General Sessions (Final agenda)

CoSMoS 2014 Preliminary Technical Program and Conference Agenda
August 11 – 13, 2014
Williamsburg Lodge, Williamsburg, VA
Sunday, August 10
Pre-conference evening reception for early arrivals
Day 1: Monday, August 11

7:30 – 8:45 am Breakfast (provided)
8:45 – 9:00 am Welcome / opening remarks Michael Balogh, President
9:00 – 10:30 am Session 1 – Orals

Chairs: Elizabeth Hamelin, CDC
Justin Stroh, Pfizer

Biology Meets Small Molecule Science
Nature has already created the most specific separation and detection tool: the antibody. Typically used by biologists, antibodies and aptamers are now used by chemists to capture and deliver small molecules. Come hear how both small and large molecule science benefits from the other’s perspective.

Understanding the potential of macromolecules in analytical method development
Jonas W. Perez
Battelle Memorial Institute, Columbus, OH

Macromolecules can be used to enhance many different analytical techniques, including analytical techniques to evaluate small molecules. Two classes of macromolecules that are of particular interest in analytical method development are antibodies and aptamers. A general understanding of these biomolecules and their use is necessary to effectively develop techniques which utilize them. Although both can provide similar functions, such as antigen recognition, they vary greatly in their strengths and limitations. This presentation will focus on proving background knowledge on antibodies and aptamers as well as some of the terminology and characteristics associated with each.

Development of an Atpasensor for the Detection of Paralytic Shellfish Toxins
Jeffrey A. DeGrasse
Center for Food Safety and Applied Nutrition, US Food and Drug Administration, College Park, Maryland

Paralytic shellfish poisoning (PSP) is a serious illness caused by consumption of shellfish contaminated with paralytic shellfish toxins (PSTs) that are produced during toxic blooms of microscopic algae.
The PSTs comprise a family of at least 24 different closely related neurotoxins and pose a major health threat worldwide. There are several reliable methods available for the detection of PSTs, including the mouse bioassay, liquid chromatographic detection, and immunoassays. The immunoassays are rapid and field deployable. However, immunoassays are challenged by antigen cross reactivity that could lead to false positive or false negative results. Continued immunoassay method development is hampered by the lack of commercially available PST antibodies. To address the challenges associated with current immunoassays, the aim of this project is to find an alternative analytical recognition element to antibodies that can be incorporated into rapid screening methods for PSTs. Aptamers are single-stranded nucleic acids that have high affinity and specificity to their target molecules. Aptamers have significant advantages over antibodies, giving them promise as a recognition element for different types of analytes. Since aptamers are synthesized in-vitro, chemical modification of aptamers with different functional groups can be done very easily and in a site-specific manner. We present structure switching aptamers that specifically bind with high affinity and specificity to small molecule shellfish toxins of interest for food safety. We then employ these selected aptamers to develop a FRET-based assay to detect PST in shellfish. We also discuss the development of a field-deployable biosensor as a fast, inexpensive method to detect the PSTs with high sensitivity at harvest in order to ensure that shellfish are safe for consumption.

**Novel ADME Strategies for ADC Drug Development**

Xiaogang Han  
*PDM NBE, Pfizer Inc.*

*Presentation sponsored by CoSMoS*

Antibody drug conjugates (ADCs) bring the promise of a much enhanced selectivity to the delivery of potent agents to a target employing immuno interactions. At the late discovery and early development stage, the candidate optimization and selection process requires understanding of the on-target cellular uptake kinetics of ADCs and quantitative descriptions of the interplay of the antibody and released payload(s) PK. The complex modality of bioconjugates pose unprecedented challenges in profiling ADME attributes due to the combination of characteristics involving a small molecule drug with an antibody, and the heterogeneity of drug product resulting from conjugation chemistry. Ligand-binding assays (ELISA) are well-established platforms for large molecule quantitation. However, they are not always best suited for quantifying conjugates. As the active moieties, the payload (especially in its conjugated state) is the critical component to measure for exposure calculation at the target site. Here we will discuss our strategy for better assessments of specificity, TI, payload delivery, and overall PK/PD profile. We discuss a few novel approaches using LC/MS platform enabled characterization of ADCs in a quantitative and reliable manner.

