-94.61%)			
LZD	2	0	373	0	455
Sensitivity (95% CI), Specificity (95% CI), PPV (95% CI)	14.25%(11.95%-16.55%) 99.20%(99.%-99.40%) 66.32%(59.60%-73.04%)	NA			

AMK	2	1	82	0	355
Sensitivity (95% CI), Specificity (95% CI), PPV (95% CI)	60.65%(57.05%-64.25%) 98.24%(97.96%-98.52%) 74.91%(71.36%-78.46%)	0.42%(0.06%-0.90%) 99.95%(99.90%-1.%) 42.86%(6.20%-79.52%)			
CAP	2	3	10	0	219
Sensitivity (95% CI), Specificity (95% CI), PPV (95% CI)	80.12%(74.05%-86.19%) 98.87%(98.40%-99.34%) 85.81%(80.32%-91.30%)	4.82%(1.56%-8.08%) 100.00%(100.00%-100.00%) 100.00%(100.00%-100.00%)			
KAN	7	1	78	0	162
Sensitivity (95% CI), Specificity (95% CI), PPV (95% CI)	55.87%(53.20%-58.54%) 94.05%(93.48%-94.62%) 65.09%(62.32%-67.86%)	0.23%(0.03%-0.49%) 99.93%(99.87%-99.99%) 37.50%(3.95%-71.05%)			
ETH	4	161	547	2	283
Sensitivity (95% CI), Specificity (95% CI), PPV (95% CI)	47.71%(45.73%-49.69%) 94.79%(94.25%-95.33%) 77.64%(75.53%-79.75%)	13.%(11.67%-14.33%) 96.76%(96.33%-97.19%) 60.34%(56.16%-64.52%)			
PAS	4	4	131	1	248
Sensitivity (95% CI), Specificity (95% CI), PPV (95% CI)	42.74%(33.78%-51.70%) 99.45%(99.13%-99.77%) 81.97%(72.32%-91.62%)	7.69%(2.86%-12.52%) 99.80%(99.60%-1.%) 69.23%(44.14%-94.32%)			
PZA	2	304	107	1	153
Sensitivity (95% CI), Specificity (95% CI), PPV (95% CI)	10.54%(8.52%-12.56%) 99.25%(98.76%-99.74%) 91.26%(85.81%-96.71%)	72.50%(70.53%-74.47%) 30.13%(27.54%-32.72%) 63.%(61.02%-64.98%)			
STM	5	10	74	2	50
Sensitivity (95% CI), Specificity (95% CI), PPV (95% CI)	94.93%(93.61%-96.25%) 96.08%(94.90%-97.26%) 96.11%(94.94%-97.28%)	17.73%(15.44%-20.02%) 96.46%(95.34%-97.58%) 83.63%(78.81%-88.45%)			

Catalogue Limitations

This study has several inherent limitations. Firstly, Version 2.0 data combines quota-based sampling from Version 1.0 with a prospective-all sampling approach by the CRyPTIC Consortium. Although this version encompasses most Indian States and Union Territories, it does not statistically represent the entire locale or the nation as a whole. Our primary objective was to systematically gather *Mycobacterium tuberculosis* (MTB) strains to assess genetic diversity and characterize mutations linked with drug resistance in India. However, it is important to acknowledge that this method may not fully encompass the diversity, and certain analysis of resistance associations may lack statistical power to accurately evaluate association measures.

Secondly, the inclusion criteria of Version 1.0 focused on patients assumed to have drug-resistant TB, resulting in a bias toward the collection, testing, and analysis of DR-TB isolates and strains. Conversely, CRyPTIC data incorporated in Version 2.0 comprises all culture-positive clinical samples (prospective all) that were prospectively included. Version 2.0 encompasses drug-sensitive TB isolates, constituting approximately 27% of the final dataset. Despite representing a large volume of DR-TB strains nationwide, this may introduce bias to the dataset, potentially resulting in incomplete associations of detected mutations among drug-susceptible strains. This bias could lead to the overestimation of mutation-associated resistance for polymorphisms not previously recognized as resistance-associated. Thirdly, as the pDST data for Bedaquiline is not available for all the isolates, hence, we could not collate and report the corresponding resistance association analysis.

Mutation Catalogue reckoner

Reading the tables

The terms and abbreviations used in drug-specific subsections and tables below are listed in **Table 3** and mirror those used in the WHO Mutation Catalogue.

Table 3. Terms used in the report and their description

Terms Used in the Mutation Catalogue	Description
Assoc w R	Associated with resistance
Assoc w RI	Associated with resistance – interim
Inf	Infinity
NA	Not Available
Undef	Undefined (0/0)
Not Assoc w R	Not associated with resistance
Not Assoc w RI	Not associated with resistance – interim
Uncert. Sig.	Uncertain significance
WHO-endorsed gDST assay	WHO-endorsed genotypic drug susceptibility testing assay
Drug	Name of drug
Mutations	Mutation, with common name where relevant
Present in R (TP)	Number of resistant isolates with the mutation
Present in S (FP)	Number of susceptible isolates with the mutation
Absent in R (FN)	Number of resistant isolates without the mutation
Absent in S (TN)	Number of susceptible isolates without the mutation
Sensitivity	True positive rate of mutation
Specificity	True negative rate of mutation
PPV	Positive predictive value of mutation
PPV|SOLO	Positive predictive value conditional on being solo
Initial confidence grading	Initial grouping of mutation
Dataset(s)	Dataset(s) used to derive the initial confidence grading
Additional grading criteria	Criterion for changing the initial confidence grading (e.g., previous WHO guidance or WHO-endorsed genotypic DST assays) to determine the final confidence grading
LoF	Loss of function
Final confidence grading	Final grouping of mutation after additional grading criteria were applied

Additional Variables Shown in the Catalogue	Description
Gene Name	Gene Name of Each Mutation
Gene ID	Gene ID for Every Variant
Present SOLO_R	Resistant isolates with the single (solo) mutation
Present SOLO_S	Sensitive isolates with the single (solo) mutation
Present SOLO_SR	Sum of resistant and susceptible isolates with the single (solo) Mutation
Sensitivity*	True positive rate of mutation
Specificity*	True negative rate of mutation
PPV*	Positive predictive value of mutation
LR+*	Positive likelihood ratio of mutation
LR-*	Negative likelihood ratio of mutation
OR*	Odds ratio of mutation
OR SOLO*	Odds ratio of solo mutation
OR SOLO_FE-sig	Fisher's exact test for the false discovery rate (FDR)-corrected *P* for the OR SOLO; TRUE = FDR-corrected $P \leq 0.05$, FALSE = FDR-corrected $P > 0.05$

* The lower bound (lb) and upper bound (ub) of the 95% CI are provided as additional columns in the Mutation Catalogue.

The tables in this report were simplified and abridged to fit the page space (i.e., all Group 3, Group 4 and Group 5 Mutations are not shown; full list available upon request).

A description of methods used to calculate and analyze data for the variables above is presented in the Statistical Analysis section of this document. The thresholds used to define the initial confidence grading are listed below; if they were met, the entry is highlighted in the colour denoted within parentheses.

Initial Confidence Grading

Group 1: Associated with resistance (Red)

1. Sum of resistant and susceptible isolates with the solo mutation (Present SOLO_SR) ≥5
2. Lower bound of 95% CI of PPV conditional on being solo (PPV | SOLO_lb) ≥25%
3. OR > 1, which always applies if criterion 4 is met
4. OR | SOLO > 1
5. Statistical significance of OR | SOLO (OR SOLO_FE-sig) with Fisher exact FDR-corrected

   $P \leq 0.05$

Group 2: Associated with resistance – interim (Orange)

1. Resistant isolates with the solo mutation (Present SOLO_R) ≥ 2
2. PPV≥50%

Group 3: Uncertain significance

Mutations that did not meet the criteria for inclusion in group 1, 2, 4 or 5.

Group 4: Not associated with resistance – Interim

1. PPV conditional on being solo (PPV | SOLO) < 40%
2. Upper bound of 95% CI of PPV conditional on being solo (PPV | SOLO_ub) < 75%

Group 5: Not associated with resistance

Mutations which have PPV less than 50% were considered as Not associated with resistance while WHO filtered those mutations which are less than 10%.

Additional Grading Criteria

Following the initial confidence grading, certain mutations originally categorized within Groups 3, 4, and 5 were reclassified into Group 2. This reclassification was guided by expert rules and precedents adhered to in the WHO Catalogue, and were motivated by the same reasons elucidated in the WHO Catalogue (Blue). Furthermore, it is worth noting that certain mutations with a robust association with resistance were not initially placed in Group 1 or Group 2 due to stringent statistical criteria. The rationales behind these reclassifications are provided in the tables (Blue). Finally, for the sake of thoroughness and precision, all the strains and mutations are presented in drug-specific tables below, regardless of their frequency.

An illustrative example

In the first example below, the drug considered is INH. The variant is in the *katG* gene, the amino acid change is at codon 315, and the amino acid change is from Serine to Threonine. This variant was found in 4877 phenotypically resistant isolates and in 203 susceptible isolates. The mutation was not found in 944 phenotypically resistant isolates and in 2869 susceptible isolates. The mutation Q190! of *katG* gene falls into Group-5 category by initial confidence grading based on its statistical classification. This mutation was moved to Group 2 (Associated with interim resistance) following the expert rule that any INDEL or premature stop codon mutation can confer INH resistance as described in WHO Mutation Catalogue (3).

Mutations	Gene Name	Present SOLO_R	Present SOLO_SR	Present in R (TP)	Present in S (FP)	Absent in R (FN)	Absent in S (TN)	PPV	PPV | SOLO	PPV | SOLO_lb	PPV | SOLO_ub	Sensitivity	Specificity	OR | SOLO	INITIAL CONFIDENCE GRADING	Additional Grading Criteria	FINAL CONFIDENCE GRADING
S315T	*katG*	2294	2521	4877	203	944	2869	96%	92%	91%	93%	84%	93%	3070	Group-1		Group-1
Q190!	katG	0	0	0	1	1745	365	0%	0%	0%	0%	0%	100%	Inf	Group-5	Indel or prema-ture stop codon	Group-2

The sensitivity, specificity, and PPV represent the performance of this mutation in the dataset. The next four columns indicate the statistical performance

of this mutation when it occurs without other mutations (defined as 'SOLO') in the genomic regions selected when assessing INH resistance. The values given are the midpoint PPV with the corresponding lower bound (lb) and upper bound (ub), and the odds ratio for the solo mutation (OR SOLO). This template is as per the WHO Mutations Catalogue.

The initial confidence grading for *katG* S315T was group 1 (Assoc w R) because:

- Present_SOLO_SR (see Mutation Catalogue) was 2521 and, consequently, ≥ 5.
- PPV|SOLO_lb of 90.7% was ≥ 25%.
- OR SOLO of 30.7 was > 1 and statistically significant.

Isoniazid

For Isoniazid, fifteen mutations were classified into Group-1 and Group-2 based on initial confidence grading. Then fourty-four mutations were moved to Group 2 based on Additional Grading Criteria (Indel or premature stop codon loss of function [LoF]) in *katG* gene. Promoter mutation was found at C-15T of *fabG1* (Group 1). Two *katG* mutations (S315T and S315N) were found in Group 1.

Mutations	Gene Name	Present SOLO_R	Present SOLO_SR	Present in R (TP)	Present in S (FP)	Absent in R (FN)	Absent in S (TN)	PPV	PPV | SOLO	PPV | SOLO_lb	PPV | SOLO_ub	Sensitivity	Specificity	OR | SOLO	INITIAL CONFIDENCE GRADING	Additional GradingCriteria	FINAL CONFIDENCE GRADING
C-15T	*fabG1/ pro-moter*	83	87	1276	44	4547	3026	96%	65%	56%	74%	24%	98%	1675.565	Group-1		Group-1
S94A	*inhA*	4	6	65	2	5758	3068	97%	67%	29%	104%	1%	100%	106.5648	Group-1		Group-1
S315T	*katG*	2294	2521	4877	203	944	2869	96%	92%	91%	93%	84%	93%	3071.327	Group-1		Group-1
S315N	*katG*	13	13	39	0	5784	3070	100%	100%	100%	100%	1%	100%	Inf	Group-1		Group-1
D142G	*katG*	2	2	3	0	5820	3070	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
G-17T	*fabG1/ pro-*	2	2	30	2	5793	3068	90%	50%	1%	99%	0%	100%	Inf	Group-2		Group-2

	moter																
G406A	*embB*	2	2	112	7	5711	3063	94%	22%	0%	49%	2%	100%	Inf	Group-2		Group-2
G-48A	*ahpC /prom oter*	2	2	43	4	5780	3066	87%	33%	0%	71%	1%	100%	Inf	Group-2		Group-2
R268H	*ndh*	11	95	144	126	5679	2944	53%	8%	3%	13%	2%	96%	6.788 586	Group-2		Group-2
S315I	*katG*	3	3	11	0	5812	3070	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
S315R	*katG*	4	4	52	3	5771	3067	95%	57%	20%	94%	1%	100%	Inf	Group-2		Group-2
T-8A	*fabG1/ pro- moter*	4	4	24	2	5799	3068	90%	67%	29%	104%	0%	100%	Inf	Group-2		Group-2
T-8C	*fabG1/ pro- moter*	2	2	125	4	5698	3066	96%	33%	0%	71%	2%	100%	Inf	Group-2		Group-2
R463L	*katG*	8	185	5105	2530	718	540	67%	0%	0%	1%	88%	18%	3.399 273	Group-2		Group-2
S315T2	*katG*	2	2	15	0	1730	366	100%	100%	100%	100%	1%	100%	Inf	Group-2		Group-2
Q190!	*katG*	0	0	0	1	1745	365	0%	0%	0%	0%	0%	100%	Inf	Group-5	Indel or prem ature stop co- don	Group-2
!741C	*katG*	0	0	0	1	1745	365	0%	0%	0%	0%	0%	100%	Inf	Group-5	Indel or prem ature stop co- don	Group-2
GACA61GA	*katG*	0	0	0	1	1745	365	0%	0%	0%	0%	0%	100%	Inf	Group-5	IN- DEL or prem ature	Group-2

																stop co-don	
K554!	*katG*	0	0	0	1	1745	365	0%	0%	0%	0%	0%	100%	Inf	Group-5	Indel or premature stop co-don	Group-2
GCCCC703GCCCCC	*katG*	0	0	0	1	1745	365	0%	0%	0%	0%	0%	100%	Inf	Group-5	IN-DEL or premature stop co-don	Group-2
CG97CGG	*katG*	0	0	1	0	4077	2704	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
GTTT105GTT	*katG*	0	0	1	0	4077	2704	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
GCCCCC372GCCCC	*katG*	0	0	3	0	1742	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or prem	Group-2

																ature stop co-don	
TC1003TCC	*katG*	0	0	2	0	1743	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
TCC1177TCCC	*katG*	0	0	2	0	1743	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
GC1367GCC	*katG*	0	0	2	0	1743	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
W728!	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	Indel or premature stop co-don	Group-2
CTTACCGCTGTAACG	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or	Group-2

