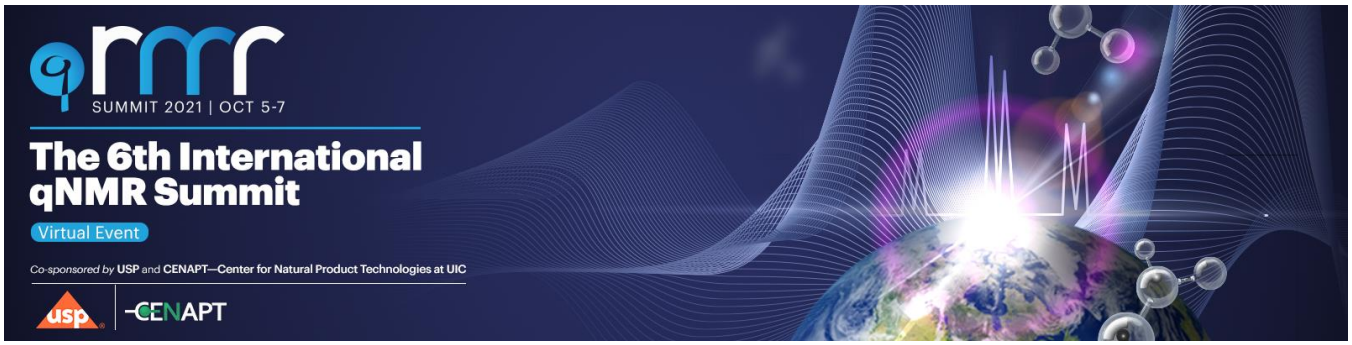


Speaker Biographies

(Listed alphabetically by last name)
October 5-7, 2021

Prabhakar Achanta, Ph.D.
Postdoctoral Research Associate
College of Pharmacy, University of Illinois at Chicago, USA

Dr. Prabhakar Achanta is a postdoctoral research associate at Prof. Guido Pauli's lab, College of Pharmacy, University of Illinois at Chicago. He has been associated with the group since October 2018. Prior to this role, he worked for about 15 months at a Contract Research Organization in Hyderabad, India in NMR division for structure confirmation and elucidation of synthesized small molecule.

Dr. Achanta did his PhD in Medicinal and Natural Products Chemistry at Kakatiya University, College of Pharmaceutical Sciences, India, during which he isolated few new malabaricanes, a rare class of tricyclic triterpenes.

Dr. Achanta's interests are in Natural Products Drug Discovery and determining purity in pharmaceuticals by NMR. At UIC, he is involved in establishing HiFSA profiles of small molecule therapeutics by deep understanding of their 1H NMR spectra through Full Spin Analysis. He also works towards identifying dentin bio-modifiers from Vitis sps.

Presentation: Day 3 - Plain 1H NMR Analysis Streamlines the Quality Control of WHO Essential Medicines

ABSTRACT: Amongst the many pharmaceuticals used worldwide, a group of ~400 is listed as Essential Medicines (EMs) by WHO for maintaining basic human health. Although quality control of every medicine is important, given the significance of EMs it is of priority. In this study, Favipiravir, a drug to treat mild COVID-19 and two EMs (Pyrazinamide and Nicotinamide) were chosen given their structural similarity, to investigate the differences in their 1H NMR spectra in high and low field spectrometers. Further, through the Quantum Mechanics (QM) supported 1H NMR iterative Full Spin Analysis (HiFSA) accurate chemical shifts (□), coupling constants (J), line widths (□½), line shape and signal intensities were determined by which NMR spectra can be calculated. The process of HiFSA, thus, enables scaling of the NMR spectra acquired on the high-field spectrometer to any benchtop spectrometer level. Quantitative aspects of these pharmaceuticals, in both high-field and low-field NMR spectra, were studied by External Calibration (EC) qNMR and via the population of spin particles as obtained from HiFSA. The present study underscores the applicability of benchtop NMR spectrometers in quality control of EMs and pharmaceuticals in general.

Ad Bax, Ph.D.
Chief of the Section on Biophysical NMR Spectroscopy
National Institutes of Health

Presentation: Day 1 - George Hanna Award: Concept, Intentions, Parameters

Lucy Botros, M.Sc.
Senior Scientist II, General Chapters
USP

As a Senior Scientist II with the General Chapters group of The United States Pharmacopeial Convention, Ms. Botros is responsible for supporting USP Expert Committees and associated Expert Panels in the development and revision of USP-NF general chapters related to chemical and physical analysis of pharmaceutical drug substances and drug products, including the suite of <85X>/<185X> spectroscopy, NMR spectroscopy and Mass spectrometry general chapters. She is also responsible for the development of new standards in Continuous Manufacturing and Process Analytical Technology.