10:30 – 11:00 am Break  
11:00 am – 12:30 pm **Session 2 – Workshop**  
**3rd Annual Method Development Olympics**  
The organizers of the CoSMoS Conference recognize the value of diversification when engaging in new analytical challenges. More exposure to a variety of techniques and approaches usually leads to a successful outcome. In order to highlight this type of thinking, CoSMoS has designed an analytical challenge to help stimulate healthy discussion on the different approaches to analytical method development. Conference participants will apply their method development strategy to an analytical problem defined by the CoSMoS organizing committee. Participants review the analytical challenge and submit their application to participate on the CoSMoS website. The top 3 finalists are invited to present their method session and the audience votes to determine the Bronze, Silver, and Gold Medalists awarded at the Tuesday evening dinner.

12:30 – 1:30 pm Lunch (provided)  
1:30 – 3:00 pm **Session 3 – Workshop**
The future of chromatography – what will separation systems look like in the next decade

Over the past decade we have seen significant progress in the field of HPLC. U(H)PLC was introduced and now every major system manufacturer has a UHPLC grade system available. Column technology has progressed at the same speed, ultimately enabling UHPLC with sub 2 um particles. These advances have allowed unparalleled chromatographic performance or accelerated analysis times – whichever you chose to be more important. Core shell particles have more recently entered the arena and allow increased performance at lower pressure drops compared to UHPLC. Monolith are making a come-back with newer versions now available with improved performance characteristics. Work is also done on column design to support these advancements in instrument design and separation media. In this session we discuss the most recent trends and take a critical look at how much impact they have on the day-to-day work of practitioners of chromatography. Will other technologies change the landscape again and what do we expect chromatographic separations to look like 10 years from now? Which trends will prevail and make a lasting impact and what will turn out to be a fad?

Featured Plenary Speaker:
The Future of Chromatography

Georges A. Guiochon
University of Tennessee, Knoxville and Oak Ridge National Laboratory Distinguished Scientist

Presentation sponsored by CoSMoS

Current trends in chromatography and their origins will be illustrated pointing out the degrees of maturation and sophistication covering high pressure, new packing materials, advanced columns, 2D-chromatography, and the use of MS and NMR as detectors.

However, for the lack of a suitable crystal-ball detector, the long-term future of chromatography remains hazy. Chromatography as an area of research results from its unique position as a powerful means to investigate the thermodynamics and kinetics of phase equilibria and is the most powerful method of separating and identifying compounds available in the life sciences. Examples of current work in an unusual application of 2D-chromatography, of potential importance investigating problems of interest in biochemistry, will be discussed.

Georges A. Guiochon graduated in 1953 with a MS degree in engineering at Ecole Polytechnique (Paris, France) and received a Ph.D. in chemistry from the University of Paris (France) in 1958. He was a Professor of chemistry at Ecole Polytechnique (1958-1985) and at the University Pierre et Marie Curie of Paris (1968-1984), then at Georgetown University, Washington, D.C. (1984-1987). In June 1987, he was appointed a Distinguished Professor at the University of Tennessee (Department of Chemistry) and a Senior Scientist at the Oak Ridge National Laboratory (Division of Chemical Sciences).
Presentation sponsored by CoSMoS

The ambient distribution of light stable isotopes in biopharmaceutical synthetic pathways permits the identification and differentiation of potentially-infringing pathways. After reviewing three cases of product identification, we examine three cases of process authentication: one of false advertising and two of process patent infringement. The three cases of product authentication demonstrate the dynamic range of the light stable isotopes in differentiating sources of pharmaceutical materials. The false-advertising case was substantially a product case because the green-tea L-Theanine and the client- and competitor L-Theanine were markedly different in carbon- (~15‰) and nitrogen isotopic (~10‰) composition. The competitor L-Theanine process was revealed from court documents and chemical-isotopic insight. The competitor was accused of falsely advertising the source of their L-Theanine. The second case of process patent infringement was a straightforward case of infringement. An infringer used synthetic intermediates that were readily available on the market to produce the infringing product. When confronted with the isotopic evidence of process infringement, an out-of-court, business resolution was reached. The third case of process infringement was a case of wrongful accusation of infringement. The carbon-isotopic records of both the product and process studies show that (i) the products are of different origins and (ii) the defendant had in fact used a different synthetic pathway so that he was not infringing the patent of the plaintiff.

