BHIMADZU

Evaluation of LC-MS Data under Ultra-High Throughput Conditions

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Overview

Purpose: To evaluate LC-MS performance under ultra-high throughput conditions.

Method: A number of UHPLC/MS methods were run to evaluate MS speed, carryover and reproducibility under high-throughput conditions.

Results: The use of a new high-speed autosampler allowed up to four LC-MS/MS runs to be completed within one minute without any load ahead or pre-injection techniques.

Introduction

High-speed injections significantly improve throughput in multi-sample processing. Recently, a high-speed autosampler was introduced that features an injection time of just 7 seconds and an analysis cycle of 14 seconds. The combination of this autosampler with a high-speed quadrupole that features a positive/negative ionization switching time of 15 msec and a high-speed scanning rate of 15,000 u/sec was tested under ultra-high throughput conditions of four analytical runs per minute.

Background of Autosampler Development

- Reduction of analysis cycle and increase of sample capacity
- Efficient sample analysis in pharmacokinetic and synthesis in drug discovery
- Carryover reduction for high-sensitivity MS detection
- Open access design for rapid synthesis-compound identification
- Reduction of column external volume for ultra-fast analysis
- Ultra-fast analysis by Shimadzu LC/MS and LC/MS/MS
- Connection to other vendor's MS instruments

Instrumentation

• UHPLC: Shimadzu Nexera UHPLC system with SIL-30ACMP autosampler

CTO-30AS column oven.

• MS: Shimadzu 8030 LC-MS/MS DUIS source

Nexera MP System

Enhanced LC/MS frontend HPLC performance with Nexera ultra-fast analysis technology

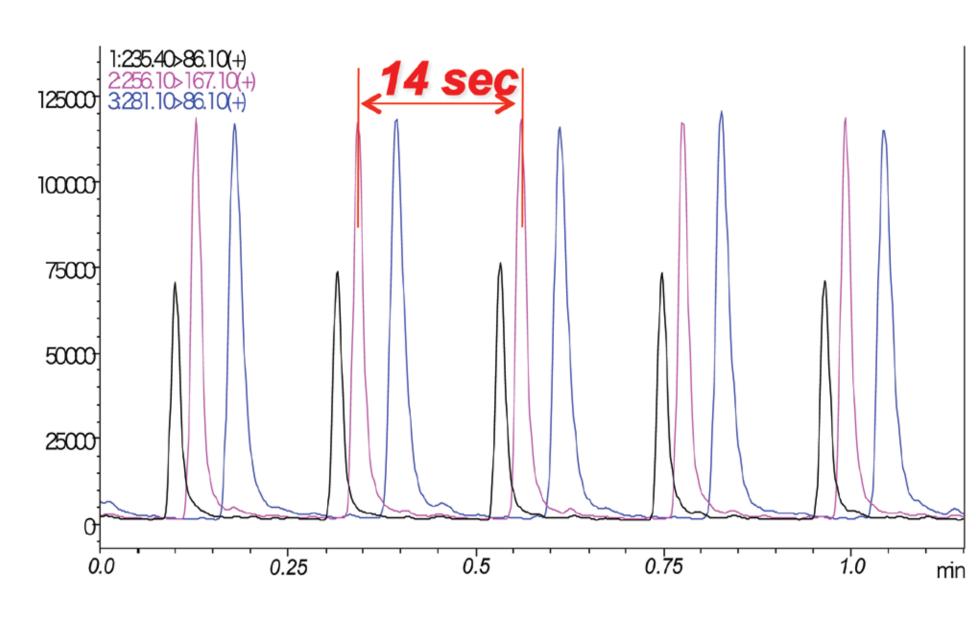
Newly-developed multiplate autosampler SIL-30ACMP and a small column oven CTO-30AS comprise the new Nexera system.



