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IQCP: A New Quality Control Option

Dave Eisentrager

On January 1, 2014 the Centers for Medicare and Medicaid Services (CMS) rolled out a new Quality Control (QC) option for laboratories to use to comply with the Clinical Laboratory Improvement Amendments (CLIA) regulations. Individualized Quality Control Plan (IQCP) will replace the existing QC regulations, Equivalent Quality Control (EQC), after an education and transition period of two years.

CMS intends to provide IQCP so non-waived laboratories will have flexibility in customizing their QC policies and procedures for the test systems they use and the unique aspects of their laboratory. The director of the laboratory will be responsible for all aspects of the QC plan chosen. During the education and transition period (Jan 1, 2014 – Jan 1,

2016), the laboratory may choose to do one of the following:

- Continue to use EQC as described in Appendix C of the current guidelines until January 1, 2016.
- Follow the default CLIA QC regulations.
- Implement IQCP based on the published guidelines under 42 CFR [493.1256\(d\)](#)¹.

After the education and transition period, labs must use options 2 or 3 above.

IQCP is applicable to all areas of the laboratory except for pathology, histopathology, oral pathology, cytology, certain parts of histocompatibility, parts of clinical cytogenetics, and immunohematology.

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Idaho's Ground Water Monitoring Program

Ernie Bader

Starting in 1990 the Idaho Department of Water Resources (IDWR), with the help from other state and federal agencies, began the Statewide Ground Water Quality Monitoring Program. This program came in response to an Idaho Senate Bill passed by the State Legislature in 1989 to maintain and improve Idaho's groundwater quality. The objectives of the Statewide Program are to:

- Characterize the groundwater quality of Idaho's major aquifers.

- Identify trends and changes in groundwater quality within Idaho's major aquifers.
- Identify potential groundwater quality problem areas.

In order to achieve these goals, IDWR monitors approximately 1200 sites every five years. The data collected is compiled into a

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A New Quality Control Option

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The new component introduced (but not really new) into IQCP is the inclusion of Risk Assessment evaluation in the QC procedures. Risk assessment is defined as “the identification and evaluation of potential failures and sources of errors in a testing process”¹. Each IQCP must include documentation of Risk Assessment,

the equipment. The Risk Assessment must also include the laboratory’s data on the instrument including proficiency testing, validation and verification, and other experiences with the equipment. This data will be used to establish the number, type, frequency of QC assays, and acceptable results of the control material.

The Quality Control Plan must ensure the accuracy and reliability of the test results and that the quality is appropriate for patient care. This plan may also include personnel training and competency assessments.

Quality Assessment monitoring must cover the five components included in the Risk Assessment. The QCP should be reevaluated if changes occur. If testing process failures occur, an investigation should be conducted to determine the root cause of the failure and its impact on patient care. Changes to the QCP should be made based on the new risk assessment information, if necessary.

To read the IQCP guideline, go to the CMS website (www.cms.gov/clia) and click the IQCP link on the left hand side of the page. Under “related links”, click *Survey and Cert letter 13-54* (see figure 1). The guideline is included as Attachment #1.

Contact the Laboratory Improvement Section at (208) 334-2235 ext. 245 or 247 with questions or for additional information.

References

¹Centers for Medicare & Medicaid Services. (2013). *Individualized Quality Control Plan (IQCP): A New Quality Control (QC) Option, Attachment #1*. Baltimore, MD. Retrieved from www.cms.gov/clia

