Quantitative Measurement of Dried Blood Spot Guanidinoacetate and Creatine for Clinical Research

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Background: Guanidinoacetate methyltransferase (GAMT) Deficiency, a cerebral creatine deficiency syndrome, was added to the United States’ Recommended Uniform Screening Panel (RUSP) in early 2023. Successful newborn screening programs that currently screen for GAMT deficiency have developed multi-tiered screening strategies that universally begin with a flow injection-tandem mass spectrometric (FIA-MS/MS) quantitative measurement of guanidinoacetate (GUAC) and creatine (CRE) from dried blood spots routinely collected for screening of inborn errors of metabolism (IEMs). At the time of the abstract submission deadline for this meeting, no test systems were on market in the USA that include GUAC and CRE, the two biochemical markers of GAMT deficiency.

Methods: Using the Waters FIA-MS/MS system (ACQUITY™ UPLC™ I-Class PLUS System, FL-injection and the XEVO™ TQD Mass Spectrometer), we have demonstrated the analytical performance of this system for these biomarkers in manufactured (contrived) extracted dried blood spots (DBS) for clinical research.

Results: Using the Waters non-derivatized in-house method containing Waters Internal Standard mix, FIAMS/MS system and in-house DBS linearity set (L1–L9) show good linearity of R2 ≥0.99 and imprecision <20% for both analytes. The average recovery was 108% (GUAC) and 91% (CRE). Additionally, CDC Linearity (2021) material was compared; the correlation between the Waters in-house method and CDC Linearity reports R2 of ≥0.99 for both analytes.

Conclusions: Whilst the preliminary data has demonstrated the analytical performance of two metabolites using the Waters Xevo TQD Mass Spectrometer, this FIA-MS/MS system is capable of testing for many metabolites for clinical research.

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