NATIONAL BIOMONITORING NETWORK

Strategy for Harmonization of Laboratory Measurements

The National Biomonitoring Network (NBN) is a performance-based system of public health laboratories engaged in human biomonitoring to inform public health practice. As such, the design of NBN member programs vary by project intent, design, scope and methodology. This flexibility affords biomonitoring programs the opportunity to customize projects to their specific needs, meet jurisdictional requirements and promotes innovation in analytical testing by encouraging method development in response to advances in analytical technology. Performance based networks including the NBN, however, have a significant challenge of harmonizing laboratory measurements among member laboratories to allow for comparison of laboratory data.

APHL reviewed the protocols of multiple networks to assist in the development of this strategy for harmonization of laboratory measurements in the NBN, as outlined in the table below:

Network	Design	Approach	Harmonization
LRN-C	Emergency Response	• Performance based • Designated analytes • Limited jurisdictional flexibility	• Performance specifications • External proficiency • Exercises
NHANES	Nationally representative statistical sample	Single laboratory	Not applicable
Canadian Health Measures Survey (CHMS)	Nationally representative statistical sample	Designated laboratories test for specified analytes	Not applicable
HBM4EU	Multi-national design	• Specified analytes • Limited jurisdictional flexibility	• Initial demonstration of capability • External proficiency challenges • Inter-laboratory and inter-network assessments
CHEAR/HHEAR	• Target analysis • Untargeted analysis to inform health research	• Performance based • Varied analytes	• Initial demonstration of capability • External proficiency testing • Inter-laboratory assessments
NBN	• Emergency response • Community investigations • Population-based surveillance	• Performance based • Varied analytes	• Initial demonstration of capability • External proficiency challenges • Inter-laboratory and inter-network assessments

The LRN-C is the network that most closely resembles the NBN in structure and philosophy and so several of the approaches to harmonizing laboratory measures in the LRN-C are included in the overall strategy for the NBN.

Comprehensive quality management system that includes the pre-analytical, analytical and post-analytical phases of biomonitoring testing.

As a requirement of membership, laboratories must attest to having a quality management system that monitors: all specimen collection, laboratory testing and reporting processes, identifying problems and opportunities for improvement, and a protocol for corrective action.

Evidence of analytical capability at specified performance levels.

Biomonitoring methods are typically mass spectrometry based Laboratory Developed Tests (LDTs) that require internal validation to assure the desired level of sensitivity, specificity, precision and accuracy for the intended project. The reporting limits for each analyte in the assay are also determined at this stage.

Demonstration of analytical proficiency.

Laboratories must successfully participate in testing challenges of unknown specimens that show the laboratory can accurately measure analytes of interest in complex biological matrices. Recognizing that external proficiency programs may not be available for all analytical targets, particularly for emerging compounds of concern, the NBN provides a hierarchical approach to proficiency testing:

- **External proficiency testing programs** that provide graded assessments of testing challenges are used when available. Several high quality programs are available from New York State, the Centre du Toxicologie du Quebec and European partners. Participation in these programs provides several benefits in that laboratories around the world are testing common specimens prepared by experienced providers, the results are analyzed and reported in systematic ways and the data afford comparison among and between participating laboratories. External proficiency data are a cornerstone of harmonization of laboratory measures across the NBN.
- **Inter-laboratory comparison** via round-robin or split sample testing is a good way to demonstrate analytical proficiency in the absence of a formal external program. Homogeneity of specimens is critical to a successful inter-laboratory assessment and should be initiated only after careful planning and preparation. Cross-network collaboration and evaluation are encouraged, and provide a unique opportunity to harmonize measurements internationally. CDC's Biomonitoring Quality Assurance Support Program is one example of inter-laboratory comparison. A second inter-laboratory program, Health Assessment Measurements Quality Assurance Program is run by the National Institute of Standards and Technology and provided reports and certificates of completion to participants, along with workshops and webinars which discuss results, as well as methodological advancements in the area of health assessment measurements.
- **Blinded internal challenges** in which the analytes and or target concentrations are unknown to the analysts are an acceptable way to demonstrate analytical proficiency. This approach may be particularly important during method development and prior to the establishment on or external proficiency or inter-laboratory assessments.

Common, traceable analytical standards, controls and certified reference materials.

Whenever practical, NBN laboratories should use common, traceable analytical standards and controls. Alternatively, inter-laboratory analysis of standards and internally prepared controls provides additional confidence in the accuracy of the measurements and evaluates laboratory bias. Judicious use of certified and standard reference materials throughout the testing process provides additional confirmation of method performance.

External assessment or certification of laboratories reporting results to participants or clinicians.

NBN member laboratories who intend to report individual biomonitoring results to participants or to their clinicians, are required to maintain an external certification or accreditation for the biomonitoring laboratory such as; CLIA, CAP or ISO 17025. These external parties provide on-site assessment of laboratory policies and procedures, analytical processes and the entire quality management system. Rather than create an additional evaluation system, the NBN relies on these established partners to conduct audits thereby, reducing the administrative burden on the member laboratories to meet multiple standards.

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