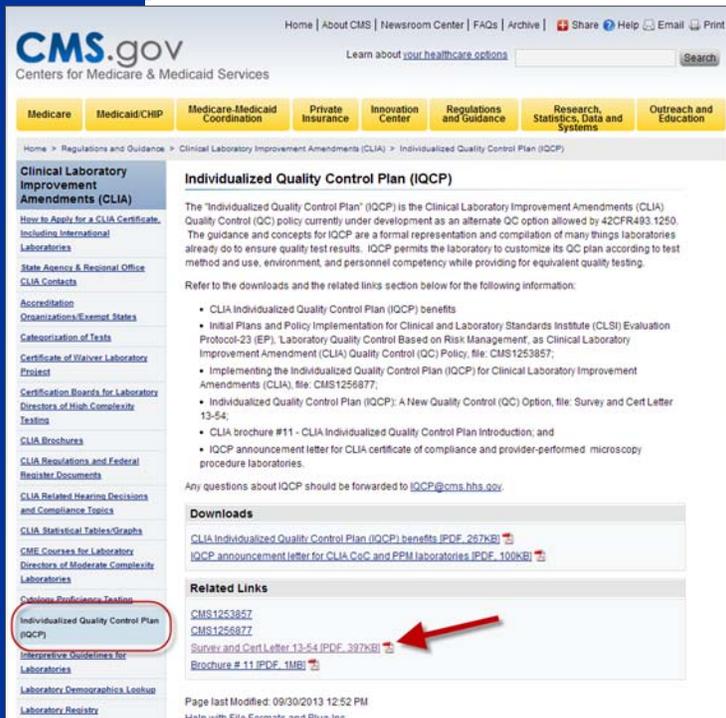


Figure 1: The IQCP guideline can be accessed at www.cms.gov/clia.

a written Quality Control Plan, and documentation of Quality Assessment.

The Risk Assessment portion must include all the phases of testing: Pre-analytic, Analytic, and Post-analytic. It must also include an evaluation of the following five components: Specimen, Environment, Reagents, Test System, and Testing Personnel. You may use the manufacturer’s package insert, operator’s manual, troubleshooting guides, and other information produced by the maker of

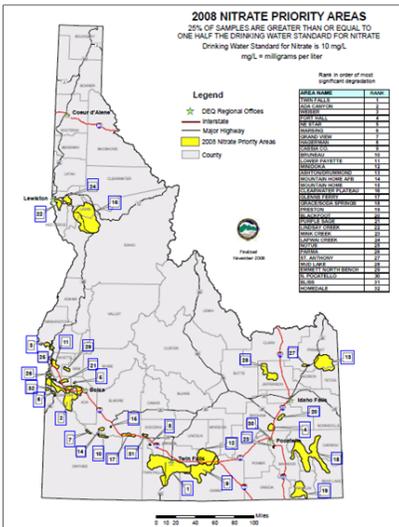


Figure 1. Areas with samples that test greater than or equal to one half of the drinking water standard for nitrate, 2008.*

a specific area. The EDMS site can be accessed at: <http://maps.idwr.idaho.gov/Groundwater/EDMS>

IDWR and the U.S. Geological Survey (USGS) worked together as partners in the program for 18 years, but IDWR assumed full responsibility for the monitoring program in 2009 due to economic challenges. For three years IDWR subcontracted out the laboratory testing portion of the program and utilized its own staff and some USGS contract workers to collect samples. Starting in the summer of 2012, IBL partnered with IDWR to provide the analytical chemistry testing and seasonal temporary lab technicians to run field tests and collect water samples for this program.

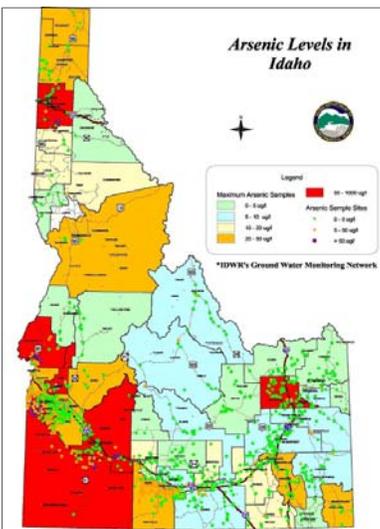


Figure 2. Arsenic levels in Idaho by region.*

The statewide groundwater data shows that most of the groundwater in Idaho meets the National Primary Drinking Water Standards designated by the U.S. Environmental Protection Agency. Southern Idaho has a higher percentage of problem sites when compared to the rest of the state. Contaminants that are the greatest concern are nitrate (Figure 1) and arsenic (Figure 2). Idaho Department of Environmental

Ground Water Program

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central database called the Environmental Data Management System (EDMS), managed by IDWR that also includes groundwater samples taken by other state and federal agencies. This data is then used by state and federal agencies to understand the aquifer characteristics and monitor trends in

Quality (DEQ) has established Nitrate Priority areas in the state to address nitrate contamination issues. Understanding nitrate trends provides information to improve land use decisions of the impacted area. The data generated from arsenic testing increases awareness of the possible health risks for private well owners.

This past summer IBL expanded our testing parameters to include several emerging contaminants (EC) that indicate anthropogenic activity in the environment. In order to handle the high volume of samples and budgetary limitations, the lab performed immunoassays as a screening procedure to identify wells that may need confirmatory analysis. Out of 201 sites monitored this past year, the following contaminants were identified: Bisphenol A (BPA) -12 sites, Caffeine-3 sites, and Triclosan- 5 sites (Figure 3).

