TB or not TB - or DR-TB? Introducing a new EQA scheme for *Mycobacterium tuberculosis* drug resistance

Heidi Berghäll[1]*, Jaana Paakkanen[1], Silja Mentula[2], Kristel Virtanen[1], Jonna Pelanti[1]

1) Labquality, Helsinki, Finland
2) Finnish Institute for Health and Welfare, Dept. Health Security, Mycobacterial Reference Laboratory, Helsinki, Finland

*heidi.berghall@labquality.com

Background

Labquality, a Finnish independent EQA provider, has introduced a new EQA scheme for *Mycobacterium tuberculosis*, drug resistance (DR), by performing a pilot study named *Mycobacterium tuberculosis*, rifampicin and isoniazid, nucleic acid detection in June 2022. The scheme covers fully susceptible *Mycobacterium tuberculosis* complex (MTBC) and rifampicin (RIF) and isoniazid (INH) resistance and is intended for clinical laboratories using different tests for *M. tuberculosis* drug resistance testing. RIF and INH are the primary tuberculosis (TB) drugs and cornestones of multi-drug resistance (MDR) definition, and therefore present a screening target for MDR-TB as well as XDR-TB (extensively drug-resistant tuberculosis). The increased incidence of drug resistance is a growing concern, and is relevant in both high and low TB incidence countries. There has been an increase of available tests for nucleic acid detection of TB drug resistance and to support the quality control of the laboratories, this new EQA scheme has been introduced.

Methods

31 laboratories registered for the pilot study. Samples were shipped without temperature control packaging. The sample material consisted of 3 artificial sputum primary samples containing non-viable microbes. Samples were pre-tested with Xpert MTB/RIF (Cepheid) and GenoType MTBDRplus 2.0 (Hain Lifescience) in order to confirm the expected result of each sample. Examinations to be performed by the participating laboratories were nucleic acid detection for *M. tuberculosis*, RIF and INH susceptibility. Participants were instructed to perform the analysis according to the test manufacturer's instructions for liquid specimen and report their results through Labquality's electronic platform LabScala. Final reports including expert comments were distributed to the participants upon closing of the round.

Results

All participants reported their results and altogether 5 different nucleic acid detection tests were used (Table 1). Rifampicin resistance detection was included in the test selection of all participants and isoniazid resistance detection was reported by 14/31 participants. Participants were allowed to report results of more than one test. The expected results and the number of tests used as well as the result distribution are shown in figure 1. The range of test targets (MTBC ± RIF ± INH) of the assays used was taken into consideration when scoring the results. The success rates were 100% for sample S001 (MTBC, INH resistant), 100 % for S002 (MTBC, fully susceptible) and 98% for S003 (MTBC, RIF resistant) where one false negative and one indeterminate result was reported. The overall success rate was thereby 99% (figure 2).

Conclusion

Based on the results of this study, pre-testing and quality controls conducted by the sample material manufacturer, the sample material can be considered homogenous, stable and suitable for external quality assessment. Considering the immediate high interest and response rate, there is a clear need for this new EQA scheme. In contrast to the limited availability of traditional growth-based TB susceptibility testing or whole genome sequencing, often centralized to the few bio-safety level 3 (BSL-3) laboratories, rapid nucleic acid detection tests can be operated in conventional BSL-2 laboratory and used to speed up the resistance screening considerably. The performance of the participants and the tests used for resistance screening as well as the response rate were good. The pilot study can be considered very successful based on the high success rates.

Test	MTBC	MTBC + RIF detection	MTBC + INH detection
BD MAX MDR-TB panel (BD)	+	+	+
ELITechGroup MDR/MTB ELITe MGB Kit	+	+	+
GenoType MTBDRplus 2.0 (Hain Lifescience)	+	+	+
Xpert MTB/RIF (-/Ultra) (Cepheid)	+	+	-
Xpert MTB/XDR (Cepheid)	+	-	+

Table 1. Nucleic acid detection tests and their targets

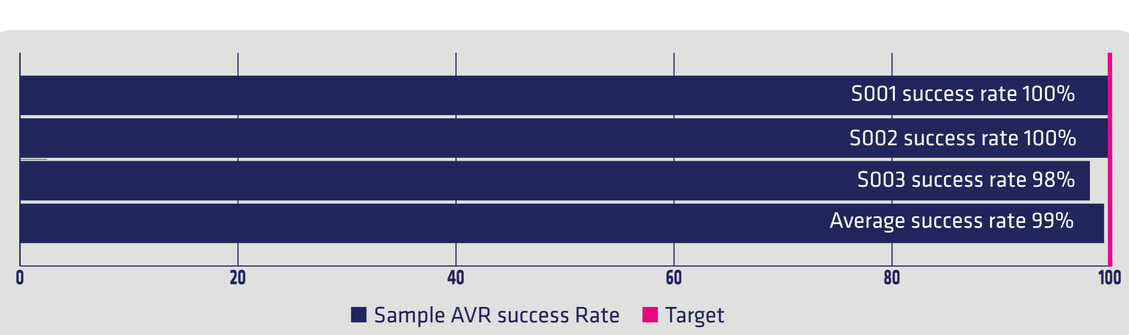

Fig. 2. Overall success rate by sample.