639C																premature stop co-don	
ACC1550ACCC	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
TTGT1734TTGTGT	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
CTT474CT	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
AGG1145AGGG	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
AC-	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-	Group-2

CTT-GCCACTGCCATCCTTGCC2060ACCTTGCC																DEL or premature stop co-don	
AGCGC1921AGCGCGC	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
ACC1334ACCCC	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
TC1868TCC	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
ACC1485ACCCC	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-	Group-2

																don	
TGGG18TGGGG	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
TGCTTGGG-GAC-CAGC1301TGC	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
GC1855GCC	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
TC29TCC	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
CCCGGCGCCG369CCCG	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature	Group-2

																stop co-don	
CTCGGGTTCGGG867CTCGGGTTCGGGTTCGGG	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
CAC-GAC-GGGAC69CAC	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
W668!	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	Indel or premature stop co-don	Group-2
TCCC644TCCCCC	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
CG486CGG	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or prem	Group-2

																ature stop co-don	
CA1614CATA	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
W39!	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	Indel or premature stop co-don	Group-2
W341!	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	Indel or premature stop co-don	Group-2
GCCCCC372GCCCCCC	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
GACAC1616GACACAC	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or prem	Group-2

																ature stop co-don	
C2106CA	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
GC1920GCC	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
CGGG717CGGGG	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
AC2081ACC	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
CCGGTGGTGG	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL	Group-2

TTTCTGTAATGGGTGGGTGTTGC41CCGGTGGTGGTTTCTGTAATGGGTGGGTGTTGCGGTGGTGGTTTCTGTAATGGGTGGGTGTTGC																or premature stop co-don	
GCCC1433GCC	*katG*	0	0	1	0	1744	366	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2
GCCC1285GCC	*katG*	0	0	1	1	1744	365	50%	0%	0%	0%	0%	100%	Inf	Group-3	IN-DEL or premature stop co-don	Group-2

Rifampicin

In case of Rifampicin, four mutations (S450L, D435V, H445Y and H445D) were classified into Group 1, and eighty-four mutations were found to span in Group 2 (Associated with interim resistance), as per the final confidence grading criteria. Based on previous WHO Guidance, mutations outside the RRDR (I491F) were moved to Group-2 from Group-5. Sixty-four Group 2 mutations were all in the RRDR, and these were classified in accordance to the expert rule which implies that any RRDR mutation, except for synonymous mutations, it should be assumed to confer RIF resistance. It should also be noted that this expert rule was first introduced by WHO in 2018 and was reaffirmed in 2021 (4, 10).

Mutations	Gene Name	Present SOLO_R	Present SOLO_SR	Present in R (TP)	Present in S (FP)	Absent in R (FN)	Absent in S (TN)	PPV	PPV | SOLO	PPV | SOLO_lb	PPV | SOLO_ub	Sensitivity	Specificity	OR | SOLO	INITIAL CONFIDENCE GRADING	Additional GradingCriteria	FINAL CONFIDENCE GRADING
D435V	*rpoB*	64	76	294	62	4525	4013	83%	51%	42%	60%	6%	98%	472.9871	Group-1		Group-1
H445D	*rpoB*	32	36	163	30	4656	4045	84%	52%	39%	64%	3%	99%	695.0172	Group-1		Group-1
S450L	*rpoB*	727	834	3891	402	926	3675	91%	64%	62%	67%	81%	90%	2696.479	Group-1		Group-1
H445Y	*rpoB*	42	47	284	66	4535	4009	81%	39%	30%	48%	6%	98%	742.5711	Group-1		Group-1

H445L	*rpoB*	19	23	60	17	4759	4058	78%	53%	36%	69%	1%	100%	405.0326	Group-2		Group-2
D435Y	*rpoB*	31	49	555	275	4264	3800	67%	10%	7%	14%	12%	93%	153.4813	Group-2		Group-2
G332S	*rpoC*	3	4	760	124	4059	3951	86%	2%	0%	5%	16%	97%	292.0177	Group-2		Group-2
G433S	*rpoC*	2	2	565	75	4254	4000	88%	3%	1%	6%	12%	98%	Inf	Group-2		Group-2
H445N	*rpoB*	16	25	223	155	4596	3920	59%	9%	5%	14%	5%	96%	151.6294	Group-2		Group-2
H445R	*rpoB*	12	12	153	18	4666	4057	89%	40%	22%	58%	3%	100%	Inf	Group-2		Group-2
I491T	*rpoC*	3	3	542	73	4277	4002	88%	4%	0%	8%	11%	98%	Inf	Group-2		Group-2
I491V	*rpoC*	11	12	3400	421	1419	3654	89%	3%	1%	4%	71%	90%	2832.558	Group-2		Group-2
L430P	*rpoB*	24	60	1049	577	3770	3498	65%	4%	2%	6%	22%	86%	61.85676	Group-2		Group-2
L452P	*rpoB*	21	45	163	113	4656	3962	59%	16%	10%	22%	3%	97%	74.45769	Group-2		Group-2
L516P	*rpoC*	2	2	141	16	4678	4059	90%	11%	0%	26%	3%	100%	Inf	Group-2		Group-2
P1040R	*rpoC*	7	7	3093	315	1726	3760	91%	2%	1%	4%	64%	92%	Inf	Group-2		Group-2
Q432L	*rpoB*	5	5	46	12	4773	4063	79%	29%	8%	51%	1%	100%	Inf	Group-2		Group-2
S431T	*rpoB*	4	7	302	240	4515	3837	56%	2%	0%	3%	6%	94%	113.3112	Group-2		Group-2
S441L	*rpoB*	6	6	10	0	4809	4075	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
S450W	*rpoB*	16	21	123	65	4696	4010	65%	20%	11%	28%	3%	98%	273.2538	Group-2		Group-2
S493L	*rpoB*	2	2	7	0	4812	4075	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
V170F	*rpoB*	2	4	28	13	4791	4062	68%	13%	0%	31%	1%	100%	84.78397	Group-2		Group-2

V483A	*rpoC*	10	10	3023	333	1796	3742	90%	3%	1%	5%	63%	92%	Inf	Group-2		Group-2
H445P	*rpoB*	1	1	11	2	4808	4073	85%	33%	0%	87%	0%	100%	Inf	Group-4	RRDR	Group-2
P434A	*rpoC*	1	1	6	2	3416	3358	75%	33%	0%	87%	0%	100%	Inf	Group-4	RRDR	Group-2
I491F	*rpoB*	11	20	23	27	4796	4048	46%	29%	15%	43%	0%	99%	103.16	Group-5	previous WHO Guidance	Group-2
Q432E	*rpoB*	0	0	0	1	3422	3359	0%	0%	0%	0%	0%	100%	Inf	Group-5	RRDR	Group-2
S431G	*rpoB*	0	0	1	3	4818	4072	25%	0%	0%	0%	0%	100%	Inf	Group-5	RRDR	Group-2
M434L	*rpoB*	0	0	0	1	1397	714	0%	0%	0%	0%	0%	100%	Inf	Group-5	RRDR	Group-2
S441!	*rpoB*	0	0	0	2	1397	713	0%	0%	0%	0%	0%	100%	Inf	Group-5	RRDR	Group-2
S441P	*rpoB*	0	0	0	3	1397	712	0%	0%	0%	0%	0%	100%	Inf	Group-5	RRDR	Group-2
P454S	*rpoB*	0	0	0	1	1397	714	0%	0%	0%	0%	0%	100%	Inf	Group-5	RRDR	Group-2
A451V	*rpoB*	0	0	0	1	1397	714	0%	0%	0%	0%	0%	100%	Inf	Group-5	RRDR	Group-2
D435A	*rpoB*	0	0	5	0	4814	4075	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	previous WHO guidance	Group-2
D435G	*rpoB*	1	3	92	16	4727	4059	85%	6%	0%	17%	2%	100%	42.93421	Group-3	previous WHO guidance	Group-2
D435N	*rpoB*	0	0	1	0	3421	3360	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
F452C	*rpoC*	0	0	7	0	4812	4075	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
F452L	*rpoC*	0	0	37	5	4782	4070	88%	0%	0%	0%	1%	100%	Inf	Group-3	RRDR	Group-2
F452S	*rpoC*	0	0	9	0	4810	4075	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2

H445Q	*rpoB*	1	1	4	1	4815	4074	80%	50%	0%	119%	0%	100%	Inf	Group-3	RRDR	Group-2
K445R	*rpoC*	0	0	68	8	4751	4067	89%	0%	0%	0%	1%	100%	Inf	Group-3	RRDR	Group-2
L430R	*rpoB*	1	1	31	6	4788	4069	84%	14%	0%	40%	1%	100%	Inf	Group-3	RRDR	Group-2
L449V	*rpoC*	0	0	10	1	4809	4074	91%	0%	0%	0%	0%	100%	Inf	Group-3	RRDR	Group-2
M434I	*rpoB*	0	0	19	7	4800	4068	73%	0%	0%	0%	0%	100%	Inf	Group-3	RRDR	Group-2
M434V	*rpoB*	0	0	6	1	4813	4074	86%	0%	0%	0%	0%	100%	Inf	Group-3	RRDR	Group-2
N437D	*rpoB*	0	0	26	25	4793	4050	51%	0%	0%	0%	1%	99%	Inf	Group-3	RRDR	Group-2
P434L	*rpoC*	0	0	7	2	4812	4073	78%	0%	0%	0%	0%	100%	Inf	Group-3	RRDR	Group-2
P434Q	*rpoC*	0	0	7	2	4812	4073	78%	0%	0%	0%	0%	100%	Inf	Group-3	RRDR	Group-2
P434R	*rpoC*	0	0	3	1	4816	4074	75%	0%	0%	0%	0%	100%	Inf	Group-3	RRDR	Group-2
P454R	*rpoB*	0	0	1	0	3421	3360	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
Q429H	*rpoB*	0	0	13	3	4806	4072	81%	0%	0%	0%	0%	100%	Inf	Group-3	RRDR	Group-2
Q432H	*rpoB*	0	0	1	0	3421	3360	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
Q432P	*rpoB*	0	1	37	19	4782	4056	66%	0%	0%	0%	1%	100%	0	Group-3	RRDR	Group-2
Q432R	*rpoB*	1	1	2	0	4817	4075	100%	100%	100%	100%	0%	100%	Inf	Group-3	RRDR	Group-2
S428A	*rpoC*	0	0	17	2	4802	4073	89%	0%	0%	0%	0%	100%	Inf	Group-3	RRDR	Group-2
S428C	*rpoB*	0	0	6	3	4813	4072	67%	0%	0%	0%	0%	100%	Inf	Group-3	RRDR	Group-2
S428R	*rpoB*	0	0	33	17	4786	4058	66%	0%	0%	0%	1%	100%	Inf	Group-3	RRDR	Group-2

S428T	*rpoB*	0	0	17	12	4801	4064	59%	0%	0%	0%	0%	100%	Inf	Group-3	RRDR	Group-2
S428T	*rpoC*	0	0	6	3	3416	3357	67%	0%	0%	0%	0%	100%	Inf	Group-3	RRDR	Group-2
S431C	*rpoB*	0	0	24	18	4795	4057	57%	0%	0%	0%	0%	100%	Inf	Group-3	RRDR	Group-2
S431R	*rpoB*	1	1	162	90	4655	3987	64%	1%	0%	3%	3%	98%	Inf	Group-3	RRDR	Group-2
S450*	*rpoB*	0	0	2	0	3420	3360	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
S450A	*rpoB*	0	0	4	0	3418	3360	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
S450P	*rpoB*	0	0	5	0	4814	4075	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
T427P	*rpoB*	0	0	1	0	3421	3360	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
V431M	*rpoC*	0	0	17	1	4802	4074	94%	0%	0%	0%	0%	100%	Inf	Group-3	RRDR	Group-2
Q432K	*rpoB*	0	0	7	6	4812	4069	54%	0%	0%	0%	0%	100%	Inf	Group-3	RRDR	Group-2
T427I	*rpoB*	0	0	2	0	1395	715	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
S450!	*rpoB*	0	0	2	0	1395	715	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
K446Q	*rpoB*	0	0	2	0	1395	715	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
G433A	*rpoC*	0	0	2	0	1395	715	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
L452V	*rpoB*	0	0	1	0	1396	715	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
L452Q	*rpoB*	0	0	1	0	1396	715	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
N437Y	*rpoB*	0	0	1	0	1396	715	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
T427A	*rpoB*	0	0	1	0	1396	715	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2

H445S	*rpoB*	0	0	1	0	1396	715	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
L449R	*rpoC*	0	0	1	0	1396	715	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
Q436P	*rpoB*	0	0	1	0	1396	715	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
R448Q	*rpoB*	0	0	1	0	1396	715	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
F433L	*rpoB*	0	0	1	0	1396	715	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
G433D	*rpoC*	0	0	1	0	1396	715	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
N438T	*rpoB*	0	0	1	0	1396	715	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
Q435P	*rpoC*	0	0	1	0	1396	715	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
L446Q	*rpoC*	0	0	1	0	1396	715	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
P434S	*rpoC*	0	0	1	0	1396	715	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
L452R	*rpoB*	0	0	1	0	1396	715	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	RRDR	Group-2
H445C	*rpoB*	1	1	4	3	1393	712	57%	25%	0%	67%	0%	100%	Inf	Group-3	RRDR	Group-2
S428I	*rpoB*	0	0	1	1	1396	714	50%	0%	0%	0%	0%	100%	Inf	Group-3	RRDR	Group-2

Ethambutol

Four EMB resistance-associated mutations were classified into Group 1, and only thirteen were classified into Group 2. Out of these thirteen mutations associated with interim resistance, twelve were within the well-characterized *embB* gene, including its *promoter* region and remaining one was found *ubiA* gene.