Ms. Botros holds an M.Sc. and B.Sc. in Chemistry from McGill University, Montreal, Canada.

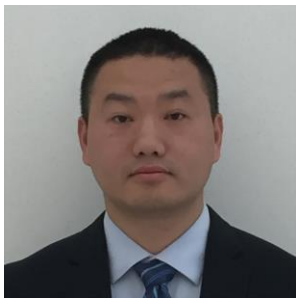
Presentation: Day 1 - Newly updated USP General Chapters <761> and <1761>
ABSTRACT: USP general chapters *Nuclear Magnetic Resonance Spectroscopy* ⟨761⟩ and *Applications of Nuclear Magnetic Resonance Spectroscopy* ⟨1761⟩ are currently being revised by the quantitative nuclear magnetic resonance (qNMR) Expert Panel. Since the last revision in 2013, there has been a surge in the utilization of NMR as a quantitative tool to determine purity of organic compounds and the composition of mixtures, and there is an urgent need to provide current guidance on the use of qNMR for applications within scope of the USP. This talk will review the current status of the general chapter revisions, and the proposals to align with soon-to-official USP general chapter *Analytical Procedure Life Cycle* ⟨1220⟩. An overview of the proposed revision will also include a discussion on NMR spectrometer qualification procedures and requirements, and standardized qNMR methods using certified reference materials (CRMs).

Anton Bzhelyansky, M.A.
Principal Scientist, Science-Dietary Supplements & Herbal Medicines
USP

Anton Bzhelyansky received a master's degree in Analytical Chemistry from the University of Maryland Baltimore County and, prior to joining the United States Pharmacopeial Convention (USP), has worked as a method developer in pharmaceutical and dietary supplement industries for thirteen years. At USP, his focus is on the botanical dietary ingredients and dietary supplements monographs, multifaceted issues of adulteration and incorporation of advanced methodologies into compendial practices and documentation. In 2013-2016, he has led the work of the USP Expert Panel on Screening for Undeclared Drugs and Drug Analogues, which culminated in the issuance of the namesake General Chapter <2251>. For the next four years, he worked to establish the USP Roman Database, an integrated resource cataloguing data on adulterants and adulterated products marketed as dietary supplements. Since 2016, in partnership with UIC-CENAPT, Anton has been

involved in instituting the qNMR Summit; he is engaged in several qNMR-related initiatives internationally and advocates broad adoption of this methodology as an important pharmacopoeial tool. Mr. Bzhelyansky is the leading scientist in preparation and issuance of the annual USP Dietary Supplements Compendium, and leads the work of the USP Modern Analytical Methods Joint Subcommittee. Anton championed the establishment of the George Hanna qNMR Award, with the inaugural award to be given at the qNMR Summit 6.0 (2021).

Moderator of Day 2, Session II: Inaugural George Hanna qNMR Award Ceremony



Kang Chen, Ph.D.
Research Chemist
U.S. Food & Drug Administration (FDA-CDER), USA

Kang Chen graduated with PhD in chemistry from New York University. He had been at NIH as a postdoc and staff scientist, developing NMR methods to study protein structure and dynamics. In 2014 he moved to the US Food and Drug Administration's Center for Drug evaluation and Research (CDER) where he develops NMR methods to research the quality of complex drug products.

Presentation: Day 2 - High Resolution 19F qNMR Reveals Mass-balanced Drug Phase Distribution in Oil-in-Water Nano-Emulsion Formulations
ABSTRACT: An oil-in-water (o/w) nano-emulsion (NE) is composed of oil globules stabilized by surfactant and dispersed in an aqueous phase. Nano-emulsions are used to formulate hydrophobic active pharmaceutical ingredient (API) and typically allow higher dosage strengths and better content uniformity. One knowledge gap for NE drug products is the lack of information about API phase distribution in the oil (o), surfactant (s) and water (w) phases, challenging to measure non-invasively in emulsions, especially for an API in (s) phase, the interface between the dispersed phase (o) and the continuous phase (w). Here, high resolution 19F quantitative NMR (qNMR) spectroscopy was applied directly on a NE drug product (DP) with difluprednate (DFPN) as the API. Specifically, the resolved chemical shifts of the F28 nucleus in DFPN depended on the type of shielding molecules in each phase. The integration of F28 peaks robustly yielded mass-balanced quantitative distribution of 1.8%, 35% and 59% per label claim (LC), for (w), (s) and (o) phases, respectively. Furthermore, the dilution dependent F28 peak line-broadening was characteristic of dynamic exchange between NE and micro-emulsion (ME) globules, suggesting that API availability could be quickly achieved using an o/w NE formulation.

