ISNS Standing Committee on Quality Assurance

Lexicon of Terms to be used in newborn screening

This lexicon has been developed by the Standing Committee on Quality Assurance of the International Society for Neonatal Screening. It consists of a number of terms common to medical laboratories in general but which are often misused or give rise to confusion as well as terms which are specific for the field of neonatal screening, but which sometimes have different meanings in different parts of the world.

Accuracy. Closeness of agreement between the result of a measurement and the true value of the measurand. [1]

Age of infant. The day of birth should be referred to as D0. The age of the infant at testing is the date of birth subtracted from the date of sample. Preferably, the age of infant should be expressed in hours for DBS collected at <96 h of age.

Analytical sensitivity. Slope of the analytical calibration function (analytical curve or standard curve)[1]

Analytical specificity. The ability of a measurement procedure to determine solely the measurable quantity it purports to measure. [1]

Blind Quality Control (QC). Quality control specimens made to look exactly like patient specimens and treated in the same way through the screening process. For newborn screening, blood or urine specimens made to look exactly like the specimens from newborns". [2]

Borderline. Screening test results either require follow-up or they do not. Results which require follow-up are positive, those which do not, are negative. Borderline is a meaningless classification in this context; this term is best avoided. See inconclusive.

Calibrator. A reference material used for calibration. (Reference material is a material or substance one of whose property values are sufficiently homogenous and well established to be used for the calibration of a measuring system, the assessment of measurement procedure or for assigning values to materials. A given reference material may be used either as a calibration material in calibration of a measuring system and in assigning values to materials, or as a control material in assessing the performance of a measurement procedure, but must not be used for both purposes in a given situation in a particular laboratory. A reference material may be in the form of a pure or mixed gas, liquid or solid. The concept reference material is subordinate to reference standard.) [1] A calibrator must be traceable to a national or international reference material where this is available.

Control material. Material used for the purposes of internal quality control or external quality assessment (proficiency testing), and subjected to measurement according to the same or part of the same measurement procedure as that used for unknown samples in order to monitor analytical performance [1.] Control material is not used for calibration purposes.

Cutoff level. The value of a test variable which distinguishes positive from negative results. It is necessary to clarify whether a result exactly at the cutoff level is regarded as being positive or negative.[3]

Date of assay. Date that sample is assayed.
NOTE: This term is preferred to date of test.

Date of specimen. Date of collection of specimen from the patient.
NOTE: This term is preferred to date of test.

Date of Test. This term is ambiguous and is best avoided.

Detection rate (diagnostic sensitivity). The proportion of affected individuals with positive test results. Expressed as a percentage A/A+C.

Diagnostic sensitivity. see detection rate.

Diagnostic specificity is the proportion of unaffected individuals with negative test results.[3] i.e. D / D+B, expressed as a percentage.

Diagnostic test. A test which implies or indicates a particular diagnosis. This does not imply the diagnosis in question is always correct. There is usually an intention to offer therapeutic intervention following a positive diagnostic test.

Diagnostic testing. The process of testing to discover whether the patient has the condition indicated as possible by the screening program.

Dried blood spot specimen (DBS) Drops of blood onto special collection paper
NOTE: Avoid the use of "Guthrie specimen" in this context.

External (interlaboratory) quality assessment. Evaluation and monitoring of the accuracy and precision of any analytical process in one laboratory by comparison of the same parameters of the same process performed between laboratories using, preferably using identical lots, and comparing results through some centralised data processing system[4]

False negative. An affected individual with a negative test result. This may be because the test result was normal or because there was an inadequate sample, a failure to communicate the test result or other reason. The false negative result is a failure of the screening programme and is not necessarily a failure of an analytical system. A false negative result is a missed case, unless there was a specific refusal for the screening. The false negative rate is (1-sensitivity) i.e. A/A+C.

False positive. An unaffected individual with a positive test. The false positive rate is the proportion of unaffected individuals with positive tests. The false positive rate is (1-specificity) i.e. B/B+D.

Follow up. The total of activities undertaken by the screening program to assure and document appropriate response to a non-negative screening test result.

Frequency. The number of cases per number screening tests. For newborn screening it is equivalent to the birth prevalence, and can be computed by dividing the total number of births by the number of cases giving a '1 per X number'.

Incidence. The number of new cases of a disorder which arise in a specified period of time and in a defined population. The incidence is thus the frequency with new cases of a condition arise.[4] True incidence of the conditions tested for in newborn screening programs is affected by prenatal loss in these conditions therefore incidence should not be used for newborn screening purposes unless true incidence is determined; birth prevalence should be used.

Inconclusive (intermediate, equivocal) test result. A test result so close to the cutoff level that there is uncertainty whether the infant is to be referred for diagnostic testing. NOTE. In most programs using such classification an inconclusive result leads to a request for a repeat specimen (see above).

In-house assay system. An assay system purchased as individual parts; some of the individual parts may be made in the laboratory.