Mutations	Gene Name	Present SOLO_R	Present SOLO_SR	Present in R (TP)	Present in S (FP)	Absent in R (FN)	Absent in S (TN)	PPV	PPV | SOLO	PPV | SOLO_lb	PPV | SOLO_ub	Sensitivity	Specificity	OR | SOLO	INITIAL CONFIDENCE GRADING	Additional GradingCriteria	FINAL CONFIDENCE GRADING
C-16T	*embA/promoter*	171	237	322	106	3461	7115	75%	69%	63%	75%	10%	98%	661.8773	Group-1		Group-1
M306L	*embB*	44	65	69	42	2994	5788	62%	51%	41%	62%	2%	99%	405.0514	Group-1		Group-1
M306V	*embB*	694	1156	1574	752	1491	5076	68%	48%	45%	51%	51%	87%	511.4009	Group-1		Group-1
Q497R	*embB*	367	669	473	381	2590	5449	55%	49%	45%	53%	15%	93%	255.6679	Group-1		Group-1
C-11A	*embA/promoter*	3	4	229	36	2114	4403	86%	8%	0%	16%	10%	99%	624.8344	Group-2		Group-2
C-12T	*embA/promoter*	2	6	69	40	2274	4399	63%	5%	0%	11%	3%	99%	96.72383	Group-2		Group-2
C-16A	*embA/promoter*	3	5	19	8	2324	4431	70%	27%	1%	54%	1%	100%	285.994	Group-2		Group-2
C-16G	*embA/promoter*	2	3	10	4	2333	4435	71%	33%	0%	71%	0%	100%	380.1972	Group-2		Group-2
D1024N	*embB*	7	14	48	40	3015	5790	55%	15%	5%	25%	2%	99%	192.0398	Group-2		Group-2
D354A	*embB*	17	30	26	17	3037	5813	60%	50%	33%	67%	1%	100%	250.3001	Group-2		Group-2
G-43C	*embA/promoter*	6	14	37	17	2306	4422	69%	26%	8%	44%	2%	100%	143.8205	Group-		Group-2

															2		
Q497K	*embB*	5	11	26	12	3037	5818	68%	29%	8%	51%	1%	100%	159.6422	Group-2		Group-2
T1082A	*embB*	6	32	391	245	2672	5585	61%	2%	1%	4%	13%	96%	48.23526	Group-2		Group-2
V188A	*ubiA*	2	2	3	0	2340	4439	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
Y319S	*embB*	8	13	15	5	3048	5825	75%	62%	35%	88%	0%	100%	305.7743	Group-2		Group-2
S347I	*embB*	2	3	15	6	3048	5824	71%	25%	0%	55%	0%	100%	382.1522	Group-2		Group-2
Y334H	*embB*	2	2	5	1	3058	5829	83%	67%	13%	120%	0%	100%	Inf	Group-2		Group-2

Fluoroquinolones – Levofloxacin, Ofloxacin and Moxifloxacin

There were Group-1 and Group-2 mutations in LFX(20), MFX (21) and OFX (13), as per the initial confidence grading. The expert rule for FLQ was applied following the WHO Mutation Catalogue criteria. This expert rule requires any *gyrA* or *gyrB* mutation associated with LFX resistance to also be classified as resistant to MFX and OFX. Hence, adhering to previous WHO catalogue, four mutations in one each from LFX, MFX and two from OFX were moved from Group-3 to Group-2, one from OFX in Group-5 was moved to Group-2, as per the expert criteria.

Drug	Mutations	Gene Name	Present SOLO_R	Present SOLO_SR	Present in R (TP)	Present in S (FP)	Absent in R (FN)	Absent in S (TN)	PPV	PPV | SOLO	PPV | SOLO_lb	PPV | SOLO_ub	Sensitivity	Specificity	OR | SOLO	INITIAL CONFIDENCE GRADING	AdditionalGrading Criteria	FINAL CONFIDENCE GRADING
LFX	A90V	*gyrA*	675	892	884	256	3423	4331	78%	73%	70%	75%	21%	94%	393.573	Group-1		Group-1
LFX	D94A	*gyrA*	204	298	301	114	4005	4474	73%	64%	59%	69%	7%	98%	242.4353	Group-1		Group-1

LFX	D94G	*gyrA*	1518	1825	1644	326	2663	4262	83%	82%	81%	84%	38%	93%	791.3629	Group-1		Group-1
LFX	D94H	*gyrA*	40	43	48	6	4258	4582	89%	87%	77%	97%	1%	100%	1434.789	Group-1		Group-1
LFX	D94N	*gyrA*	233	279	278	50	4028	4538	85%	82%	78%	87%	6%	99%	570.6543	Group-1		Group-1
LFX	D94Y	*gyrA*	182	216	199	39	4106	4550	84%	82%	77%	87%	5%	99%	593.1778	Group-1		Group-1
LFX	S91P	*gyrA*	124	166	160	50	4146	4538	76%	71%	65%	78%	4%	99%	323.1526	Group-1		Group-1
MFX	A90V	*gyrA*	600	893	812	328	4489	3266	71%	65%	62%	68%	15%	91%	148.9876	Group-1		Group-1
MFX	D94A	*gyrA*	207	298	308	107	4991	3488	74%	66%	61%	71%	6%	97%	158.971	Group-1		Group-1
MFX	D94G	*gyrA*	1504	1826	1632	338	3668	3257	83%	82%	80%	83%	31%	91%	414.7443	Group-1		Group-1
MFX	D94N	*gyrA*	236	279	280	48	5018	3548	85%	83%	79%	87%	5%	99%	388.0579	Group-1		Group-1
MFX	D94Y	*gyrA*	176	216	193	45	5104	3551	81%	80%	74%	85%	4%	99%	306.1207	Group-1		Group-1
MFX	S91P	*gyrA*	122	166	158	52	5140	3544	75%	70%	63%	77%	3%	99%	191.1779	Group-1		Group-1
OFX	D94G	*gyrA*	509	513	565	6	662	879	99%	99%	98%	100%	46%	99%	16896.19	Group-1		Group-1
OFX	A90V	*gyrA*	251	259	342	7	885	877	98%	97%	95%	99%	28%	99%	3109.138	Group-1		Group-1
OFX	D94N	*gyrA*	84	85	106	1	1120	885	99%	99%	97%	101%	9%	100%	6637.5	Group-1		Group-1
OFX	D94A	*gyrA*	72	80	107	8	1119	878	93%	90%	83%	97%	9%	99%	706.1662	Group-1		Group-1
OFX	D94Y	*gyrA*	61	61	72	2	1153	885	97%	97%	92%	101%	6%	100%	Inf	Group-1		Group-1
OFX	S91P	*gyrA*	39	41	57	2	1169	884	97%	95%	89%	102%	5%	100%	1474.594	Group-1		Group-1
LFX	D461N	*gyrB*	9	13	17	9	4289	4579	65%	50%	27%	73%	0%	100%	240.2133	Group-2		Group-2
LFX	D89N	*gyrA*	3	7	4	4	4302	4584	50%	43%	6%	80%	0%	100%	79.91632	Group-2		Group-2
LFX	D94V	*gyrA*	2	2	2	0	3213	3567	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
LFX	E501D	*gyrB*	11	29	52	24	4254	4564	68%	31%	16%	47%	1%	99%	65.56444	Group-2		Group-2
LFX	E501V	*gyrB*	2	3	2	1	4304	4587	67%	67%	13%	120%	0%	100%	213.1506	Group-2		Group-2
LFX	G88A	*gyrA*	6	9	14	3	4292	4585	82%	67%	36%	97%	0%	100%	213.6533	Group-2		Group-2
LFX	G88C	*gyrA*	20	25	21	5	4285	4583	81%	80%	64%	96%	0%	100%	427.818	Group-2		Group-2
LFX	N499T	*gyrB*	7	13	29	12	4277	4576	71%	37%	15%	59%	1%	100%	124.8227	Group-2		Group-2
LFX	R446C	*gyrB*	3	5	15	3	4291	4585	83%	50%	10%	90%	0%	100%	160.2773	Group-2		Group-2
LFX	R446H	*gyrB*	4	7	9	3	4297	4585	75%	57%	20%	94%	0%	100%	142.2698	Group-2		Group-2
LFX	S447F	*gyrB*	2	4	8	4	4298	4584	67%	33%	0%	71%	0%	100%	106.6543	Group-2		Group-2

LFX	T500N	*gyrB*	4	7	26	6	4279	4583	81%	40%	10%	70%	1%	100%	142.806	Group-2		Group-2
MFX	D461N	*gyrB*	7	13	14	12	5284	3584	54%	37%	15%	59%	0%	100%	79.13197	Group-2		Group-2
MFX	D89N	*gyrA*	5	7	6	2	5292	3594	75%	71%	38%	105%	0%	100%	169.7846	Group-2		Group-2
MFX	D94H	*gyrA*	39	43	47	7	5251	3589	87%	85%	74%	95%	1%	100%	666.4016	Group-2		Group-2
MFX	D94V	*gyrA*	2	2	2	0	4283	2497	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
MFX	E501D	*gyrB*	23	29	63	13	5235	3583	83%	64%	48%	80%	1%	100%	262.3655	Group-2		Group-2
MFX	E501V	*gyrB*	2	3	2	1	5296	3595	67%	67%	13%	120%	0%	100%	135.7628	Group-2		Group-2
MFX	G88A	*gyrA*	6	9	12	5	5286	3591	71%	55%	25%	84%	0%	100%	135.8683	Group-2		Group-2
MFX	G88C	*gyrA*	20	25	21	5	5277	3591	81%	80%	64%	96%	0%	100%	272.2001	Group-2		Group-2
MFX	N499T	*gyrB*	6	13	29	12	5269	3584	71%	33%	12%	55%	1%	100%	58.30328	Group-2		Group-2
MFX	R446C	*gyrB*	5	5	18	0	5280	3596	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
MFX	R446H	*gyrB*	4	7	8	4	5290	3592	67%	50%	15%	85%	0%	100%	90.5356	Group-2		Group-2
MFX	S447F	*gyrB*	2	4	9	3	5289	3593	75%	40%	0%	83%	0%	100%	67.93345	Group-2		Group-2
MFX	T500N	*gyrB*	4	7	26	6	5271	3591	81%	40%	10%	70%	0%	100%	90.83665	Group-2		Group-2
MFX	M291I	*gyrB*	3	79	770	660	4528	2936	54%	0%	0%	1%	15%	82%	2.559513	Group-2		Group-2
LFX	N499D	*gyrB*	4	5	9	2	4297	4586	82%	67%	29%	104%	0%	100%	426.9025	Group-2		Group-2
MFX	N499D	*gyrB*	4	5	9	2	5289	3594	82%	67%	29%	104%	0%	100%	271.8094	Group-2		Group-2
OFX	D94H	*gyrA*	14	14	21	0	1205	886	100%	100%	100%	100%	2%	100%	Inf	Group-2		Group-2
OFX	T500N	*gyrB*	2	2	12	0	1213	887	100%	100%	100%	100%	1%	100%	Inf	Group-2		Group-2
OFX	G88C	*gyrA*	7	7	7	0	1219	886	100%	100%	100%	100%	1%	100%	Inf	Group-2		Group-2
OFX	E501D	*gyrB*	2	7	15	5	1211	881	75%	29%	0%	62%	1%	99%	29.09992	Group-2		Group-2
OFX	N499D	*gyrB*	3	3	4	0	1222	886	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
OFX	D461N	*gyrB*	2	3	6	1	1220	885	86%	67%	13%	120%	0%	100%	145.082	Group-2		Group-2
OFX	D89N	*gyrA*	2	5	3	3	1223	883	50%	40%	0%	83%	0%	100%	48.13301	Group-2		Group-2
OFX	E501V	*gyrB*	0	1	0	1	1226	885	0%	0%	0%	0%	0%	100%	0	Group-5	previous WHO guidance	Group-2

LFX	A504V	*gyrB*	1	1	15	1	4291	4587	94%	50%	0%	119%	0%	100%	Inf	Group-3	previous WHO guidance	Group-2
MFX	A504V	*gyrB*	1	1	15	1	5283	3595	94%	50%	0%	119%	0%	100%	Inf	Group-3	previous WHO guidance	Group-2
OFX	A504V	*gyrB*	0	0	8	0	1218	886	100%	Inf	Inf	Inf	1%	100%	Inf	Group-3	previous WHO guidance	Group-2
OFX	G88A	*gyrA*	0	1	4	1	1222	885	80%	0%	0%	0%	0%	100%	0	Group-3	Previous WHO guidance	Group-2

Pyrazinamide

About 48 mutations were classified into Group-1 and Group-2 category, as per the initial grading criteria and application of expert rule which implies that any nonsense mutation and indel in the coding region of *pncA*, as well as all non-synonymous mutations are presumed to cause loss of function resistance phenotypes (unless disproven) in rifampicin-resistant isolates, 258 mutations of Group-3, Group-4 and Group-5 were moved to Group-2 in final grading resulting in 306 mutations in Group-1 and Group-2 category. There were two promoter region mutations: A-11G and A-11C observed in *pncA* gene. In addition, a single mutation(R212R) in *rpsA* gene was also classified into Group-1 based on the initial confidence grading criteria.