Anna Codina, Ph.D.
Director Pharmaceutical Business Unit
Bruker BioSpin

Anna has a degree in Chemistry and a PhD in Protein NMR from the University of Barcelona, Spain. She undertook her post-doc in protein NMR at the MRC Laboratory of Molecular Biology in Cambridge, UK, and following that worked in the Analytical R&D department of Pfizer for eight years, becoming proficient in low level impurity structure elucidation, reaction monitoring, qNMR and the preparation of regulatory documentation. She joined Bruker in 2011 as Material Characterisation Laboratory Manager and she is now the Director of the Pharmaceutical Business Unit at Bruker BioSpin.

Presentation: Day 3 - Development of a Quantitative Performance Qualification Standard
ABSTRACT: Adherence to compliance with GxP is mandatory for everybody working in regulated environments such as those in the development or manufacturing space of the pharmaceutical industry including CROs, CMOs and other service providers. Important requirements are data integrity and instrument qualification. Qualification typically includes Installation Qualification (IQ), Operational Qualification (OQ) and Performance Qualification (PQ). Additionally, a Computer System validation document must also be successfully completed.

We describe the development of a certified reference material (CRM) for PQ tailored to qNMR. A novel, two-component mixture that is manufactured under ISO/IEC 17025 and ISO 17034 accredited workflows is the basis of the new qPQ test. This qPQ test is now incorporated within NMR automation software, allowing automated qPQ. Superior level of compliance is achieved with a soft¬ware suite directly analogous to the accepted standard for GxP operations, offering secure access to the instrument and the option to manage one or more instruments in a network, under GxP.

Bernd Diehl
Professor
Spectral Service (Germany)

Presentation: Day 1 - Quantitative Analysis of Heparin in Heparinoid Unfractionated Raw Materials
ABSTRACT: Forthcoming

Bruno Garrido, Ph.D.
Researcher
National Institute of Metrology Standardization (Brazil)

Bruno Garrido works as a Researcher at the Brazilian National Metrology Institute (Inmetro). His research focuses in organic analytical methods such as NMR, MS, HPLC and GC and their application in the resolution of measurement problems for various fields of application such as clinical analyses, food analyses, toxicology, forensic sciences and fuel analyses. Specifically in NMR, he is interested in new pulse sequences and applications for qNMR and TD-NMR.

Presentation: Day 1 - Recent qNMR Applications in Metrology
ABSTRACT: Metrology is the measurement science. In order to have reliable research, there is a preeminent need to improve measurement processes worldwide and NMR is not an exception. The presentation focuses on how the research at Inmetro intends to help the development of better measurement methods in qNMR with improved reliability and comparability.

Patrick Giraudeau, Ph.D.
Professor
University of Nantes (France)

Prof. Patrick Giraudeau studied physics and chemistry at the University of Nantes, where he received his Ph.D. degree in 2008. He worked for one year each as a postdoctoral researcher in the Department of Chemical Physics at the Weizmann Institute o f Science (Israel). In 2009, he became an associate professor at the University of Nantes, where he became a full professor in 2017. In 2014, he became a fellow of the Institut Universitaire de France, and received a consolidator grant from the European Research Council in 2018. His research activities at the CEISAM research institute are focused on the development of quantitative NMR methods for the analysis of complex mixtures, including applications to metabolomics and fluxomics. Research highlights include the development of fast multi-dimensional quantitative experiments at high fields and also on benchtop spectrometers, as well as recent investigations in dissolution dynamic nuclear polarization.

