Speaker Biographies

(Listed alphabetically by last name)
September 22-23, 2020

Meg Brunell, M.S.
Senior Scientist
Merck

Meg Brunell obtained her M.S. degree in Chemistry from Villanova University in Radnor Township, PA. She specialized in fundamental studies of metal complexes with ligands in different protonation states, including the use of experimental techniques, electrochemistry and UV/Visible spectroscopy. Prior to her M.S. work, Margaret obtained her B.S. degree in Chemistry from Saint Joseph's University in Philadelphia, PA. In 2015, she started her career as a pharmaceutical scientist at Merck located in Rahway, NJ. As a member of Analytical Sciences within Merck Research Laboratories, she has focused on chemical and physical stability testing of drug products during early development of final market formulations. Specifically, she has been involved in the development of a number of sterile parenteral programs, including highly potent compounds.

Presentation: Day 2 - Osmolarity Measurements in Highly Potent Drug Products

ABSTRACT: As the pharmaceutical landscape evolves, research and development of new drug products has become focused on more specialized medicines, including large molecules/biologics, co-formulation or co-administration formulations, unique routes of administration, specialized devices, and potent compounds. An increasing number of new chemical entities in development are deemed potent, posing certain safety and handling risks for scientists working with these compounds in the lab. Some of the risk factors of working with potent compounds include, method of handling, physical form of material, quantity handled, and exposure duration/frequency. The impact of potent compound handling to analytical testing involves longer handling times, reduced flexibility, additional personal protective equipment/engineering controls, and additional waste streams. The use of automated systems for analytical testing of potent compounds provides a solution to the difficulties associated with potent compound handling by improving accuracy and precision, increasing efficiency, and minimizing analyst exposure. Automation equipment for analytical testing includes the Tablet Processing Workstation (TPW) for liquid and solid sample preparation, automated pH meters, and automated osmometers. Specifically, the OsmoTech osmometer from Advanced Instruments requires only a small sample size of ~20 µL. In addition, the A2O Advanced Automated Osmometer from Advanced Instruments offers fully automated multi-sample capability with a completely contained system. These automated systems not only improve efficiency, but also significantly decrease sample size, which becomes important due to high manufacturing costs for potent compound products due to complex processes and safety requirements.

Wen-Li Chung, M.S.
QC Scientist/Validation Manager
Genentech

Wen-Li Chung is currently a QC scientist and Global Technical Expert for Compendial/Generic Methods in Genentech/Roche. She received her B.S. in Zoology from National Taiwan University and a Master's Degree in Biochemistry from Auburn University. An expert on of pharmaceutical products, Wen-Li has extensive experience on Formulation, Analytical Method Development, Validation, Protein Characterization, and Quality Control. She worked at a number of biopharmaceutical companies including Biogen, Pfizer, Millennium, and Abbvie before joining Genentech in 2013. Wen-Li has 5 issued patents and is one of the inventors for liquid formulation Avonex.

Presentation: Day 1 - Vapor Pressure Osmometers: Comparison Between Models, Calibration Challenges, Quantitation Limits and Robustness

ABSTRACT: Osmolality is a required general test for releasing protein drug substance and product. However, vapor pressure depression osmolality method is seldom used due to lack of Pharmacopeia requirements. As a result, companies routinely leverage the freezing point depression method acceptance criteria in order to claim method compliance with the compendial guidance. In this presentation, three vapor pressure depression osmometers were compared for osmolality measurement, followed by review of limitations of the instrument, calibration challenges and quantitation limits. In addition, considerations for setting up specifications and validation characteristics will also be discussed.

Presentation: Day 1 - Impact of Test Volume/Osmometer Models on Accuracy and Robustness for the Analysis of Biotherapeutics – Method Selection and Suitability Verification (with Ann Woys)

ABSTRACT: Osmolality is a required general test for releasing protein drug substance and product. Common methods used for osmolality determination include freezing point determination and vapor pressure detection. Three freezing depression osmometers with differing samples volumes and freezing initiation mechanisms were evaluated: (Advanced Instrument (AI) 3250 (250 µL), AI 3320 (20 µL), and Gonotech Osmomat 3000 (50 µL)). One vapor pressure depression osmometer (Wescor 5600) was included for comparison. All osmometers were tested with varying concentrations of eight antibody formulations to check the dependence of determine the impact of protein concentration and viscosity on results. Eight protein samples were tested at both high concentration (≥100 mg/mL) and lower concentration (50 mg/mL). At the lower protein concentration, results are in general comparable among the three freezing depression osmometers tested and are within ±10% of the theoretical value, but the vapor pressure osmometer is significantly more accurate. At high concentrations, results generated by the AI 3250 and Wescor 5600 are all within ±10% of the theoretical value, but those generated by the AI 3320 and Osmomat 3000, are all consistently higher than the theoretical values and 4 out of 8 are greater than 10% from the theoretical values. There is no apparent correlation between osmolality readout accuracy and either viscosity or protein concentration of the samples with all the osmometers tested. These results indicate that is critical to evaluate the comparability in osmometer models between labs before method transfer. Precision and robustness (i.e. consistency in freezing) should be considered for selection of the osmometer for testing as well as prior to setting up specifications for protein analysis.