Mutation	Gene Name	Present SOLO_R	Present SOLO_SR	Present in R (TP)	Present in S (FP)	Absent in R (FN)	Absent in S (TN)	PPV	PPV | SOLO	PPV | SOLO_lb	PPV | SOLO_ub	Sensitivity	Specificity	OR | SOLO	INITIAL CONFIDENCE GRADING	AdditionalGrading Criteria	FINAL CONFIDENCE GRADING
V139A	*pncA*	6	8	42	2	850	1206	95%	75%	45%	105%	5%	100%	425.6471	Group-1		Group-1
A-11G	*pncA /promoter*	8	12	52	7	839	1202	88%	53%	28%	79%	6%	99%	286.5316	Group-1		Group-1
R212R	*rpsA*	19	182	500	191	392	1017	72%	9%	5%	13%	56%	84%	30.24133	Group-2		Group-2
I5S	*pncA*	2	3	36	2	856	1206	95%	50%	1%	99%	4%	100%	281.7757	Group-2		Group-2
ACC392 ACCCC	*pncA*	3	4	26	4	866	1204	87%	43%	6%	80%	3%	100%	417.0901	Group-2		Group-2
V139G	*pncA*	5	5	11	0	881	1208	100%	100%	100%	100%	1%	100%	Inf	Group-2		Group-2
T76P	*pncA*	3	4	12	1	880	1207	92%	75%	33%	117%	1%	100%	411.4773	Group-2		Group-2
V128G	*pncA*	3	3	9	0	883	1208	100%	100%	100%	100%	1%	100%	Inf	Group-2		Group-2
W68G	*pncA*	3	3	8	0	884	1208	100%	100%	100%	100%	1%	100%	Inf	Group-2		Group-2
W68R	*pncA*	5	5	7	0	885	1208	100%	100%	100%	100%	1%	100%	Inf	Group-2		Group-2

F94L	*pncA*	5	5	5	0	887	1208	100%	100%	100%	100%	1%	100%	Inf	Group-2		Group-2
L4W	*pncA*	2	2	5	0	887	1208	100%	100%	100%	100%	1%	100%	Inf	Group-2		Group-2
G97D	*pncA*	3	3	4	0	888	1208	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
P62L	*pncA*	3	3	4	0	888	1208	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
V7G	*pncA*	4	4	4	0	888	1208	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
A-11C	*pncA//promoter*	2	2	4	0	888	1208	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
Q141P	*pncA*	2	2	4	0	888	1208	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
V180F	*pncA*	5	5	5	1	887	1207	83%	83%	54%	113%	1%	100%	Inf	Group-2		Group-2
K96R	*pncA*	5	6	5	1	887	1207	83%	83%	54%	113%	1%	100%	680.3833	Group-2		Group-2
D12A	*pncA*	2	3	6	2	886	1206	75%	50%	1%	99%	1%	100%	272.2348	Group-2		Group-2
ACC392 ACCC	*pncA*	2	3	6	2	886	1206	75%	50%	1%	99%	1%	100%	272.2348	Group-2		Group-2
F58L	*pncA*	2	2	3	0	889	1208	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
G162R	*pncA*	2	2	3	0	889	1208	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
P62T	*pncA*	3	3	3	0	889	1208	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
Q10K	*pncA*	2	2	3	0	889	1208	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
T135P	*pncA*	3	3	3	0	889	1208	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
P54R	*pncA*	3	3	3	0	889	1208	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
P54L	*pncA*	2	2	3	0	889	1208	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
A3P	*pncA*	2	2	3	0	889	1208	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
S67P	*pncA*	2	2	3	0	889	1208	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
L35P	*pncA*	2	3	4	1	888	1207	80%	67%	13%	120%	0%	100%	271.8468	Group-2		Group-2
TCC473 TCCC	*pncA*	2	2	2	0	890	1208	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2

TGGTATCGG502TGGTATCGGTATCGG	*pncA*	2	2	2	0	890	1208	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
V180L	*pncA*	2	2	2	0	890	1208	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
K96T	*pncA*	2	2	2	0	890	1208	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
CCGACCACATCGACC395CCGACC	*pncA*	2	2	2	0	890	1208	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
T47I	*pncA*	2	2	2	0	890	1208	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
A46T	*pncA*	2	2	2	0	890	1208	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
AT408ATT	*pncA*	2	2	2	0	890	1208	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
TGG91TG	*pncA*	2	2	2	0	890	1208	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
A171E	*pncA*	2	2	2	0	890	1208	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
A146T	*pncA*	2	2	3	1	889	1207	75%	67%	13%	120%	0%	100%	Inf	Group-2		Group-2
T47A	*pncA*	2	2	5	3	887	1205	63%	40%	0%	83%	1%	100%	Inf	Group-2		Group-2
Q10P	*pncA*	2	3	4	2	888	1206	67%	50%	1%	99%	0%	100%	271.6216	Group-2		Group-2
G132D	*pncA*	2	3	3	2	889	1206	60%	50%	1%	99%	0%	100%	271.3161	Group-2		Group-2
T76I	*pncA*	2	3	2	1	890	1207	67%	67%	13%	120%	0%	100%	271.236	Group-2		Group-2
GC418GCC	*pncA*	2	2	2	1	890	1207	67%	67%	13%	120%	0%	100%	Inf	Group-2		Group-2
Q10!	*pncA*	2	2	2	2	890	1206	50%	50%	1%	99%	0%	100%	Inf	Group-2		Group-2
G108R	*pncA*	1	1	10	2	882	1206	83%	33%	0%	87%	1%	100%	Inf	Group-4	pncA_mutation	Group-2

S67W	*pncA*	1	1	2	2	890	1206	50%	33%	0%	87%	0%	100%	Inf	Group-4	pncA_mutation	Group-2
Y103H	*pncA*	1	2	1	2	891	1206	33%	33%	0%	87%	0%	100%	135.3535	Group-4	pncA_mutation	Group-2
S65S	*pncA*	12	444	171	519	721	689	25%	2%	1%	4%	19%	57%	2.654492	Group-5	pncA_mutation	Group-2
!187W	*pncA*	0	1	1	2	891	1206	33%	0%	0%	0%	0%	100%	0	Group-5	pncA_mutation	Group-2
F58V	*pncA*	0	0	1	3	891	1205	25%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
C138F	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
C138C	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
V155L	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
E181D	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
V169A	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
V183L	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
E174Q	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
C184G	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
S179C	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
V183V	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
A170P	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
A170A	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
H137R	*pncA*	0	2	0	2	892	1206	0%	0%	0%	0%	0%	100%	0	Group-5	pncA_mutation	Group-2

F94V	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
Q141!	*pncA*	0	1	0	1	892	1207	0%	0%	0%	0%	0%	100%	0	Group-5	pncA_mutation	Group-2
M1K	*pncA*	0	1	0	1	892	1207	0%	0%	0%	0%	0%	100%	0	Group-5	pncA_mutation	Group-2
D63A	*pncA*	0	2	0	2	892	1206	0%	0%	0%	0%	0%	100%	0	Group-5	pncA_mutation	Group-2
L27R	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
TGGTAGTCCGCCGCTTCGGCCAGGTAGTC125TGGTAGTC	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
CGGCCG496CGGCCGGGCCG	*pncA*	0	1	0	1	892	1207	0%	0%	0%	0%	0%	100%	0	Group-5	pncA_mutation	Group-2
TCC239TC	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
L35L	*pncA*	0	1	0	1	892	1207	0%	0%	0%	0%	0%	100%	0	Group-5	pncA_mutation	Group-2
AG172AGG	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
S66L	*pncA*	0	1	0	1	892	1207	0%	0%	0%	0%	0%	100%	0	Group-5	pncA_mutation	Group-2
P62Q	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
TC167TCC	*pncA*	0	1	0	1	892	1207	0%	0%	0%	0%	0%	100%	0	Group-5	pncA_mutation	Group-2
P69L	*pncA*	0	1	0	2	892	1206	0%	0%	0%	0%	0%	100%	0	Group-5	pncA_mutation	Group-2

CAATA400CAATAATA	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
CG385CGG	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
TGG170TGGGG	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
D63G	*pncA*	0	1	0	1	892	1207	0%	0%	0%	0%	0%	100%	0	Group-5	pncA_mutation	Group-2
CAA413CAAA	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
CTT288CT	*pncA*	0	1	0	1	892	1207	0%	0%	0%	0%	0%	100%	0	Group-5	pncA_mutation	Group-2
V130M	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
T168I	*pncA*	0	2	0	2	892	1206	0%	0%	0%	0%	0%	100%	0	Group-5	pncA_mutation	Group-2
AC307A	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
D63E	*pncA*	0	1	0	2	892	1206	0%	0%	0%	0%	0%	100%	0	Group-5	pncA_mutation	Group-2
S59F	*pncA*	0	1	0	1	892	1207	0%	0%	0%	0%	0%	100%	0	Group-5	pncA_mutation	Group-2
L116M	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
L116Q	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
G17A	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
Y41D	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
GCGAGCC55GCGAGCCCGAGCC	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2

G24V	*pncA*	0	1	0	1	892	1207	0%	0%	0%	0%	0%	100%	0	Group-5	pncA_mutation	Group-2
S65P	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
G55V	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
CTGGCG536C	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
CGGG86CGG	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
GC526GCC	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
V21A	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
P77L	*pncA*	0	1	0	1	892	1207	0%	0%	0%	0%	0%	100%	0	Group-5	pncA_mutation	Group-2
D49V	*pncA*	0	0	0	1	892	1207	0%	0%	0%	0%	0%	100%	Inf	Group-5	pncA_mutation	Group-2
S59Y	*pncA*	0	1	0	1	892	1207	0%	0%	0%	0%	0%	100%	0	Group-5	pncA_mutation	Group-2
T153I	*pncA*	0	1	0	1	892	1207	0%	0%	0%	0%	0%	100%	0	Group-5	pncA_mutation	Group-2
A28T	*pncA*	0	1	0	1	892	1207	0%	0%	0%	0%	0%	100%	0	Group-5	pncA_mutation	Group-2
L27P	*pncA*	1	1	91	1	801	1207	99%	50%	0%	119%	10%	100%	Inf	Group-3	pncA_mutation	Group-2
G132A	*pncA*	1	2	91	4	801	1204	96%	20%	0%	55%	10%	100%	150.3121	Group-3	pncA_mutation	Group-2
L182S	*pncA*	0	0	17	0	875	1208	100%	Inf	Inf	Inf	2%	100%	Inf	Group-3	pncA_mutation	Group-2
T177P	*pncA*	0	0	15	2	877	1206	88%	0%	0%	0%	2%	100%	Inf	Group-3	pncA_mutation	Group-2
D136G	*pncA*	1	1	9	0	883	1208	100%	100%	100%	100%	1%	100%	Inf	Group-3	pncA_mutation	Group-2
A3E	*pncA*	0	0	8	0	884	1208	100%	Inf	Inf	Inf	1%	100%	Inf	Group-3	pncA_mutation	Group-2

L172P	*pncA*	1	1	7	0	885	1208	100%	100%	100%	100%	1%	100%	Inf	Group-3	pncA_mutation	Group-2
C138R	*pncA*	1	1	7	0	885	1208	100%	100%	100%	100%	1%	100%	Inf	Group-3	pncA_mutation	Group-2
D49G	*pncA*	1	1	5	0	887	1208	100%	100%	100%	100%	1%	100%	Inf	Group-3	pncA_mutation	Group-2
A134V	*pncA*	1	1	5	0	887	1208	100%	100%	100%	100%	1%	100%	Inf	Group-3	pncA_mutation	Group-2
H71Y	*pncA*	0	1	8	2	884	1206	80%	0%	0%	0%	1%	100%	0	Group-3	pncA_mutation	Group-2
G78V	*pncA*	0	0	4	0	888	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
D49A	*pncA*	1	1	4	0	888	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
CG394CGG	*pncA*	1	1	3	0	889	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
GA18GAA	*pncA*	0	0	3	0	889	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
H57Y	*pncA*	1	1	3	0	889	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
L4S	*pncA*	1	1	3	0	889	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
T160A	*pncA*	0	0	3	0	889	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
A146V	*pncA*	1	1	3	0	889	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
M1I	*pncA*	1	1	3	0	889	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
M175V	*pncA*	1	1	3	0	889	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
A46V	*pncA*	1	1	3	0	889	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
S104R	*pncA*	1	1	3	0	889	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
H51P	*pncA*	1	1	3	0	889	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2

