been originally validated to detect constitutional copy number abnormalities from peripheral blood will require a separate full validation to detect somatic alterations but may only require a more limited study to allow for a different specimen such as saliva to be used.

If an array has been validated for constitutional copy number alterations from fresh/frozen tissue, every potential tissue source (lung, liver, kidney, etc.) does not require separate validation, unless they potentially include interfering substances (eg, mucin).

Validations can be augmented by, but not supplanted with, additional reference materials (eg, characterized cell lines, cell lines with spiked in nucleic acids). Matrix-appropriate samples must be included.

Evidence of Compliance:
- ✓ Records of validation studies

CYG.49575 Assay Performance Monitoring **Phase I**

Assay performance is monitored for each run and quality metrics are verified prior to reporting results.

NOTE: The monitoring of assay performance includes the review and recording of the quality metrics of each run. This may include:
- *DNA labeling verification (using detection of label, purification and quantitation of labeled DNA fragments, or electrophoretic techniques)*
- *Review of DLRs (Derivative Log Ratio)*
- *Genotyping performance (SNP arrays only)*
- *Number of suboptimal samples*
- *Monitoring the number of copy number alterations per sample*
- *Other quality metrics provided by the array software*

Criteria for acceptable performance must be defined. This includes hardware and analytical software.

Evidence of Compliance:
- ✓ Records of verification

REFERENCES

1) South ST, Lee C, Lamb AN, Higgins AW, Kearney HM, Working Group for the American College of Medical Genetics and Genomics Laboratory Quality Assurance Committee. ACMG standards and guidelines for constitutional cytogenomic microarray analysis, including postnatal and prenatal applications: revision 2013. *Genet Med.* 2013; 15(11):901-9.
2) Shao L, Akkari Y, Cooley LD, et al. Chromosomal microarray analysis, including constitutional and neoplastic disease applications, 2021 revision: a technical standard of the American College of Medical Genetics and Genomics (ACMG). *Genet Med.* 2021;23(10):1818-1829.
3) Vermeesch JR, Fiegler H, de Leeuw N, Szuhai K, Schoumans J, Ciccone R, Speleman F, Rauch A, Clayton-Smith J, Van Ravenswaaij C, Sanlaville D, Patsalis PC, Firth H, Devriendt K, Zuffardi O. Guidelines for molecular karyotyping in constitutional genetic diagnosis. *Eur J Hum Genet.* 2007 Nov;15(11):1105-14
4) Clinical and Laboratory Standards Institute. *Genomic Copy Number Microarrays for Constitutional Genetic and Oncology Applications. 1st ed.* CLSI guideline MM21-Ed1. Clinical and Laboratory Standards Institute, Wayne, PA; 2015.

CYG.49580 Array Analytical Wet Bench **Phase II**

The laboratory follows a defined process for performing the array analytical wet bench.

NOTE: The procedure must include:
- *A description of the analytical target regions (eg, targeted or genome-wide)*
- *A description of acceptable sample types (see CYG.49545)*
- *Methods and reagents used for isolating, labeling, and hybridization of nucleic acids, as applicable*
- *Controls (including in silico)*
- *Instrument software and version*
- *Acceptance and rejection criteria for the results generated by the wet bench. These should include criteria for determining when the wet bench process has failed or is suboptimal.*