Noemi Dorival-Garcia, Ph.D.
Research Fellow
National Institute for Bioprocessing Research and Training, Ireland

Noemí holds a Ph.D. in Analytical Chemistry from the University of Granada, Spain, which was focused on the development of analytical methods for the determination of pharmaceuticals, endocrine disruptors and emerging contaminants in environmental and biological matrices. She joined the Characterisation and Comparability Lab at NIBRT in 2015 on a project entitled “Facility of the future: the plastic factory, enabling single use technologies”, focusing on the characterisation of E&L compounds from single-use technology solutions, using different mass spectrometry-based analytical techniques, and modern sample preparation approaches. In the same line of investigation, she is currently leading the technical part of another Project in collaboration of Janssen Sciences Ireland about “Determining the Reduction Capacity of Ultrafiltration/Diafiltration for Removing Leachables from Process Streams”, which is about the evaluation of UF/DF as a widely used downstream process unit operation for the potential removal of leachables from the process stream, elucidating the risk that these substances might pose to patients if they persist during the process and accumulate in the final drug product.
She was also part of a project entitled “Continuous Quality – Multi-Attribute Continuous Product Characterisation for Increased Process Control”, in collaborative partnership with Pfizer, to develop an on-line real time multi-attribute CQA assessment platform using high resolution LC-MS for monoclonal antibodies and Fc fusion proteins for increased process understanding, optimisation, intensification and control.

Presentation: Day 2 – Osmolality as Important Component of a Multi-Attribute Continuous Product Characterisation Platform for Increased Process Control Monitoring

ABSTRACT: Biopharmaceuticals are complex molecules produced by mammalian cells through recombinant DNA technology. During manufacturing and storage, therapeutic proteins are subject to various post-translational modifications (PTMs), which may affect bioactivity or stability and are classified as critical quality attributes (CQAs). The cell culture process control is crucial, as levels of PTMs can be induced or modified during production. It is often difficult to characterise samples taken from the bioreactor due to low product levels during early stages and presence of interfering components. Furthermore, process parameters monitoring and multiple analytical results are needed, meaning that data may not available for several days, thereby slowing process development and preventing “real-time” adjustment to the manufacturing process.
Here, we describe the development of an automated solution for purification, titre determination and sequential evaluation of CQAs (aggregation, charge variants, sequence confirmation and PTMs using middle down analyses) for monoclonal antibodies; also including simultaneous monitoring of the critical process parameters, nutrients, metabolites and osmolality. Samples from a bioreactor were automatically sampled using a MAST□ system and transferred to a cell removal system. Using a Gilson□ liquid handler, cell-free samples were injected into an UltiMate□-3000 UHPLC adapted to work with 5 columns and coupled to UV and Orbitrap™ MS detectors. The autosampler of the UHPLC was configured to perform the injection, fraction collection, and reinjection of fractions using a rapid multiattribute LC−MS analysis, as well as performing required sample preparation steps, as antibody neutralisation after the purification/preconcentration stage to isolate antibody product from the free-cell culture media samples; and also the antibody reduction for the subunit mass analysis. MAST□ controller was responsible for all process automation and Chromeleon□ managed the full automatic analytical cascade and generation of reports, including LC-MS data.
The system demonstrated correlations between process parameters and CQAs including aggregation, charge variant proportions and certain glycans levels. Osmolality that was determined off-line proved to be an excellent parameter to measure cell culture health status and also antibody productivity and quality. The full described platform is versatile to be used to monitor other attributes and applied across the biopharmaceutical industry for the analysis of biosimilars and fusion proteins. Its simplicity of use

overcomes the inherent complexity of mass spectrometry methods and complicated data analysis software offering a feasible alternative for implementation in the regulated environment.

