IMPACT OF STORAGE AND HANDLING CONDITIONS ON A HUMAN PLASMA STANDARD REFERENCE MATERIAL TO ASSESS THE ANALYTICAL BIAS IN METABOLOMIC STUDIES

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Metabolomics attempts to understand biological function or disease through broad surveys of metabolites in relevant samples by means of many different analytical methodologies. These approaches are qualitative, quantitative, or a combination, and can offer insights into mechanisms of disease or markers for diagnostics. To allow comparisons across studies, these metabolites need to be unambiguously identified, quantified and referenced in a standardized manner. NIST is developing a Standard Reference Material, Metabolites in Human Plasma (SRM 1950), to serve as a common material to help researchers evaluate qualitative and quantitative analytical methods. The intended use of SRM 1950 should significantly contribute in the current steps towards standardized metabolomic approaches.

SRM 1950 is a human plasma pool designed to represent a normal metabolome. It was obtained from a representative mixture of healthy male and female donors in a narrow age range, with a racial distribution similar to that of the U.S. population. The concentrations of approximately 70 metabolites were determined; most with isotope-dilution mass spectrometry. An additional approximately 250 metabolites were identified in the plasma using GC/MS, LC/MS and NMR instrumentation.

The study presented here has systematically evaluated the influence of SRM 1950 handling and storage conditions on the plasma metabolome by monitoring 70 representative metabolites with two-dimensional gas chromatography coupled to time-of-flight mass spectrometry (GC x GC-TOFMS). This report compares the endogenous and some exogenous metabolites measured in SRM 1950 stored at -80°C with those obtained after five freeze-thaw cycles (-20°C and room temperature) over 5 weeks and under different laboratory conditions (1 h, 4 h and 24 h in a hood). In addition, the experimental design included a 48 hour study at a temperature that might occur during sample transport (e.g. 60°C). A detailed characterization of the effect of these common and extreme laboratory sample handling practices on the plasma metabolome will be presented during this lecture with the objective to highlight potential analytical bias.