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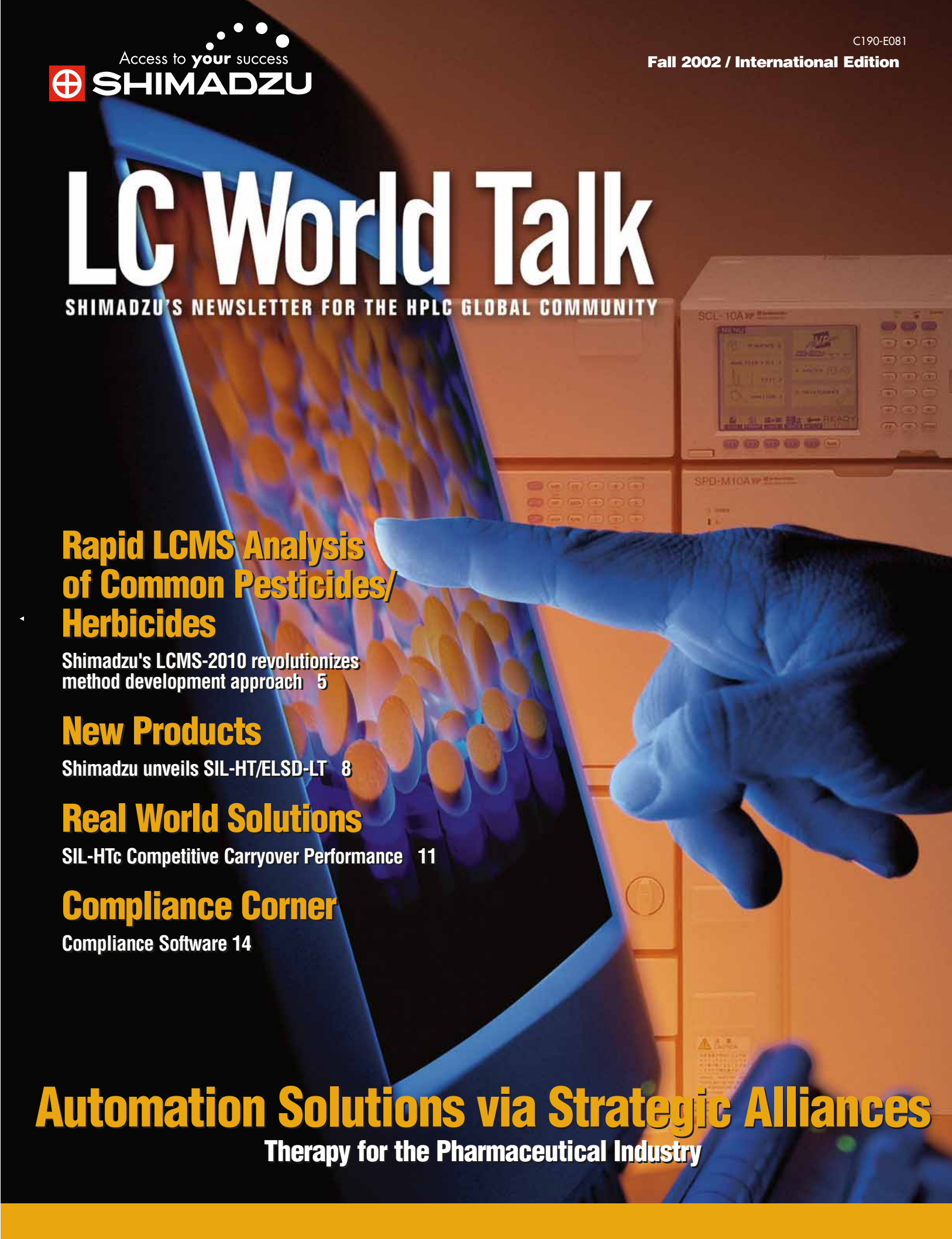
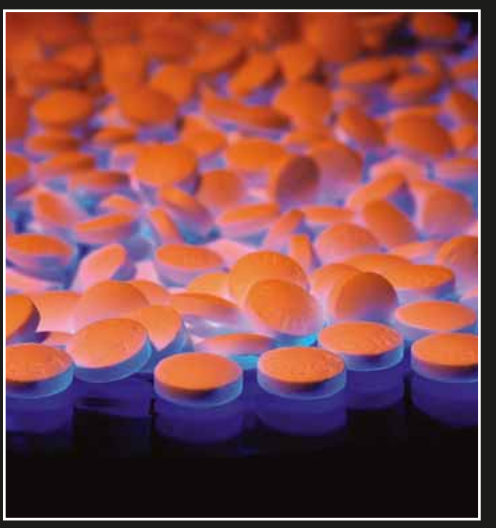
LC World Talk

SHIMADZU'S NEWSLETTER FOR THE HPLC GLOBAL COMMUNITY



Automation Solutions via Strategic Alliances

Therapy for the Pharmaceutical Industry



Automation Solutions via Strategic Alliances

Therapy for the Pharmaceutical Industry

"Make this faster, more reliable and flexible?" The request to automate, speed analysis and purification of compounds in the areas of drug discovery and development has been the mandate issued to analytical instrument companies!

The message is clear: if you watch…it will happen without you and your company."

Rapid technological advances in combinatorial chemistry, genomics and proteomics have dramatically altered drug discovery and development during the past twenty years. The pace in the pharmaceutical industry and life sciences marketplace has escalated from a comfortable canter to an all out sprint in order to deliver drug-to-market. In turn, this has driven the technology industry beyond imagination to automate high throughput sample preparation and analysis. The driving engine being: "How can you make this faster, more reliable and flexible?" The request to automate, speed analysis and purification of compounds in the areas of drug discovery and development has been the mandate issued to analytical instrument companies! The message is clear: if you watch…it…will happen without… you and your company. That is "old news," but one discipline defines the other's destiny. Automate now or perish!

