SUPPLEMENTARY INFORMATION (SI)

Towards harmonized criteria in Quality Assurance and Quality Control of non-targeted LC-HRMS analytical workflows for screening of emerging contaminants in human biomonitoring

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SI-1. Harmonised definitions

The following definitions have been drawn from European legislation [1], international organisations, such as UNODC and IUPAC [2–6], scientific networks, like NORMAN, Eurachem and CITAC [7,8], and specialized literature [9–14].

Accuracy: the closeness of agreement between a test result and the accepted reference value. It is determined by determining trueness and precision.

Aliquot: a representative portion of a homogenous sample, assumed to be taken with negligible sampling error.

Analyte: the substance subject to analysis for its detection, identification, and/or quantitation.

Analytical method: the set of operations used in the performance of a specific chemical analysis, systematically presented in the order in which they have to be executed.

Annotation: the act of linking a detected mass spectrometric feature with a chemical. This action corresponds with the levels 3 and 4 from the Schymanski´s scale [15]

Background signal: the null signal, obtained in the absence of analyte or interference derived signals.

Baseline signal: the summation of the background signal plus signal in the analyte (peak) region of interest due to interferents or contamination.

Batch: the set of samples that comprises a worklist analysed without stopping the equipment or without making big changes.

Bias: the difference between the test result and an accepted reference value.

Biomarker of effect: a change in biological response, which can be related to exposure to or toxic effects of chemicals.

Biomarker of exposure: the chemicals and their metabolites measurable in an organism that are related to the exposure of the organism to a chemical.

Calibrator: the pure analyte in a suitable solvent or matrix used to prepare the calibration curve.

Certified reference material (CRM): a material that has had a specified analyte content assigned to it, and whose property values are given by a procedure which establishes traceability to an accurate realization of the unit in which the property values are expressed, and for which each value is accompanied by an uncertainty at a stated level of confidence.

Clean-up: a process to partially remove the matrix, which may cause the matrix effect, from the test portion.

Comparability: the degree to which different methods or results can be represented as similar.

Comparable results: the set of measurement outputs, for quantities of a given kind, which is metrologically traceable to the same reference.

Contamination: unintended introduction of the analyte or interferent that can interfere in the analysis into a sample, extract, or internal standard solution at any stage of the analytical method.

Cross-contamination: the response of contaminants or interferents in a run analysis that comes from a different run analysis or sample.

Detection: analytical signal that may be assigned to an analyte or substance present in a sample.

Determination: the application of the complete analytical process for detecting, identifying, and quantifying an analytical parameter of an analyte.

False negative rate: the fraction of incorrect (false negative) results obtained when a test is applied to positive samples.

False positive rate: the fraction of incorrect (false positive) results obtained when a test is applied to positive samples.

Feature (mass spectrometric): an instrumental response that is characterized by retention time, MS spectra and optionally MS/MS spectra data. This information anable the annontation process.

Field blank: a sample without the test portion or using an equivalent amount of suitable solvent in place of the test portion, that is subjected to all aspects of sample collection, field-processing preservation, and transportation to which the complete analytical procedure is applied. It can be used as synonym of procedural blank sample though usually the last ones are implemented into the laboratory. That means the procedural blank samples do not cover the sampling stage.

Fortified sample: a sample enriched with a known amount of analyte(s).

Harmonisation: bringing about agreement on terminology, concepts, etc. so those different entities can interact based on the same terms of reference.

Human matrix: any discrete biological material of human origin that can be sampled and processed. Examples are blood, serum, plasma, urine, faeces, saliva, sputum, and various discrete tissues.

Identification: assigning a detected analytical signal by non-targeted or suspect screening to one individual analyte or to a group of compounds based on matching their properties. This action corresponds with the levels 1 and 2 from the Schymanski´s scale [15]

Identification level (or level of identification confidence): an approach for communicating identification confidence. The common approach used (in environmental research) includes five levels and was proposed by Schymanski et al. [15].

Interference effect: a systematic error in the analysis caused by a substance in the sample that contributes to the response of the analytical measurement, without influencing its sensitivity for the analyte of interest.

Interferent: any substance other than the analyte that gives a similar analytical response to the analyte or alters the analytical result.

Interlaboratory comparability investigation (ICI): a measure to harmonize analytical methods and their application this way improving the comparability of analytical results. For this purpose control materials (reference materials) can be used. ICIs are even necessary when the laboratories use the same analytical standard operating procedure (SOP).

Interlaboratory comparison study: the organisation, performance, and evaluation of tests on the same sample by two or more laboratories under documented conditions to determine testing performance, which results are compiled into a single report. The results of the laboratories are compared to the consensus values, calculated from results of all the participants after the elimination of the outliers values.

Internal Standard (IS): a substance not contained in the sample with physical-chemical properties as similar as possible to those of the analyte that has to be identified, which is added to the sample in known concentration.

Laboratory reference sample: a sample that has had a specified analyte content assigned to it, that is prepared and tested (homogeneity and stability) by a specific laboratory to be used within interlaboratory study. The analyte amount is given by the laboratory and ensures its traceability.

Limit of detection: the minimum amount of an analyte that can be measured by the analytical method and that can be reliably distinguished from baseline signal.

Linearity: the ability of an analytical method to elicit signals that are directly proportional to the amount of the given analytes or analytical parameters in samples within a given range.