Ashish Garg, Ph.D.
Senior Consultant Engineer
Eli Lilly and Company

Ashish Garg is currently Sr. Consultant Engineer, at Eli Lilly and Company. He earned his Bachelors & Masters of Technology from Indian Institute of Technology, Bombay, in 2003, and his PhD in from the University of Minnesota in 2009, working with Prof. Efrosini Kokkoli. During his Ph.D. he focused on development of novel synthetic peptide and aptamer amphiphiles for drug delivery using stealth liposomes, to specifically target the molecule of interest on cell surfaces and deliver a payload intracellularly. After completing his PhD, Ashish accepted a position as a Senior Scientist at TEVA Pharmaceuticals where he worked for 6 years. During that time, he focused on development of complex injectable formulations based on liposomes and polymeric microspheres. He joined Eli Lilly and Company in 2016 and since than he is focusses on development and commercialization of peptides, insulin and siRNA based parenteral formulations. Ashish has a strong physical chemistry background in pre-formulation and formulation development. As an engineering by training he is skilled in scaleup of sterile products and design/build out of a pilot/commercial scale manufacturing plant for aseptic processing. Ashish has over 10+ years of experience in developing control strategy, justifying drug product specifications and writing CMC sections for regulatory submissions.

Presentation: Day 1 - Considerations for Formulation Development to Improve Patient Experience

ABSTRACT: Osmolality is a critical quality parameter for pharmaceutical dosage forms. For parenteral administration, formulations are typically designed to stabilize the active ingredient and make the composition isotonic. It is believed that formulations with the above characteristics will be safe, acceptable and well tolerated by patients. However, patient experience depends on variety of factors. This presentation will elaborate on patient centric design of formulations for parenteral administration and on developing a Control Strategy for Osmolality as a critical quality attribute (CQA).

Michael Lally
Application & Validation Specialist
Lighthouse Instruments

Michael is responsible for methods development, methods validation and methods transfer of laser headspace analysis technology for pharmaceutical applications. He is a Chemical Engineer with 40 years of experience working in cGLP/cGMP environment. Applications include container closure integrity testing of parental products, process monitoring for oxygen sensitive formulations, water activity of oral solid dosage forms, and moisture in lyophilized products.

Presentation: Day 2 – Osmolality and the new USP <922> Water Activity General Chapter

ABSTRACT: The USP published a new General Chapter USP<922> Water Activity in the Pharmacopeia Forum (PF) that includes a description of the relationship between water activity and osmolality. This presentation will explain how water activity compliments osmolality while providing unique information that is different than molarity, osmolality, and total water content. We will review how water activity impacts critical quality attributes of oral solid dosage products with examples from formulation development, packaging development, long term stability and microbiology.

Chetan Pujara, Ph.D.
Vice President, Pharmaceutical Sciences
Abbvie

Chetan Pujara is Vice President, Pharmaceutical Sciences at Abbvie, Irvine, CA. His organization designs and develops dosage forms and drug-device combination products intended for clinical trials and commercialization primarily for EyeCare, Aesthetics and Neuroscience therapeutic areas.
Prior to Allergan's acquisition by Abbvie, he was Vice President in Global R&D at Allergan plc, Irvine, CA in a similar role. His organization was responsible for formulation & manufacturing process development, analytical & microbiology development, packaging development, clinical supplies manufacture and GMP lab systems & operations departments. He also represented CMC functions on Allergan's eye care and medical aesthetics governance boards that were accountable for creating therapeutic area strategy and delivering on late-stage project pipeline.
Chetan started his career at Abbott Laboratories, IL, where over 10 years he held various positions in Global Pharmaceutical R&D gaining experience in development of solid oral dosage forms and pediatric oral suspensions.
Chetan contributes to the pharmaceutical sciences community by volunteering for several non-profit organizations. He is a member of the USP Dosage Forms Expert Committee and USP <771> Ophthalmic Preparation Expert Panel. He is an Adjunct Professor in the Department of Industrial and Physical Pharmacy, Purdue University, IN and a Scientific Advisor to the Editors of J. Pharm Sci. He also serves on the Industrial Advisory Board of Dane O. Kildsig Center for Pharmaceutical Processing Research and on the Board of Directors of IQ Consortium for Pharmaceutical Development.
Chetan received his PhD in Pharmaceutics from Purdue University, West Lafayette, IN and B.S. degree in Pharmacy from BITS, Pilani, India.

Presentation: Day 2 – Osmolarity & Tonicity – Considerations for Topical Ophthalmic Products
ABSTRACT: Topical ophthalmic dosage forms are sterile products mainly intended to deliver medicines to local ocular tissues in the anterior segment of the eye. Due to the specialized anatomy and physiology of the eye, in general, topical ophthalmic formulations have a relatively short time frame to deliver drug to the tissues. Therefore, quality attributes such as pH, Viscosity, Osmolarity & others can have a meaningful impact on the intended performance of the product. This presentation will cover basic anatomy & physiology of the eye, ophthalmic dosage form design and impact of formulation osmolarity/tonicity on performance of topical ophthalmic dosage forms.

