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ETG AND ETS: ETHANOL BIOMARKERS

Ethyl Glucuronide (EtG) and Ethyl Sulfate (EtS) - Direct Biomarkers or Metabolites of Ethanol

Ethyl Glucuronide (EtG) and Ethyl Sulfate (EtS) are direct biomarkers or metabolites of ethanol, and they are called that because they are direct products of the metabolism of ethanol. Although most alcohol that is consumed is metabolized by oxidative processes in the liver, a very small amount is broken down non-oxidatively, creating EtG and EtS and these biomarkers can be measured for a longer period of time than ethanol itself can be. EtG/EtS concentrations generally represent about 0.02%-0.06% of total ethanol elimination. EtG and EtS are most reliably measured in urine specimens. Recently hair and oral fluid have been proposed as alternative matrices that can be used to measure these biomarkers, but urine is still the most researched and preferred matrix. Because of the chemical composition of the hair shaft, only EtG can be tested in hair, not EtS. There is very little peer reviewed data that support EtG testing in oral fluid.

Published literature indicates that EtG is detectable in urine 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.

EtG and EtS urine confirmations are performed using LC/MS/MS methodology. The cutoff level for EtG confirmation may be 100 ng/mL, 250 ng/mL, 500 ng/mL or higher; the EtS confirmation cut-off level is 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. Neither EtG nor EtS testing can absolutely distinguish between beverage alcohol consumption and incidental or unintentional alcohol exposure from foods, personal hygiene products, cleaning or sanitizing agents or other environmental sources based on the EtG/EtS levels alone. If the lower of the cut-off levels mentioned above are used, it is strongly recommended that the 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. Additionally, urine specimens being testing for EtG/EtS should arrive at the testing laboratory within 5 days of specimen collection. There are no published reports of in-vitro synthesis of EtS or degradation of EtS stability in urine specimens.

While EtG and EtS testing can be effective tools to assist in alcohol abuse relapse prevention and monitoring, use of appropriate cut-off levels and a thorough medical review or clinical correlation of any EtG/EtS positive test results are essential. Use of EtG testing with a cut-off level lower than 250ng/mL is not recommended and EtS testing with a cut-off of 75-100 ng/mL is recommended to help rule out in-vitro EtG production.

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"

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

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