Possible Addendum: Online process analysis of natural-abundance stable isotopes affords a marked opportunity to monitor bioreactors and chemical-production systems in real time. Advances in theory and in technology over the last decade plausibly afford the opportunity for online monitoring of the state of such systems. I will review the development of a Stable Isotopic Indirect Calorimeter (http://www.naturesfingerprint.com/abstracts/abstract_i10272000.shtml) as an example of a bioreactor / gas purifier / offline isotope-analytical system which could readily be converted to an online system. Next, I will briefly review the contemporary stage of online isotope-ratio monitored, continuous reactors.

Analytical Testing for the Cannabis Industry: Application of Ultra Performance Convergence Chromatography

Christopher Hudalla
Proverde Laboratories, Franklin, MA

The cannabis industry has been thriving for many years, with the use of cannabis tracing back thousands of years. However, the illicit status of the herb throughout much of the world has stifled commercialization and research, forcing most activities underground, often times with high risk and minimal accountability. As a result of this, technological advances in science and analytical instrumentation have found little to no application to this diverse field. Recent advances throughout the world in legislation, regulation and public acceptance have opened the door for legitimacy of this industry. This provides the new opportunity for the use of the latest advances in scientific instrumentation and methodologies to be applied to different aspects of this industry, including ensuring consumer safety, basic research, optimization of cultivation practices, and the design and development of Marijuana Infused Products (MIPs). At the same time, as the industry transitions to the forefront of legitimacy, increased regulatory requirements demand the application of more accurate and precise testing methodologies.

Here we present the application of UltraPerformance Convergence Chromatography (UPC2) to the study of cannabis and cannabis products. In combination with stationary phases designed specifically for UPC2, this technique results in the analysis of cannabinoids in about 4 minutes. In addition, Convergence Chromatography minimizes the consumption of mobile phase solvents (e.g. acetonitrile) thereby generating less waste for disposal and significantly reducing the cost of analysis per sample. Based on the theory of Supercritical Fluid Chromatography (SFC), UPC2 provides detailed cannabinoid profiling...
of marijuana flower and derived products, including tinctures, salves, infusions and a wide variety of consumable goods. In addition to satisfying regulatory requirements, the resulting data is also being used to optimize cultivation and production processes, to understand the physiological effects of the various cannabinoids, and to determine appropriate strains and dosing for individual patient needs.

**Forensic Toxicology: Analytical Strategies For Detecting And Reporting Compounds In A Legal Environment.**

Lucas Zarwell  
*Office of the Chief Medical Examiner, Public Safety & Justice Cluster, Washington, D.C*  
*Presentation sponsored by CoMoS*

As an applied science, forensic toxicology continues to be one of the most challenging to implement both operationally and analytically. This is largely due to the abundance of possible analytes and addressing the legal burden of proof both quantitatively and qualitatively.

This presentation will discuss analytical approaches and advances in testing postmortem and human performance casework. Techniques will include discussion of how spectrophotometry, GC/MS, LC/MS/MS, and TOF technologies are applied. Issues with legal challenges, quality assurance, and interpretation will be discussed.

5:00 – 6:00 pm  
Poster session and reception  
6:00 pm  
Dinner (on your own)

**Day 2: Tuesday, August 12**

7:30 – 9:00 am  
Breakfast (provided)

9:00 – 10:30 am  
**Session 5 – Orals**

**Predictive Technology**  
*Chairs: Karen Alsante, Pfizer*  
*Steven Baertschi, Lilly*

Stress testing is an important tool for the prediction of stability-related problems and impacts many areas of pharmaceutical research beyond analytical, formulation, and packaging development. Accurate shelf-life predictions are best made with data from formal long-term stability studies that require a significant time investment, although recent studies utilizing an “accelerated stability assessment protocol” have demonstrated a high degree of kinetic predictability with much less time required. The quantitative interpretation of stress testing results is an underdeveloped area that has made significant progress in recent years. This session will feature presentations on current research efforts to develop better stability predictive tools for the future.

