Quality Control in the Evolving Landscape of Molecular Diagnostics Testing

Quality Control

A Bio-Rad Technical Article

A laboratory in a cutting-edge field like molecular infectious disease testing merits an exceptional quality control program to strengthen confidence in lab performance and support excellent patient care. However, for the relatively new segment of molecular diagnostics, QC standards and regulations are not as well-defined as more traditional areas of *in vitro* diagnostics. The rapid innovation and evolving regulations of molecular infectious disease testing can make it difficult to create and maintain an effective QC program that takes quality, efficiency, and regulatory requirements into account. This informative article will highlight relevant QC considerations for molecular diagnostics and present you with effective QC solutions to support a dynamic and evolving molecular laboratory.

Bio-Rad is an industry leader in quality control with a growing menu of molecular infectious disease control materials. With powerful QC data management software, expert customer service, and educational QC resources, Bio-Rad is excellently suited to guide your molecular laboratory on the path to a stronger quality control program. Incorporating objective and automated QC practices can improve a laboratory's ability to detect and correct errors, helping your laboratory to produce higher quality results and increase lab efficiency.

The following concepts will be explored:

Improving lab performance with comprehensive QC strategies

Adhering to thorough QC procedures can help molecular laboratories closely monitor testing for random or systematic error and identify immediate data shifts or abnormal long-term trends.

Streamlining QC with data management software

- **Difficulties of data management in molecular laboratories**
  As molecular diagnostics grows more popular and many laboratories increase their volume of molecular testing, the amount of QC data to collect and analyze will continue to increase, making manual data management more difficult.
- **Supporting the molecular laboratory with Unity software**
  Integrating Bio-Rad's Unity Real Time QC data management software into your molecular laboratory is a transformative step in modernizing and simplifying lab procedures.

Effectively evaluating assay performance with independent control materials

From a trusted provider of quality products and services, Bio-Rad's molecular controls are a valuable building block in an effective, comprehensive quality control program.

Investing in laboratory excellence

Effective quality control programs work to limit the risks of considerable economic consequences, damage to a laboratory's reputation, or possible patient harm.

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Improving lab performance with effective QC practices

Systematic quality control is a laboratory's first line of defense against potentially disastrous mistakes or problems. This is especially true for clinical laboratories, where lab results directly advise patient treatment. However, any change in the test system or process, from new reagent lots to new instruments, could potentially affect result quality and integrity. Procedural errors, instrument malfunctions, environmental changes, and other variables can also alter test results. While some of their effects are obvious, other changes are more subtle and can only be detected by a methodical quality control analysis.

A standard quality control program might rely on in-kit controls and proficiency surveys, but supplementing those with independent third party controls and QC data management software will help strengthen QC measures.

Adhering to thorough QC procedures can help molecular laboratories closely monitor testing for random or systematic error and identify immediate data shifts or abnormal long-term trends. Detecting errors early allows laboratories to quickly address issues before they adversely affect patient data.

A standard quality control program might rely on in-kit controls and proficiency surveys, but supplementing those with independent third party controls and QC data management software will help strengthen QC measures. A rigorous quality control program will not only help fulfill regulatory requirements, it will increase result confidence, enhance efficiency, minimize budgetary waste, and simplify lab procedures.

Streamlining QC with data management software

Integrating Bio-Rad's Unity Real Time QC data management software into your molecular laboratory is a transformative step in modernizing and simplifying lab procedures. Following a rigorous quality control program is essential, especially when dealing with patient samples. It can be challenging to prioritize quality while saving time, complying with regulations, and minimizing expenses, but automated data management can greatly simplify the QC process.

Challenges with molecular QC data management

Many molecular laboratories spend hours manually entering and analyzing QC data in spreadsheets or basic software programs. In addition to taking up valuable time, this process can be long, tedious, and error-prone. Random error is often unavoidable when manually recording data. Lab staff may also be spending a great deal of time performing QC collection and recording tasks, but this may squander valuable time that could be spent elsewhere.

An effective QC analysis takes into account QC results over time and compares those results with peer lab data. Performing this level of analysis by manually gathering data from detailed spreadsheets and sourcing outside data can be challenging, and it can take longer to notice errors or variations in the data. Time is everything in a clinical lab—the longer it takes to identify errors, the more data could be affected.

As molecular diagnostics grows more popular and many laboratories increase their volume of molecular testing, the amount of QC data to collect and analyze will continue to increase. However, automated software makes managing and analyzing high volumes of data simple and efficient. Effective QC data management software can streamline data collection and analysis processes, supporting your growing molecular laboratory and its quality goals.

Supporting the molecular laboratory with Unity Real Time

A comprehensive data management system can support your molecular laboratory's QC needs, especially as your lab continues to grow. A powerful QC data management software program like Unity Real Time can automate the steps of a QC data system, from collection to organization to analysis.

With Unity connectivity solutions, data flows directly from lab instruments and LIS systems to the Unity Real Time software, eliminating the need for time-consuming manual data recording. This automated flow of data also reduces defect opportunities in the data entry process. Instead, results are digitally communicated to create a reliable, accurate, and standardized database of results.

