![College of American Pathologists logo]

Quantitative Image Analysis of Human Epidermal Growth Factor Receptor 2 Immunohistochemistry for Breast Cancer: Guideline from the College of American Pathologist[1]

Accuracy - The degree of correctness or true values of a given laboratory result comparing to a gold standard. Accuracy also implies freedom from error.[2]

Algorithm - A sequential set of instructions used in calculations or problem solving. A diagnostic algorithm or a therapeutic algorithm consists of a stepwise series of instructions with branching pathways to be followed to assist a physician in coming to a diagnosis or deciding on a management strategy, respectively.[3] Image analysis algorithms are used to assist image-based assessment of digital pathology slides.

Batch analysis - An analysis in which all of the samples collected for a specific, nonemergent assay undergo the same testing process at the same time or sequentially.[4]

Function Check - Confirmation that an instrument or item of equipment operates according to manufacturer's specifications before routine use, at prescribed intervals, or after minor adjustment. Depending on the type of system, function checks may include calibration.[5]

Instrument calibration - A process of comparison in which an instrument is used to measure or is measured by a calibration standard, and the result is compared to two things: the known value and uncertainty of the standard and the performance specifications required by the customer. It quantifies the relationship between the readings of a measurement standard under controlled and specified conditions.[6]

Inter-run reproducibility - Also known as within-run precision. Replicates of the same sample across different run demonstrate high correlation.[7]

Intra-run reproducibility - Replicates of samples demonstrate high correlation in the same run. This is to monitor sample to sample variation.[7]

Laboratory developed test (LDT) - A type of in vitro diagnostic test that is designed, manufactured and used within a single laboratory according to the laboratory's own procedures.[8]

Metadata - Data/information that provides information about other data which include descriptive, structural and administrative metadata.[9]

Precision - The closeness of agreement between independent results of measurements obtained under stipulated conditions.[2]

Quantitative image analysis (QIA) - 1) A process whereby quantitative and meaningful information is acquired from the digital images of a specimen, and
2) The computer-assisted detection or quantification of specific features in an image following enhancement and processing of that image, including analysis of immunohistochemistry samples, DNA analysis, morphometric analysis, and *in situ* hybridization.[5]

Quantitative image analysis (QIA) system - A system that integrates automated microscopy, high-quality image acquisition, and powerful analytical algorithms to detect, count, and quantify areas of interest and includes the hard-wares (computer, scanner, monitor, informatics network, etc.) as well as soft-wares (algorithms).[10]

Region of interest (ROI) - Also called a potential target or image-subregion; a portion of an image that is of interest and upon which an image analysis will be performed on.[11]

Reproducibility - The ability of a test or study to be duplicated either by the same researcher or by someone else working independently.[12]

Revalidation - A procedure used to assess a previously validated test's accuracy and reliability in detecting the marker of interest when there has been a change in test conditions (e.g. methods, equipment, or specimen or fixative types). The degree of revalidation required depends on the nature of the change.

Validation - A documented program that provides a high degree of assurance that a specific process, system or test method will consistently produce a result that accomplishes its intended purpose, meeting predetermined acceptance criteria.[13]

Verification - The process of evaluating a test or a product of a development phase to determine whether it meet the specified requirements. In the post-development phase, verification procedures to endure the product continuously meeting the initial design specifications.[13]

References

1.   Bui MM, Riben MW, Allison KH, et al. Quantitative image analysis of human epidermal growth factor receptor 2 immunohistochemistry for breast cancer: guideline from the College of American Pathologists. *Arch Pathol Lab Med*. 2019;143(10):1180-1195. doi: 10.5858/arpa.2018-0378-CP

2.   Wagar EA. Laboratory laws and regulations. In: Wagar EA, Horowitz RE, Siegal GP, eds. *Laboratory Administration for Pathologists*. Northfield, IL: College of American Pathologists Press; 2011:215-234.

3.   Martin E. Oxford Concise Medical Dictionary, 9th ed. Oxford, United Kingdom: Oxford University Press; 2015. http://www.oxfordreference.com/abstract/10.1093/acref/9780199687817.001.0001/acref-9780199687817-e-282?rskey=lZze6d&result=321. Accessed July 15, 2018.

4.   Venes D, ed. *Tabers Cyclopedic Medical Dictionary*. 23rd ed. Philadelphia, PA: F. A. Davis Company; 2017. https://www.tabers.com/tabersonline/view/Tabers-Dictionary/743387/0/batch_analysis?q=analysis+batch. Accessed July 15, 2018.

5.   College of American Pathologists. Accreditation checklists. College of American Pathologists website. http://www.cap.org/web/home/lab/accreditation/accreditation-checklists?_afrLoop=18507313584783#!%40%40%3F_afrLoop%3D18507313584783%26_adf.ctrl-state%3Do5jzhyem6_30. Accessed: July 16, 2018.

6.   Payne GC. Calibration: What Is It? Quality Progress. asq.org/quality-progress/2005/05/measure-for-measure/calibration-what-is-it.html. Published May 2005. Accessed July 16, 2018.

7.   Chesher D. Evaluating assay precision. *Clin Biochem Rev*. 2008;29(Suppl 1):S23-26.

8.   U.S. Food & Drug Administration. Laboratory Developed Tests. U.S. Food & Drug Administration website. Updated March 26, 2018. Accessed July 16, 2018.

9.   Riley J. *Understanding Metadata: What is metadata, and what is it for? A Primer*. Baltimore, MD: NISO Press; 2017.

10.   van der Hall PO, Kraan MD, Tak PO. Quantitative image analysis of synovial tissue. *Methods Mol Med*. 2007;135:121-143.

11.   Si J, Lin H, Abousleman G. Electronic imaging and signal processing: detecting regions of interest in images. *SPIE Newsroom*. http://spie.org/newsroom/0414-detecting-regions-of-interest-in-images?SSO=1. Published November 2006. Accessed July 18, 2018.

12.   Samsa G, Samsa L. A guide to reproducibility in preclinical research [published online July 10, 2018]. *Acad Med*. doi: 10.1097/ACM.0000000000002351

13.   U.S. Department of Health and Human Services, Food and Drug Administration. Quality System Regulation, General Provisions, Definitions. 21 CFR §820.3 2012.