**Predicting Rates of Degradation as a Function of Dosage Strength**  
*Allison Dill*  
*Lilly, Indianapolis, IN*

A model for predicting the rate of degradation as a function of drug load was recently developed (J. Pharm. Sci., 101(11), 2012, 4170-4177). In this case study, we explore both the mathematical model as well as the conceptual construct from which the model was developed. We applied the model to a pediatric formulation of prasugrel hydrochloride of varying drug loads. Our results confirm the validity of the mathematical model, but call into question the proposed conceptual construct. We will discuss the generality of the model and how the use of this model can speed development of lower dose drug formulations typically found in pediatric dosing regimens.

**Water Activity Measurements: The Achilles Heel of Accelerated Stability Predictions**

*Brian Pack*  
*Lilly, Indianapolis, IN*
Water activity measurements have been utilized for many years in the pharmaceutical industry in order to demonstrate that drug products are not likely to support microbial growth. In addition, scientists have tried to correlate degradation rates with water activity values, as it is this water that is considered available for reaction. More recently, water activity measurements have been utilized in support of accelerated stability projections. This presentation will first address water activity measurement fundamentals (i.e., how to measure accurately during a stability study) and errors introduced by common practices. In addition, techniques to determine water activity values outside the typical instrument operating range (e.g., 60 °C, 70 °C, and 80 °C) will be discussed along with the impact to accelerated stability predictions.

Oxidative Prediction: Azo Initiator Pharma Consortium Effort and Results

Marcela Nefliu
Merck, Sharp & Dohme, NJ

Azoalkane initiators such as 2,2-azobisisobutyronitrile (AIBN) and 2,2'-azobis-2-methyl-propanimidamide (AAPH) are widely employed by the pharmaceutical industry in simple solution stress testing studies to evaluate the susceptibility of drugs to autoxidation. For model pharmaceutical compounds containing primary and secondary amine groups we report the formation of drug like artifacts according to the general scheme below, that are not derived from the free radical chain process characteristic to this standard oxidative stress test. The effect of experimental parameters on the yield of the artifacts as well as detailed mechanistic studies to gain further understanding into their formation such as isotopic labeling studies and measuring the level of cyanide in the stressed samples will be discussed.

10:30 – 11:00 am
Break

11:00 am – 12:30 pm
Session 6 – Workshop
USP Standards and Monograph Modernization
Kevin Hool, Vice President of R&D
USP, Rockville, MD
Presentation sponsored by CoSMoS
Jon Clark, Vice President of Chemical Medicines
USP, Rockville, MD

USP standards are used by the FDA for guidance in the approval of food and drug products. With the advancement of analytical tools and techniques, the modernization of USP monographs is required to reflect current technologies, ensure continued practicality and relevance, and meet regulatory expectations. This workshop will discuss the current status and future direction of the USP, and areas of priority for modernization of monographs.

12:30 pm – 1:30 pm
Lunch (provided)

1:30 – 3:00 pm
Session 7 – Orals
Modern Structure Elucidation
The need to elucidate chemical structure from spectroscopic data has existed since chemists discovered molecules. Fortunately, instrumentation and data interpretation techniques have made great strides since the days of prism spectrosopes. In this sessions, three speakers will describe the 21st century approaches to structure elucidation, covering advanced instrumental techniques, databases, and the Internet cloud.

The mzCloud: Cloud Computing in Mass Spectrometry
Robert Mistrik
HighChem, Slovakia

Identification of unknown compounds using mass spectrometry was traditionally limited to library search techniques and manual
spectral interpretation. A few years ago, Precursor Ion Fingerprinting (PIF) was developed. This innovative approach identifies substructural information through the comparison of product ion spectra of structurally related compounds. Structural information is derived by utilizing previously characterized ion structures stored in mzCloud database and matching them with unknown product ion spectra. PIF is a very powerful technique that heavily depends upon libraries containing spectra of precursor ions of various chemical classes acquired at various experimental conditions.

To enable elucidation of unknowns using the precursor ion fingerprinting method, a cloud solution has been developed which is implemented in a relational database that is freely accessible through a public domain web site (mzcloud.org).