"Use of independent third party controls should be considered, either instead of, or in addition to, any control materials supplied by the reagent or instrument manufacturer." ISO 15189:2012 5.6.2.2 Quality control materials

The automation of QC documentation and analysis saves time and presents you with the information you need to monitor quality more efficiently while devoting your time to problem-solving and other important tasks.

Because test results are transmitted to the data management software, laboratories can monitor data in real time. This means that meaningful errors that might otherwise go unnoticed can be quickly identified, allowing urgent issues to be addressed as soon as possible. For example, in molecular infectious disease testing, cycle threshold values (which can indicate potential performance issues) can be observed in real time, providing insight into the efficiency of those reactions.

Once results are transmitted, the powerful statistical capabilities of Unity Real Time can conduct a comprehensive QC analysis. For quality control, bias (how much results differ from reference results) and imprecision (how much variation exists between results) are key statistics in evaluating quality. Unity Real Time automatically calculates and tracks this data over time, presenting you with an analytical window into the workings of your lab. Not only can the software alert you to immediate shifts that may need problem-solving, but it can also monitor values over time to identify more subtle trends that could be affecting lab performance. As reagent and calibrator lots are switched out, test operators change, instrument maintenance occurs, and small environmental changes happen, Unity Real Time monitors QC results and identifies shifts or concerning trends.

Unity Real Time also provides access to data from peer groups, an invaluable resource for comparing your molecular lab testing performance against other laboratories. Peer lab data allows laboratories to compare result data and long term trends, which can help identify problem areas. InstantQC reports provide a snapshot comparison of your lab data and interlaboratory data, a tool that is especially useful for troubleshooting specific problems. Monthly reports provide a detailed analysis of lab performance, highlighting potential issues and monitoring results over time.

The automation of QC documentation and analysis saves time and presents you with the information you need to monitor quality more efficiently while devoting your time to problem-solving and other important tasks. This automated documentation process also makes regulation compliance more straightforward. Rather than spending time compiling data from spreadsheets, detailed QC reports can easily be printed for auditors to review.

Every feature of Unity Real Time helps molecular laboratories take control of their QC and develop a comprehensive awareness of performance strengths and weaknesses. A quality control program monitored by powerful data management and analysis tools, available in Unity Real Time, can help save time and increase result confidence.

Evaluating assay performance with independent control materials

Bio-Rad's independent quality control materials bring molecular infectious disease testing one step closer to the ideal of standardization and uniformity in clinical testing. From a trusted provider of quality products and services, Bio-Rad's molecular controls are a valuable building block in an effective, comprehensive quality control program.

A quality control program is only as effective as its control materials. If QC materials do not perform as expected, small, but potentially harmful, errors could go unnoticed. Even a careful data analysis procedure cannot catch mistakes if the data does not accurately present them.

For the molecular infectious disease market, Bio-Rad offers multilevel, multianalyte controls that accurately and objectively assess assay performance. Bio-Rad's quality control materials allow laboratories to evaluate QC factors over time with one set of control materials. This way, if there is any variation between reagent or calibrator lots, environmental changes, or instrument issues, using one set of control materials will more likely reflect any performance differences. These QC materials are liquid and ready to use, with no need to worry about reconstitution and the potential room for error in the reconstitution process.

Currently, Bio-Rad offers three controls for molecular infectious disease testing.

- **Amplichek I** monitors performance of quantitative assay procedures for viral load assays for Human Immunodeficiency Virus (HIV-1), Hepatitis B Virus (HBV), and Hepatitis C Virus (HCV).
- **Amplichek II** monitors the performance of Healthcare Associated Infection (HAI) assays for Methicillin Resistant *Staphylococcus aureus* (MRSA), Methicillin Sensitive *Staphylococcus aureus* (MSSA), *Clostridium difficile (C diff.)*, and Vancomycin Resistant *enterococci* (VRE or vanR)
- **Amplichek STI** monitors testing for three common sexually-transmitted infections: *Chlamydia trachomatis* (CT), *Neisseria gonorrhoeae* (NG or GC), and Human Papillomavirus (HPV) for genotypes 16, 18, and 68.

Because these controls contain multiple analytes, they can free up valuable space on a multiplexed assay. Using one control to monitor assays for several analytes at once also reduces the number of control materials needed, easing budgetary and inventory concerns.

However, one of the most clinically valuable features of Bio-Rad's independent controls is their similarity to patient specimens. Because assay controls monitor the test system, it is important that controls perform similarly to patient samples. Each Bio-Rad molecular control is designed with intact inactivated pathogens in order to mimic the performance of real patient samples. This allows controls to reflect inconsistencies or changes in a similar manner to patient samples.

Because assay controls monitor the testing of patient samples, it is important that controls perform similarly to patient samples.

Many in-kit controls are made from synthetic materials and optimized to function with specific assay platforms and materials. Their performance would more closely mimic assay calibrators because they were constructed under the same conditions with the same materials. If an issue affected a calibrator, the in-kit control might react in the same manner, making everything appear normal while the underlying issue may continue to affect patient results. It is important to use effective QC materials that will more likely respond to small shifts in assay performance in order to effectively survey lab performance.