Presentation: Day 2 - Quantitative 2D NMR Methods for Complex Mixtures

ABSTRACT: NMR spectroscopy is a major tool for quantitative analysis, owing to its high reproducibility, its non-destructive character and its ability to quantify multiple analytes relying on a single internal or external standard. However, the quantitative analysis of complex mixtures is hampered by strong and numerous peak overlaps that make accurate quantification difficult. To face this limitation, our group and others have developed several methodological approaches to achieve absolute quantification by 2D NMR methods. Relying on practical examples, we will introduce and compare the principles, the potential and limitations of various quantitative 2D NMR methods.

Gennady Khirich, Ph.D.
Scientist, Analytical Operations
Genentech

Gennady Khirich is a Scientist in the small molecule process impurities group within Analytical Operations at Genentech, where he has been working as an NMR spectroscopist since 2016. He specializes in rapid development and execution of unconventional qNMR techniques in complex matrices both for R&D and process validation purposes. Prior to joining Genentech, he completed a B.S. in physics from the City College of New York, followed by completion of his Ph.D. in biophysical chemistry at Yale University.

Presentation: Day 2 - Exploring Concepts in qNMR with Monte Carlo Simulations: Facts, Fiction, and a Few Surprises

ABSTRACT: Monte Carlo (MC) methods provide a well-established means by which the distribution describing a target outcome may be generated via repeated random sampling. Simulation of noise-corrupted NMR signals using MC methods offers a particularly simple and convenient path towards elucidating and understanding the underlying metrological performance of various qNMR strategies. In this talk, I will focus on salient results and conclusions drawn from recent qNMR MC simulations of a simple noise-corrupted Lorentzian singlet, which may be further generalized to other lineshapes. Topics touched upon include the integration of white Gaussian noise as a Wiener Process; integration slope/bias “correction”; the integration accuracy/precision trade-off; and, the counterintuitive effect of exponential apodization on quantification by integration.

Michael Levy, M.Sc., MBA
Senior Vice President, Digital and Innovation
USP

Michael Levy is Senior Vice President, Digital and Innovation. In this role, Mr. Levy oversees several forward-looking pillars of activity, including Research and Innovation, Digital & Informatics, and the Pharmaceutical Supply Chain Center.

Research & Innovation identifies, assesses, and as appropriate, incubates emerging technologies that may impact the industries USP works in, the way USP standards are used, or the way those standards are produced.

Digital & Informatics focuses on digitizing USP’s standards to better integrate them into digital environments, fostering standards for digital solutions, and enhancing USP’s digital delivery of content.

The Pharmaceutical Supply Chain Center leverages a unique, integrated data set and analytics to explore complex medicine supply chains, identify potential vulnerabilities, and recommend risk mitigating interventions.

Mr. Levy’s diverse background includes shaping public policy through advocacy, counseling biopharmaceutical and healthcare regulatory executives and staff as a management consultant, and providing deep scientific and technical expertise to academic and industry researchers. Prior to his current role, Mr. Levy was the creator and first Head of USP’s Quality Institute. Previously, he served as Deputy Vice President, Science & Regulatory

Advocacy, at the Pharmaceutical Research and Manufacturers of America (PhRMA), where he shaped the drug development and regulatory review processes—with an emphasis on using non-traditional data and advanced analytics to inform clinical trial design and regulatory decision making. Mr. Levy also served as an Associate Principal at McKinsey & Company, where he supported biopharmaceutical companies and regulators on a broad set of topics in Research and Development and technology enablement. Earlier in his career, Mr. Levy was part of the team that sequenced Human Chromosome XIV as part of the Human Genome Project, and he was the lead bioinformatician in a bioinformatics start-up.

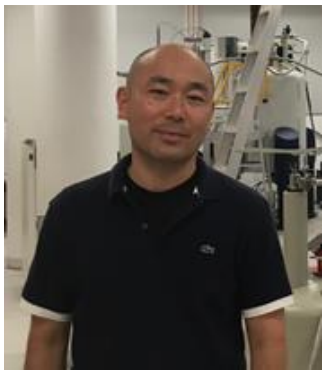
Mr. Levy earned his Masters of Business Administration Degree from Cornell University's Johnson Graduate School of Management, and his Master of Science and Bachelor of Science degrees from Concordia University in Montreal, Canada.