**Higher Order Tandem MS Applied to Natural Product Structure and Reactivity Elucidation**

Kevin A. Schug  
*The University of Texas at Arlington, Arlington TX*  
*Presentation sponsored by Shimadzu’*

Nature makes a variety of polyphenolic compounds that can act as natural antioxidants when consumed. HPLC-MS and MS/MS are gold standard techniques for trace quantitative analysis, and sometimes qualitative analysis, of these compounds from a variety of matrices ranging from foods to biofluids. However, the sheer number of different isoforms and substitution patterns that can be expressed in different polyphenolic structures can lead to difficulties in their clear differentiation. Additionally, small changes in structure can lead to large changes in antioxidant capacity. We have exploited the benefits of ion-trap – time-of-flight (IT-TOF) MS technology, which includes higher order tandem MS and high mass accuracy (< 5 ppm) capabilities, to further differentiate similarities in anthocyanin compounds common in fruits and flowers. We have also interfaced in-line reaction manifolds to IT-TOF-MS to investigate the mechanisms of oxidation for a model polyphenol, quercetin. With this instrumentation, we are able to probe some structures of products that have not been reported previously due to their limited lifetime. Further, computational calculations have helped us elucidate various pathways and structures along the way.

**Application of Structure Elucidation Techniques and Topochemical Principles to Understand Solid-State Photoreactivity.**

Greg Sluggett  
*Pfizer, Groton, CT*

Although it is well established that crystal form can influence solid-state thermal stability, there are relatively few examples which demonstrate a significant impact of crystal form on photoreactivity. This presentation will highlight the extraordinary impact of crystal form on the solid-state photoreactivity of axitinib. Photolysis of three different anhydrous axitinib crystal forms afforded remarkably unique product distributions. In each case, the structures of the major photoproducts were elucidated using state of the art NMR and mass spectroscopic techniques. The product distributions can be explained on the basis of topochemical principles in conjunction with the single crystal X-ray structures of each crystal form.
field’. Have you considered a late stage career change? Not sure where to start? Join industry leaders in an informal discussion of current industry trends, career opportunities, and thoughts on how to successfully make a transition.

5:00 – 6:00 pm
Poster session and reception

6:00 – 9:00 pm
Conference banquet
Featured speaker: Executive Chef Rhys Lewis, “Wine, Wit & Wisdom”

Day 3: Wednesday, August 13

7:30 – 9:00 am
Breakfast (provided)

9:00 – 10:30 am
Session 9 – Orals
Understanding Complex Samples
Advances in instrumentation and technique have made it possible to tackle the analysis of increasingly complex materials, and more powerful computing techniques have made whole sample comparisons tractable. The goal of this session is cross-pollination, where speakers with extremely complex characterization problems show how a shared set of tools has facilitated their analyses, and get you thinking about how those same techniques might work on your problems.

Targeted Petroleomics: Lessons Learned over the Past 15 Years
Ryan P. Rodgers
Future Fuels Institute, National High Magnetic Field Laboratory, Florida State University

High field FT-ICR mass spectrometry has changed the utility and expectations of complex mixture analysis by mass spectrometry over the past decade. The inherent high resolving power and high mass accuracy enables direct determination of elemental compositions to tens of thousands of individual components by mass measurement alone. Modern ionization methods facilitate the selective ionization of components based coarsely on chemical functionality, which combined with FT-ICR MS, reveals acidic, basic, and aromatic contributions to complex mixtures at a molecular level. Here, we expand on previous work in the field to expose chromatographic, non-covalent adduct, and novel ionization methods that further refine the ability to selectively monitor species in complex mixtures at the molecular level. The primary targets of these efforts are high heteroatom-containing species (N₂O₂S₂) that are either naturally occurring, or are produced by biotic / abiotic modification of the source material. Chemical “targets” are isolated by preparative chromatography prior to mass spectral analysis and the efforts facilitate a more in-depth molecular characterization. Applications span the fields of environmental, geochemical, analytical, toxicology, and petroleum science. In one noteworthy environmental example, comparison of the source oil (spilled into the Gulf of Mexico) to samples collected along the Gulf Coast months after the spill, reveal a > 2-fold increase in compositional complexity due to oxidative weathering. The results match bulk elemental analyses that revealed a > 4-fold increase in oxygen in the environmental field samples. Subsequent targeted chromatographic isolation of oxygen-containing species documents the diversity of oxygenated species and catalogues more than 30,000 environmental transformation products of the original spilled oil. Most important, the oxygenated species were previously unidentified, as they lie well outside the analytical window of GC-based techniques commonly employed in environmental analyses. Work supported by NSF OCE-1057417, the BP/The Gulf of Mexico Research Initiative to the Deep-C Consortium, NSF DMR-11-57490, Florida State University Future Fuels Institute, and the State of Florida.