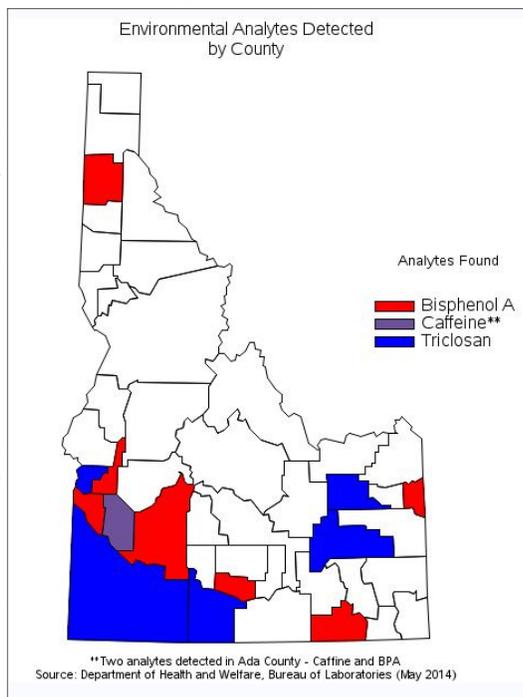


Figure 3. Emerging contaminants were identified in 20 of 201 sites in Idaho's counties in 2013. Emerging contaminant (EC) concentration ranges include the following: BPA, low 0.05 ng/mL- high 1.8 ng/mL; Caffeine, low 0.026 ng/mL-high 0.58 ng/mL; Triclosan, low 0.075 ng/mL- high 0.152 ng/mL.

Our initial data on EC indicates that human sources of contamination are showing signs of ground water impact in densely populated areas in the state. Continued monitoring and confirmatory tests will help establish EC baselines for the program's established monitoring wells, thus allowing us a greater understanding of how to manage human impact on water quality.

To learn more information about ground water quality in Idaho, please visit: <http://www.deq.idaho.gov/water-quality/ground-water.aspx>

*Figures used with permission by Idaho DEQ.

Molecular Detection of Drug Resistance in TB Isolates

Amanda J. Bruesch, MS

Mycobacterium tuberculosis (TB) is a disease of great public health importance around the globe.¹ The detection of cases, appropriate treatment, and management of disease are vital to controlling the spread of tuberculosis.² Laboratorians work to reduce the burden of the disease through rapid TB identification testing and detection of drug resistance.

TB presents many laboratory challenges due to its slow growth characteristics. Because it can take 6-8 weeks for the recovery of *M. tuberculosis* complex in culture, rapid methods for detection of TB DNA in primary specimens have become a very important tool in the TB laboratory. At the Idaho Bureau of Laboratories (IBL), a rapid method (TB NAAT) was optimized and implemented in 2011 to detect TB DNA in primary specimens. This test is generally completed within 24 hours of receipt of the sample and can make a significant impact on the treatment of the patient by initiating treatment sooner or allowing isolation orders to be discontinued.

In an effort to expand our capabilities in rapid testing of *M. tuberculosis* complex organisms, IBL has undertaken the task of validating molecular methods for detection of DNA mutations associated with first-line drug resistance. The first stage in validating this method involved testing acid fast growth identified as TB complex in either liquid or solid culture. Validation of this method in these matrices will allow IBL to perform Molecular Detection of Drug Resistance (MDDR) testing in-house, rather than sending it out to CDC.

Three gene targets (*inhA*, *katG*, and *rpoB*) have been identified as regions subject to mutation that confer resistance to two important drugs used to treat TB infection: rifampin and isoniazid.^{3,4,5,6} Approximately 95% of all rifampin-resistant TB isolates contain a mutation in the *rpoB* gene. Around 85% of isoniazid resistant TB isolates have a mutation in either the *inhA* or *katG* genes. Using methods previously published, we were able to amplify these three gene regions from more than twenty different isolates and generate high-quality sequence data. From analysis of the sequence data, we were able to detect several mutations that are correlated with resistance to rifampin or isoniazid. The molecular results from these tests showed 100% concordance with the phenotypic results of antimicrobial susceptibility testing of the TB isolates (Table 1). IBL will now perform molecular drug resistance detection on all TB isolates submitted and all growth in liquid culture that is identified as TB.