High-Speed LC-MS/MS Analysis

• 14 sec cycle time analysis

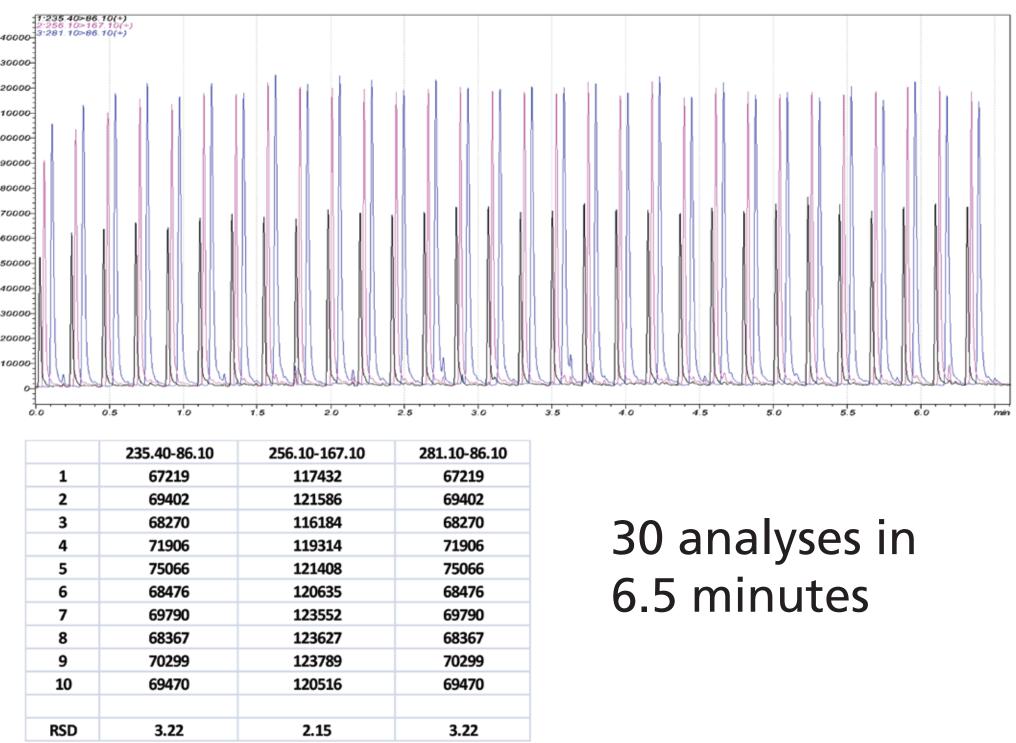
Ultra-fast analysis by combination of SIL-30ACMP and LCMS-8030 Ultra-fast LC/MS analysis without compromise on performance



Event #	Compound	Q1 m/z	Q3 m/z
1	Lidocaine	235.4	86.1
2	Diphenhydramine	256.1	167.1
3	Imipramine	281.1	86.1