Frontiers in Selective Low Level Detection of Genotoxic Impurities
chemical derivatization in conjunction with mass spectrometry for quantitation of genotoxic impurities
David Liu  
*GlaxoSmithKline, King of Prussia, PA*

Genotoxic impurities in drug substances or drug products have received considerable attention in recent years due to their potentials for being carcinogenic to humans. Genotoxic impurities are usually present at trace levels which can be critical in drug development, and if the risk is not mitigated, could lead to clinical holds or delayed drug approval. Accurate quantitation of these impurities at parts-per-million (ppm) levels requires highly sensitive analytical methodologies and developing such methods is non-routine. As such, hyphenated mass spectrometry techniques play a key role in this field owing to their high selectivity, sensitivity, and speed. Many genotoxic impurities, however, lack ionizable functional moieties and/or are too labile to be analyzed by LC/MS or GC/MS directly. Therefore, combining various chemical derivatization approaches with mass spectrometry widen its horizons in low level detection of genotoxic impurities. This talk will discuss selective case studies highlighting analytical challenges with respect to trace analysis of genotoxic synthetic impurities or genotoxic degradants formed via common degradation pathways.

The chemical nature of hydrocarbon-based biofuels from algae viewed by recent advances in separations, mass spectrometry and informatics

Patrick G. Hatcher  
Batten Endowed Chair of Physical Sciences  
*Old Dominion University, Norfolk, VA*  
*Presentation sponsored by Sierra Analytics*

Biofuels from algae are being considered seriously as renewable alternative fuels for the transportation and energy industry. We have developed a process for producing hydrocarbon-based biodiesel from a hydrothermal liquefaction process and present the application of advanced separation and mass spectrometric tools for characterizing the algae oils produced. The analytical approaches include ultrahigh pressure liquid chromatography, GC x GC / mass spectrometry, Ion Mobility mass spectrometry, and Fourier transform ion cyclotron resonance mass spectrometry. We couple the chromatographic data with advanced informatics approaches to differentiate among samples prepared by different approaches.

10:30 – 11:00 am  
Break

11:00 am – 12:30 pm  
**Session 10 – Orals**

**Real-Time Sampling**

Instrumentation has become small and rugged, and data interpretation fast and reliable enough that analyses that formerly could only be done in the laboratory (or not at all) can now be done at-line, in-line, or in the field. Likewise, laboratory instruments can now sample quickly enough to monitor fast reactions. Our speakers in this session will describe current applications in real-time sampling in several areas of analysis.

**Process Analytical Technology and Online Reaction Monitoring Techniques**

Ruchi Mehta  
*Pfizer, Groton, CT*

Chemical reactions in a reactor require a fast and efficient method to measure the consumption of reactants as well as the formation of products and by-products in order to optimize an industrial process in the shortest time and yet the most efficient way. During early stages of drug development, the most commonly used analytical technique for in-process controls has been conventional off-line chromatography. Assessing reaction completion by HPLC/UPLC on small scale lab reactions is fairly convenient due to the ease of sampling. However, in some cases, the reacting species and/or the product may not be amenable to HPLC/UPLC...
due to instability or heterogeneity of the reaction mixture. Another inconvenience arises when reaction dynamics are unknown and may require more frequent sampling of the reaction mixture in order to assess reaction completion. Furthermore, on a larger scale, sampling may be particularly difficult especially for high temperature or high pressure reactions. On the other hand, online technology such as in-situ Raman and IR Reaction Monitoring provides chemists with direct access to real-time experiment data. This robust analytical solution provides real-time insight into reaction monitoring for various processes and enables process development teams to look into the progress of chemical reactions as they happen. These can be very useful tools in examining chemistry that is difficult to monitor by normal offline methods, or chemistry that involves reactive/unstable intermediates, critical endpoints, high energy reagents or ambiguous reaction completion time.