Successful and competitive delivery of drug-to-market requires streamlined high throughput analytical procedures and, therefore, automation when and wherever possible in both drug discovery and development. The pace at which pharmaceutical companies are moving has put an extreme demand on analytical instrument companies to develop faster, more robust instruments to address the exponentially increasing amount of samples that need to be analyzed. To develop the necessary equipment to satisfy the immediate market demand of high throughput is a challenge involving software and hardware. Instrument companies must weigh the risk of producing a new product to address the current market

demand against whether or not that instrument will spontaneously become obsolete due to the rapidly evolving marketplace. However, there are several options to this dilemma:

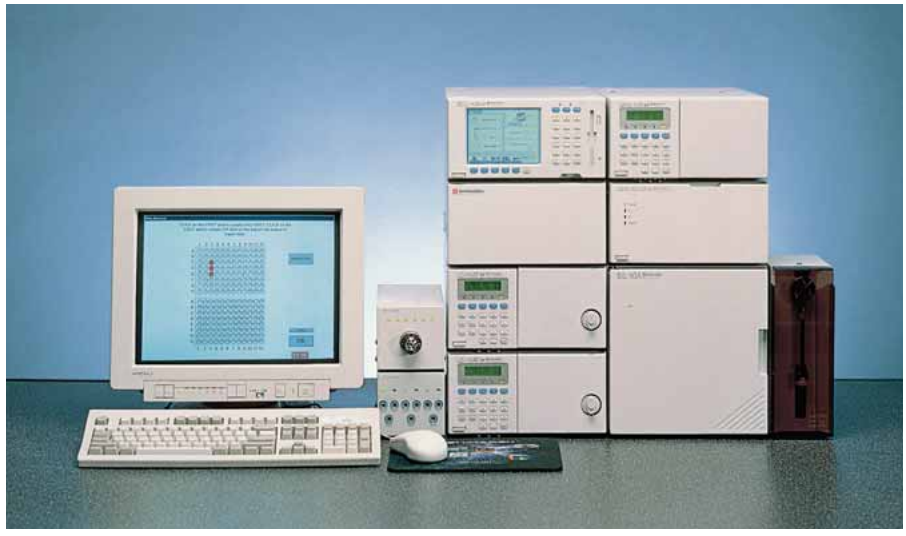
1. Take a slightly more conservative approach in manufacturing a more "mainstream" product.
2. Form strategic alliances or partnerships with pharmaceutical companies to enhance or modify existing hardware or software.
3. Combine technologies available from your own company and third parties into an Integrated Solution targeted to the needs of a specific market segment.
4. Provide "virtual instrument" plug-ins so others can control your product.

In the pharmaceutical market segment all options find their way into the proverbial think tank and are often times not mutually exclusive. However, the second option of forming strategic alliances is one that has suited Shimadzu to move swiftly and strategically in cadence with the radically changing pharmaceutical market. It is a bold move for a conservative company, but the strategy has yielded new product innovation and technologies that would not have been realized operating individually. Shimadzu has been pioneering strategic alliances, providing almost immediate automation technologies using an existing state-of-the-art HPLC product line.

Cutting-Edge Technologies via Key Strategic Alliances: A Brief History

The key to success for any company is to excel in producing a quality product and good customer service.

Discovery VP™ Preparative System



Discovery VP™ Analytical System

How is that accomplished in the rapidly evolving pharmaceutical market? Dynamic strategic vision and leadership are critical ingredients to success, but equally important is forming strategic alliances with key customers. Through these types of alliances the pharmaceutical industry and Shimadzu have been able to work closely together with the customer/collaborator to address immediate demands and expand upon the functionality of existing equipment. Fortunately, Shimadzu HPLC equipment, through its open architecture, inherently affords this flexibility. This provides the opportunity to modify or enhance existing functionality and the ability to plug into equipment from third-party vendors. This also opens the door for researchers to explore the full potential of the equipment and sets the stage for strategic alchemy with Shimadzu. Shimadzu Marketing Center's pursuit of these types of alliances was initially and intricately involved with Dr. Harold

Weller at **Bristol-Myers Squibb (BMS)**. Dr. Weller has been and is actively pioneering efforts to automate all aspects of sample handling, analysis and purification in the Early Lead Discovery group at BMS.

New Enabling Tools For Drug Discovery—Discovery VP

This collaboration has resulted in developing new enabling tools for drug discovery: namely the Discovery VP™ Analytical and Preparative fully automated HPLC systems. The Discovery VP systems were described in detail in LC World Talk Volume 5, Number 1, April 2000. Discovery VP was one of the early and complete walk-up automation chromatography systems that addressed: multiple column selection, scalable multiplexing of HPLC components, microtiter plates, UV and photodiode array detection, fraction collection, intuitive user interface with e-mail notification to both user and system administrator.

Basically, the Discovery VP systems have successfully addressed most of the demands for automated analytical and preparative HPLC analyses with easy to use queue-based control software and multiplexing capability. The intuitive interface and minimal required parameters enable users to become proficient with little training. The easily mastered software operates the entire system, so the laboratory chemist need not spend time learning how to properly operate and control HPLC equipment, optimize methodology, or adjust data acquisition conditions. Essentially, the original idea behind these automated systems is to take the chromatography out of the chemistry, allowing the combinatorial chemist to spend more time performing syntheses. The original idea and technology have evolved over the past few years.

New Evolving Technologies: Automation Enhancement

From Discovery VP to a New Broad Spectrum Automated HPLC/MS System

Shimadzu has always endeavored to provide technology to key target markets and once again provides new software and hardware enhancements in our new automated LCMS system. Built upon the featured requisite demands from the major pharmaceutical market already contained in the Discovery VP, Shimadzu's enhanced automated LCMS system now employs the highly sensitive Shimadzu LCMS-2010 Mass Spectrometer (below) in addition to its predecessor the QP8000 MS.

