



Harmonizing Laboratory Test Results for Clinical Trials

A procedure for managing variability in multiple central laboratories

INTRODUCTION

Most, if not all, central laboratories conduct clinical and anatomic pathology testing among a variety of laboratories—a situation that has intensified with the globalization of clinical trials as well as the dramatic increase in highly specialized laboratory testing. As a result, no central laboratory today conducts 100 percent of its testing on identical analytical platforms across all of its labs, so it's not surprising that there are many different approaches to managing variability.

Unique among central laboratories, LabConnect processes and infrastructure were specifically designed to leverage the benefits of a distributed laboratory model. The benefits of the distributed “decentralized central lab” model include reduced logistical costs, improved sample quality and regional testing expertise.¹ LabConnect has developed a global network of regional laboratories to support both routine and highly specialized testing for clinical trials ranging from single-site studies to large multinational trials.

Establishing the accuracy, precision and consistency of study samples is of paramount importance if the data are to meet the standards of international regulatory agencies. To ensure results from multiple labs will be considered viable for clinical trial purposes, LabConnect has developed a rigorous program of harmonization procedures to be used in conjunction with an ongoing internal quality control program.

The following paragraphs outline the methodology LabConnect uses to establish and maintain data harmony within the network.

THE HARMONIZATION PROCESS

LabConnect collaborates with the Canadian External Quality Assessment Laboratory (CEQAL) to establish and maintain testing accuracy, data management and analytical support among and between LabConnect network laboratories in the U.S., Europe, Asia-Pacific, Ukraine, South America and India.

The process:

- Define and standardize. One laboratory is designated as the laboratory of reference for the establishment of standard reporting units and common reference intervals.
- Provide consistent samples. CEQAL prepares and distributes commutable control samples of testing materials in large lots to ensure consistency.
- Monitor precision. All network laboratories receive three levels of internal quality control (IQC) samples for monitoring analytical precision within-day and between-day.
- Baseline assessment. Network laboratories undergo a baseline assessment of their analytical performance using common sets of human serum samples covering the clinical range of interest for the analytes measured. To check accuracy (“trueness”), many of the analytes within these samples have target values assigned by credentialed reference methods that can be traced to international standards. Post-analytical normalization equations correct for any calibration bias.
- Critical analytes assessment. Customized, accuracy-based, internal quality control samples for critical analytes are also prepared. These samples have target values assigned by credentialed reference methods and serve as an accuracy base to ensure that the calibration of the testing systems for critical analytes does not change over the course of the study.



- Ongoing monitoring. Lastly, harmonized laboratories must take part in an ongoing externally blinded monitoring program in which a large number of U.S. and international clinical laboratories participate. These results are aggregated to form a robust data set that can be used to assess the ongoing performance of the participating laboratories within the LabConnect network.

ASSESSING PERFORMANCE

LabConnect uses three levels of criteria to establish laboratory performance: minimum, desirable and optimum. The minimum standard is the same as that used to certify hospital laboratories in the U.S.; the latter two categories require greater accuracy and precision.

Using biological variation data, LabConnect calculates a Total Error Allowable (TEa) by combining figures for allowable bias and allowable imprecision.

During periodic testing, harmonized test results from the network are used to calculate the observed percentage change for each laboratory relative to the network reference laboratory. From these data, the CV index of biological variation (observed vs. desirable) is calculated. An index greater than 1 indicates that an intervention is warranted.

In clinical trials where precise, accurate measurement of a particular analyte is required, CEQAL prepares customized human serum accuracy (CHSA) samples. These commutable samples have target values assigned by internationally credentialed reference methods for the critical analytes. Tested at the same time as the harmonization samples, CHSA samples provide an independent metric for monitoring calibration bias.

CONCLUSION

The precision, accuracy and overall quality of laboratory test results used in clinical trials are of the utmost importance.

LabConnect has partnered with CEQAL, an international leader in its field, to develop a superior program to monitor and standardize laboratory testing within a distributed laboratory network at the highest possible level.

The human serum samples CEQAL provides are commutable, free of additives and stabilizers, and have target values assigned by credentialed reference methods. CEQAL's objective analysis of the resulting data is an independent verification of individual laboratory performance.

By utilizing a meticulously executed program of laboratory harmonization, LabConnect assures clients that global clinical trial data from multiple laboratories on different continents have the same or higher comparability as data produced by a single facility.

¹Tomasz Anyszek, Eric Hayashi, Frank D. Morrow, "Decentralized Central Labs," International Clinical Trials, August 2010 Issue

ABOUT LABCONNECT

Founded in 2002, LabConnect provides global central laboratory services including routine and esoteric laboratory testing, kit building, sample management, biostorage and scientific support services for biopharmaceutical and CRO clients. LabConnect's unique combination of state-of-the-art technology, world-class laboratories, easy access to emerging markets and extensive specialized testing expertise means the drug development industry can rely on a single provider for all of their central laboratory service needs.

