Alcohol is one of the most commonly used and abused chemicals. Alcohol has a significant suppressive effect on the central nervous system activity, and can significantly increase the risk of severe side effects when co-administered with other CNS suppressants such as opioids and benzodiazepines. To help physicians identify recent alcohol consumption among patients, American Clinical Solutions currently offers an UPLC-MS-based test for two ethanol metabolites -- ethyl glucuronide (EtG) and ethyl sulfate (EtS). EtG and EtS are formed through hepatic UDP-glucuronosyltransferase and sulfotransferase-mediated ethanol metabolism.

Physicians can use EtG/EtS test to do the following:

1. **Confirm alcohol consumption in patients.** EtG/EtS are highly specific biomarkers for alcohol consumption. Traditional alcohol tests directly measure alcohol in urine or blood. Diabetic patients are particularly prone to have false positive urine results due to the bacterial fermentation of glucose. In contrast, detection of a significant amount of EtG and EtS in urine can only result from recent consumption of alcohol.

2. **Determine when patients might have consumed alcohol.** Previous studies have clearly delineated the kinetics of urine excretion of EtG/EtS after ethanol intake [1, 2]. EtG/EtS becomes detectable in urine about one hour post-consumption. The peak values of EtG/EtS appear around 4-6 hours after alcohol consumption. EtG/EtS remain detectable until 24-36 h after last exposure [1]. In heavy drinkers, the detection windows for EtG/EtS can extend to 72 h [2]. Therefore, the detection of EtG/EtS suggests the exposure occurred apparently within 24-36 hours. Higher values of EtG/EtS in urine might suggest more recent exposure.

3. **Monitor alcohol consumption in an alcohol rehabilitation program.** Traditional urine alcohol test can detect alcohol ingestion within 12 hours. The longer detection windows of EtG/EtS allow detecting even short-term relapses during alcohol dependence treatment.
Urine EtG/EtS levels cannot be used to extrapolate the amount of alcohol consumed. Theoretically, in a well-controlled study, blood concentrations of drugs are generally correlated well with doses administered. Higher doses lead to proportionally higher blood concentrations. However, a previous study fails to establish a direct link between blood EtG/EtS concentrations and the amount of alcohol consumption, much less between urine EtG/EtS and the amount of alcohol consumption [3].

Also, the metabolic pathway leading to formation of EtG/EtS is a minor one, only contributing to < 0.2% of an alcohol dose [1]. The bulk of alcohol consumed is converted to acetaldehyde and acetic acid through alcohol dehydrogenase and aldehyde dehydrogenase, respectively. Urine EtG and EtS concentrations can be easily influenced by variations in metabolic capacity of enzymes in the alcohol metabolic pathway.

Finally, during application of urine EtG/EtS test, it has been found that a majority of urine samples tested positive for EtG are also positive for EtS. However, a small percentage of samples (< 10%) were found to be positive only for EtG or EtS. The exact reason for this phenomenon remains unknown. One possible explanation is genetic polymorphism of human genes encoding UDP-glucuronosyltransferase and sulfotransferase, which results in significant less UDP-glucuronosyltransferase or sulfotransferase activities in certain populations.