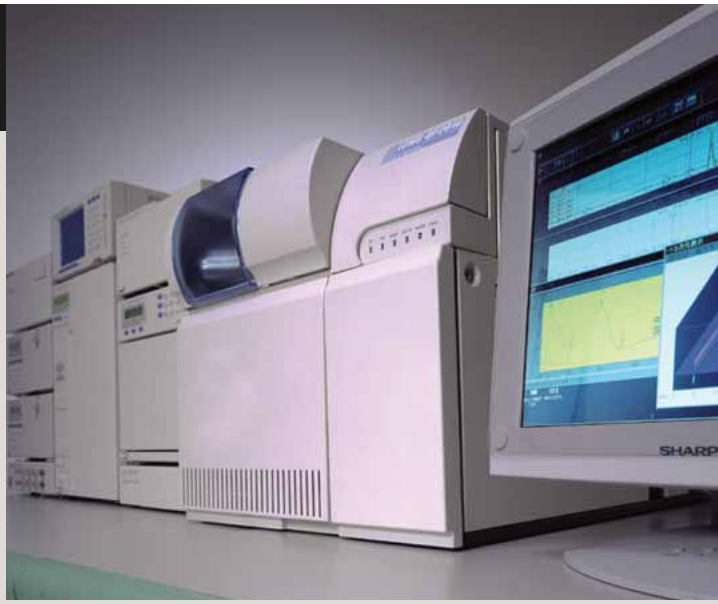
Conclusion

The applications and automated chromatography tools presented here may seem intuitively simple, but the implementation or putting the technology in place is not a trivial matter. The genesis of these cutting-edge technologies was made possible through key strategic alliances with Dr. Weller and BMS and would not have been possible without this collaborative effort. Shimadzu and Bristol Myers Squibb are successful companies that have joined in scientific excellence to attain therapeutically useful goals. Strong strategic alliances with key people in both the pharmaceutical industry and Shimadzu have afforded the opportunity to stay on the cutting edge while adding value to customer demand.

New Evolving Technologies

Feature Enhancements of Shimadzu's new fully automated LCMS System in addition to those of Discovery VP include:

- New and more robust 32 Bit Chromatography Automation Software Package
- Shimadzu's LCMS-2010 High Sensitivity Mass Spectrometer
- Mass-Directed Fraction Collection (prep. system)
- Multiple mass targeting
- Highly Accurate Ratio Sample Injection
- Dual wavelength UV detection
- Up to 10 Column Switching (analytical system)
- Reinjection capability
- Reproducible flow splitting capability



LCMS-2010

Rapid LCMS Analysis of Common Pesticides/Herbicides

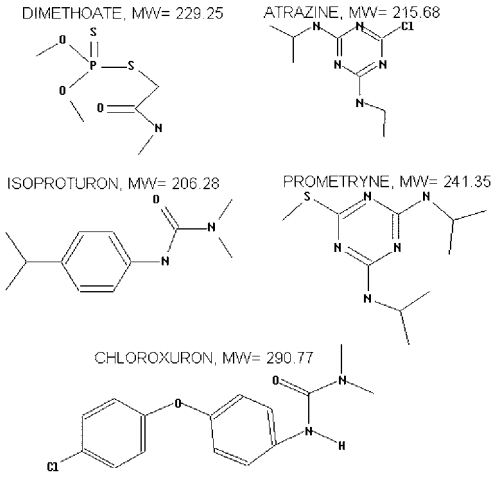
"The Shimadzu LCMS-2010 can be an effective analytical tool for developing robust qualitative and quantitative analyses for pesticides and herbicides. The versatility built into LCMS Solution® software streamlines the time and effort spent on developing these methods."

The importance of rapid and reliable determination of pesticides and herbicides in health, nutrition, and environmental studies cannot be overstated. The use of Liquid Chromatography/Mass Spectrometry (LCMS) offers some distinct advantages for such measurements, including the capability of direct measurement of pesticides and herbicides without the need for derivatization. Productivity is thereby increased as a result of higher sample throughput.

In this communication, we report on rapid LCMS analysis techniques for certain herbicides and pesticides using the Shimadzu LCMS-2010 and demonstrate enhanced productivity, increased capabilities during data acquisition, and reductions in total run time.

Shorter run times are used when employing fast gradient techniques and baseline separation is no longer needed for most LCMS applications.

LC coupled with MS increases the selectivity and sensitivity of traditional HPLC methods. Shimadzu's new LCMS-2010 offers a highly sensitive Single Quadrupole Mass Spectrometer with improved throughput, allowing end users to dramatically increase their productivity.



Structures of pesticide and herbicide standards

Conditions

Instrumentation:
Shimadzu LC-10ADvp Pumps
Shimadzu SIL-HT Autosampler
Shimadzu CTO-10ASvp Column Oven

Conditions:
Flow Rate: 0.700 ml/min
Injection Volume: 2 µl
Column: ES Industries Premier C18 2.1cm x 50mm, 5 microns
Mixer Volume: 100 µl
Column Temperature: 60°C

Mobile Phase:
A: Water (0.1% Formic Acid, v/v)
B: Methanol (0.1% Formic Acid, v/v)

Materials and Methods

The pesticide standards: Dimethoate, Atrazine, Isoproturon, Prometryne and Chloroxuron were obtained from **Chem Service**, West Chester, PA. Methanol was obtained from **Burdick and Jackson Inc.**, Muskegon, MI. TOC grade water was used for all experiments. The analytical LCMS column was obtained from **ES Industries**.

The robustness of the method is indicated by excellent retention time repeatability for the test compounds, as indicated in Table 1.

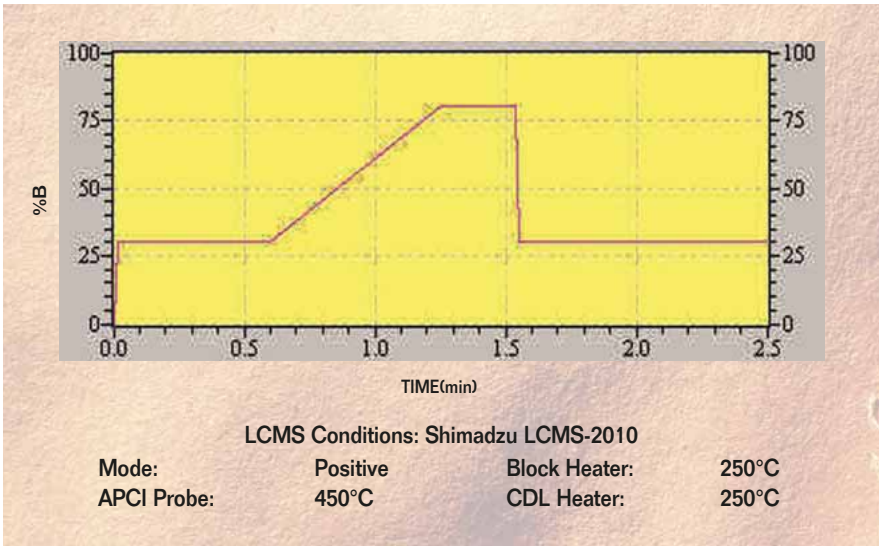
Table 1. Retention Time Repeatability

Compound	Retention Time RSD
Dimethoate	0.5%
Atrazine	0.2%
Isoproturon	0.2%
Prometryne	0.3%
Chloroxuron	0.5%

Analysis

Sensitivity was not compromised, as indicated by LOD's of at least 1ng/mL (2 pg on-column) for all of the compounds. The minimum S/N was 5 in the case of Dimethoate, while the remaining components in the test mixture had S/N values ≥10.

