TECHNOPATH
CLINICAL DIAGNOSTICS

Why use Multichem® Third Party Controls?

THE QUALITY CONTROL COMPANY

The importance of quality medical services is recognised globally with several accreditation bodies existing internationally including ISO (International Organisation for Standardisation) who have developed a set of guidelines and quality systems to ensure clinical laboratories provide reliable test results. ISO 15189:2012 was designed to outline the "requirements for competence and quality that are particular to medical laboratories". Laboratory competence and quality are critical in patient diagnosis and care to ensure they meet the need of the requesting clinicians & patients.

ISO 15189:2012 recommends the use of *"third party control materials, either instead of, or in addition to, any control materials supplied by the reagent or instrument manufacturer"*

Choosing a control material is as important as choosing an instrument, method, and assay. Laboratories need to consider multiple factors when selecting quality controls. One key consideration is the ability of the control to correctly monitor the performance of the method on the basis of the inherent analytical quality of an assay.

Control material may be provided by the instrument manufacturer or by an independent control manufacturer. The control materials provided by the manufacturer of the instrument or reagents are often referred to as "kit" controls. The control materials provided by an independent manufacturer are often referred to as "third party" controls.

The term "third party" is used to describe a quality control product that helps provide an independent assessment of a diagnostic device or method, and is not optimized for any specific instrument or reagent system. Third party controls are manufactured independently of the test system calibrators and reagents. Such controls generally begin with a human base matrix that helps provide a product analogous to a patient sample. Third party controls with a longer shelf life allow use of the same control lot over multiple changes in reagents and calibrators, giving the laboratory the ability to detect shifts that may occur with new reagents or calibrators over the shelf life of the control. Multichem® Third Party Controls routinely have a shelf life up to 36 months, which allows end users the opportunity to minimize the transitions between different lots, and adhere to a long term monitoring goal by remaining on the same lot until expiry.

Multichem® Third Party Controls have distinct advantages over kit controls that are linked into reagent/calibrator/analyser systems in that these kit controls are designed for use only on their own test systems. More importantly, kit controls are often manufactured from the

same materials as the calibrators. Consequently, the control may mimic the calibrator, making it less sensitive to changes in device performance. This can lead to acceptance of patient test results with analytical error that could be medically important. Often times a laboratory using an instrument manufacturer or kit control may receive a different control lot with each new reagent lot. This does not provide the laboratory with the benefits of long-term QC monitoring as mentioned earlier.

Benefits of the Multichem® Third Party Controls as they relate to Laboratory QC practice.

Matrix effect evaluations are designed to help users to determine whether matrix effects are the source of unexpected results that are sometimes observed with processed samples when two measurement procedures are compared; to identify and quantify the magnitude of the effects; and to ensure that laboratory performance is evaluated fairly if matrix effects are present (reference CLSI EP14-A2 Evaluation of Matrix Effects, Approved Guideline, second edition). Matrix effect phenomena involve the interplay of four major components in analytical test set up: instrument design, reagent formulation/ measurement principle, calibrator material composition and control material composition; as well as processing technique. Elimination or reduction of matrix effects requires either an improvement in the analytical specificity of the measurement procedures or in the materials used for calibrator and quality control.

As a control manufacturer, Technopath has limited power to manage for system matrix effects that involve the interplay of all the major components in the analytical test set up of an IVD system, i.e. instrument design, reagent formulation/measurement principle and calibrator material composition. Therefore matrix compatibility to patient specimens is an important characteristic for third party controls and calibrators to avoid the potential for significant deviation in performance from patient specimens. Technopath Multichem® Controls are designed for inherent safety and all claims are verified. Wherever possible, Technopath controls are formulated from a human base matrix, using raw material analytes that are also derived from human origin. Critical aspects of product functionality are then QC tested for every lot prior to release, and all released products are intended to be used for monitoring of a specific list of analytes on automated analyser platforms. Technopath's approach to Value Assignment encompasses variability of IVD test systems through selection of multiple reagent lots and calibrator where possible and/or multiple calibration events and analyser runs over multiple days, simulating the laboratory's routine

IQC operation. Such control material can therefore be described as commutable and will enable the control material to react to the examining system in a manner as close as possible to the patient sample.

The following are some examples of other international regulatory standards and guidelines that recognize the requirements and benefits of using third party controls as part of a clinical laboratory internal quality control programme.

"...quality control materials should be different from the calibrator materials to ensure that the QC procedure provides an independent assessment of the measurement procedure's performance in its entirety, including the procedure for calibration of the measurement" [1.]

"For each test system, the laboratory is responsible for having control procedures that monitor the accuracy and precision of the complete analytical process. Control materials must be tested in the same manner as patient samples" [2].

"Controls independent of those produced by the manufacturer of the test or analyser should be used." "The laboratory must have a system of long-term monitoring of internal quality control results to assess method performance" [3].

"Medical laboratories shall perform internal quality control. Use of third party human matrix quality control is recommended for all analytes" [4].

1. CLSI C24-A3, Statistical Quality Control for Quantitative Measurement Procedures: Principles and Definitions; Approved Guideline—Third Edition, 6.2.1 Relation to Calibrators

2. 42 CFR Part 493.1256 Medicare, Medicaid, and CLIA Programs; Laboratory Requirements Relating to Quality Systems and Certain Personnel Qualifications; Final Rule.

3. NATA (National Association of Testing Authorities)AS 4633 (ISO 15189), Australia, 5.6.1 Internal Quality Control

4. Essential Standards for Registration of Medical Testing Laboratories in India, Quality Council of India, 3.5.2 Quality Assurance