Internal (intralaboratory) quality control. Operational techniques and activities within a laboratory that are used to fulfill requirements for quality. In the medical laboratory internal quality control is aimed both at monitoring a process to assess whether results of measurement are reliable enough to be released and at eliminating causes of unsatisfactory performance at relevant stages of the quality loop. [1]

Kit. (in vitro diagnostic measuring system) Measuring system that is intended by the manufacturer to be used in vitro for the measurement of samples, including blood and tissue donations, derived from the human body, solely or principally for the purpose of providing information concerning physiological state, state of health or disease, or congenital abnormality or to determine the safety or compatibility with potential recipients. May include reagent and calibrator material. [5]

Lower limit of detection (minimum quantifiable value). The lowest result of a measurement that can be obtained by a stated measurement procedure, and that can be given with a statement of uncertainty of measurement. [1]

Measurand (analyte). A measurable quantity subject to measurement.[1]

Positive predictive value (PPV) or Odds of being affected given a positive result (OAPR). The proportion of individuals with positive test results who have the condition screened for (The likelihood that a presumptive positive is a true positive). From the table above, positive predictive value is (A/A+B) as % and OAPR is A/A+B as a ratio.

Positive test result. A test result above or below the cutoff. Recall action will be initiated by a positive test result.

Precision. Closeness of agreement between independent results of measurements obtained under stipulated conditions. [1]

Prevalence. The number of cases of a disorder (old and new) present at a point in time, or during a specified period, in a defined population. Prevalence is therefore the proportion of a population that is affected by a disorder at a particular time.[3] For newborn screening, birth prevalence is used.

Proficiency Testing. Determination of laboratory measurement performance by means of interlaboratory measurement comparison. [1]

Quality Assurance. The planned and systematic activities implemented within the quality system, and demonstrated as needed, to provide adequate confidence that an entity will fulfill the requirements for quality (the totality of characteristics of an entity that bear on its ability to satisfy stated and implied needs. [1]

Reanalysis. Reexamination of the same analyte in another sample from the original specimen. The technology used for the reanalysis may be the same or different from that used in the original analysis. NOTE: This term is preferred to retest

Recall rate. The percentage of specimens, for a particular disorder screening test or laboratory process, which require follow up (whatever the final diagnosis), i.e. those samples with results above or below (as appropriate) the cutoff for the screening test.

Recall specimen. This term is ambiguous and is best avoided (see repeat specimen).

Repeat rate. The percentage of specimens which were inadequate or unsuitable for testing (for whatever reason) and initiated follow up action.
NOTE: do not confuse “recall rate” with “repeat rate”

Repeat specimen. A second specimen from the same individual requested by the screening program because of an *abnormality or inadequacy* of any stage of the screening process.
NOTE: This term is preferred to recall specimen

Retest. This term is ambiguous and is best avoided (see reanalysis).

Sample. The part of the specimen, representative of the specimen as a whole that is used in the test or analysis[1]

Screening. The systematic application of a test or inquiry, to identify individuals at sufficient risk of a specific disorder to benefit from further investigation or direct preventive action, among persons who have not sought medical attention on account of symptoms of that disorder.[6] **A screening test is not intended to be diagnostic**. Persons with positive screening tests must be referred for diagnosis and treatment if necessary.

Screening outcome. The combined results of the whole screening process in terms of epidemiological parameters (see Table 1).

Table 1 Definition of epidemiological parameters with respect to screening.

Screening result	Affected	Unaffected	Total
Positive	True positive (A)	False positive (B)	Screen positive (A+B)
Negative	False negative (C)	True negative (D)	Screen negative (C+D)
Total	Total affected (A+C)	Total unaffected (B+D)	

Screening results. Laboratory analytical results of measurements in dried blood spot specimens

Second Screen. A specimen from the same individual received as part of the in advance planned duplication of the testing process in the population at some time later than the first screen.
NOTE: Avoid the use of "repeat specimen" in this context

Specimen. A specimen is the portion of the blood or other body fluid that is taken from the patient[1]

References

1 Vocabulary for Use in Measurement Procedures and Description of Reference Materials in Laboratory Medicine. Dybkaer R, Eur J Clin Chem Clin Biochem 1997; 35:141-173

2 Legal liability and Quality Assurance in Newborn Screening. American Bar Foundation, Chicago, 1985

3 Cuckle, HS and Wald. NJ (1984) Maternal serum alpha-fetoprotein measurement: a screening test for Down's syndrome. Lancet, i, 926–929

4 National Committee for Clinical Laboratory Standards. Nomenclature and Definitions for Use in NRSCL and Other NCCLS Documents - Second Edition; Proposed Guideline. NCCLS document NRSCL8-P2 (ISBN 1-56238-185-7). NCCLS, 771 East Lancaster Avenue, Villanova, Pennsylvania 19085), 1993.

5 Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices

6 Wald NJ. Guidance on terminology. J Med Screen 1994;1:76