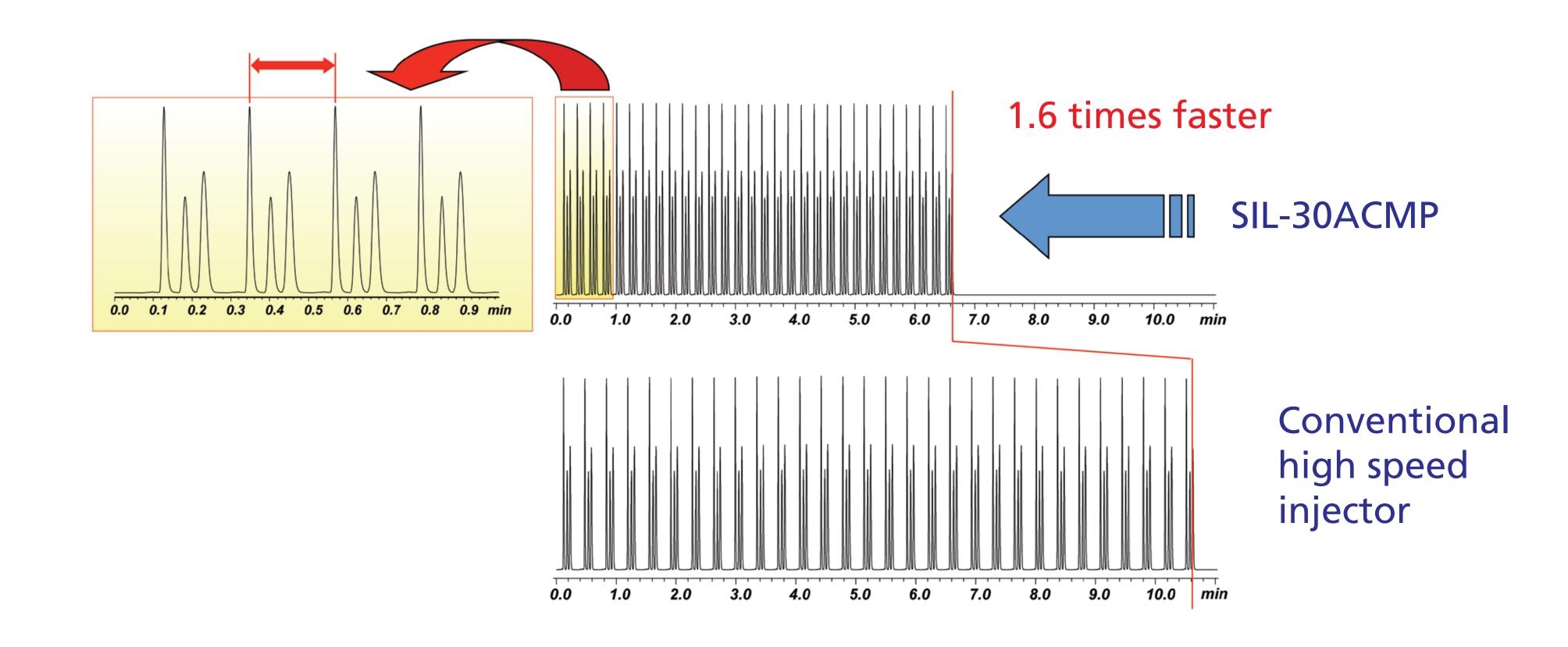
Flow rate: 1.2 mL/min onization : ESI(+)