These data are shown in Table 2. The figure on the following page displays the data on the sensitivity determination for Prometryne.



Gradient for separation of pesticide mixture

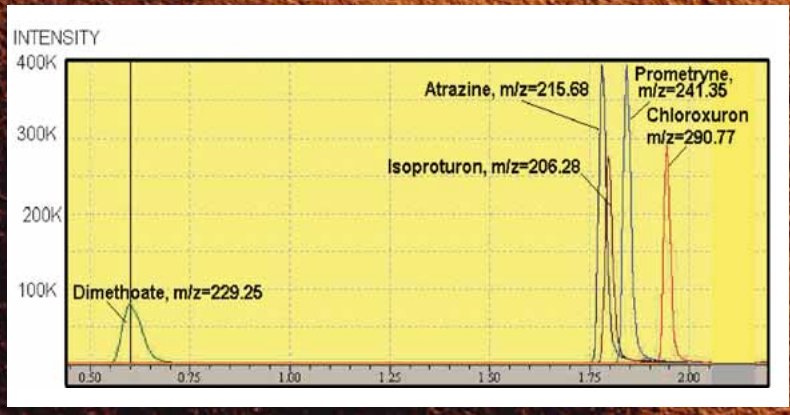
Table 2. Signal-to-Noise Values

Compound	Conc.	S/N
Dimethoate	1 ng/ml	5:1
Atrazine	1 ng/ml	24:1
Isoproturon	1 ng/ml	11:1
Prometryne	1 ng/ml	18:1
Chloroxuron	1 ng/ml	28:1

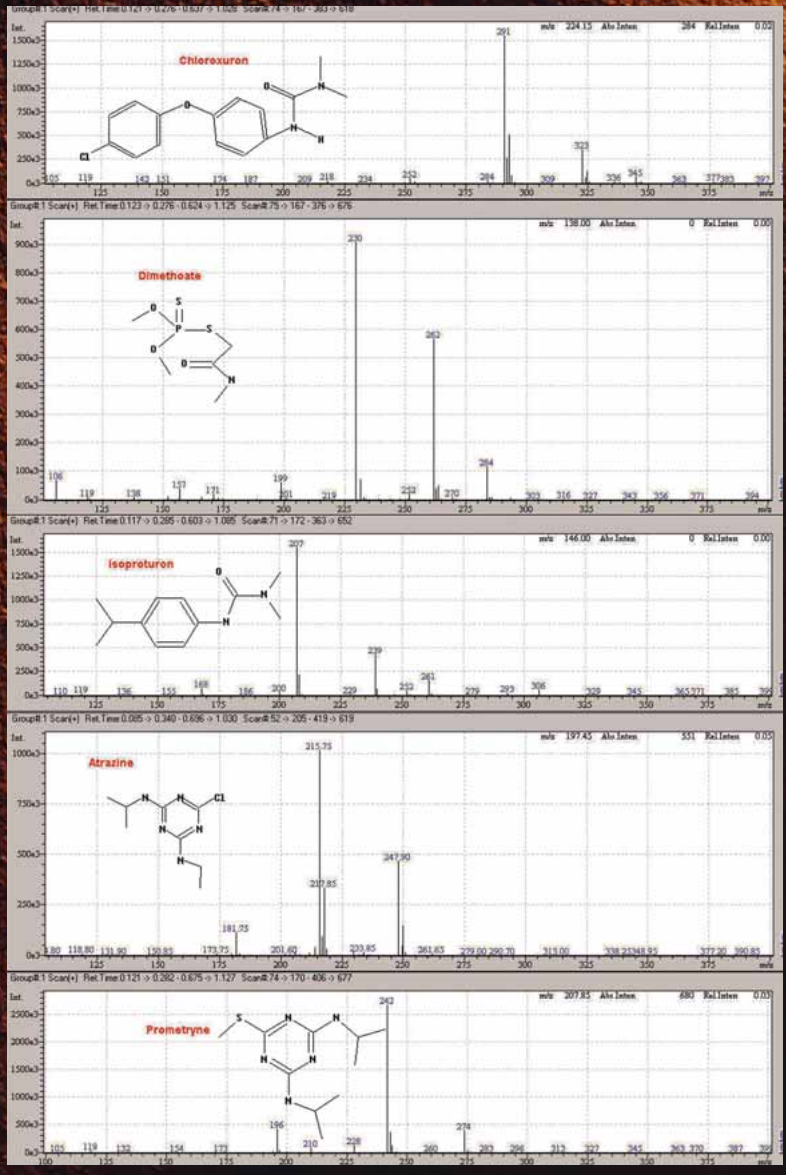
Conclusion

The Shimadzu LCMS-2010 can be an effective analytical tool for developing robust qualitative and quantitative analyses for pesticides and herbicides. The versatility built into LCMS Solution® software streamlines the time and effort spent on developing these methods. Overall throughput increases, but without compromising data integrity. The Shimadzu LCMS-2010 can revolutionize method development approach, reaching low levels of detection unmatched by any other single-quad MS.