Sample ID	Sample Type	Target	Phenotypic Result	Molecular Result
H37Rv	Isolate	<i>inhA</i>	Susceptible	WT
		<i>katG</i>		WT
		<i>rpoB</i>	Susceptible	WT
Strain F	Isolate	<i>inhA</i>	Susceptible	WT
		<i>katG</i>		WT
		<i>rpoB</i>	Resistant	His526Tyr
Strain J	Isolate	<i>inhA</i>	Resistant	WT
		<i>katG</i>		Ser315Thr
		<i>rpoB</i>	Susceptible	WT
Strain M	Isolate	<i>inhA</i>	Susceptible	WT
		<i>katG</i>		WT
		<i>rpoB</i>	Resistant	Ser531Leu
MDR-TB	Isolate	<i>inhA</i>	Resistant	WT
		<i>katG</i>		Ser315Thr
		<i>rpoB</i>	Resistant	Ser531Leu
498	Sputum	<i>inhA</i>	Susceptible	WT
		<i>katG</i>		WT
		<i>rpoB</i>	Susceptible	WT
1453	Sputum	<i>inhA</i>	Resistant	-15CtoT
		<i>katG</i>		WT
		<i>rpoB</i>	Susceptible	WT
276	Sputum	<i>inhA</i>	Resistant	-15CtoT
		<i>katG</i>		WT
		<i>rpoB</i>	Susceptible	WT
401	Sputum	<i>inhA</i>	Susceptible	WT
		<i>katG</i>		WT
		<i>rpoB</i>	Susceptible	WT

Table 1. Phenotypic and molecular results for samples included in the validation of molecular detection of drug resistance for *M. tuberculosis*. WT – wild type (no mutation detected); all other molecular results indicate a mutation at the indicated region

Next, IBL plans to validate the test method on primary samples that test positive for TB DNA through our TB NAAT. This is a much larger undertaking, as it will be more difficult to address all of the possible matrices, inhibitors, and low concentration of organisms in a primary specimen. We look forward to completing this stage of the process and being able to offer results to our providers even sooner.

If you have any questions regarding the testing or services offered for *M. tuberculosis*, please call our TB lab at 208-334-2235 ext. 253.

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Going the Extra Mile with IBL’s Testing Services

Lisa Smith

In 2013, Idaho Bureau of Laboratories (IBL) received a number of unique requests that allowed staff the opportunity to extend testing capabilities and collaboration beyond normal activities. Below are a few examples.

Swimming pool outbreak: In April, a pediatrician saw patients with non-healing hand and foot wounds who recently swam in the same public pool. *Mycobacterium abscessus-chelonae* was identified following sample submission for culture testing. The organism was detected in 3 additional patient samples, leading to an epidemiological investigation with the local health department to determine the source. Several clinical and environmental samples from in and around the pool area were received at IBL, and *M. abscessus-chelonae* was isolated in multiple samples. Further testing was performed to determine if the patient and environmental strains were related to each other. The analysis revealed that the strains were related but not indistinguishable. However, limited information is available on how much normal variation exists in the *M. abscessus/chelonae* genome. This particular case utilized expertise of staff in multiple labs and demonstrated effective collaboration with public health districts and state epidemiologists.

Unusual susceptibility request-: In July, IBL received a request to perform antimicrobial susceptibility testing (AST) on an isolate from a pediatric kidney transplant patient with sepsis. The suspected organism, a *Bacillus* species, is not typically tested for antimicrobial susceptibilities. However, this patient’s sepsis was proving difficult to treat, and the physician wanted to determine drug resistance, as treatment options for a pediatric patient with an organ transplant can be limited. IBL identified the blood isolate as belonging to the *Bacillus cereus* group of organisms. Because AST testing for *Bacillus* species is not commonly requested, IBL contacted the CDC for guidance, who promptly provided relevant documents for testing and interpretive criteria. IBL then performed disk testing and produced a detailed report with pictures and inhibitory zones for IBL’s on-hand supply of antimicrobial disks and eTest strips. Concurrently, IBL shipped an isolate to the CDC for susceptibility testing by broth microdilution. A comparison between IBL’s data and CDC’s data showed that IBL correctly identified four drugs that could be used for patient treatment, and the patient was subsequently released from the hospital.