Presentation: Day 1 - Opening: USP Introduction

Yang Liu, Ph.D.
Incubated Projects Manager, Product Quality & Analytical Methods
United States Pharmacopeia (USP), USA

Dr. Yang Liu is quantitative NMR (qNMR) expert and Incubated Projects Manager in USP's Product Quality & Analytical Method Department. Dr. Liu collaborates with scientific experts to bring more qNMR applications into USP, including high-field and benchtop qNMR applications, development of computer-aid methodologies, and compendial qNMR applications. Dr. Liu is a guest scientist at the National Institute of Standards and Technology (NIST), concentrating on the evaluation of benchtop (q)NMR instrumentation pharmacopeial and forensic applications. Dr. Liu is working with the USP qNMR Expert Panel for updating General Chapters <761> and <1761>. Dr. Liu as USP expert, has been also invited by ISO Working Group (ISO/TC 34, WG 24), in reviewing ISO/DIS24583, qNMR standards. Dr. Liu's scientific expertise includes qNMR method development and validation for measurement. He has published over 20 peer-reviewed articles and has been an invited speaker or workshop organizer for numerous scientific conferences.

Moderator: Day 2, Sessions I & II



Toru Miura, Ph.D.
Senior Researcher of Functional Materials Research Laboratories
FUJIFILM Wako Pure Chemical Corporation, Japan

Toru Miura is Senior Researcher of Functional Materials Research Laboratories within FUJIFILM Wako Pure Chemical Corporation. He has been with FUJIFILM Wako Pure Chemical Corporation since 2011. Prior to joining FUJIFILM Wako, he worked as a researcher of the National Metrology Institute of Japan (NMIJ), mainly focusing on development of Certified Reference Materials using mass balance, freezing point depression method and quantitative NMR (qNMR). He is a working group member of the Japanese Pharmacopeia herbal medicine and chemical pharmaceutical related to qNMR methodology, a drafting committee member for the Japanese Industrial Standard (JIS) K 0138 (General Rules for Quantitative Nuclear Magnetic Resonance Spectroscopy) and an expert of WG24 on qNMR established in ISO/TC34 (Food products). Since 2020, he serves as a member of the United States Pharmacopeia Expert Panel for qNMR to develop revisions of USP NMR General Chapters <761> and＜1761＞.

Presentation: Day 1 - Practice of Life Cycle Approach to Method Validation for QNMR Analytical Procedure

ABSTRACT: USP General Chapters ⟨761⟩ Nuclear Magnetic Resonance Spectroscopy and ⟨1761⟩ Applications of Nuclear Magnetic Resonance Spectroscopy are currently being revised by the quantitative nuclear magnetic resonance (qNMR) Expert Panel. One major purpose of this revision is to align with the proposed new USP General Chapter: The Analytical Procedure Lifecycle <1220>, which is aligned with Analytical Quality by Design (AQbD) concepts and offers a lifecycle approach to method validation, method transfer and verification of analytical procedures. In this presentation, I will discuss the outline of the practice of life cycle approach to method validation for qNMR analytical procedure, focusing on the concepts of Analytical Target Profile (ATP), Quality Risk Management (QRM), instrument qualification and evaluation of measurement uncertainty.

Yulia Monakhova, Ph.D.
Project Manager
Spectral Service (Germany)

Education: Habilitation, 2017 in Analytical chemistry and chemometrics
Dr. rer. nat, 2011 in Analytical chemistry and chemometrics
Dipl. Chemist, 2008
(Saratov State University, Saratov, Russia)

Employments:
Since 01/2021: Professor, University of Applied Sciences Aachen
Since 10/2014: Project manager, Spectral Service, Cologne, Germany
07/2011 - 10/2014: Senior researcher, Chemistry and Veterinary Investigation Agency (CVUA), Karlsruhe / Bruker Biospin, Rheinstetten, Germany
10/2010 - 03/2011: Postdoc researcher, CVUA, Karlsruhe, Germany
10/2008 - 06/2011: Post-graduate student, Institute of Chemistry, Saratov State University, Saratov, Russia

Publication activity:
Author of more than 80 peer-review papers
Reviewer for 15 journals

Presentation: Day 2 - Simplification of NMR Workflows by Standardization Using the 2D Integral of Deuterated Solvents as Applied to Aloe vera Preparations

ABSTRACT: In this presentation a novel NMR standardization approach by 2H integral of deuterated solvent for quantitative multicomponent analysis of complex mixtures is presented. As a proof of principle the existing NMR routine for the analysis of Aloe vera products was modified. Instead of using of absolute integrals of targeted compounds and internal standard (nicotinamide) from 1H-NMR spectra, quantification was performed based on the ratio of a particular 1H-NMR compound integral and 2H-NMR signal of deuterated solvent D2O. Validation characteristics (linearity, repeatability, accuracy) were evaluated and the results showed that the method has the same precision as internal standardization in case of multicomponent screening. Moreover, a dehydration process by freeze-drying is not necessary for the new routine. Now our NMR profiling of Aloe vera products needs only limited sample preparation and data processing.