Reproducibility Inj 21-30

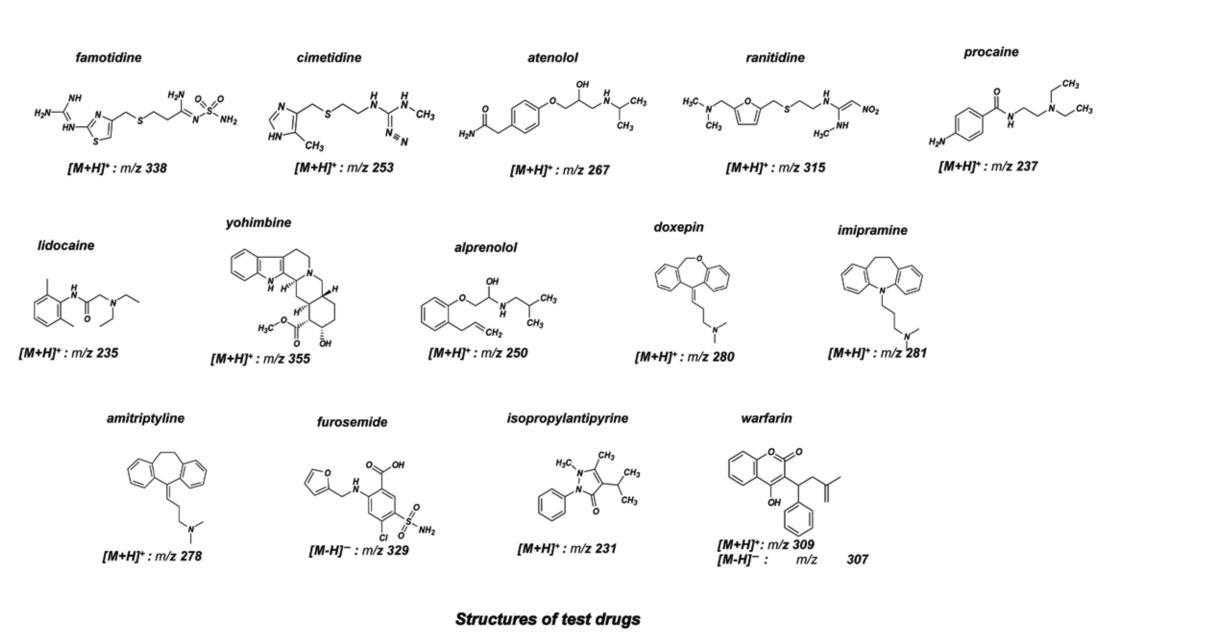


Increased Autosampler Throughput

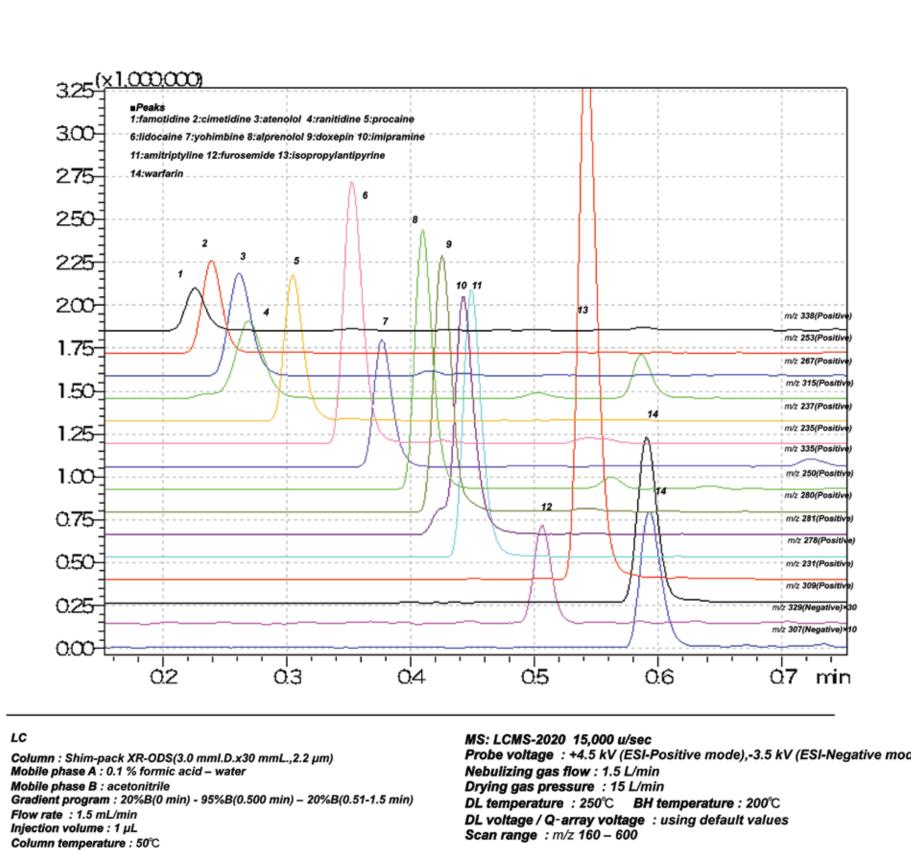
Injection cycle: 14 sec peak to peak!



High-Speed LCMS Analysis

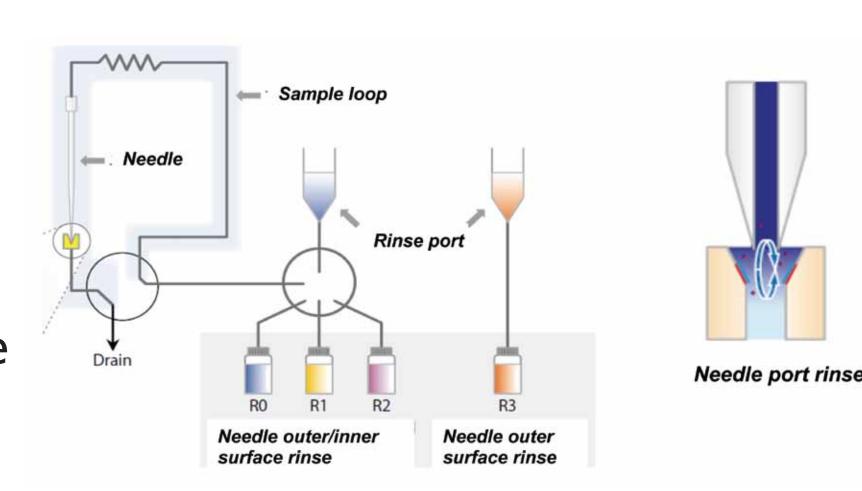


High Scan Speed LCMS Analysis



Multi Rinse Function

- Multi rinse function to minimize carryover (4 rinse solvents are available)
 - Rinse of needle surface
 - (2 rinse solutions)
- Rinse of needle inner surface and needle port (3 rinse solutions)
- Support high-sensitivity LC/MS/MS analysis