C. perfringens in homemade soup: In July, a district health department received a report from a physician of suspected foodborne illness in a hospitalized teen. The district epidemiologists obtained medical records on the reported index case and contacted the family to determine if a foodborne illness outbreak had occurred and the potential for ongoing transmission. Upon further investigation, four out of six family members had developed symptoms, which resolved in 1 day. The index case was hospitalized for 20 days with septic shock with continued recovery at home. The suspect mode of transmission for this outbreak was the homemade soup the family consumed. The family made the soup then left it out at room temperature overnight and ate it the next day. After the index patient’s blood and stool specimens tested negative for suspect bacteria, parasites, and toxins, the health district requested stool samples to be sent to

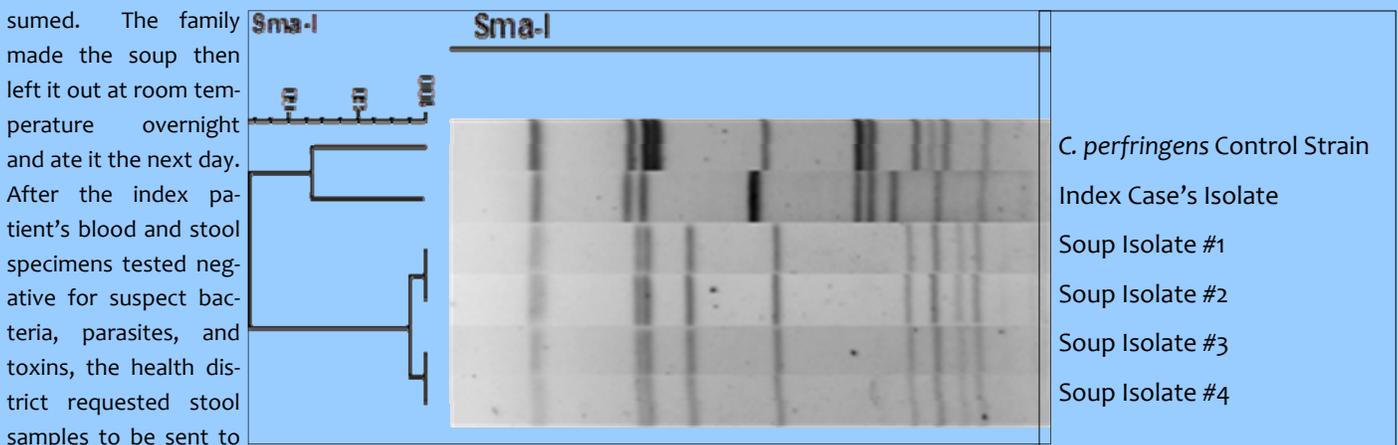


Figure 1. PFGE Analysis of *C. perfringens* Outbreak.

IBL reported that the index case’s stool was positive for *Clostridium perfringens* by 16S rDNA sequence analysis. Additionally, IBL was able to use 16S rDNA sequence analysis to identify *C. perfringens* in a soup specimen also submitted to IBL. IBL conducted PFGE analysis on one *C. perfringens* isolate from the index case and four *C. perfringens* isolates from the soup (Figure 1). The PFGE patterns show that

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IBL's Testing Services

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the soup isolates are very similar to each other but different from the index case's isolate.

The fact that such a large number of *C. perfringens* organisms were found in this family's soup suggests that *C. perfringens* was the etiologic agent and the soup was the vehicle for infection in this outbreak. Leaving the soup at room temperature overnight likely created an anaerobic environment for this organism to multiply. Unfortunately, reheating leftover soup in the microwave was likely not sufficient to kill this organism prior to consumption. Many outbreaks involving *C. perfringens* have been associated with inadequately heated or reheated meats, stews, meat pies, and meat gravies. Although the PFGE patterns in the soup were not identical matches to that of the index case, it is possible that many strains of *C. perfringens* grew in the soup and the few isolates that were randomly selected for PFGE analysis were simply not a match to the clinical isolate. This is indicative of some outbreaks in which data appear to have a close relationship but are not exact matches.