Results and Discussion



Separation of Standards



Mass Spectra of Standards

NEW PRODUCTS : SIL-HT ELSD-LT

New Liquid Chromatography products from Shimadzu find wide acceptance in many laboratory settings

Figure 1—The SIL-HT Autosampler

SIL-HT AUTOSAMPLER

Autosampler enhances analysis throughput by fast sample injection and high sample capacity

In any laboratory today, the single common denominator is the need for multi-tasking in equipment as well as in staff. Gone are the days when a single instrument operated by a single expert can be dedicated to a single task. This is especially true for laboratories engaged in liquid chromatography techniques. The maturation of High Performance Liquid Chromatography (HPLC) as an analytical discipline has dictated that the systems be easily operated by operators who are not necessarily experts in chromatography. An additional requirement is that the equipment possesses the maximum capacity for self-validation and reporting. There can be little doubt that mass detection is becoming more and more important in HPLC, and there is always the critical need for increased sample capacity, high sample throughput, maximum data repeatability and accuracy, and minimum sample carryover. As the needs of the analyst can change rapidly, the cross compatibility of hardware and software becomes more and more important.

The requirements described above are daunting, but Shimadzu has continued its tradition of excellence in HPLC with the introduction recently of three outstanding products. Shown in Figure 1 is the SIL-HT high performance stand-alone autosampler. The unit is available in two models, the SIL-HTa and the SIL-HTc with sample cooling. The SIL-HT enhances analysis throughput by fast sample injection and high sample capacity. Injection speed is 18 seconds for injecting samples of 10µL (1/2 of SIL-10ADvp). Quite simply, this autosampler is the finest available and has unmatched sample throughput, data repeatability (Figure 2), and linearity (Figure 3). Recent evaluation of the SIL-HT by pharmaceutical companies has met with a most favorable response, as have similar evaluations by contract laboratories such as **Covance**. All of these enterprises require the highest performance and versatility in an autosampler for LC and LCMS applications, including using the SIL-HT as an autosampler for triple-quad MS.

Seeing is believing, so the saying goes, and the data on repeatability and carryover for the SIL-HT is really worth seeing: 100 injections of 0.05 mg/mL caffeine, 10µL each, no rinsing, %RSD=0.230.

Carryover in the SIL-HT is guaranteed to be less than 0.01%, unmatched among commercially available LC autosamplers. In the test results shown in Figure 3, there was no detectable carryover in blank injections following 10 repeat injections of naphthalene.

Conditions

Flow rate: 1 mL/min
Mobile phase: methanol/water (60/40 v/v)
Wavelength: 254 nm

To minimize carryover, the outer surface of the sampling needle of the SIL-HT's autosampler is coated using a special, innovative surface processing technology (patent pending). Furthermore, by employing newly developed rotor seals and needle seals made of PEEK, the SIL-HT dramatically reduces contamination, even with the most highly adsorbent sample compounds. As a result, the SIL-HT demonstrates nearly zero sample carryover.

The SIL-HT uses a needle-in-the-flow-path injection design (also called a direct injection method or total volume injection method) and high-performance measuring pump (6nL step resolution) for enhanced accuracy. This results in superior repeatability over conventional autosamplers. In addition, precious samples are not wasted since the total volume aspirated is injected.

The SIL-HT also has excellent sample capacity:

350 x 1mL vials (SIL-HTa/c)

210 x 1.5mL vials (SIL-HTa) and 140 x 1.5mL vials (SIL-HTc)

100 x 4mL vials (SIL-HTa/c)

4 x MTP (1536 samples) (SIL-HTa/c)

96-well Standard and Deep Well

384-well Standard.

The high sample capacity, high-speed injection capability, injection volume repeatability, and ultra-low carryover make the SIL-HT an unsurpassed performer in high performance LC autosamplers.