H51R	*pncA*	1	1	3	0	889	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
C14!	*pncA*	0	0	4	1	888	1207	80%	0%	0%	0%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
T142A	*pncA*	0	1	4	1	888	1207	80%	0%	0%	0%	0%	100%	0	Group-3	pncA_mutation	Group-2
D12G	*pncA*	1	2	4	1	888	1207	80%	50%	0%	119%	0%	100%	135.9234	Group-3	pncA_mutation	Group-2
E91K	*pncA*	0	0	2	0	890	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
AG451AGG	*pncA*	0	0	2	0	890	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
G97S	*pncA*	1	1	2	0	890	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
H51Y	*pncA*	0	0	2	0	890	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
F106L	*pncA*	0	0	2	0	890	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
T47P	*pncA*	0	0	2	0	890	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
R121P	*pncA*	0	0	2	0	890	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
W119!	*pncA*	0	0	2	0	890	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
L120R	*pncA*	1	1	2	0	890	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
L159R	*pncA*	1	1	2	0	890	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
H57R	*pncA*	0	0	2	0	890	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
L120P	*pncA*	1	1	2	0	890	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
H51Q	*pncA*	1	1	2	0	890	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
A146E	*pncA*	1	1	2	0	890	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2

G17D	*pncA*	1	1	2	0	890	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
Y41!	*pncA*	0	0	2	0	890	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
!187R	*pncA*	0	0	2	0	890	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
L85R	*pncA*	1	1	2	0	890	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
H57D	*pncA*	1	1	2	0	890	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
T167I	*pncA*	1	2	2	1	890	1207	67%	50%	0%	119%	0%	100%	135.618	Group-3	pncA_mutation	Group-2
V125F	*pncA*	1	2	2	1	890	1207	67%	50%	0%	119%	0%	100%	135.618	Group-3	pncA_mutation	Group-2
T100P	*pncA*	1	2	2	1	890	1207	67%	50%	0%	119%	0%	100%	135.618	Group-3	pncA_mutation	Group-2
D49E	*pncA*	1	2	2	1	890	1207	67%	50%	0%	119%	0%	100%	135.618	Group-3	pncA_mutation	Group-2
V7A	*pncA*	1	2	2	1	890	1207	67%	50%	0%	119%	0%	100%	135.618	Group-3	pncA_mutation	Group-2
F106C	*pncA*	0	0	2	1	890	1207	67%	0%	0%	0%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
CG54CGG	*pncA*	0	1	2	1	890	1207	67%	0%	0%	0%	0%	100%	0	Group-3	pncA_mutation	Group-2
H82R	*pncA*	1	2	2	1	890	1207	67%	50%	0%	119%	0%	100%	135.618	Group-3	pncA_mutation	Group-2
Q10R	*pncA*	0	1	2	1	890	1207	67%	0%	0%	0%	0%	100%	0	Group-3	pncA_mutation	Group-2
ACATCGACCTCATCGAC389ACATCGAC	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
TG183T	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2

CGTGT261CGTGTGT	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
P69R	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
CCGCTGTCAGG484CCGCTGTCAGGCGCTGTCAGG	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
CG419CGG	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
TG16TGG	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
GCC455GCCCC	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
GCC315GCCC	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
GGT475GGTGT	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
ATGTGGAAGTCCTTG155ATG	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
ACC396ACCC	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
GCC339GCCC	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
I6L	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
GCATACGTCCACCATACGT4GCATA	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2

CGT																	
TA296T	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
C522CA	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
AAACCAACTCGA550AA	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
TGCGC529TGCGCGC	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
CA292CAA	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
V169I	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
G162S	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
GGCACCCTTGT294G	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
GCC72GCCCC	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
TGGCCA457TGGCCAGGCCA	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
TCC257TCCC	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
GCC315GCCCC	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
L4!	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
AGG295AGGG	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
TG259T	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_m	Group-2

GG																utation	
CG97C	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
G97V	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
TGG457TGGGG	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
CGGG232CGG	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
ACCC486ACC	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
GCCGCTGTACGCTCCG315GCCG	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
TCC119TCCCC	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
GC420G	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
TCCAGACTGGGATGGAAG257TCCAGACTGGGATGGAAGCCAGACTGGGATGGAAG	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
TCACC167TC	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
K48T	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
K48N	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_m	Group-2

																utation	
E107Q	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
TCC239TCCC	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
V9A	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
R140G	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
CAA400CAAA	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
D12D	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
T142M	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
G132S	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
T114P	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
L159P	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
C72Y	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
S59P	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
W119R	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
C14G	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
CG342C	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
V155G	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
D12E	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
T142P	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_m	Group-2

																utation	
H137P	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
V139M	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
A171V	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
H71R	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
A102P	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
D136E	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
T135N	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
E91!	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
I133T	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
TC407TCC	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
G97R	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
CGAGGA198C	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
K48E	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
L116V	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
L85P	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
L116P	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
T160P	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
TGG422	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_m	Group-2

TGGG																utation	
G17V	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
E127!	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
W68!	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
G132C	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
A143G	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
V131G	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
Y34D	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
A134G	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
D8G	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
S164P	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
H43P	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
Q10H	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
I5T	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
GGCAATACCG402GG	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
GC528GCC	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
ATAGTCCGGTGT192AT	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2

GGCCAGCGCGGCGCCACCGGTTACCGCCAGCG84GGCCAGCG	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
CGACGG508C	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
G132V	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
AG56A	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
S164!	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
GCC107GCCCC	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
Q10E	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
CGAGGAATAGTCCGGTGTGCCGGAGAAGTGGTCACCCGGGTCGATGTGGA198CGA	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
G105R	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
H71P	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
C138G	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_m	Group-2

																utation	
S88!	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
V7F	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
M1T	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
F58C	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
W119C	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
V163A	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
V155M	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
H82D	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
V93G	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
D136Y	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
V130A	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
L19P	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
A46P	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
Y103C	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
G97C	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
C138!	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
H57Q	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
CGG532	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_m	Group-2

CGGG																utation	
H71Q	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
G97A	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
S104G	*pncA*	1	1	1	0	891	1208	100%	100%	100%	100%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
E37!	*pncA*	0	0	1	0	891	1208	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	pncA_mutation	Group-2
!187G	*pncA*	0	0	3	3	889	1205	50%	0%	0%	0%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
V157A	*pncA*	1	1	1	1	891	1207	50%	50%	0%	119%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
K96E	*pncA*	1	2	1	1	891	1207	50%	50%	0%	119%	0%	100%	135.4658	Group-3	pncA_mutation	Group-2
G105D	*pncA*	1	1	1	1	891	1207	50%	50%	0%	119%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
T61P	*pncA*	1	2	1	1	891	1207	50%	50%	0%	119%	0%	100%	135.4658	Group-3	pncA_mutation	Group-2
P62S	*pncA*	0	0	1	1	891	1207	50%	0%	0%	0%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
P69S	*pncA*	0	0	1	1	891	1207	50%	0%	0%	0%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
CGG76CGGG	*pncA*	0	0	1	1	891	1207	50%	0%	0%	0%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
CGACGAGGAATAG201C	*pncA*	0	0	1	1	891	1207	50%	0%	0%	0%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
P54S	*pncA*	0	0	1	1	891	1207	50%	0%	0%	0%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
L156P	*pncA*	0	0	1	1	891	1207	50%	0%	0%	0%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
A102V	*pncA*	0	0	1	1	891	1207	50%	0%	0%	0%	0%	100%	Inf	Group-3	pncA_mutation	Group-2
C14R	*pncA*	0	0	1	1	891	1207	50%	0%	0%	0%	0%	100%	Inf	Group-3	pncA_m	Group-2

																utation	
V9G	*pncA*	0	1	1	1	891	1207	50%	0%	0%	0%	0%	100%	0	Group-3	pncA_mutation	Group-2

Linezolid

Only two mutations (C154R, G2814T) in the linezolid resistance-associated genes, *rpl*C and *rrl* were classified as Group 1.

Mutations	Gene Name	Present SOLO_R	Present SOLO_SR	Present in R (TP)	Present in S (FP)	Absent in R (FN)	Absent in S (TN)	PPV	PPV | SOLO	PPV | SOLO_lb	PPV | SOLO_ub	Sensitivity	Specificity	OR | SOLO	INITIAL CONFIDENCE GRADING	Additional GradingCriteria	FINAL CONFIDENCE GRADING
C154R	*rplC*	102	159	108	56	776	7953	66%	65%	57%	72%	12%	99%	1833.98	Group-1		Group-1
G2814T	*rrl*	13	21	18	8	866	8001	69%	62%	41%	83%	2%	100%	1501.342	Group-1		Group-1

para-aminosalicylic acid

In total, eight mutations were found in three PAS resistance-associated genes (*thyA*, *folC* & *ribD*). Four mutations (*thyA* T22A, *folC* I43T, *ribD* TCCCCC83TCCCC, and *folC* R49W) were classified as Group 1, including one deletion. Four mutations *(thyA* R126G, R99! and T22N, as well as *folC* E40G) were classified as Group 2, which includes a nonsense mutation.

Mutations	Gene Name	Present SOLO_R	Present SOLO_SR	Present in R (TP)	Present in S (FP)	Absent in R (FN)	Absent in S (TN)	PPV	PPV | SOLO	PPV | SOLO_lb	PPV | SOLO_ub	Sensitivity	Specificity	OR | SOLO	INITIAL CONFIDENCE GRADING	Additional Grading Criteria	FINAL CONFIDENCE GRADING
T22A	*thyA*	30	37	30	7	87	1988	81%	81%	68%	94%	26%	100%	9793.103	Group-1		Group-1
I43T	*folC*	6	10	9	4	108	1991	69%	60%	30%	90%	8%	100%	2765.278	Group-1		Group-1
TCCCCC83TCCCC	*ribD*	6	6	6	0	111	1995	100%	100%	100%	100%	5%	100%	Inf	Group-1		Group-1
R49W	*folC*	5	5	5	0	112	1995	100%	100%	100%	100%	4%	100%	Inf	Group-1		Group-1
R126G	*thyA*	3	5	3	2	114	1993	60%	60%	17%	103%	3%	100%	2622.368	Group-2		Group-2
E40G	*folC*	2	2	2	0	115	1995	100%	100%	100%	100%	2%	100%	Inf	Group-2		Group-2
R99!	*thyA*	2	3	2	1	115	1994	67%	67%	13%	120%	2%	100%	3467.826	Group-2		Group-2
T22N	*thyA*	2	3	2	1	115	1994	67%	67%	13%	120%	2%	100%	3467.826	Group-2		Group-2

Amikacin, Streptomycin, Capreomycin and Kanamycin

In case of Amikacin resistance genes, only two mutations were found to span in Group-1 as per the initial confidence grading (A1401G and G1484T) and other mutation namely, C1402T was moved from Group-5 to Group-2 based on expert final grading criteria. For, capreomycin resistance genes, five mutations were classified as Group-1 and Group-2 mutation. Kanamycin resistance genes, featured eight mutations in Group-1 and Group-2 category. And streptomycin resistance genes harboured sixteen mutations in Group-1 and Group-2 category.