Mass accuracy: the average of the difference between the accurate measured mass to charge (m/z) of an ion and the exact mass to charge, of *n* individual measures.

Matrix: all constituents of a sample other than the analytes.

Matrix effect: a systematic error in the analysis caused by the influence of matrix constituent on the sensitivity of the analytical measurement of the analyte by suppression or enhancement.

Monitoring: the continuous or repeated observation, measurement, and evaluation of a process in a certain field of application, according to given schedules in space and time.

Noise: a set of undesirable fluctuations of the baseline or background signal of an instrument.

Outlier: a result that appears to differ unreasonably from the population of the other results.

Performance characteristic: the parameter that defines the functional quality of an analytical method. This may be for instance selectivity, accuracy, trueness, precision, repeatability, reproducibility, recovery, detection capability, or stability.

Population: a finite or infinite set of individuals (people, things or events) that have at least one trait in common.

Precision: the closeness of agreement between independent test results obtained under stipulated (predetermined) conditions. The measure of precision is computed as the standard deviation of the test result.

Procedural blank or blank sample: a sample without the test portion or using an equivalent amount of suitable solvent in place of the test portion, to which the complete analytical procedure is applied.

Qualitative method: an analytical method that determines the presence or absence of a known constituent or identifies a substance based on its chemical, biological, or physical properties.

Quality assurance (QA): the set of system of activities whose purpose is to provide the confidence that the analytical method or the system fulfills the defined standards of quality with a stated level of confidence.

Quality control (QC): the overall system of activities whose purpose is to control the quality of the results.

Quantitative method: an analytical method which determines the amount or mass fraction of an analyte in a sample.

Range (in the analytical sense): the interval between the upper and the lower amount of the analyte in the sample for which it has been determined that the method is applicable or analytical parameter is accepted.

Recovery: the percentage of the true amount of an analyte, present in or added to the test portion, which is recovered during the analytical procedure. It is determined during validation instead of trueness when no certified reference material is available.

Repeatability: the precision for independent test results, which are obtained with the same method on identical test portions, in the same laboratory by the same operator using the same equipment within short intervals of time.

Representativeness: the consistency between the results and the laboratory samples, and between them, the analytical object and the analytical problem.

Reproducibility: the precision for independent test results, which are obtained with the same method on identical test portions, but the laboratory, operator, and/or equipment can be different within larger intervals of time than one run analysis.

Response: the output of an analytical system as a reaction to a certain stimulus.

Result: a set of analytical values being attributed to a measured compound together with any other available relevant information as the uncertainty of the measurement.

Robustness or ruggedness: capability of an analytical method to remain unaffected by small changes in experimental conditions.

Sample preparation: the set of operations required to convert the test portion into the treated portion.

Sample: the totality of an analysis material having an identical composition or quality.

Sampling: the set of operations needed to obtain a sample or specimen including planning, collecting, recording, labelling, sealing, shipping, etc.

Screening method: a procedure used to detect the presence of an analyte or class of substances at the level of interest.

Selectivity/Specificity: the ability to discriminate between the analyte (*specificity)* or a number of analytes (*selectivity)* to be determined and other materials in the test sample. Matrix influences may affect the analyte signal directly by the interference effect either indirectly by the matrix effect. This characteristic is predominantly a function of the measuring technique described but can vary according to the class of compound or matrix.

Sensitivity: the smallest detectable change in the response of a measuring instrument of the analytical method, typically expressed as the slope of the calibration curve.

Signal to noise ratio: the measurement of the precision of the instrumental signal, expressed mostly by the ratio of the net signal value to a baseline noise parameter (standard deviation or peak to peak distance).

Signal: the response of an instrument to certain stimuli. A signal is characterized by at least three parameters: position, intensity, and width (symmetry, shape).

Solvent blank: the mixture of all the solvents used during sample preparation and/or aliquot of solvent for checking instrumental performance and background contamination.

Stability: the resistance to decomposition or other physicochemical changes of a sample along the time.

Standard operating procedure (SOP): the set of written instructions that describes a repetitive activity followed by an organization.

Subsample: the quantity of material drawn from the test sample on which the analysis is carried out.

Substance: the matter of particular or definite chemical constitution and its metabolites.

Suspect compound: the known compounds in terms of chemical name and molecular formula which are expected to be present in a sample. For these compounds, either no reference standard or incomplete mass spectrometric reference data are available.

Synthetic matrix: a sample where the test portion is substituted by a mixture of the main components of the matrix under study; or by a commercial matrix with a different source origin.

System suitability: the holistic ensuring that an analytical system performs properly against documented performance specifications, for a specific analytical method.

Target compound: the compounds of known chemical name and structure and of which full mass spectrometric reference data, including MS/MS fragmentation and retention time, is available to enable annotation. Reference data have been usually acquired with certified reference standards and quantitative targeted methods are available, alongside some exposure and risk assessment data.

Test sample: a sample prepared from a laboratory sample and from which test portions will be taken.

Trueness: the closeness of agreement between the average value obtained from a large series of test results and an accepted reference value.

Unknown compound: a compound whithout any structure or identity information prior to the analytical workflow.

Validation: a process by which it is evaluated if the performance characteristics of the analytical method meet the particular requirements of specific intended use in quantitative terms.

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