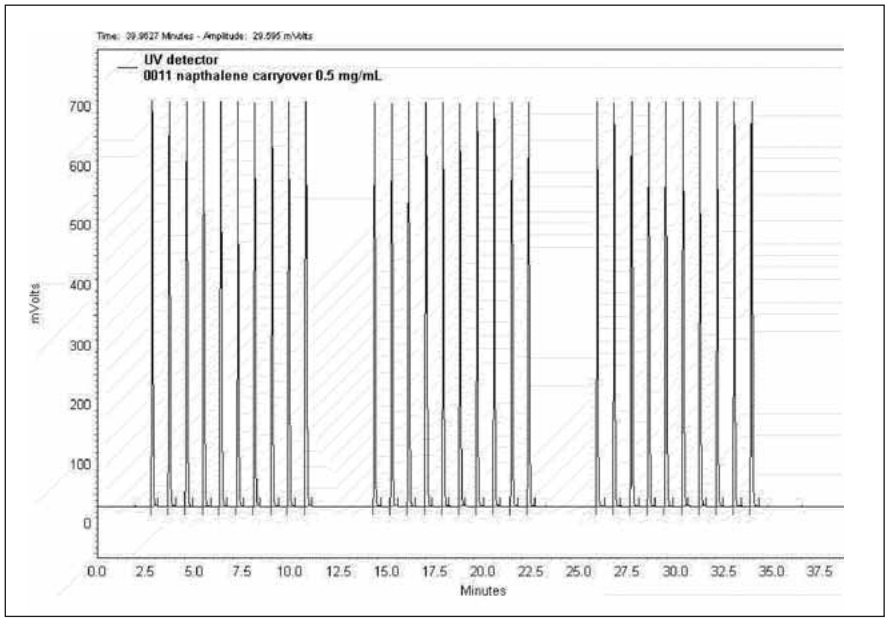


Figure 3—Injection Repeatability Carryover of Naphthalene in the SIL-HT

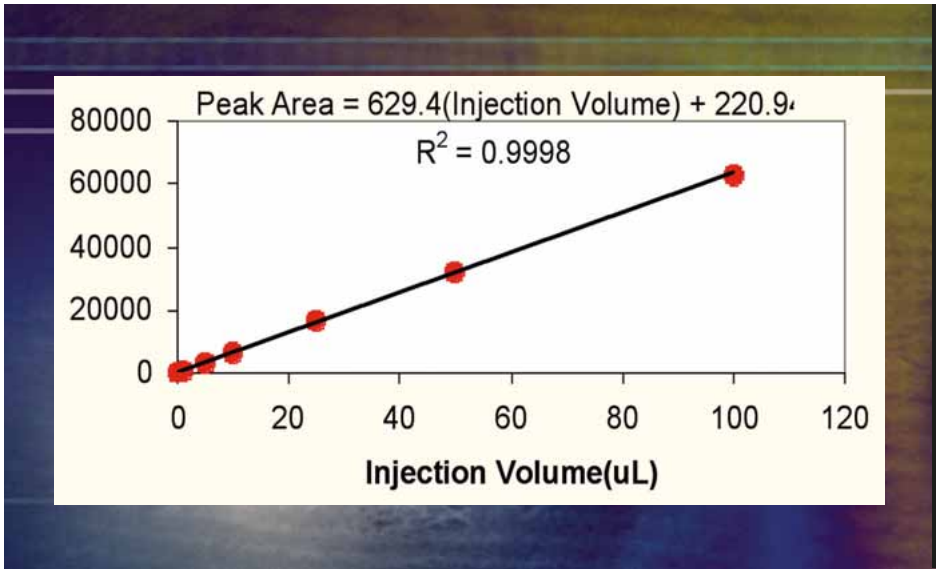


Figure 2

SIL-HT Injection Volume Linearity

Conditions:
SIL-HTc
LC-10ADvp, SPD-10AV
VP-ODS column 4.6 x 150 mm
60%MeOH:H2O/No Rinse
0.05 mg/mL caffeine, 254 nm
Sample Injection Speed = 3 µL/s
5 X 1, 5, 10, 25, 50, and 100 µL

ELSD-LT

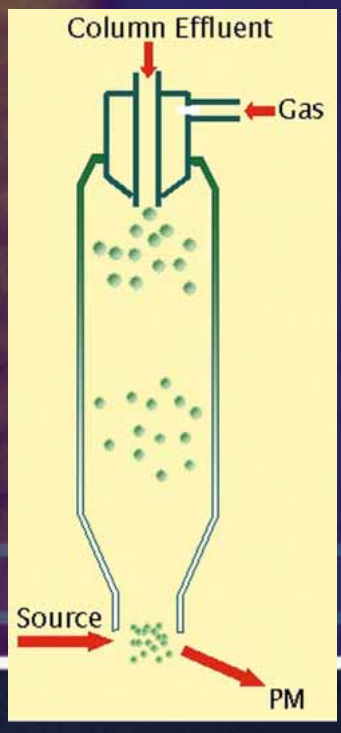
Shimadzu Introduces the Low-Temperature Evaporative Light Scattering Detector

Shimadzu has now completed the family of HPLC detectors with the introduction of the ELSD-LT. The ELSD-LT is ideally suited for applications in drug discovery, natural products development, combinatorial chemistry, and food and beverage industries. Analytes are detected regardless of their chromophoric properties. Essentially, all compounds are detected even if they do not contain a chromophore or an electroactive group.

Shimadzu's ELSD-LT low-temperature evaporative light scattering detector transforms a target compound to particulate form by evaporating the mobile phase, and then measures the light scattered by these particles to detect the compound. In general, the detector will deliver a signal for all compounds that do not evaporate or decompose during the mobile phase evaporation stage. Further, the detector produces stable baselines during gradient elution chromatography as its response is independent of the bulk spectral properties of the eluent. The ELSD-LT produces nearly uniform detection sensitivity for the majority of analytes, regardless of their physical properties. The low-temperature integrated design prevents the decomposition of thermally labile compounds, resulting in increased assay sensitivity.

The ELSD-LT is a universal mass sensitive detector with the following key benefits:

- **Low temperature operation–**
  The ELSD-LT optimizes sensitivity of thermally labile compounds by low-temperature evaporation of the mobile phase using a three-step process. This system can evaporate a mobile phase consisting of 100% H_2O at 32˚C. Other systems require a special accessory to evaporate the mobile phase. ELSD-LT has an integrated design for optimizing sensitivity, performance and ease of operation.
- **New Cell Design Reduces Band Broadening–**
  The innovative cell design minimizes band broadening providing a similar bandwidth as UV, UV-VIS detectors.
- **Excellent Performance using Gradients–**
  The ELSD-LT provides excellent resolution of analytes since gradients can be used to optimize separations. The mobile phase is removed from the eluent even at high flow rates such as 4ml/min. with uncompromised resolution.
- **Quantitation of all Analytes in a Sample–**
  Essentially all compounds in a sample provide a signal allowing accurate quantitation. The detector response is related to the mass of the compound, not UV absorbance, making this detector extremely useful for the combinatorial chemist. The ELSD-LT is a universal detector.



REAL WORLD SOLUTIONS

SIL-HTc COMPETITIVE CARRYOVER PERFORMANCE ANALYZED BY LC-MS/MS:

A Collaborative Study between Shimadzu Marketing Center* and Covance Laboratories**

S.M. Wishnies*, M. Nishimura*,

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S. Maruyama*, A. Ueyanagi*,

T.D.J. Halls**, S. Zhou** and X. Jiang**

(Shimadzu Corp., Kyoto, Japan* and Covance Laboratories, Inc., Madison, WI, USA**)

SIL-HTc High Throughput Autosampler

ADVANCES IN THE FIELD OF DRUG DISCOVERY have resulted in a tremendous production of potentially therapeutic compounds and, thus, another "bottleneck" downstream from synthesis to drug development. Candidate compounds need to be rapidly analyzed for structure elucidation and evaluated for efficacy and toxicity. Bioanalysis is now perhaps the most prominent activity in drug development and the preferred tools for these types of analyses are High Performance Liquid Chromatography (HPLC) coupled with triple quadrupole mass spectrometry (LC-MS/MS). Successful development of accurate and dependable bioanalytical methods is therefore extremely critical. Method development to determine levels of drugs and their metabolites in biological fluids can present an array of analytical problems that can interfere with the assay. The causes of assay interference are often attributed to sample carryover, particularly with "sticky" compounds having an affinity for the flow-path composition and/or uncleared micro dead volumes in the HPLC system and, in particular, the autosampler. In addition, the increased sensitivity of triple quadrupole mass spectrometry tends to magnify the detection of carryover. Carryover has been conventionally reported using UV detection. Mass spectrometry was used in this collaborative study with **Covance Laboratories** (Madison, WI, USA) as a more sensitive determination of sample carryover using the new high throughput SIL-HTc autosampler. Carryover performance of the SIL-HTc was compared to that of other commercially available HPLC autosamplers on the market.