Drug	Mutations	Gene Name	Present SOLO_R	Present SOLO_SR	Present in R (TP)	Present in S (FP)	Absent in R (FN)	Absent in S (TN)	PPV	PPV | SOLO	PPV | SOLO_lb	PPV | SOLO_ub	Sensitivity	Specificity	OR | SOLO	INITIAL CONFIDENCE GRADING	Additional GradingCriteria	FINAL CONFIDENCE GRADING
AMK	A1401G	*rrs*	265	522	417	120	291	8066	78%	69%	64%	73%	59%	99%	2858.1	Group-1		Group-1
KAN	C-12T	*eis /promoter*	91	211	121	151	1207	6538	46%	43%	36%	49%	9%	97%	354.82	Group-1		Group-1
KAN	C-14T	*eis /promoter*	30	34	39	9	1289	6491	81%	77%	62%	92%	3%	100%	4936.53	Group-1		Group-1
KAN	G-10A	*eis /promoter*	43	55	48	16	1280	6494	70%	68%	54%	82%	3%	100%	923.03	Group-1		Group-1
KAN	G-10C	*eis /promoter*	61	94	63	34	1265	6515	66%	65%	55%	76%	5%	99%	870.03	Group-1		Group-1
KAN	A1401G	*rrs*	425	509	446	91	881	6760	83%	82%	79%	86%	34%	99%	3882.22	Group-1		Group-1
KAN	C1402T	*rrs*	6	6	7	0	1321	6466	100%	100%	100%	100%	1%	100%	Inf	Group-1		Group-1

AMK	G1484T	*rrs*	23	30	13	24	696	8161	35%	49%	35%	63%	2%	100%	3852.69	Group-1		Group-1
CAP	A1401G	*rrs*	128	151	128	22	38	1922	85%	85%	80%	91%	77%	99%	28148.28	Group-1		Group-1
CAP	G1484T	*rrs*	5	5	5	0	161	1944	100%	100%	100%	100%	3%	100%	Inf	Group-1		Group-1
KAN	G-37T	*eis /promoter*	15	21	18	7	1310	6473	88%	88%	65%	110%	3%	100%	6055.96	Group-1		Group-1
STM	K43R	*rpsL*	654	662	755	9	311	1037	99%	99%	98%	100%	71%	99%	27258.76	Group-1		Group-1
STM	K88R	*rpsL*	69	69	82	0	985	1045	100%	100%	100%	100%	8%	100%	Inf	Group-1		Group-1
STM	A1401G	*rrs*	21	48	121	29	946	1016	81%	42%	28%	56%	11%	97%	83.53	Group-1		Group-1
STM	C517T	*rrs*	27	28	27	1	1040	1044	96%	96%	90%	103%	3%	100%	2710.38	Group-1		Group-1
STM	A514C	*rrs*	23	25	27	2	1040	1043	93%	92%	81%	103%	3%	100%	1153.32	Group-1		Group-1
KAN	C-15G	*eis /promoter*	3	5	3	5	1325	6464	50%	50%	10%	90%	0%	100%	624.41	Group-2		Group-2
CAP	C1402T	*rrs*	4	4	4	0	162	1944	100%	100%	100%	100%	2%	100%	Inf	Group-2		Group-2
CAP	GT293G	*gid*	2	2	2	0	164	1944	100%	100%	100%	100%	1%	100%	Inf	Group-2		Group-2
CAP	E121Q	*gid*	2	2	2	0	164	1944	100%	100%	100%	100%	1%	100%	Inf	Group-2		Group-2

STM	A1401G	*rrs*	21	48	121	29	946	1016	81%	42%	28%	56%	11%	97%	83.53	Group-2		Group-2
STM	A906G	*rrs*	16	19	19	3	1048	1042	86%	84%	68%	101%	2%	100%	530.28	Group-2		Group-2
STM	A908C	*rrs*	9	10	11	1	1056	1044	92%	90%	71%	109%	1%	100%	889.77	Group-2		Group-2
STM	K88M	*rpsL*	8	8	8	0	1059	1045	100%	100%	100%	100%	1%	100%	Inf	Group-2		Group-2
STM	C905G	*rrs*	5	5	6	0	1061	1045	100%	100%	100%	100%	1%	100%	Inf	Group-2		Group-2
STM	P75R	*gid*	5	5	5	0	1062	1045	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
STM	K88T	*rpsL*	5	5	5	0	1062	1045	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
STM	A908G	*rrs*	2	2	4	0	1063	1045	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
STM	A514T	*rrs*	4	5	5	1	1062	1044	83%	80%	45%	115%	0%	100%	393.22	Group-2		Group-2
STM	A134E	*gid*	2	2	2	0	1065	1045	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
STM	L79S	*gid*	2	5	3	3	1064	1042	50%	40%	0%	83%	0%	100%	65.29	Group-2		Group-2
AMK	C1402T	*rrs*	0	5	3	4	706	8181	43%	0%	0%	0%	0%	100%	0	Group-5	WHO-end. gDST	Group-2

Ethionamide

In case of Ethionamide, twenty-eight mutations were classified as Group-1 and Group-2 based on initial confidence grading. One hundred and thirty-seven mutations were moved to Group-2 based on expert criteria, wherein any premature stop codon and indel in *ethA* is considered to be associated with ETO resistance. L203L in *fabG1* gene was moved to Group-2 adhering to WHO catalogue criteria. Thus, finally four mutations were classified as Group-1 and one hundred and sixty-two mutations were classified into Group-2, as per the final confidence grading.

Mutations	Gene Name	Present SOLO_R	Present SOLO_SR	Present in R (TP)	Present in S (FP)	Absent in R (FN)	Absent in S (TN)	PPV	PPV | SOLO	PPV | SOLO_lb	PPV | SOLO_ub	Sensitivity	Specificity	OR | SOLO	INITIAL CONFIDENCE GRADING	Additional GradingCriteria	FINAL CONFIDENCE GRADING
C-15T	*fabG1 /promoter*	906	1182	1034	285	1412	6163	75%	74%	71%	77%	42%	95%	1287.25	Group-1		Group-1
S94A	*inhA*	18	27	40	15	1784	4943	73%	55%	38%	72%	2%	100%	554.15	Group-1		Group-1
T-8C	*fabG1 /promoter*	58	84	68	30	1756	4928	69%	66%	56%	76%	4%	99%	626.04	Group-1		Group-1
T-8C	*ethA*	7	13	25	6	596	1485	81%	54%	27%	81%	4%	100%	290.69	Group-1		Group-1
G-17T	*fabG1 /promoter*	11	19	11	10	1813	4948	52%	52%	31%	74%	1%	100%	375.26	Group-2		Group-2
Y84D	*ETOA*	2	3	2	1	1822	4957	67%	67%	13%	120%	0%	100%	544.13	Group-2		Group-2
S266R	*inhA*	9	65	60	59	561	1432	50%	13%	5%	21%	10%	96%	41.02	Group-2		Group-2
L203L	*inhA*	10	19	18	9	603	1482	67%	53%	30%	75%	3%	99%	273.08	Group-2		Group-2
Y84D	*ethA*	9	10	9	1	612	1490	90%	90%	71%	109%	1%	100%	2191.18	Group-2		Group-2

S94A	*ethA*	3	4	10	2	611	1489	83%	60%	17%	103%	2%	100%	731.1	Group-2		Group-2
G-17T	*ethA*	4	7	8	3	613	1488	73%	57%	20%	94%	1%	100%	323.65	Group-2		Group-2
A341V	*ethA*	4	4	4	0	617	1491	100%	100%	100%	100%	1%	100%	Inf	Group-2		Group-2
CTTT365CTTTT	*ethA*	4	4	4	0	617	1491	100%	100%	100%	100%	1%	100%	Inf	Group-2		Group-2
R207C	*ethA*	3	4	5	1	616	1490	83%	75%	33%	117%	1%	100%	725.65	Group-2		Group-2
CAAAA1243CAAA	*inhA*	7	14	10	7	611	1484	59%	50%	24%	76%	2%	100%	242.88	Group-2		Group-2
T342A	*ethA*	2	2	3	0	618	1491	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
W455!	*ethA*	2	2	2	0	619	1491	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
Y276!	*ethA*	2	2	2	0	619	1491	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
S390F	*ethA*	2	2	2	0	619	1491	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
G43S	*ethA*	2	2	2	0	619	1491	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
T88I	*ethA*	2	2	2	0	619	1491	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
TGTAGGTGGG634TGTAGGTGGGTAGGTGGG	*ethA*	2	2	2	0	619	1491	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
TGCGC141TGCGCGC	*ethA*	2	2	2	0	619	1491	100%	100%	100%	100%	0%	100%	Inf	Group-2		Group-2
C137R	*ethA*	3	5	3	2	618	1489	60%	60%	17%	103%	0%	100%	361.41	Group-2		Group-2

L134R	*ethA*	2	3	2	1	619	1490	67%	67%	13%	120%	0%	100%	481.42	Group-2		Group-2
W21!	*ethA*	2	2	2	1	619	1490	67%	67%	13%	120%	0%	100%	Inf	Group-2		Group-2
G42D	*ethA*	2	3	2	1	619	1490	67%	67%	13%	120%	0%	100%	481.42	Group-2		Group-2
G182D	*ethA*	2	2	2	2	619	1489	50%	50%	1%	99%	0%	100%	Inf	Group-2		Group-2
GTTT T342G TTT	*ethA*	1	3	2	2	619	1489	50%	33%	0%	87%	0%	100%	120.27	Group-4	INDEL or premature stop codon	Group-2
Y143!	*ethA*	1	2	1	2	620	1489	33%	33%	0%	87%	0%	100%	240.16	Group-4	INDEL or premature stop codon	Group-2
TGGG 241TG G	*ethA*	1	1	1	2	620	1489	33%	33%	0%	87%	0%	100%	Inf	Group-4	INDEL or premature stop codon	Group-2
GGCG C756G GCGC GC	*ethA*	0	1	1	2	620	1489	33%	0%	0%	0%	0%	100%	0	Group-5	INDEL or premature stop codon	Group-2
GTT10 35GT	*ethA*	0	0	0	1	621	1490	0%	0%	0%	0%	0%	100%	Inf	Group-5	INDEL or premature stop codon	Group-2
W109!	*ethA*	0	1	0	1	621	1490	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or premature stop codon	Group-2
TGG7	*ethA*	0	2	0	2	621	1489	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or	Group-2

61TG																premature stop codon	
C253!	*ethA*	0	0	0	5	621	1486	0%	0%	0%	0%	0%	100%	Inf	Group-5	INDEL or premature stop codon	Group-2
CGG977CG	*ethA*	0	1	0	1	621	1490	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or premature stop codon	Group-2
TGG88TG	*ethA*	0	1	0	1	621	1490	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or premature stop codon	Group-2
ATT281AT	*ethA*	0	0	0	2	621	1489	0%	0%	0%	0%	0%	100%	Inf	Group-5	INDEL or premature stop codon	Group-2
CAGCCA687CAGCCAAGCCA	*ethA*	0	2	0	2	621	1489	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or premature stop codon	Group-2
TC1033T	*ethA*	0	1	0	1	621	1490	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or premature stop codon	Group-2
AGG631AG	*ethA*	0	2	0	2	621	1489	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or premature stop codon	Group-2

Y140!	*ethA*	0	0	0	1	621	1490	0%	0%	0%	0%	0%	100%	Inf	Group-5	INDEL or premature stop codon	Group-2
ATGT1394ATGTGT	*ethA*	0	0	0	1	621	1490	0%	0%	0%	0%	0%	100%	Inf	Group-5	INDEL or premature stop codon	Group-2
GT131GTT	*ethA*	0	0	0	1	621	1490	0%	0%	0%	0%	0%	100%	Inf	Group-5	INDEL or premature stop codon	Group-2
GT75GTT	*ethA*	0	0	0	1	621	1490	0%	0%	0%	0%	0%	100%	Inf	Group-5	INDEL or premature stop codon	Group-2
G441GA	*ethA*	0	0	0	1	621	1490	0%	0%	0%	0%	0%	100%	Inf	Group-5	INDEL or premature stop codon	Group-2
AGGATGGG245AGG	*ethA*	0	1	0	1	621	1490	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or premature stop codon	Group-2
Q215!	*ethA*	0	0	0	1	621	1490	0%	0%	0%	0%	0%	100%	Inf	Group-5	INDEL or premature stop codon	Group-2
TGG812TG	*ethA*	0	0	0	1	621	1490	0%	0%	0%	0%	0%	100%	Inf	Group-5	INDEL or premature	Group-2

																stop codon	
TA816T	*ethA*	0	1	0	1	621	1490	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or premature stop codon	Group-2
Q359!	*ethA*	0	0	0	1	621	1490	0%	0%	0%	0%	0%	100%	Inf	Group-5	INDEL or premature stop codon	Group-2
CA62C	*ethA*	0	0	0	1	621	1490	0%	0%	0%	0%	0%	100%	Inf	Group-5	INDEL or premature stop codon	Group-2
GCC502GC	*ethA*	0	1	0	1	621	1490	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or premature stop codon	Group-2
Q347!	*ethA*	0	1	0	1	621	1490	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or premature stop codon	Group-2
GAA906GA	*ethA*	0	0	0	1	621	1490	0%	0%	0%	0%	0%	100%	Inf	Group-5	INDEL or premature stop codon	Group-2
GT633GTT	*ethA*	0	0	0	1	621	1490	0%	0%	0%	0%	0%	100%	Inf	Group-5	INDEL or premature stop codon	Group-2
TGA3	*ethA*	0	1	0	1	621	1490	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or	Group-2

16TGAGA																premature stop codon	
AG1043A	*ethA*	0	1	0	1	621	1490	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or premature stop codon	Group-2
Q269!	*ethA*	0	1	0	1	621	1490	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or premature stop codon	Group-2
AGG1037AGGG	*ethA*	0	1	0	1	621	1490	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or premature stop codon	Group-2
GTC1392GTCTC	*ethA*	0	1	0	1	621	1490	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or premature stop codon	Group-2
GGTGT948GGTGTGT	*ethA*	0	0	0	1	621	1490	0%	0%	0%	0%	0%	100%	Inf	Group-5	INDEL or premature stop codon	Group-2
GAA300GA	*ethA*	0	2	0	2	621	1489	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or premature stop codon	Group-2
AGG1037AG	*ethA*	0	0	0	1	621	1490	0%	0%	0%	0%	0%	100%	Inf	Group-5	INDEL or premature stop codon	Group-2