More Flexibility (CTO-30AS Oven)

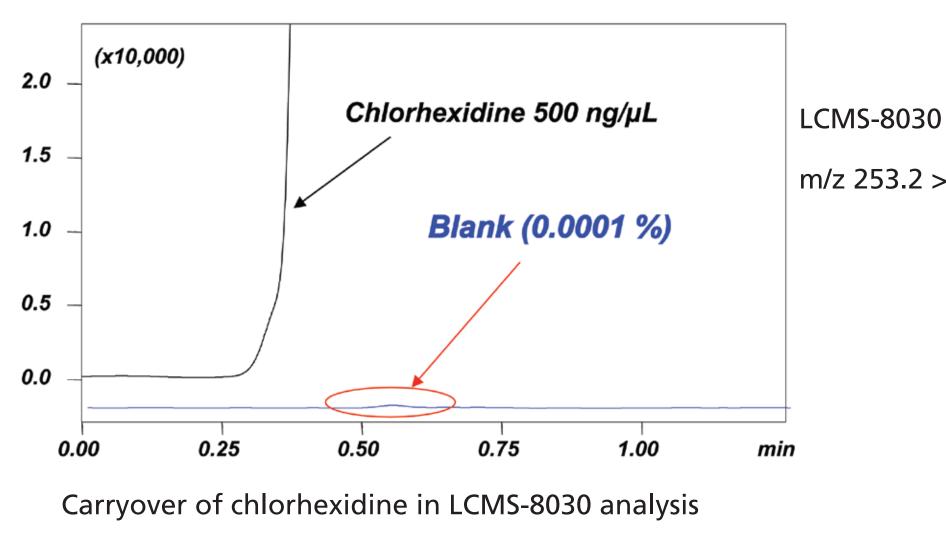
- Flexible angle from horizontal to vertical Minimized pipe length between LC/MS interface and column
- 1 column (50mm length), (room temp. + 10 °C to 85 °C)

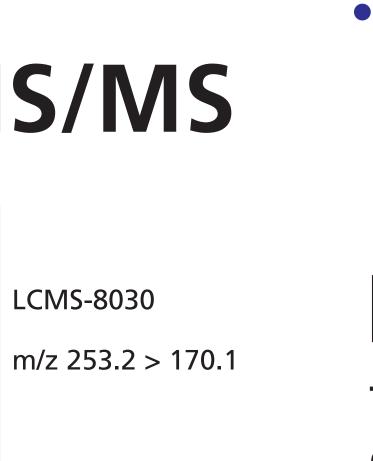
- Ultimate LC/MS frontend UHPLC More Speed
- World's fastest cycle time (14 sec) to support Ultra-high throughput analysis More Reliable