Dieter Roethlisberger, Ph.D.
Head DP Technical Project Leaders
Lonza AG, Switzerland

Dr. Dieter Röthlisberger studied Pharmacy at the University of Lausanne, Switzerland and graduated in 1981. After a 2 years job abroad for the Swiss red Cross he joined the research group of Prof. Bernard Testa Institute of Medicinal Chemistry at the University of Lausanne, where he got his PhD degree in 1987. He spent 30 years at Hoffman-La Roche, Basel, in different positions in formulation development, clinical manufacturing of biopharmaceuticals, outsourcing management and development of parenteral dosage forms for pharmacokinetic and mass balance studies. Since June 2018 Dr. Dieter Röthlisberger holds the position of Head of Technical Project Leadership at Lonza AG, Drug Product Services in Basel, Switzerland.

Presentation: Day 2 – Osmolality – Considerations for Parenteral Biotech Drug Products

ABSTRACT: The presentation has been divided in three parts. The first will focus on clinical aspects, show the complexity and efficacy of the main physiological osmolality control mechanisms. The difference in sensitivity of osmo- and baroreceptors will be explained and the clinical use of osmolal gap and hydration status discussed. Some special cases of injection solutions will illustrate the difference between isotonicity and isoosmolality.
A second part is dedicated to the estimation of potential damage at the injection site and the systemic risk of any major osmolality deviation. It will be completed by a list of hypertonic marketed drug products, which will allow the audience to retrieve concrete examples in the Dailymed database about how those drug products are administered and dosed in practice.
Finally some specific insight in the field of the biotech drug products will be given by showing the potential impact of isotonizing agents on formulation stability.

Erinc Sahin, Ph.D.
Principal Scientist, Drug Product Science & Technology
Bristol-Myers Squibb

Dr. Sahin received his B.Sc. in Molecular Biology and Genetics in METU (Turkey), M.Sc. in a joint program between Bioengineering and Materials Science & Engineering departments in Sabanci University (Turkey); and his Ph.D. in a joint program between Biochemistry and Materials Science & Engineering departments in University of Delaware (USA). Prior to joining BMS in 2011, Dr. Sahin worked on aggregation of therapeutically relevant proteins as a post-doctoral fellow in Roberts group in Department of Chemical and Biomolecular Engineering in University of Delaware.

Since joining BMS in 2011, Dr Sahin has taken roles with increasing complexities and responsibilities in a group that develops formulations, manufacturing processes, and patient-centric product presentations for injectable drug products, from their discovery to commercialization.

Presentation: Day 1 – Freezing Point Based versus Vapor Pressure Based Osmometers on High Concentration Protein Formulations: Instrument Selection Matters
ABSTRACT: Osmolality is a critical attribute for injectable formulations, as well as a valuable in-process test that informs overall solute content of a formulation. Therefore, osmolality is typically part of the specifications for parenteral products. Being so, accuracy and precision of osmolality measurements have strong implications on demonstrating success in manufacturing.
At high protein (polymer) concentrations, osmometers are shown to deviate from calculated osmolality values to varying degrees depending on their working principles. These deviations have critical impact on analytical strategy and execution as well as specification setting, particularly within the context of technology transfer and involvement of multiple testing sites.

Marc Stranz, Pharm.D.
Chief Clinical Officer
BioMatrix SpRx

Marc Stranz, PharmD, is Chief Clinical Officer for BioMatrix Specialty Pharmacy. Dr Stranz has a long history in drug compounding, infusion therapy, and specialty infusion. He summarized the current knowledge of drug-induced vascular tissue damage in a 2002 article and has continued to update that work with new research. He speaks frequently on the correlation of drug pH, osmolarity, and cytotoxicity with phlebitis and extravasation injury, as well as interventions to prevent injury.

Presentation: Day 1 – The Application of Osmolality to Drug Administration
ABSTRACT: Drug-induced damage to the vascular glycocalyx and epithelial cells is a well known clinical problem. Guidelines for drug formulation lack foundation, as animal data is limited and human research inconsistent. This presentation is a topical summary of the myriad factors that influence drug-induced vascular damage and the data available on controlling injury.

Bingchuan Wei, Ph.D.
Genentech Research Early Development Scientist
Genentech

Bingchuan works as a scientist in Genentech research and early development (gRED). He has extensive experience in analytical development of biological products and small molecule drugs. His current research interest is in chromatography, spectroscopy and real time release use, as well as using data modelling tools to link the biological product quality with process, protein structure and function. He earned his B.S. in chemistry and mathematics from Peking University and Ph.D. in analytical chemistry from Purdue University.

