Longitudinal Patient Envelopes for Specimen Authenticity and Improved Patient Access Across Traditional, Telehealth, and Hybrid Care Facilities

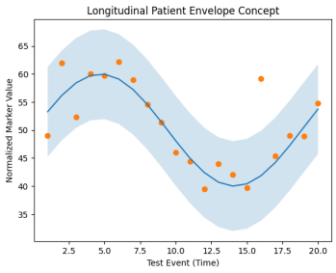
R. Patrick Rainey, Ph.D., DABT

Abstract. Longitudinal interpretation of quantitative urine drug testing enables the development of patient-specific biologic "envelopes" that support specimen authenticity and patient safety. Using high-specificity analytical methods such as LC-MS/MS, clinicians can evaluate longitudinal parent drug and metabolite relationships, sex-specific hormones, human-specific excretory metabolites to help distinguish true ingestion from tampering, dilution, or substitution. This framework establishes a clinically reliable model for authenticity and adherence assessment. Importantly, this approach can be extended beyond traditional office-based testing into telehealth and hybrid care models, including at-home collections, improving access for rural and underserved populations while maintaining clinical integrity. [1-6]

Urine drug monitoring is widely used to support adherence, risk management, and clinical decision-making in patients receiving controlled substances, medication management, and SUD/MOUD treatments. Central to this process is typically immunoassay specimen validity testing, including creatinine, specific gravity, pH, and oxidant/adulterant detection, which helps identify dilution, substitution, and chemical interference. While these measures do not establish donor identity, they confirm that a specimen is physiologically plausible and suitable for interpretation. [1,2]

LC-MS/MS testing provides the analytical foundation for longitudinal interpretation. Unlike immunoassay screening, LC-MS/MS offers high specificity and sensitivity, enabling precise quantitation of parent drugs, drug metabolites, and human biomarkers like sex hormones and urine-specific excretory metabolites. In the case of longitudinal testing, simultaneous measurement of parent drug and their metabolites allows for evaluation of metabolic consistency. Clinical studies demonstrate that abnormal parent-to-metabolite relationships, such as disproportionately high parent drug with low metabolite, are associated with urine spiking or non-physiologic conditions, while more typical patterns reflect ingestion and metabolism. [3,4]

Across serial testing events, quantitative LC-MS/MS data enables the development of a longitudinal patient envelope **see Figure**. This envelope represents the expected range of variation for an individual patient, incorporating gender-appropriate hormones, urine-specific metabolites, creatinine-normalized parent drug-to-metabolite relationships, and total concentration scale. Using this approach, results tend to remain within a coherent biologic and sex-specific range and provide strong evidence of authentic, patient-specific specimen identity. Significant deviations from this envelope can be identified as implausible and clinically actionable. [4,5]



Importantly, this framework is not limited to in-office testing. The same principles can be applied to telehealth and hybrid care models that incorporate at-home urine collections. When combined with specimen validity testing and LC-MS/MS analysis, longitudinal patient envelopes allow providers to interpret unobserved samples with confidence, supporting decision-making while maintaining clinical rigor.

This has meaningful implications for access and equity. Patients in rural or underserved areas, who may not have convenient access to clinic-based collection, can still participate in structured monitoring programs. By leveraging longitudinal data rather than relying solely on direct observation, providers can extend care safely and effectively without compromising patient safety or data integrity.

Accordingly, the literature supports a clinically grounded approach: LC-MS/MS-based longitudinal patient envelopes provide a practical and scientifically supported method for evaluating specimen authenticity and supporting patient safety. This approach enhances provider confidence, improves monitoring capabilities, and enables broader access to care across traditional, telehealth, and hybrid models. [1-6]

References

1. Raouf M, Bettinger JJ, Fudin J. A Practical Guide to Urine Drug Monitoring. Fed Pract. 2018;35(4):38-44.
2. Wissenbach DK, Binz TM, Steuer AE. Advances in testing for sample manipulation in clinical and forensic toxicology - Part A: urine samples. Clin Biochem. 2023;119:110634.
3. Donroe JH, Holt SR, O'Connor PG, Sukumar N, Tetrault JM. Interpreting quantitative urine buprenorphine and norbuprenorphine levels in office-based clinical practice. Drug Alcohol Depend. 2017;180:46-51.
4. Accurso AJ, Lee JD, McNeely J. High prevalence of urine tampering in an office-based opioid treatment practice detected by evaluating the norbuprenorphine to buprenorphine ratio. J Subst Abuse Treat. 2017;83:62-67.
5. Furo NA, Schwartz RP, Gryczynski J, Mitchell SG, Jaffe JH, O'Grady KE. Buprenorphine Dosage and Urine Quantitative Buprenorphine, Norbuprenorphine, and Creatinine Levels in an Office-Based Opioid Treatment Program. Subst Abuse. 2021;15:11782218211064531.
6. Furo NA, O'Grady KE, Gryczynski J, Schwartz RP, Mitchell SG, Jaffe JH. Association Between Buprenorphine Dose and the Urine Norbuprenorphine to Creatinine Ratio: Revised. Subst Abuse. 2023;17:11782218231156735.