EXPERIMENTAL

LC-MS/MS Components:

(1) SIL-HTc High Throughput Autosampler with Cooling Capability and built-in system controller (below).

(2) Commercially Available HPLC Autosamplers denoted as: A, B, C and D.

All autosamplers were configured with the same two Shimadzu LC-10ADvp analytical pumps (high pressure mixing) and MS/MS (Sciex API 365) for direct comparison of carryover performance.

LC-MS/MS Conditions

The Shimadzu LC system was configured with the SIL-HTc and the commercially available autosamplers (A, B, C or D) and coupled with a Sciex API 365 triple quadrupole mass spectrometer operated in positive turbo ionspray mode. A typical C18 (50 x 4.6mm, 3.5µm particle size) column was employed; flow rate: 0.400mL/ min.; column temperature: 40°C; injection volume: 20µL.

The mobile phase consisted of: (a) 5 mM ammonium formate in 0.1% formic acid: 0.1% formic acid in acetonitrile (55:45, v:v). The mass spectrometer was operated in positive ionspray mode. MRM ions for Compound X: 386.3/167.1; dwell time: 300 msec; capillary voltage: 2.5 kV; source temperature: 400°C; collision gas: N_2; collision energy: 37V.

FIGURE 1: TYPICAL CHROMATOGRAM of SIL-HTc CARRY OVER

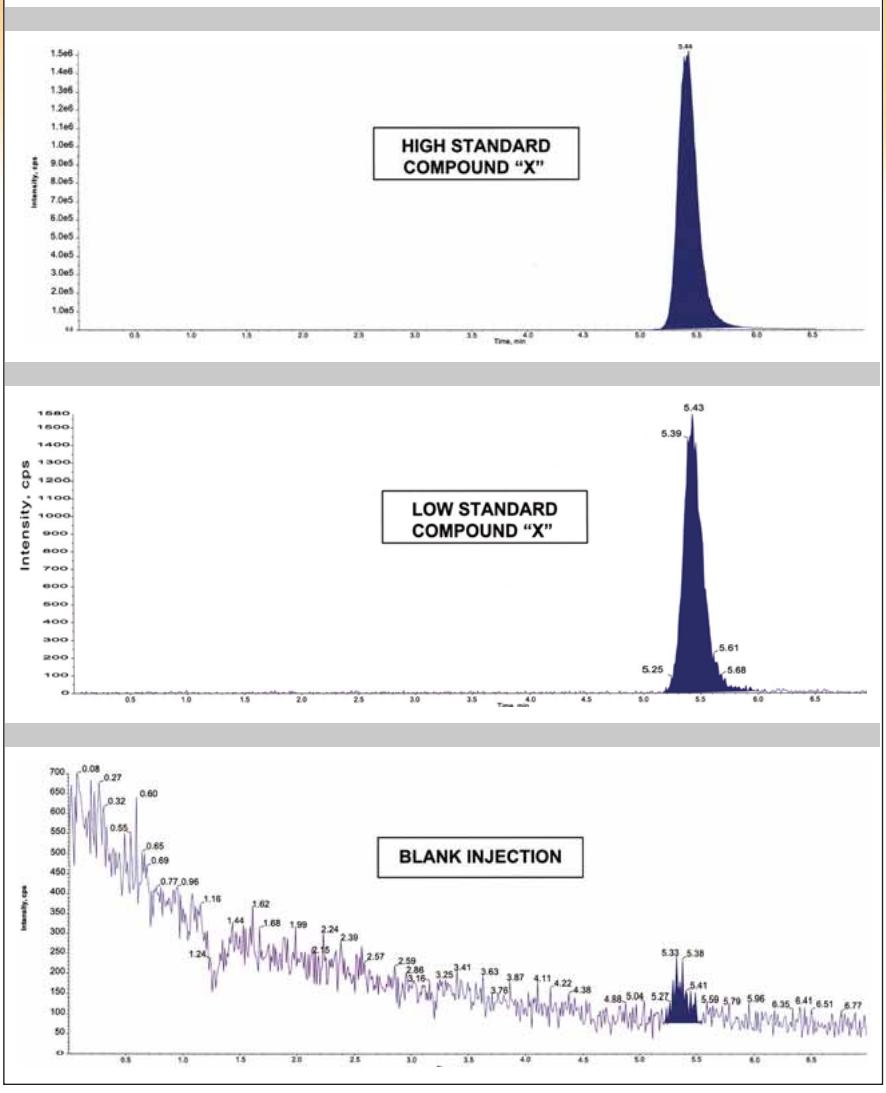

Table 1. Percent Carryover Comparison of the Commercial Autosamplers and the SIL-HTc.

RESULTS

AUTOSAMPLER	% CARRYOVER
A	0.0129
B	0.00924
C	0.0170
D	0.0144
Shimadzu SIL-HTc	0.00572

According to the results in Table 1, the SIL-HTc autosampler outperformed or gave the least amount of measurable carryover (~ 2 to 3 times less) compared to the other autosamplers tested (see FIGURE 1). As mentioned in Note 2, extensive rinsing, multiple rinse solvents (when applicable) and/or both were used for the other autosamplers. Extensive rinsing correlates with increased cycle time. The SIL-HTc was tested using the default injection routine consisting of a 20-sec injection cycle time without employing extensive rinsing.

SAMPLE PREPARATION

Sample Compound X (**Covance Laboratories**, Madison, WI, USA) was used as the model compound for testing the carryover of various HPLC autosamplers. Sample solutions were prepared by diluting the stock standard solution of Compound X (1.00 mg/mL in methanol) with methanol/water (1:1,v/v). The tested samples included high standard (1.00 µg/mL), low standard (0.500 ng/mL) and blank solvent (5 mM ammonium formate: acetonitrile: formic acid, 60:40:0.1 v: v: v).

Test Procedure

For each test, 20 µL of a blank sample was injected into the LC-MS/MS immediately after a high calibration standard. The carryover (%) was calculated as the relative peak area of the blank against that of the high calibration standard.

Note 1: The sample for the study was proprietary and therefore structural information was not available; however, the sample was described to be basic and very hydrophobic

Note 2: The rinse protocols for the other autosamplers may have included extensive rinsing with one or more solvents to eliminate carryover. The SIL-HTc was used in default, 20-second cycle time without extensive rinsing.

