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The Power of Precision

Accelerating turnaround time in high-throughput ADME pipelines

LeadScape® 3.0 Analyze software for the Echo® MS system

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One of the key steps in pharmaceutical drug discovery is the analysis and optimization of lead drug candidates through precision data that speaks to their in-vitro and in-vivo bioavailability, metabolism and pharmacological effects. Absorption, distribution, metabolism and excretion (ADME) groups analyze these pharmacokinetic properties and often utilize LC-MS/MS strategies to properly characterize safety and efficacy of these drug candidates to make informed decisions that influence preclinical assessments and clinical phases.

Advances in high throughput screening and medicinal chemistry along with requirement to bring ADME studies earlier into development cycle have necessitated development of high throughput approaches in ADME labs. Researchers require increased efficiency, sensitive and reproducible data to deliver unequivocal results with fast turnaround times for large sample sets. With Acoustic Ejection Mass Spectrometry (AEMS) employed on the Echo® MS system, sample volumes as low as 2.5 nL are delivered by an Open Port Interface (OPI) that is connected to the SCIEX Triple Quad 6500+ mass spectrometer.[1]

A carrier solvent is used to deliver the sample into the electrospray ionization OptiFlow Turbo V ion source to analyze samples at rates as fast as 1 second per sample with minimal carryover.

However, method optimization and batch curation can often be a bottleneck when analyzing hundreds to thousands of compounds. Figure 1 outlines the optimization and analysis workflow implemented to improve turnaround time whilst reducing number of manual steps (as low as 5 clicks per batch) and amount of sample consumption (as low as 2.5 nL per sample) in the lab. First, the optimization of compound parameters is performed on the SCIEX Triple Quad 6500+ mass spectrometer partnered with an ExionLC system using DiscoveryQuant software. Then, LeadScape Analyze software, coupled with the Echo® MS system, accelerates the workflow by importing MRM parameters from an existing LIMS system (DQ database) into SCIEX OS software. Here, sample batches are easily generated and submitted to SCIEX OS software for data acquisition and data processing. Here, using LeadScape Analyze software with the Echo® MS system, a 384 well plate was analyzed in 11 min compared to 160 min needed using DiscoveryQuant software with LC-MS/MS.
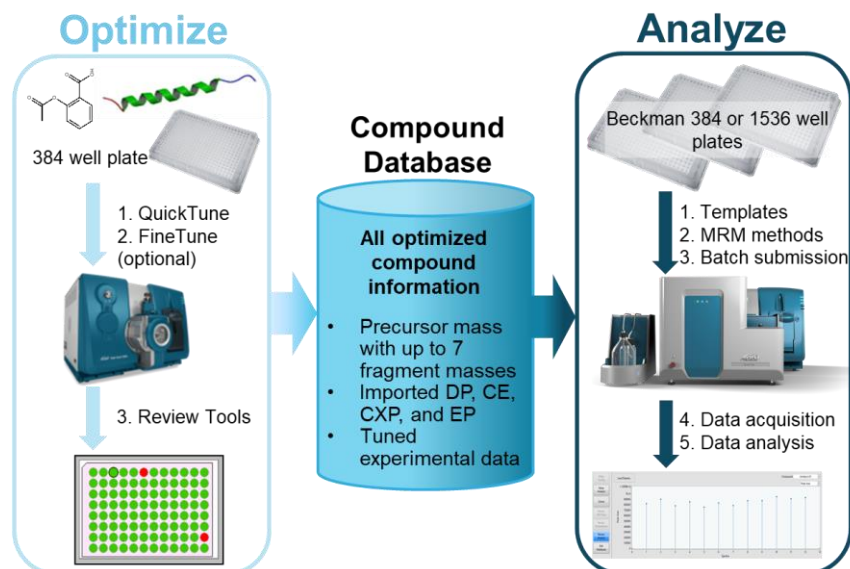

Figure 1. Leveraging DiscoveryQuant software with LeadScape Analyze software to streamline high throughput analysis in HT-ADME laboratories. The combined workflow highlighted above provides a faster, simplified workflow to increase throughput and turn-around-time by 14x. Optimized compound MRM conditions generated by DiscoveryQuant software can be imported from DQ database into LeadScape Analyze software. Multiple batches can be created and submitted for data acquisition in SCIEX OS software in an automated manner.

Key features of the LeadScape Analyze software for high-throughput ADME screening

- Ability to import existing compound databases (LIMS) as text files for analysis on the Echo® MS system
- LeadScape Analyze software seamlessly integrates with SCIEX OS software to provide method optimization and batch curation to minimize time spent on manual method creation during compound analysis on the Echo® MS system
- Processing methods are automatically created to provide results files on demand
- Use of LeadScape Analyze software increased turnaround time by up to 14x compared to conventional LC-MS/MS

References

1. Rapid MS/MS analysis with Acoustic Ejection Mass Spectrometry (AEMS) - Using the SCIEX Echo® MS system to break bottlenecks in quantitative mass spectrometry throughput. SCIEX technical note, RUO-MKT-02-11385-A.

2. Clark GT. (2015) HT-ADME in a contract research organization laboratory: can you ensure bioanalytical quality in a highly automated environment? *Bioanalysis*. **7(4)**: 403-406.

3. Automating high-throughput ADME assays with LeadScape® Analyze software on the Echo® MS system. SCIEX technical note, RUO-MKT-02-14841-A.

4. 10x increased throughput for metabolic stability assays - featuring LeadScape® Analyze software on the Echo® MS system. SCIEX technical note, RUO-MKT-02-14849-A.