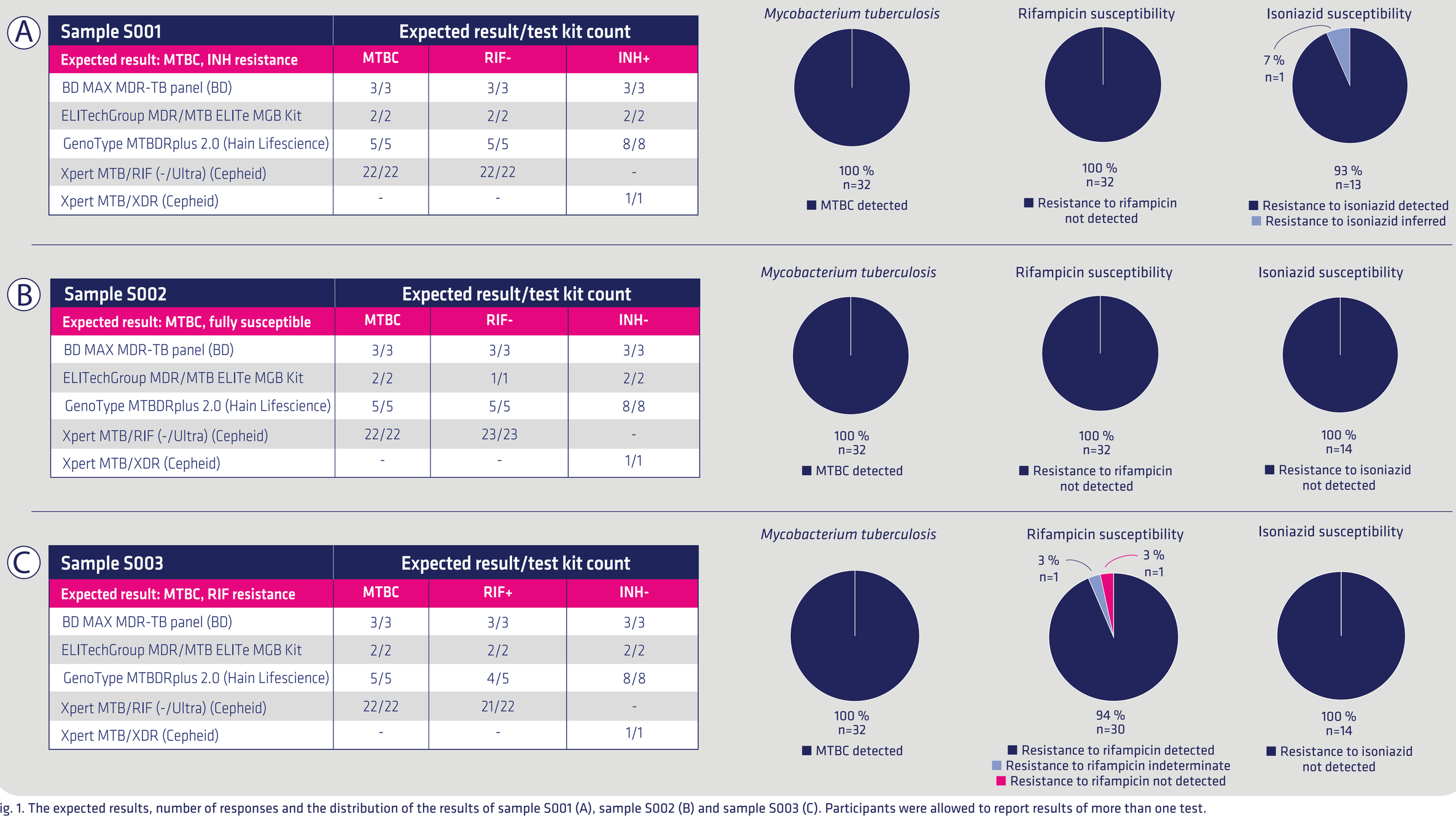

Fig. 1. The expected results, number of responses and the distribution of the results of sample S001 (A), sample S002 (B) and sample S003 (C). Participants were allowed to report results of more than one test.