**The Automated Temperature Controlled Analysis of Antibody-Drug Conjugates and Advanced Logistics & Robotic Liquid Handling Quality Concepts for use in Regulated Bioanalysis**

Joseph A. Tweed  
*Pfizer Groton, CT*

The use of robotic liquid handling platforms have continually demonstrated a measurable increase in speed by which discovery and regulated bioanalysis drug candidates progress through portfolio milestones. However, of critical importance is maintaining a balance between quality and speed as drug candidates reach the GLP and cGLP stages of drug development. At Pfizer, we are building upon our previous successes in automation to enhance the quality of our existing operations and deliver cutting-edge solutions in the emerging area of antibody-drug conjugate (ADC) study specimens bioanalysis. In this presentation, we demonstrate how the use of advanced sample management logistics and barcode tracking (1-D and 2-D) allows for improved chain-of-custody from sample receipt to analysis on the robotic platform. In addition, the use of new technology such as total aspirate and dispense monitoring (TADM) allows for complete tractability of all pipetting steps used within any given bioanalytical assay performed on a robotic liquid handling platform. Lastly, as assay complexity increases, it is imperative to ensure that the scientific, regulatory compliance and business needs of the organization are being meet and where possible, exceeded for any given automation strategy. The implementation of these fundamental concepts are being demonstrated in the temperature controlled, automated bioanalysis of preclinical and clinical antibody-drug conjugate study specimens samples. Antibody-drug conjugate study specimen bioanalysis requires meticulous attention to detail, efficiency and speed (as stability is often a concern) and solid laboratory pipetting skills because the sample preparation and extractions are typically performed manually and on ice(4C). By moving the bioanalysis of the antibody-drug conjugate study specimen samples into an automated temperature controlled workflow, we will demonstrate how overall assay performance is enhanced and provide a rationale for the use of advanced logistics, liquid class optimization and pressure monitoring technology for routine portfolio support.

**Chemical process understanding using RxnNMR**

David Anthony Foley  
*Pfizer, CT*

*Presentation sponsored by CoSMoS*

The use of online NMR technology in the development of organic reaction processes provides information rich data which can be used to gain a deeper understanding of the process under investigation. This technique has been employed in process
development at Pfizer for a number of years, predominantly at the development stage of pharmaceutical research. Much of this work has been conducted at high field (400 MHz). The development of an NMR reaction monitoring platform will be discussed, including a novel flow cell designed for increased flexibility of use, compared to fixed flow cells. The implementation of this technology will also be demonstrated; citing specific examples of reactions developed and optimized employing online NMR

12:30 pm – 1:30 pm
Lunch (provided)

1:30 – 3:00 pm
Session 11 – Orals

New Horizons and Trends in Analytical Chemistry Techniques
Technology is constantly evolving, providing analytical scientists with a toolbox of unique techniques and innovative approaches for solving complex problems. In this session, CoSMoS offers a series of presentations that highlight new technology and applications that are currently on the horizon and stand to make an impact in modern analytical chemistry.

Analysis of leachables in silicone caps using 2D LC/MS/MS
Claude R. Mallet
Waters Corporation, Milford, MA

The final extract of a sample preparation protocol is usually transferred into a 96-well plate or a 2 mL glass vial. Those containers are then sealed with a flexible material to allow easy puncture and re-sealability. In 2000, LC/MS rapidly became the pre-dominant choice for analytical work, thus displacing the decade long tested LC/UV solution. As early as 2005, reports of ghost peaks with newer generation of mass spectrometers started to show up at level never seen before. These observations lead to noticeable variations during quantification. Those variations were attributed to “extractables” and “leachables”, or E&L, referring to compounds that can be extracted under extreme conditions and to compounds that can migrate or leach by direct contact under normal conditions. With single chromatography dimension, the final solvent composition is crucial to ensure proper sample focusing during the injection process. Therefore, to achieve acceptable quantification performance at trace level, the extraction protocol usually includes a large sample enrichment process. Since current LC/MS and GC/MS are still limited to small injection volumes for analysis, extraction protocol must include a sample volume reduction and a solvent conversion step.