Presentation: Day 2 – Multi-attribute Raman Spectroscopy (MARS) as a New Technology for Osmolality Measurement
ABSTRACT: Rapid release of biopharmaceutical products has raised a lot of attention towards more efficient drug manufacturing. Simultaneously targeting several critical quality attributes(CQAs) with one method is an essential pillar of a rapid release strategy. In this study, combining Raman spectroscopy, Design of Experiment (DoE) and multivariate data analysis (MVDA), we develop a novel, rapid and non-destructive multi-attribute Raman spectroscopy (MARS) method to measure multiple CQAs of the formulated protein therapeutics. Our assessment shows that MARS is capable of measuring formulation related CQAs including protein concentration, osmolality, pH, concentration of formulation additives (PS20, methionine and N-acetyl tryptophan etc.) and protein purity related CQAs such as size and oxidation variants for the formulated protein therapeutics. Remarkably, osmolality and other CQAs like protein concentration could be determined using a multiproduct generic model. The variable importance in projection (VIP) analysis successfully correlates each MVDA model with the chemical basis of the targeted CQA for model interpretation. MARS is potentially a powerful tool to improve the efficiency and reduce the turnaround time of biopharmaceutical development and manufacture by replacing multiple existing QC assays with one rapid spectra scan without sample processing.

Ann Woys, Ph.D.
Pharmaceutical Development Scientist
Genentech

Ann Woys is currently a Pharmaceutical Development scientist and leader of the Compendial Methods Analytical Expert Team at Genentech – Roche. Ann received her Ph.D. in physical chemistry at the University of Wisconsin – Madison while developing a new spectroscopy for membrane and aggregating protein structures. She expanded her spectroscopy tool kit as a postdoctoral researcher at Northwestern University, before joining PIKE Technologies as a leader in the engineering department, where her teams developed new spectroscopy and microscopy products. At Genentech, Ann has led Stage A to D formulation development, supported the compendial methods, and wrote a Donnan Effect modeling program for non-ideal mixed buffers systems.

Presentation: Day 1 - Impact of Test Volume/Osmometer Models on Accuracy and Robustness for the Analysis of Biotherapeutics – Method Selection and Suitability Verification (with Wen-Li Chung)

ABSTRACT: Osmolality is a required general test for releasing protein drug substance and product. Common methods used for osmolality determination include freezing point determination and vapor pressure detection. Three freezing depression osmometers with differing samples volumes and freezing initiation mechanisms were evaluated: (Advanced Instrument (AI) 3250 (250 µL), AI 3320 (20 µL), and Gonotech Osmomat 3000 (50 µL)). One vapor pressure depression osmometer (Wescor 5600) was included for comparison. All osmometers were tested with varying concentrations of eight antibody formulations to check the dependence of determine the impact of protein concentration and viscosity on results. Eight protein samples were tested at both high concentration (≥100 mg/mL) and lower concentration (50 mg/mL). At the lower protein concentration, results are in general comparable among the three freezing depression osmometers tested and are within ±10% of the theoretical value, but the vapor pressure osmometer is significantly more accurate. At high concentrations, results generated by the AI 3250 and Wescor 5600 are all within ±10% of the theoretical value, but those generated by the AI 3320 and Osmomat 3000, are all consistently higher than the theoretical values and 4 out of 8 are greater than 10% from the theoretical values. There is no apparent correlation between osmolality readout accuracy and either viscosity or protein concentration of the samples with all the osmometers tested. These results indicate that is critical to evaluate the comparability in osmometer models between labs before method transfer. Precision and robustness (i.e. consistency in freezing) should be considered for selection of the osmometer for testing as well as prior to setting up specifications for protein analysis.

Kristeena Wright, Ph.D.
Application Scientist
Advanced Instruments, LLC

Kristeena Wright has been an Application Scientist at Advanced Instruments since 2018. She has a background in drug manufacturing support and is a motivated biomedical researcher and spokesperson for scientific advancements, as shown by multiple presentations and collaborations with other subject matter experts. Kristeena holds a Ph.D. in Biomedical Sciences from Marshall University and a B.S. in Biomedical Engineering from Duke University.

Presentation: Day 1 - Osmolality, Osmolarity and Tonicity – Understanding the Measurements

ABSTRACT: Determination of solution concentration is an integral part of drug manufacturing and process development practices. Osmolality, osmolarity and tonicity all describe similar properties of these bioprocessing solutions but are not interchangeable. Here we explore differences in these terms and how they are best measured and/or used.