## Efficacy of urine EtG and PEth C-DBS in the monitoring of alcohol consumption in an abstinence-oriented inpatient treatment setting

## Summary

Biological markers like blood alcohol concentration (BAC), carbohydrate-deficient transferrin (CDT), glutamyltransferase (GGT) and ethyl glucuronide (EtG) are widely used to monitor alcohol consumption. Frequent applications are the control of abstinence in traffic medicine and the monitoring of therapeutic efforts in the treatment of alcohol use disorder (AUD). However, established markers like GGT or CDT have a low sensitivity, while BAC or EtG have only a short half-time and therefore, a punctual alcohol consumption may remain undetected. Recently, phosphatidylethanol (PEth) has been introduced as a new biomarker. It's sensitivity is comparable to EtG, the most commonly used biomarker. At the same time, it has a longer half-life in the blood and therefore, a continued alcohol consumption may better be detected. In a pilot study, we have analyzed the depletion of PEth in alcohol withdrawal in patients with AUD and found a continued degradation. We also found, that the usage of capillary- dried blood spots (C-DBS) obtained from the finger-tip proved to provide identical results as DBS generated from venous blood. However, although a few studies have shown PEth to be appropriate as alcohol biomarker, valid reference values and an evidence based clinical application have not been developed, yet.

This study proposal has the aim to conduct a head-to-head comparison of the alcohol biomarkers EtG and PEth in terms of efficacy to identify alcohol consumption in abstinent patients with AUD in an inpatient treatment setting. We expect that PEth will outperform urine EtG with regard to sensitivity in the detection of alcohol consumption in the study participants. We expect a higher sensitivity of PEth to be measured in low- to- moderate alcohol consumption and a longer retrospective latency in the detection of heavy drinking days. The study will be conducted in two inpatient treatment centers for AUD in the Canton of Bern (PZM; Klinik Südhang). 60 relapses will be investigated and compared, using EtG in urine, PEth C-DBS and the patients` self-report. Directly after each relapse that is identified, EtG and PEth samples will be collected during one week. Quantification of EtG in urine and PEth in C-DBS will take place by the use of liquid chromatography coupled to mass spectrometry (LC-MS/MS) at the IRM Bern.

PEth is a promising alcohol biomarker in the field, due to its high specificity and sensitivity as well as its window of detecting alcohol consumption. Furthermore, capillary blood withdrawal in combination with dried blood spots has several advantages: The collection of samples can be done by non-medical personnel as no venipuncture is necessary. The transportation is easy, as no special containers or cooling is required. Capillary blood withdrawal is less invasive compared to venipuncture. In general, blood withdrawals are less prone to manipulation compared to urine samples. Besides our pilot project ALPHATA, only a few studies with several limitations have compared EtG and PEth in a clinical setting. Because of the aforementioned advantages, PEth C-DBS has the potential to be routinely implemented into clinical routine (AUD treatment, transplantation medicine), as well as in the field of medico-legal investigations (e.g. traffic and aviation medicine, forensic psychiatry). Especially for the latter, the exact knowledge of reference values, concentrations and kinetics of biomarkers are strongly required. This deserves thoroughly planned and conducted studies like our proposal, as critical decisions in this sensitive area have to rely on a clinical evidence with the best possible data.