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LETTER TO THE EDITOR

WILEY

Consensus for the use of the alcohol biomarker phosphatidylethanol (PEth) for the assessment of abstinence and alcohol consumption in clinical and forensic practice (2022 Consensus of Basel)

Letter to the Editor

Phosphatidylethanols (PEths) are a group of abnormal phospholipids that can serve as direct alcohol biomarkers. They are formed within the human body from phosphatidylcholines upon enzymatic catalysis by phospholipase D, by exchange of the choline group against ethanol, when alcohol is present. The use of PEths as alcohol biomarker became popular, as they accumulate in red blood cells (RBC), prolonging the window of detection up to several weeks.[1] This can be advantageous for abstinence monitoring when compared with ethyl glucuronide (EtG) and ethyl sulfate (EtS) in urine.[2] Currently, more than 48 analogs of PEth are known.[3] The most prominent analog is PEth 16:0/18:1, which contains a palmitic and an oleic acyl group in the sn-1 and sn-2 position of the glycerol backbone, respectively. Currently, the quantification of PEth 16:0/18:1 is being applied for a variety of purposes, including the follow-up of alcohol-impaired drivers, for the diagnosis and treatment of alcohol use disorders, for newborn screening regarding fetal alcohol syndrome, for organ transplantation to exclude prior alcohol abuse, and within the security environment and workplace testing.[1] Generally, a lower and an upper threshold concentration are applied for PEth 16:0/18:1, which permits the classification into three groups; see Table 1.

During the past decade, many laboratories have been researching and analyzing PEth extensively, and various cutoff concentrations, practices, and methodologies—often country-specific—have emerged. Furthermore, the published data have increased the global interest in PEth, and the number of commercial laboratories that are starting to analyze PEth is ever-increasing. To harmonize PEth analysis and interpretation on a global scale, the Society of PEth Research (PEth-NET) was established in the autumn of 2020. This was followed by a first online symposium in 2021 and the realization of an overview article regarding PEth harmonization by a small group of PEth-NET members.[1] This article lay the basis for the *PEth in Mind* Symposium that took place as an in-person meeting in Basel, Switzerland, on May 19–20, 2022. The second day of the symposium was aimed at having a harmonization discussion among the 36 international participants from 25 different organizations. As a deliverable of the harmonization discussion during this meeting, the *2022 Basel Consensus Document on PEth* was unanimously voted into action by the conference participants. It represents the first internationally established harmonization document on PEth. It is an important document to further increase the use of PEth as a valuable alcohol biomarker in the clinical or forensic toolbox. Moreover, it should also facilitate the integration of PEth into recommendations and guidelines regarding alcohol-related issues and allow the streamlining of PEth quantification, based on clear recommendations for analytical and preanalytical procedures. The consensus defines the target measurand (PEth 16:0/18:1 in whole blood), cutoff concentrations (20 and 200 ng/ml), and minimal requirements for the applied analytical method (accuracy and precision within 15%).

All the key findings of the consensus document are listed below:

Introduction

1. Abstinence from alcohol means no intake of any alcoholic beverages or other alcohol-containing products over a pre-defined period. Chronic excessive alcohol consumption corresponds to an average consumption of 60 g or more of pure ethanol on a single drinking day over a prolonged duration for men and 40 g for women (according to the World Health Organization[4]).
2. The group of ethanol metabolites, phosphatidylethanol, is measured in whole blood as a direct marker of alcohol consumption.
3. When alcohol is consumed, PEth concentrations in the human blood reach an equilibrium (plateau) between formation and elimination (or degradation), which reflects alcohol intake.[5,6]
4. For the assessment of alcohol consumption, the major phosphatidylethanol analog, PEth 16:0/18:1 (further simply being referred to as "PEth"), is quantified, and cutoff concentrations are applied as decision limits.
5. PEth has a biphasic half-life and a detection window of up to several weeks.

General considerations

1. The possibility of post-sampling alteration of PEth concentrations must be taken into account.
2. Validity of results should be demonstrated using accepted standards of practice, such as—but not limited to—inter-laboratory comparisons and/or proficiency testing.
3. Commutability[7] of calibrators and quality control samples with authentic samples should be demonstrated.

TABLE 1 Cutoff concentrations for PEth 16:0/18:1 in whole blood reflecting alcohol intake within the month prior to sampling

PEth 16:0/18:1 concentration cutoff	Interpretation
<20 ng/ml	Compatible with abstinence or low alcohol consumption
≥20 ng/ml but <200 ng/ml	Alcohol consumption
≥200 ng/ml	Strongly suggestive of chronic excessive alcohol consumption

Cutoff concentrations

1. PEth concentrations should be interpreted considering all relevant factors surrounding the case.
2. Occasional drinking events may not be detected.
3. A single determination of a PEth concentration may not give a full insight into drinking patterns.
4. Cutoff concentrations for PEth 16:0/18:1 are applied as listed above:
5. The accuracy and precision of the validated method used for the determination of PEth should be within 15% at the above-specified cutoff concentrations.

Calibration

1. The reference material for the quantification of PEth should be as pure as possible. Special attention must be paid to the sn1-/sn2-regioisomeric purity (e.g., PEth 16:0/18:1 vs. PEth 18:1/16:0). The primary reference material is preferentially compatible with ISO 17034.
2. The calibration window must cover the applied cutoff concentrations.

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