I Feel the Need. The Need for Speed: Integrated Solid Phase Extraction/Autosampler for Support of ADME Assays in Drug Discovery
Panos Hatsis
Novartis Institute for Biomedical Research, Cambridge, MA

A significant amount of effort in drug discovery is devoted to the optimization of a drug’s Absorption, Distribution, Metabolism and Excretion (ADME) parameters, since these parameters drive exposure and disposition. ADME assays can be readily performed in multi-well format, and automated using sample preparation robotics. Consequently, the timeliness of results delivery is predominantly dictated by the analysis of samples, and for this reason breakthroughs in analysis technology are always desirable. This presentation will describe the authors’ experience with an integrated solid phase extraction/autosampler platform, i.e., RapidFire™ coupled to a mass spectrometer, for the analysis of samples from in-vitro ADME assays, e.g. solubility, permeability (PAMPA) and protein binding. Samples from each assay were split and run using the conventional method and RapidFire™.

The results from each assay were compared using correlation plots, and showed good agreement. These assays have been historically run using liquid chromatography/mass spectrometry or liquid chromatography/ultraviolet detection (LC/UV) with a sample-to-sample cycle time of approximately 1 – 2 minutes. The RapidFire™, however has a cycle time of approximately 10
seconds, which represents an improvement of over 80%. The reduction in analysis time was not at the expense of robustness or data quality. The impact of data analysis on the overall turnaround time was also considered since it can become a significant part of the workflow with high-throughput analyses. The importance of commercially available software packages, as well as in-house programs, on the overall data turnaround time will be discussed.

Recent Advances in Column Technology: Active Flow Technology

R.A. Shalliker
Australian Centre for Research on Separation Science, School of Science and Health, University of Western Sydney, Parramatta, NSW

The wall effect is a serious cause of the loss of performance in chromatographic separations, so too is frictional heating in high speed/pressure applications involving columns packed with small particles. Band profiles inside chromatography columns are therefore not narrow cylindrical disks, rather, band profiles more likely resemble partially filled bowls. These bowls may be flat on the leading edge, but hollow in the tailing section with solute dispersed in the wall region. To overcome wall effects and frictional heating a new type of HPLC column has recently been designed. These columns are referred to as Active Flow Technology (AFT) columns. These columns isolate the wall region of mobile phase flow from the radial central region of flow, consequently, presenting to the detection source a more chromatographically efficient solute band. Far fewer plates are required to separate just the leading surfaces of bowl shaped elution profiles than the entire bowl complete with trailing wall region. An added advantage of AFT columns is that the volume of the solute band is reduced, and in fact can be tuned to suit the requirements of the detection source. This makes this type of column ideal for applications involving LC-MS, since the volume load to the MS is reduced, and the solute concentration is higher. Mobile phase flow rates through AFT columns can easily reach 5 mL/min even when MS detection is employed, reducing analysis times to seconds.

3:00 pm
Closing remarks / Conference adjourns

- Founding Sponsors
  - Agilent Technologies
  - Thermo Scientific
  - ACS
  - Waters
  - Shimadzu

- Highlights and Announcements
  CoSMoS 2015 abstract submissions are now being accepted.
  Oral abstract deadline - March 30
  Poster abstract deadline - June 30
Compete with colleagues for the Gold medal

CoSMoS 2015 Flyer: Click Here

CoSMoS 2015 Preliminary Agenda Download

• Tuesday evening’s guest speaker

"Stories from Research with African species" Based on his passion for conservation research with rare and endangered species Dr. Matt Anderson, Director of Behavioral Ecology at the San Diego Zoo Institute for Conservation Research brings us insights to such topics as the secret language of elephants and the intriguing story of the African cheetah.

Dr Matt Anderson is the Director of Behavioral Biology at the San Diego Zoo Institute for Conservation Research. In this position he oversees, and is actively involved in, projects which utilize the study of animal behavior for the conservation of species in our collection and in the wild. This innovative approach is multifaceted and includes the study of animal communication (with emphasis upon bioacoustics), the monitoring of sex steroid and stress hormone levels in relation to many aspects of behavior and the assessment of animal welfare in the collection. Prior to arriving in San Diego, Matt received an undergraduate degree in Zoology (with honors) from the University of Liverpool, UK and subsequently studied behavior, reproduction, bioacoustics and anatomy in nocturnal primates for his PhD (biological anthropology). During his PhD he studied and also lectured at Oxford Brookes University, Oxford University, the Zoological Society of London and the University of Cambridge.

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