CONCLUSION

Sample carryover has progressively become more of a problem in drug development, especially in the area of bioanalysis, for a number of reasons. Given that carryover is dependent upon compound structure and thus the resulting chemical properties of that structure in a multitude of different environments, there are other obvious variables to consider. The sample matrix or vehicle is critical when developing an accurate and quantitative assay. The compound and its metabolites are most likely in biological fluids such as blood, urine plasma and/or serum to name a few, which further complicates assay development because of the very nature of these fluids (proteins, salts and other interfering components).

The compound/metabolites then usually need to be extracted before reconstituting into an appropriate solvent or buffer for LC-MS/MS analyses. Providing that most of these problems have been addressed, the analytical equipment is then suspect and the carryover seems to be magnified by employing the increased sensitivity of a mass spectrometer as the detector. The autosampler would then be the most logical component of the HPLC system contributing to sample carryover.

Shimadzu has approached the carryover problem with a newly designed high throughput autosampler, the SIL-HTc. The rapid cycle time does not sacrifice throughput and the extremely low carryover makes it the perfect autosampler for these types of LC-MS/MS applications and others. It was clear that the SIL-HTc had the least amount of carryover in this study. Shimadzu incorporated several new design features in the SIL-HTc to accomplish this. The newly engineered SIL-HTc development features include:

- **A** Special metallic coating of the sample needle
- **B** Use of a PEEK™ rotor seal
- **C** Modification of the flow paths

As a result, the new SIL-HTc had the least amount of sample carryover, minimal rinsing with a rapid cycle time of 20 seconds.

ACKNOWLEDGEMENTS

Shimadzu Marketing Center (Shimadzu Corporation) would like to acknowledge and extend great thanks to Timothy D.J. Halls, Ph.D. (Vice President of Pharmaceutical Chemistry) at Covance Laboratories Inc. Madison, WI for allowing Shimadzu to collaborate with Covance in this study at Covance Labs, and for the expertise of Shaolin Zhou, Ph.D. and Xiangyu Jiang, Ph.D. for performing the experiments and data analyses in their labs at Covance. We deeply appreciate your efforts.

Compliance Corner is a new section to LC World Talk that will be dedicated to updates and activities related to regulatory issues. The editor also welcomes questions to be addressed in the next issue. Please e-mail questions to LCWorldTalk@shimadzu.com. Please visit our Web site at www.shimadzu.com.

Shimadzu Offers a Software Suite to

Assist Customer Compliance to Title 21, Code of Federal Regulations, Part 11

Shimadzu Corporation's Dr. Hayakawa (Shimadzu Liquid Chromatography Business Unit) presented work on Shimadzu's state-of-the-art compliant data archiving software package, CLASS-Agent.

IT IS NOW CRUNCH TIME for the pharmaceutical industry, CROs, and biotech businesses alike to consult quality standards, (ISO, EN, TICKIT, GMP, GLP, GCP, ANSI, ASTM, GALP), streamline their processes, perform GAP analyses and remediation to prepare for that inevitable FDA audit. Once your company files claim to be 21 CFR Part 11 to the FDA, the flag is up. Failure to comply can be quite drastic and can result in the FDA issuing a warning letter, pulling product from market, astronomical fines, criminal investigation and/or closing down the shop. Since the introduction of 21 CFR Part 11 (Electric Records and Signatures) in 1997, industry has had time to perform GAP analyses and explore ways to effectively execute plans to comply.

During this time Shimadzu Corporation has provided global seminars on regulatory issues involving 21 CFR Part 11 and how Shimadzu as a vendor provides the tools necessary to assist customer compliance, from hardware to software solutions. Before introducing the suite of enabling compliance technologies, we have asked attendees some critical questions that are essential in building an effective compliance initiative:

Has a company-wide validation plan been devised to identify all systems that are required to be validated and has this list been prioritized? Have personnel been trained and has a timeline been

established to realistically implement these goals?

Has necessary software and computer systems been validated according to internal and FDA guidelines such that they comply with the recommended steps for regulatory compliance - testing and validating computer hardware, software, and analytical system configurations which acquire, store and manage critical data?

What vendor can provide you with the necessary tools to best suit your needs and can they be used to build validation into the system acquisition process?

So the question remains: have you selected the best vendor to assist regulatory compliance? For the past 3 to 5 years, Shimadzu has been taking part as a vendor to go aboard to help customers understand 21 CFR Part 11 through a series of seminars sponsored by Shimadzu or co-sponsored with other vendors and organizations such as the Institute of Validation Technologies (IVT). Just recently, Shimadzu co-sponsored an IVT seminar on Regulatory Compliance in Tokyo, Japan to introduce Shimadzu's suite of software compliance tools: Lab Solutions, CLASS-VP and CLASS-Agent for data acquisition, storage, archiving, and audit trail, that comply with 21 CFR Part 11. Some vendors market compliance, but Shimadzu has painstakingly addressed all points of 21 CFR Part 11 and is confident these software tools enable the end user to comply.

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Lab Solutions, CLASS-VP and CLASS-Agent comprise the Shimadzu regulatory toolbox to assist end users on the road to compliance. Compliance with 21 CFR Part 11 is achieved through the integrated data management system for all common laboratory instruments. Instruments included in this suite management system are LC, GC, GC-MS, LC-MS, UV, FTIR, AA and balances. CLASS-Agent provides electronic record and electronic signature with secure database archiving that is required for compliance. In addition, a network-based browser is provided for review and authorization of data packages including raw data, all processed results files, meta files and descriptive notes.

As a global vendor of Chromatography Instruments, Data and Data Archiving Software Systems, Shimadzu can assist you with your regulatory needs.

SHIMADZU exhibit at IVT seminar in Tokyo, Japan.

LC World Talk

LC WorldTalk *is a complimentary newsletter published for the benefit of Shimadzu customers to keep you apprised of the latest HPLC techniques and applications. Comments and suggestions, or requests to receive LC WorldTalk may be e-mailed to LCWorldTalk@shimadzu.com.*

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If accepted for publication, a representative from Shimadzu will contact you.

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