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White Paper

Infectious disease assay development: choosing the appropriate external controls

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During the development of a molecular-based assay for infectious disease research, or when using a pre-qualified assay or sequencing tool, it is important to select appropriate external controls to evaluate and verify the performance of each process. This testing is imperative in tracking drift and run-to-run variation within a procedure. Here, we will discuss the importance of choosing the appropriate external controls, and will provide information on how to select the appropriate cultures and nucleic acids for your tests.

There are a number of different types of external controls that should be employed as part of your good laboratory practices when developing, validating, or evaluating a novel molecular-based assay or tool. These controls are positive or negative references that are treated in parallel with test specimens to verify technical performance and interpret the quality of data. When used properly, external controls can both confirm that a test is performing correctly as well as help identify problems in the event of a test failure[1-3].

External controls can be used to test a number of sources of variability, including sample collection, nucleic acid extraction procedures, sample preparation, and data acquisition. For example, let's say you are evaluating a quantitative real-time PCR assay for the detection of a specific pathogen. When processing each batch of samples, you would want to include external controls that represent the strains of the targeted pathogen. These control samples should be prepared, extracted, and tested in the exact same manner as each sample. Subsequently, the derived results from the control samples during each stage of your procedure should then be analyzed prior to examining the sample results. If the assay does not perform as expected, all results for each of the samples should be considered invalid, and the assay re-run.

The difficulty in obtaining and employing the ideal controls lies in how reliable and suitable it is for a particular assay. A control that may work for one type of assay or platform may not necessarily work for another. For this reason, it is essential that the external controls used are optimized for the specific assay or platform being tested. To aid in assay validation, ATCC offers an expansive array of authenticated cultures and nucleic acid preparations for use as external controls in nucleic acid extraction, process verification, amplification, and proficiency testing. Each of these products are prepared as high-quality, authenticated materials backed by meticulous quality control procedures, making them ideal as external controls for process validation.

Overall, choosing the ideal external control is critical in the evaluation, verification, and validation of novel assays or tools. Through the use of appropriate authenticated strains and nucleic acids, run-to-run variation, sample preparation, and assay execution can be properly analyzed.

References

1. OIE. Terrestrial Manual. Chapter 1.1.5. Principles and Methods of Validation of Diagnostic Assays for Infectious Diseases, 2013.
2. Lee MA, *et al.* Internal and External Controls for Reagent Validation. Current PCR. http://www.gene-quantification.com/lee-et-al-horizonpress-2008.pdf, 2008.
3. Dasgupta A, Sepulveda JL. Accurate Results in the Clinical Laboratory – A Guide to Error Detection and Correction. Elsevier, 2013.

Additional Resources

- Quality Control Strains for Commercial Kits
- Clinical Research Tools
- Quantitative Nucleic Acids

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