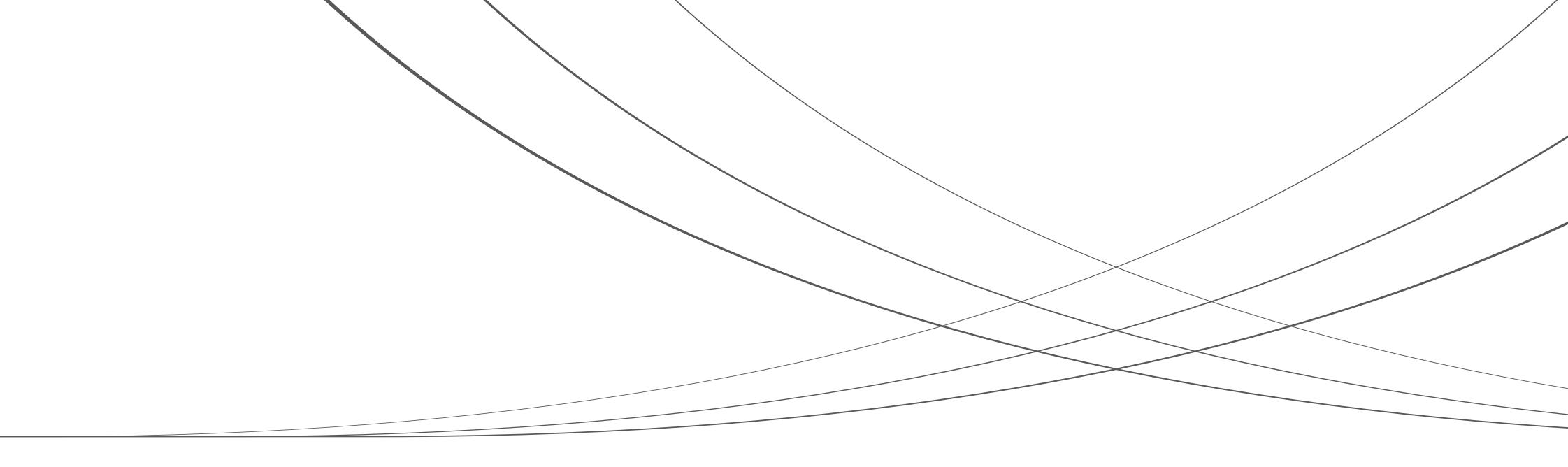
Minimized Carryover to Support LC/MS/MS

• Carryover level of chlorhexidine

Very low carryover of a stubborn 2.0 compound, chlorhexidine Chlorhexidine 500 ug/mL \rightarrow carryover 0.0001%!





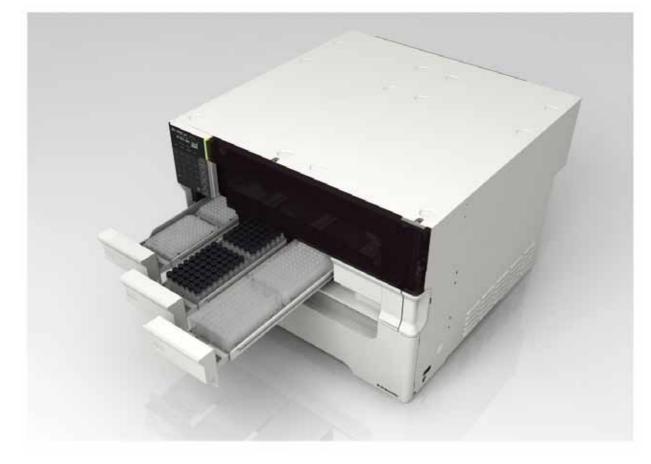


More Capacity & Flexibility

• Flexible use of plate types and easy access to samples Accommodates 6 plates

(384MTP 2304, 96MTP 576, 1.5mL vial 324) Different plate types are available between 3 racks Mixed use of microplates and 1.5mL vial racks is available

 Open access design to set samples on analysis Safely sample access in closed environment



• To maximize LC/MS performance

- Adjustable oven position for nearest
- connection to LC/MS interface
- 3 position-variable on levels

Summary

- Expanded application range by precise low-volume injection
- (1.0%RSD at 0.5 uL injection)
- Minimized carryover to support high-sensitivity LC/MS/MS
- (≦ 0.0015 %)
- More Capacity
 - Accommodates 2304 samples
 - (3 times higher capacity than SIL-30AC)
- More Flexibility
- Continuous analysis using 3 types of plates
- Flexible sample setting by open access rack design Optional column oven for LC/MS



Results

The use of LC-MS/MS coupled with a high-speed injector (injection speed 7 seconds, cycle time 14 seconds) allowed up to four analyses to be completed within a oneminute timeframe.

A low carryover autosampler design allows throughput to be optimized.

High scanning (15,000 u/sec) and polarity switching speeds (15 msec) allow LC/MS and LC/MS/MS to keep up with ultra-high throughput UHPLC.