CAAA141CAA	*ethA*	0	0	0	1	621	1490	0%	0%	0%	0%	0%	100%	Inf	Group-5	INDEL or premature stop codon	Group-2
Y286!	*ethA*	0	1	0	1	621	1490	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or premature stop codon	Group-2
CTTCTCG672C	*ethA*	0	0	0	1	621	1490	0%	0%	0%	0%	0%	100%	Inf	Group-5	INDEL or premature stop codon	Group-2
Y382!	*ethA*	0	1	0	1	621	1490	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or premature stop codon	Group-2
E274!	*ethA*	0	1	0	1	621	1490	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or premature stop codon	Group-2
TGGGG1308TGGGGG	*ethA*	0	0	0	1	621	1490	0%	0%	0%	0%	0%	100%	Inf	Group-5	INDEL or premature stop codon	Group-2
TGGG628TGGGG	*ethA*	0	0	0	1	621	1490	0%	0%	0%	0%	0%	100%	Inf	Group-5	INDEL or premature stop codon	Group-2
AG94AGG	*ethA*	0	1	0	1	621	1490	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or premature	Group-2

																stop codon	
CCA867C	*ethA*	0	0	0	1	621	1490	0%	0%	0%	0%	0%	100%	Inf	Group-5	INDEL or premature stop codon	Group-2
TGTCGATTCC286T	*ethA*	0	1	0	1	621	1490	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or premature stop codon	Group-2
GCCC33GCC	*ethA*	0	1	0	2	621	1489	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or premature stop codon	Group-2
TGCGC555TGCGCGC	*ethA*	0	0	0	1	621	1490	0%	0%	0%	0%	0%	100%	Inf	Group-5	INDEL or premature stop codon	Group-2
TGG305TGG	*ethA*	0	1	0	1	621	1490	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or premature stop codon	Group-2
TAA1223TA	*ethA*	0	1	0	1	621	1490	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or premature stop codon	Group-2
GCCC33GCCCC	*ethA*	0	0	0	1	621	1490	0%	0%	0%	0%	0%	100%	Inf	Group-5	INDEL or premature stop codon	Group-2
TCG16	*ethA*	0	1	0	1	621	1490	0%	0%	0%	0%	0%	100%	0	Group-5	INDEL or	Group-2

7TCGCG															premature stop codon	
GT12G	*ethA*	0	0	0	1	621	1490	0%	0%	0%	0%	0%	100%	Inf	Group-5	INDEL or premature stop codon	Group-2
GCC743GCCC	*ethA*	0	0	0	1	621	1490	0%	0%	0%	0%	0%	100%	Inf	Group-5	INDEL or premature stop codon	Group-2
L203L	*fabG1*	0	0	36	27	1788	4931	57%	0%	0%	0%	2%	99%	Inf	Group-3	WHO catalogue	Group-2
ATCGGCCCGACGAAATCCTCCGAGCCGGCGAATCTCGGC482ATCGGC	*ethA*	0	0	13	0	608	1491	100%	Inf	Inf	Inf	2%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
TAGTTCTGATTCAG1382TAG	*ethA*	0	0	3	0	618	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
AAC1301AACAC	*ethA*	1	1	2	0	619	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2

TC313TCC	*ethA*	0	0	2	0	619	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
TG374TGG	*ethA*	0	0	2	0	619	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
AGGCCG61AGGCCGGCCG	*ethA*	0	0	2	0	619	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
GTAGCCA1158G	*ethA*	0	0	2	0	619	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
AGGG1291AGG	*ethA*	1	1	2	0	619	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
W69!	*ethA*	1	2	2	0	619	1491	100%	100%	100%	100%	0%	100%	240.87	Group-3	INDEL or premature stop codon	Group-2
TC1154TCC	*ethA*	1	1	2	0	619	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
ACCCC826ACCC	*ethA*	1	2	2	1	619	1490	67%	50%	0%	119%	0%	100%	240.71	Group-3	INDEL or premature	Group-2

																stop codon	
AGC674AGCGC	*ethA*	1	2	2	1	619	1490	67%	50%	0%	119%	0%	100%	240.71	Group-3	INDEL or premature stop codon	Group-2
CAAAAA1048CAAAAAA	*ethA*	1	2	2	1	619	1490	67%	50%	0%	119%	0%	100%	240.71	Group-3	INDEL or premature stop codon	Group-2
GTTTT342GTTTTT	*ethA*	0	1	2	1	619	1490	67%	0%	0%	0%	0%	100%	0	Group-3	INDEL or premature stop codon	Group-2
S308!	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
ACC371ACCC	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
TCGCCG1063TCG	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
TGG308TGGG	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
CAAA	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or	Group-2

AA1048CAAAA																premature stop codon	
TGAG624TGAGGAG	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
GACAGACAAAC1210G	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
Y92!	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
GAA300GAAA	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
AGCGC581AGCGCGC	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
GTCTC695GTCTCTC	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
CGG172CG	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2

TGG697TGGG	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
GC568GCC	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
K370!	*ethA*	0	1	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	0	Group-3	INDEL or premature stop codon	Group-2
TGG710TGG	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
TCGC676TCGCGC	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
ATCGGCACTGATCACCTT324ATCGGCACTGATCACCTTCGGCACTGATCACC	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2

TT																	
GTT861GT	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
ATCTTC788ATC	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
Q271!	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
Y235!	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
TCGC1263TCGCGC	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
TC1187TCC	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
GC81G	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
C27!	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or	Group-2

																premature stop codon	
CG215C	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
GCC1128GCCCC	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
CGGG84CGG	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
TC1391TCC	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
AGG902AGGG	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
TGCG1038TGCGCG	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
TG1015TGG	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2

TGGGG1308TGGG	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
TG778TGG	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
GT1387G	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
GAA906GAAA	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
CA687CAA	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
TGGGCG1433TG	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
TG218TGG	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
ACGCG1356ACGC	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature	Group-2

GCG																stop codon	
CA801CAA	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
GCC1142GC	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
W391!	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
ACCCC826ACCCCC	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
AG581AGG	*ethA*	0	0	1	0	620	1491	100%	Inf	Inf	Inf	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
G1152GC	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
CT1299CTT	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
TGG8	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or	Group-2

72TG																premature stop codon	
GA606G	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
GCC59GCCC	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
GA727G	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
GTT1036GTTT	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
Q363!	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
GCCC345GCC	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
ACAACGTCGAGGT23A	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2

GCC1288GC	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
Y351!	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
Q246!	*ethA*	1	1	1	0	620	1491	100%	100%	100%	100%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
C131!	*ethA*	1	2	1	1	620	1490	50%	50%	0%	119%	0%	100%	240.32	Group-3	INDEL or premature stop codon	Group-2
Y461!	*ethA*	0	0	1	1	620	1490	50%	0%	0%	0%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
CTTTT111CTTTA	*ethA*	0	1	1	1	620	1490	50%	0%	0%	0%	0%	100%	0	Group-3	INDEL or premature stop codon	Group-2
AT779A	*ethA*	0	0	1	1	620	1490	50%	0%	0%	0%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
GC673GCC	*ethA*	0	1	1	1	620	1490	50%	0%	0%	0%	0%	100%	0	Group-3	INDEL or premature	Group-2

																stop codon	
AGGGG865AGGG	*ethA*	0	0	1	1	620	1490	50%	0%	0%	0%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
W289!	*ethA*	0	0	1	1	620	1490	50%	0%	0%	0%	0%	100%	Inf	Group-3	INDEL or premature stop codon	Group-2
TC1117TCC	*ethA*	0	1	1	1	620	1490	50%	0%	0%	0%	0%	100%	0	Group-3	INDEL or premature stop codon	Group-2
TCCC137TCCCC	*ethA*	0	1	1	1	620	1490	50%	0%	0%	0%	0%	100%	0	Group-3	INDEL or premature stop codon	Group-2

Methods and Approaches:

Across India, MTB isolates and processed sputum specimens were collected and their phenotype-genotype correlation data were utilized to develop this catalogue. The developing process is as follows:

a) Raw high-quality whole genome sequencing reads were produced using an Illumina MiSeq instrument

b) A comprehensive and a validated bioinformatics pipeline (CamNIRTResPred) and customized python/shell scripts were used for generation of variant sequencing data interrogation, annotation, resistance determination, and lineage prediction (7)

c) Phenotypic culture and DST data were generated using WHO-endorsed methods (LJ solid culture and BACTEC MGIT 960 liquid culture)

d) Sequencing and phenotypic DST testing for strains with initial discordance between gDST and pDST were repeated for any anti-TB drug

e) Based on the WHO Mutation Catalogue, the procedures outlined in the above-mentioned Initial Confidence Grading and Additional Confidence Grading sections, the variants were classified into “Associated with resistance” and “Not associated with resistance” categories.

Phenotypic Drug Susceptibility Testing

Mycobacterial Growth Indicator Tubes (MGIT) in BACTEC™ MGIT™ 960 system (BD, Franklin Lakes, NJ, USA) following the WHO-recommended critical concentrations for the year 2018 [Rifampicin (1.0µg/ml), Isoniazid (0.1µg/ml), Ethambutol (5.0µg/ml), Pyrazinamide (100µg/ml), Levofloxacin (1.5µg/ml), Moxifloxacin (0.5µg/ml), Ofloxacin (2.0µg/ml), Linezolid (1.5µg/ml), Amikacin (1.0µg/ml), Capreomycin (2.5µg/ml), Kanamycin (2.5µg/ml), Streptomycin (1.0µg/ml), Ethionamide (5.0µg/ml), and P-aminosalicylic acid (4.0µg/ml)] were used for generating Phenotypic DST. Before the release of the updated ‘2021 WHO Technical Report on critical concentrations for drug susceptibility testing of isoniazid and the rifamycins (rifampicin, rifabutin and rifapentine)’, the critical concentrations from 2018 report were used for phenotypic DST. Future MGIT-based DST will use the updated critical concentrations to maximize detection of phenotypic susceptibility and resistance. For instance, if genotypic and phenotypic results were discordant, pDST was repeated.

Genomic DNA Isolation

A conventional CTAB method was used for isolation of genomic DNA from LJ-amplified isolates of MTB. Genomic DNA Clean and Concentrator kit (ZYMO Research, Irvine, CA, USA) was used for DNA purification. Quality-checking and quantification of isolated genomic DNA were analyzed using NanoDrop (Thermo Fisher Scientific, Waltham, MA, USA) and the Qubit dsDNA Assay (Invitrogen, Waltham, MA, USA) respectively.

Whole Genome Sequencing

NexteraXT DNA Library Preparation and Index kits (Illumina, San Diego, CA, USA) were used for generating DNA libraries. The Bioanalyzer 2100 System (Agilent Technologies, Santa Clara, CA, USA) was used for measuring library sizes which tends to be ~850 bp on an average and were normalized in equimolar concentrations. The 2 × 251 cycles of paired-end read sequencing was generated using MiSeq Reagent Kit v3 (Illumina, San Diego, CA, USA) and Miseq sequencer (Illumina, San Diego, CA, USA).

Quality Control

The Sequencing data were then aligned to the H37Rv reference genome (NC_000962.3) and their coverage, depth and breadth were calculated. To identify the primary species for each isolate and their percentage of relatedness to other species, Kraken tool was used (6). Besides applying filter quality in variant calling, as depicted in the Variant Calling and Resistance Prediction section below, the following criteria were employed to eliminate low-quality isolates from downstream analysis:

- Sequences with breadth coverage less than 85% were excluded from further analysis, as these isolates were deemed to be contaminated.

- Isolates exhibiting contamination with genomes from other species during Kraken analysis were also excluded from downstream analytics to ensure MTB-specific genomes were scrutinized for variant calling and resistance determination.

Variant Calling and Resistance Prediction

The filtered genomes were subjected to analysis using CamNIRTResPred, an in-house, validated genomic analytics pipeline (7). A total of 6,782 whole genome sequences passed quality control, with reads having at least 60 base pairs and a minimum base quality of 20. Further the sequences were trimmed using Trimmomatic software v0.36 (LEADING:20 TRAILING:20 SLIDINGWINDOW:4:20 MINLEN:60) (8). Genome index for the H37Rv reference genome was build using bwa v0.7.12, and the samtools faidx option (v1.3.1) (9, 10). The bwa v0.7.12 mem with default parameters was used for alignment of the reads to the H37Rv reference genome. Picard v2.2.4 and GATK v3.5 were used for sorting, duplicate removal, and indel mapping correction (11, 12).

Variants were called using Samtools and bcftools v1.3.1 with the following parameters (samtools mpileup -d 8000 -t DP -B -u -g -m 4 and bcftools call -m -v -o) respectively (13). The variant quality filter metrices such as base quality >50, mapping quality >30, read depth >5, and at least one read mapping in either direction was further applied. Homozygous and heterozygous sites were classified by variants with >75% of the mapped reads and by variants with <75% of the mapped reads. RD-analyzer was used to predict the lineages of the isolates (14).

At the end, to predict the variants association with resistance, the filtered variants were annotated and compared against a database of mutations containing published resistance-associated mutations for first- and second-line antituberculosis drugs.

Statistical Analysis

The number of drug-resistant and drug-susceptible samples with and without mutations were determined using genotype and phenotype comparisons and were merged into 2x2 contingency tables (refer **Table 4).** Sensitivity, Specificity, Positive Predictive Values (PPVs), and Odds Ratios (ORs) were calculated with corresponding Confidence Intervals (CIs). Fisher's exact test was used to determine p-values based on the hypergeometric distribution. A Benjamini-Hochberg correction procedure with a False Discovery Rate (FDR) of 5% was used to handle multiple testing (15). Isolates with a single (SOLO) mutation were included in the count of SOLO mutations instead of including all isolates with a given mutation and were compared with the corresponding

numbers of isolates without mutation. To calculate the PPVs and ORs for SOLO mutations (PPV SOLO and OR SOLO) as per the WHO Mutations Catalogue, the same statistical procedure was applied as represented below:

- $\text{PPV SOLO} = \frac{\text{Present SOLO\_R}}{\text{Present SOLO\_R + Present in S}}$

- $\text{OR SOLO} = \frac{\frac{\text{Present SOLO\_R}}{\text{Absent in R}}}{\frac{\text{Present SOLO\_S}}{\text{Absent in S}}}$

Table 4. Phenotype - Genotype Comparison Conditions

Diagnostic List	Phenotype Results	Genotype Results
True Positive (TP)	R	R
False Positive (FP)	S	R
False Negative (FN)	R	S
True Negative (TN)	S	S

The above-said analyses were performed using R v.4.1.0 and MedCalc, v.19.2.6 (16, 17).

