Ethyl Glucuronide (EtG), Ethyl Sulfate (EtS) and Phosphatidyl ethanol (PEth) are Direct Biomarkers or Metabolites of Ethanol

Ethyl Glucuronide (EtG), Ethyl Sulfate (EtS), and Phosphatidyl Ethanol (PEth) are direct biomarkers or metabolites of ethanol. They are termed “direct” because they are direct products of the metabolism of ethanol, and no other alcohols metabolize this way. Although most alcohol that is consumed is metabolized by oxidative processes in the liver, a very small amount is broken down non-oxidatively, thereby creating these biomarkers that can be measured for a longer period of time than ethanol itself remains detectable. EtG and EtS are usually measured in urine specimens. PEth can be measured either in whole blood or one laboratory uses blood spot testing.

EtG/EtS concentrations generally represent about 0.02%-0.06% of total ethanol elimination. Published literature indicates that EtG may be detectable for up to 80 hours after alcohol ingestion. The EtG and EtS “windows of detection” are dependent on cut-off levels used, individual metabolism, alcohol usage patterns, and the concentration of the urine specimen being tested.

The presence of EtG and EtS in urine specimens is confirmed using LC/MS/MS methodology. The cutoff level for EtG confirmation may be 100 ng/mL, 250 ng/mL or 500 ng/mL or higher; the EtS confirmation cut-off level is usually 75- 100 ng/mL.

Because of the sensitivity of both EtG and EtS testing it is possible for exposure to alcohol from use of personal hygiene products, foods containing alcohol, and cleaning or sanitizing products to result in a positive EtG and/or EtS result. EtG/EtS testing cannot absolutely distinguish between beverage alcohol consumption and incidental or unintentional exposure from these ethanol containing sources based on the EtG/EtS levels alone. It is strongly recommended that low level EtG/EtS results be interpreted with consideration of non-drinking exposure to alcohol. It is also strongly recommended that MRO review be considered for all EtG/EtS positive results.

Recent studies have indicated that EtG can be either formed or degraded in a urine specimen when certain conditions are present. EtG is subject to degradation by some bacteria at room temperature. Also, under certain conditions, in-vitro (outside of the body, in the specimen container) formation of EtG may occur when certain bacteria and ethanol or ethanol-producing bacteria are both present in a urine specimen. Because of these two factors related to EtG degradation and in-vitro production, FSSolutions strongly recommends that EtS testing be conducted in conjunction with testing for EtG because unlike EtG, EtS is completely stable once it is formed. There are no published reports of in-vitro synthesis of EtS or degradation of EtS stability in urine specimens. Additionally, urine specimens being testing for EtG/EtS should arrive at the testing laboratory within 5 days of specimen collection to minimize EtG level changes.
For programs that choose to use EtG and EtS testing for monitoring alcohol abstinence, the following comments contained in the US SAMHSA’s Center for Substance Abuse Treatment (CSAT) Advisory July 2012 revision should be noted:

Because of the common use of EtG to document abstinence in various settings and the grave consequences for false positive, much attention has been given to the cutoff values of EtG. Although further research is needed before firm cutoffs for EtG can be established, sufficient research has been completed to reach the following conclusions:

- A “high” positive (e.g., >1,000 ng/mL) may indicate:
  - Heavy drinking on the same day or previously (e.g., previous day or two)
  - Light drinking the same day
- A “low” positive (e.g., 500–1,000 ng/mL) may indicate:
  - Previous heavy drinking (previous 1–3 days)
  - Recent light drinking (e.g., past 24 hours)
  - Recent intense “extraneous” exposure (within 24 hours or less)
- A “very low” positive (100–500 ng/mL) may indicate:
  - Previous heavy drinking (1–3 days)
  - Previous light drinking (12–36 hours)
  - Recent “extraneous” exposure

**Phosphatidyl Ethanol (PEth)** While EtG and EtS testing can be effective tools to assist in alcohol abuse relapse prevention and monitoring, the use of PEth testing either by itself or as a follow-up to non definitive EtG/EtS results can be a great help in differentiating between innocent or extraneous ingestion of alcohol and drinking. PEth is a blood test and has a detection period of 2-4 weeks depending on the amount and pattern of alcohol consumption. PEth research has been published in peer reviewed literature since the 1980’s and no false positives have been reported. Only the consumption of 60 gm (3-4 six ounce glasses of wine) or more will cause a PEth positive at the 20 ng/mL cutoff which is currently used by FSSolutions’ laboratory partners.

Incidental or unknowing ingestions of ethanol have not been shown to cause PEth positives. Negative PEth tests when performed within the detection period after non definitive EtG/EtS positives are extremely helpful in supporting claims of abstinence. Conversely, positive PEth results performed as follow ups to those same EtG/EtS results can help to determine whether or not drinking actually occurred.

PEth, EtG and EtS are all laboratory developed tests (LDT’s). There is no national oversight agency for any LDT so the selection of laboratories to perform these tests is critical. Only laboratories with the highest overall standards and certifications should be used, and FSSolutions will not partner with any laboratories that don’t meet such high standards. Given that, laboratory protocols may vary and laboratory results may differ. Care is recommended in the interpretation of all biomarker results, and we are always available for collaboration and consultation about those results. Please read the FSSolutions Report on Laboratory Certificates: What They Mean to You.

For further information please contact FSSolutions at 800-732-3784 / info@FSSolutionssolutions.com