C. difficile submissions: In October, IBL was contacted by an Idaho hospital that was concerned they might have a common source *Clostridium difficile* infection spreading to several patients. In order to determine if these patients were infected with the same strain of *C. difficile*, they requested culture for and PFGE of any resulting isolates. Normally this is a test IBL would send to the CDC, but due to the government shutdown, the CDC was unable to accept the samples. We performed anaerobic culture on the stools using selective and differential media and isolated multiple colonies of *C. difficile* from each patient. PFGE testing was subsequently done which required significant optimization, as this organism is difficult to work with. PFGE patterns were successfully generated and data analysis undertaken. It appears that these patients had unrelated strains of *C. difficile* and that there is not a common source for these infections based on PFGE interpretation. This is good news for the hospital and helped to alleviate the concerns of their infection control staff regarding a common source spreading throughout their facility. IBL typically performs this type of testing procedure when identifying potential outbreaks related to organisms including *Salmonella* and Shiga toxin-producing *E. coli* and was pleased to be able to extend this capability for *C. difficile*.

IBL would like to thank our clinical partners for reaching out for assistance with these challenging samples and interesting requests. Our laboratorians are always willing to think outside the box to address these atypical situations. By allowing us to assist with your unique cases, we are able to further expand our capabilities and better serve you—our clients.

References

¹Centers for Disease Control and Prevention (26 May 2011). Human Jamestown Canyon Virus Infection—Montana, 2009. *Morbidity and Mortality Weekly Report*. Retrieved from <http://www.cdc.gov/media/mmwrnews/2011/0526.html#3>

Word Scramble

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1. IANRSCE

2. TIRAETN

3. FIFAEENE

4. UAIQTYL SESSNSTAME

5. SRTODLICMIU NSGEEPNFIR

6. RSTMECIYH

7. ATDNWUORRGE

8. YPTSIIBTESLIUC

9. NRCAIBIAIOMLT

10. ASNNMITTONAC

11. IGDELTPMIOSOIE

12. SRIK ESESNTMSAS

13. RCBMMOCAEIYTU

Word Scramble Solution

1. ARSENIC
2. NITRATE
3. CAFFEINE
4. QUALITY ASSESSMENT
5. CLOSTRIDIUM PERFRINGENS
6. CHEMISTRY
7. GROUNDWATER
8. SUSCEPTIBILITY
9. ANTIMICROBIAL
10. CONTAMINANTS
11. EPIDEMIOLOGIST
12. RISK ASSESSMENT
13. MYCOBACTERIUM



Image from <http://www.fightbac.org/>

Drug Resistance in TB Isolates

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References

- ¹Brewer, T.F., & Heymann, S.J. (2005). Long Time Due: Reducing Tuberculosis Mortality in the 21st Century. *Arch Med Res* 36, 617-621.
- ²Campbell, P., Morlock, P.G., Sikes, D., Dalton, T., Metchock, B., Starks, A., Hooks, D., Cowan, L., Plikaytis, B., & Posey, J. (2011). Molecular Detection of Mutations Associated with First- and Second-Line Drug Resistance Compared with Conventional Drug Susceptibility Testing of *Mycobacterium tuberculosis*. *Antimicrobial Agents and Chemotherapy*, 2032-2041.
- ³Mani, C., Selvakumar, N., Narayanan, S. & Narayanan, P.R. (2010). Mutations in the rpoB Gene of Multidrug-Resistant *Mycobacterium tuberculosis* Clinical Isolates from India. *Journal of Clinical Microbiology* 39(8), 2987.
- ⁴Halse, T.A., Edwards, J., Cunningham, P.L., Wolfgang, W.J., Dumas, N.B., Escuyer, V.E., & Musser, K.A. (2010). Combined Real-Time PCR and rpoB Gene Pyrosequencing for Rapid Identification of *Mycobacterium tuberculosis* and Determination of Rifampin Resistance Directly in Clinical Specimens. *Journal of Clinical Microbiology* 48(4), 1182.
- ⁵Engstom, A., Morcillo, N., Imperiale, B., Hoffner, S.E., and Jureen, P. (2012). Detection of First- and Second-Line Drug Resistance in *Mycobacterium tuberculosis* Clinical Isolates by Pyrosequencing. *Journal of Clinical Microbiology* 50(6), 2026.
- ⁶Garcia-Sierra, N., Lacoma, A., Prat, C., Haba, L., Maldonado, J., Ruiz-Manzano, J., Gavin, P., Samper S., Ausina, V., & Dominguez, J. (2011). Pyrosequencing for Rapid Molecular Detection of Rifampin and Isoniazid Resistance in *Mycobacterium tuberculosis* Strain and Clinical Specimens. *Journal of Clinical Microbiology* 49(10), 3683.