Executive Summary

To summarize, this mutation catalogue version 2.0 is a collation of MTB-specific mutations that are graded into five categories based on TB drug-resistance association. This was achieved by comparing genotypic and phenotypic data for a vast collection of strains collected throughout India. Based on the availability of high-quality genotypic (whole genome sequencing) and phenotypic (TB culture) drug susceptibility testing data, a total of 8894 MTBC isolates were chosen for the investigation. Based on the 2021 WHO Mutations Catalogue approach (3), which includes categorizing mutations into "Groups" according to the strength of their evidence-based link with TB treatment resistance, the downstream analysis was performed which resulted in 10,673 variants. Following the first version, the second version will serve as a standard reference for the interpretation of mutations linked to drug-resistant tuberculosis in India, guiding national activities for disease prevention and surveillance.

The Version 2.0 catalogue has been enhanced with descriptions of 52 mutations, in addition to those documented in catalogue version 1.0. The key contributor gene is *rpoC*, with 25 mutations. Additionally, the current version includes new genes: *ndh*, *ubiA*, *rrl*, and *fabG1*, for which mutations were not reported in Version 1.0. A general comparative analysis of both catalogues and the differences in terms of genes and number of mutations are tabulated in Table 5a. Furthermore, in Version 2.0, additional mutations in isoniazid resistance genes, namely *inhA*, *embB*, and *ndh* (new addition in Version 2.0), were observed. Similarly, concerning rifampicin, ethambutol, linezolid, and ethionamide, Version 2.0 features additional genes: *rpoC*, *ubiA*, *rrl*, and *fabG1*, respectively. The contrast of differences in mutations between Version 1.0 and Version 2.0 is tabulated in Table 5b. In summary, out of 14 drugs studied in Version 2.0, additional drug-resistant mutations were reported for 11 drugs. In Version 2.0, we observed 3 indels in *katG*, *fabG1*, and *ethA* genes.

Table 5a: The General comparative analysis of mutations in Version 1.0 and Version-2.0 (new genes added in version 2.0 are highlighted in yellow colour)

Drugs	Version 1.0		Version 2.0	
	Genes	**No of Mutations**	**Genes**	**No of Mutations**
Rifampicin	*rpoB*	60	*rpoB*	63
			rpoC	25
Isoniazid	*katG*	46	*katG*	51
	fabG1 /promoter	1	*fabG1//promoter*	4
	ahpC /promoter	1	*inhA*	1
			embB	1
			ahpC//promoter	1
			ndh	1
Ethambutol	*embB*	6	*embB*	10
	embA//promoter	1	*embA*	6
			ubiA	1
Levofloxacin	*gyrA*	10	*gyrA*	11
	gyrB	5	*gyrB*	10
Moxifloxacin	*gyrA*	10	*gyrA*	11
	gyrB	5	*gyrB*	11
Ofloxacin	*gyrA*	9	*gyrA*	10
	gyrB	4	*gyrB*	6
Linezolid	*rplC*	1	*rplC*	1
			rrl	1

Amikacin	*rrs*	2	*rrs*	3
Capreomycin	*rrs*	3	*rrs*	3
	gid	4	*gid*	2
Kanamycin	*eis /promoter*	5	*eis/promoter*	6
	rrs	3	*rrs*	2
Ethionamide	*fabG1/ promot-er*	1	*fabG1/promoter*	3
	inhA	3	*inhA*	4
	ethA	159	*ethA*	157
	ethR	8		
	mshA	8	*fabG1*	1
Para-aminosalicylic acid	*thyA*	4	*thyA*	4
	folC	3	*folC*	3
	ribD	1	*ribD*	1
Pyrazinamide	*pncA*	297	*pncA*	303
	pncA /promoter	2	*pncA/promoter*	2
	rpsA	1	*rpsA*	1
Streptomycin	*rpsL*	4	*rpsL*	4
	rrs	8	*rrs*	8
	gid	8	*gid*	3

Table 5b. Details of unique genes and mutations between version 1.0 and version 2.0

Drugs	Genes	Mutations												
Rifampicin	*rpoB*	S493L	Q432E	P454S	D435N	P454R	Q432H	S450*	S450A	T427P	H445S			
	rpoC	G433S	I491T	I491V	L516P	P1040R	V483A	P434A	F452C	F452L	F452S	K445R	L449V	
		P434L	P434Q	P434R	S428A	S428T	V431M	G433A	L449R	G433D	Q435P	L446Q	P434S	G332S
isoniazid	*katG*	D142G	S315I	S315R	CG97CGG	GTTT105 GTT								
	fabG1/prc	G-17T	T-8A	T-8C										
	inhA	S94A												
	embB	G406A												
	ahpC /prc	C-81T/G48A												
	ndh	R268H												
ethambutol	*embB*	S347I	Y334H	T1082A	M306L									
	embA	C-11A	C-12T	C-16A	C-16G	G-43C								
	ubiA	V188A												
linezolid	*rrl*	G2814T												
Amikacin	*rrs*	C1402T												
capreomycin	*gid*	GCCCCC1 03GCCCC	GCCCCC3 52GCCCC											
kanamycin	*eis /prom*	C-12T	C-15G	CG-7C										
	rrs	G1484T												
Streptomycin	*gid*	Q125!	Q127!	E103!	S136!	E40!								
P-aminosalicylic acid	*No additions*													
levofloxacin	*gyrA*	D94V												
	gyrB	N499T	R446C	R446H	S447F	T500N								
moxifloxacin	*gyrA*	D94V												
	gyrB	N499T	R446C	R446H	S447F	M291I	T500N							
ofloxacin	*gyrA*	G88A												
	gyrB	E501V	A504V											
Ethinoamide	*fabG1/prc*	T-8C	G-17T	C-15T										
	inhA	S94A												
	fabG1	L203L												
	ethR	GC753GC C	W116!	AGGG386 AGGGG	TC694TCC	G103GC	TGG710T GGGG	GA286G	S186!					
	mshA	GCC193G C	CGG509C GGG	y155!	AGCCCCG CCACTGG ACGCC14 03AGCCC CGCCACT GGACGC CCCGCCA CTGGACG CC	GCGC879 GCGCCGC	TG878TG GCG	TG878TG G	GGTG519 GGTGTG					
Pyrazinamide	*pncA*	S65S	C138C	V183V	A170A	L35L	D12D							

	Genes/Mutations present in Version 1.0 but not in Version 2.0
	Newly reported mutations for existing genes (Version 1.0) in Version 2.0
	Genes reported first time with respect to specific drug in Version 2.0

Grouping of mutations in version 2.0:

According to the additional grading criteria adopted in this study, the mutations were reclassified in Version 2.0. The number of mutations spanning each group for Version 1.0 and 2.0 are tabulated in Table 6. It should be noted that, in the case of Version 1.0, it comprised 45 mutations in Group 1 and 638 mutations in Group 2. Moreover, in Version 2.0, 14 new mutations were added in Group 1 and 38 were added in Group 2.

Table 6. Summary of mutation grouping details in Version 1.0

	Drugs	Group 1:V1	Group 1:V2	Group 2:V1	Group 2:V2	Group 3:V1	Group 3:V2	Group 4:V1	Group 4:V2	Group 5:V1	Group 5:V2
RIF	Rifampicin	3	4	57	84	767	1652	121	1	850	392
INH	Isoniazid	2	4	46	55	1336	1730	26	0	106	107
EMB	Ethambutol	0	4	7	13	70	432	26	0	893	822
LFX	Levofloxacin	5	7	10	14	115	385	9	0	228	176
MOX	Moxifloxacin	6	6	9	16	112	398	10	0	230	159
OFX	Ofloxacin	7	6	6	10	118	186	10	0	226	165
LZD	Linezolid	1	2	0	0	304	373	10	0	477	455
AMK	Amikacin	2	2	0	1	48	82	0	0	383	355
CAP	Capreomycin	2	2	5	3	5	10	0	0	222	219
KAN	Kanamycin	5	7	3	1	23	78	0	0	103	162
ETH	Ethionamide	2	4	177	161	233	547	1	2	312	283
PAS	Para-aminosalic	4	4	4	4	72	131	2	1	306	248
PZA	Pyrazinamide	2	2	298	304	47	107	0	1	220	153
STM	Streptomycin	4	5	16	10	34	74	4	2	83	50

Comparative analysis of WHO catalogue vs. Version 2.0:

In Version 2.0, we observed a total of 716 mutations and compared them with the 2023 WHO mutation catalogue. We found that 32% of drug resistant were common to those reported by WHO. The remaining mutations were confined to the Indian mutation catalogue Version 2.0. These 2 mutations correspond to 10 drugs and 16 genes/promoter. The most prevalent drug resistance mutations between WHO and Version 2.0 were observed for rifampicin, pyrazinamide, and fluoroquinolones. Moreover, 19 new mutations in Version 2.0, which were not reported in Version 1.0 but were common with WHO, were observed. These 19 mutations correspond to 8 genes/promoter feature resistance to 6 drugs (see Table 7).

Table 7. List of additional mutations in version 2.0 which are common to WHO catalogue with corresponding confidence grading

Drug	Gene name	Mutation	Final confidence grading version 2.0
Ethambutol	*embA/Promoter*	C-12T	Group 2
	embB	M306L	Group 1
	embB	T1082A	group 2
Linezolid	*rrl*	G2814T	Group 1
Rifampicin	*rpoC*	E1092D	Group 2
	rpoC	G594E	Group 2
	rpoC	A172V	Group 2
	rpoC	P601L	Group 2
	rpoC	P906A	Group 2
	rpoC	A621T	Group 2
	rpoC	D271G	Group 2
	rpoC	R69P	Group 2
	rpoC	E784Q	Group 2
Isoniazid	*inhA*	S94A	Group 1
	katG	D142G	Group 2
	katG	S315I	Group 2
	katG	S315R	Group 2
	ndh	R268H	Group 2
Ethionamide	*inhA*	S94A	Group 1
Pyrazinamide	*pncA*	V139A	Group 1

References

1. Global tuberculosis report 2021. Geneva: World Health Organization; 2021. Licence: CCBY-NC-SA 3.0 IGO
2. India TB report 2023. https://tbcindia.gov.in/showfile.php?lid=3680
3. WHO Catalogue of mutations in *Mycobacterium tuberculosis* complex and their association with drug resistance. 2021. https://apps.who.int/iris/handle/10665/341981
4. Walker TM et al The 2021 WHO Catalogue of *Mycobacterium tuberculosis* complex mutations associated with drug resistance: A genotypic analysis. Lancet Microbe. 2022Apr;3(4):e265-e273. doi10.1016/S2666-5247(21)00301-3.
5. Indian Catalogue of *Mycobacterium tuberculosis* Mutations and their Association with Drug Resistance – 2022. https://www.nirt.res.in/pdf/2022%20India%20Mutations%20Catalogue_CDC%20Cleared.pdf
6. Wood, D.E., Salzberg, S.L. Kraken: ultrafast metagenomic sequence classification using exact alignments. Genome Biol 15, R46 (2014). https://doi.org/10.1186/gb-2014-15-3- r46
7. Tamilzhalagan S, Shanmugam S, Selvaraj A, Suba S, Suganthi C, Moonan PK et al. Whole-Genome Sequencing to Identify Missed Rifampicin and Isoniazid Resistance Among Tuberculosis Isolates-Chennai, India, 2013-2016. Front Microbiol. 2021 Nov22;12:720436.
8. Bolger AM, Lohse M, Usadel B. Trimmomatic: a flexible trimmer for Illumina sequence data. Bioinformatics. 2014 Aug 1;30(15):2114-20. doi: 10.1093/bioinformatics/btu170. Epub 2014 Apr 1. PMID: 24695404; PMCID: PMC4103590.
9. Li H. (2013) Aligning sequence reads, clone sequences and assembly contigs with BWA-MEM. arXiv:1303.3997v2 [q-bio.GN].
10. Li H, Handsaker B, Wysoker A, Fennell T, Ruan J, Homer N, Marth G, Abecasis G, Durbin R; 1000 Genome Project Data Processing Subgroup. The Sequence Alignment/Map formatand SAMtools. Bioinformatics. 2009 Aug 15;25(16):2078-9
11. Picard - http://broadinstitute.github.io/picard/

12. McKenna A, Hanna M, Banks E, Sivachenko A, Cibulskis K, Kernytsky A, Garimella K, Altshuler D, Gabriel S, Daly M, DePristo MA. 2010. The Genome Analysis Toolkit: AMapReduce framework for analyzing next-generation DNA sequencing data. Genome Res20:1297–1303.

13. Danecek P, Bonfield JK, et al. Twelve years of SAMtools and BCFtools. Gigascience(2021) 10(2):giab008

14. Faksri, K., Xia, E., Tan, J.H. et al. In silico region of difference (RD) analysis of *Mycobacterium tuberculosis* complex from sequence reads using RD-Analyzer. BMCGenomics 17, 847 (2016). https://doi.org/10.1186/s12864-016-3213-1

15. Benjamin Y, Hochberg Y. Controlling the false discovery rate: a practical and powerfulapproach to multiple testing. JR Statist Soc B. 1995;57(1):289–300.

16. R Core Team (2021). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria.

17. MedCalc Statistical Software version 19.2.6 (MedCalc Software bv, Ostend, Belgium;https://www.medcalc.org; 2020)