Bio-Rad's molecular control materials are designed with intact inactivated pathogens. When the control is run, this intact pathogen undergoes the same process as pathogens in patient samples, allowing the entire analytical process of extraction, amplification, and detection to be monitored. Not every control can objectively monitor the full analytic process. Some in-kit controls are lysates (which do not monitor the extraction process) or are composed of partial sequences, providing an unclear representation of the testing process.

Using Bio-Rad's independent control materials allows molecular laboratories to assess every step of the analytic process for a rigorous QC evaluation. Bio-Rad's growing line of multianalyte molecular controls can streamline lab processes, increase efficiency, and consolidate inventory space. Ultimately, choosing quality control materials that serve as objective assessors of the molecular infectious disease testing process is a step towards greater result confidence.

Investing in laboratory excellence

Quality control is, at its core, a form of risk mitigation. Effective quality control programs work to limit the risks of possible patient harm, economic consequences or damage to a laboratory's reputation. Implementing a comprehensive quality control program provides an extra layer of security to screen for possible complications or mistakes, potentially saving a laboratory from damaging economic or legal fallout.

Clinical laboratories, like any businesses, are constantly under pressure to increase efficiency and lower spending. While a supplemental layer of control materials and QC software might seem like an unnecessary added expense, a more limited quality control program may ultimately cost a laboratory much more. Money not spent up front on problem detection and prevention can result in much higher costs in the long run.

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Some control materials may be more inexpensive, but costs should not be prioritized above quality testing. For all their convenience, in-kit controls that use synthetic materials and are optimized for specific instruments or reagents may not be as attuned to nuanced variations in patient samples. Supplementing a quality control program with independently-manufactured control materials can contribute to a comprehensive analysis of instrument performance. Using Bio-Rad's molecular controls may also help minimize inventory waste, since their usage is not restricted to a single reagent lot.

"The laboratory shall use quality control materials that react to the examining system in a manner as close as possible to patient samples."

ISO 15189:2012 5.6.2.2 Quality control materials

Integrating the UnityReal Time QC data management platform into a molecular laboratory promotes efficiency, and quickly address potential performance issues. The ability to monitor all QC data in real time with powerful analytical software helps detect any errors or irregularities that may adversely affect patient results, whether they are sudden shifts or more gradual trends over time.

Investing in a comprehensive quality control program lowers the risk of inconsistent or inaccurate results that, if allowed to leave the laboratory, could result in expensive retesting or could potentially lead to misdiagnoses. By catching mistakes before any invalid results leave your lab, an effective quality control program avoids potentially drastic consequences for your laboratory.

Because a molecular testing laboratory's first priority should be to their patients, adopting rigorous quality control measures is an investment in a higher standard of patient care. Supplementing a laboratory's quality control program with independent quality control materials and data management software tools demonstrates the laboratory's dedication to economic efficiency, forward-thinking and exceptional patient care.

References

- International Organization for Standardization. ISO 15189: 2012 Medical laboratories – Requirements for quality and competence. 2012. https://www.iso.org/standard/56115.html

Further reading

- www.qcnet.com/molecular
- www.qcnet.com/costofquality
- "Digital management of quality control: a critical tool for the modern lab" by Nico Vandepoele http://www.qcnet.com/molecular/pdf/MLO-1411.pdf

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For further information, please contact the Bio-Rad office nearest you or visit our website at www.qcnet.com/molecular

Clinical Diagnostics Group

Website *www.bio-rad.com/qualitycontrol* ***Australia*** *61-2-9914-2800* ***Austria*** *43-1-877-8901* ***Belgium*** *32-9-385-5511* ***Brazil*** *+55 (31)3689-6600* ***Canada*** *1-514-334-4372* ***China*** *86-21-61698500* ***Czech Republic*** *420-241-430-532* ***Denmark*** *+45-4452-1000* ***Finland*** *358-9-804-22-00* ***France*** *33-1-47-95-60-00* ***Germany*** *+49 (0)89-318-840* ***Greece*** *30-210-7774396* ***Hong Kong*** *852-2789-3300* ***Hungary*** *+36-1-459-6100* ***India*** *1800-180-1224* ***Israel*** *972-3-9636050* ***Italy*** *+39-02-216091* ***Japan*** *81-3-6361-7070* ***Korea*** *82-2-3473-4460* ***Mexico*** *+52 (55)5488-7670* ***The Netherlands*** *+31-318-540666* ***New Zealand*** *64-9-415-2280* ***Norway*** *+47-23-38-41-30* ***Poland*** *48-22-3319999* ***Portugal*** *351-21-472-7700* ***Russia*** *+7-495-721-1404* ***Singapore*** *65-6415-3170* ***South Africa*** *27-11-442-85-08* ***Spain*** *34-91-590-5200* ***Sweden*** *+46-8-555-127-00* ***Switzerland*** *+41 (0)26-674-55-05/06* ***Taiwan*** *886-2-2578-7189* ***Thailand*** *662-651-8311* ***United Kingdom*** *+44 (0)20-8328-2000*