The new standardization methodology provides an appealing alternative for multicomponent NMR screening. In general, this novel approach, using standardization by 2H integral, benefits from reduced sample preparation steps and uncertainties, and is recommended in different application areas (purity determination, forensics, pharmaceutical analysis, etc.).

Jeff Moore, Ph.D.
Senior Director, Scientific Affairs & Strategy
USP

Dr. Jeff Moore is the head of Scientific Affairs & Strategy at US Pharmacopeia. He holds a PhD in food chemistry from the University of Maryland and a BS from Michigan State University. He leads a team of scientists responsible for growing USP scientific voice and presence globally and led USP's COVID-19 treatments initiative in 2020. He is the author of the most cited manuscript on food fraud and led the development of USP's Food Fraud Database in 2012. He has extensive experience in the areas of risk-based systems approaches to food safety, food authenticity testing, non-targeted testing, food fraud mitigation, food chemical safety, and international food additive regulations. He serves on the EU-China SAFE and EU Food Integrity advisory boards and University of Maryland's Global Leadership Council. He has authored more than 30 manuscripts in peer reviewed journals and book chapters. Prior to joining USP Jeff was a research scientist at Nestlè.

Presentation: Day 2 - The qNMR Method in the Remdesivir Toolkit and beyond
ABSTRACT: This presentation will provide an overview of USP's recently published Methods to Assist in Detecting Falsified Remdesivir with a focus on lessons learned from the qNMR method development and validation work.

Jose Napolitano, Ph.D.
Senior Scientist
Genentech

José G. Napolitano obtained his Ph.D. in Chemistry from Universidad de La Laguna (Tenerife, Spain) in 2010. He then moved to University of Illinois at Chicago for postdoctoral work on qNMR applications. His career in pharma began in 2013 at AbbVie's Discovery Chemistry and Technology (DCaT) organization in Lake County, IL. In late 2019, he joined Genentech's Small Molecule Pharmaceutical Sciences (SMPS) department in South San Francisco, CA. His research interests lie in the interface between computational and spectroscopic approaches to solve complex structure elucidation problems, as well as the application of NMR to advance our understanding of chemical transformations.

Presentation: Day 3 - The Impact of qNMR in Small-Molecule Pharmaceutical R&D
ABSTRACT: NMR is a well-established analytical technique that offers a unique perspective into atomic structure and molecular dynamics, providing critically important information for both organic and analytical chemists. As a result, the use of NMR is deeply ingrained into pharmaceutical research and development, from early discovery phases and all the way into manufacturing operations. This presentation will highlight how quantitative NMR (qNMR) has expanded the realm of NMR applications even further, with specific examples of how the implementation of quantitative procedures is changing the role of the NMR spectroscopist in small-molecule pharmaceutical development.

Matthias Niemitz
Entrepreneur
NMR Solutions (Finland)

Experience: > 25 years in quantum mechanical spectral analysis using qNMR.

Presentation: Day 2 - Quantum Mechanical Analysis
ABSTRACT: Quantum mechanical analysis provides two unique features that enable the analysis of very complex spectral data in qNMR applications:
1. By using chemical shifts, coupling constants and populations rather than spectral line frequencies and intensities the quantum mechanical approach considerably reduces the number of unknowns to be determined. This enables unambiguous quantification of very complex NMR data.
2. The additional information about the relationship between coupled spins provided by the quantum mechanical description of the spin systems dramatically reduces the degree of freedom in the assignment and quantitation process. This enables the separation and accurate quantitation of even completely overlapping lines.
Quantum mechanical analysis used to be a standard approach in the early days of NMR because it was the only means for fully understanding NMR data from the low field instruments common at that time. However, the lack of computational power and user friendly software limited its use, which was further reduced by the development towards higher field. Recent progress in the computer technology now meets the renaissance of low field instruments and especially in qNMR applications the quantum mechanical approach is superior also for high field data because prior knowledge about chemical shifts and coupling constants can be applied to the analysis of NMR data measured at any field.

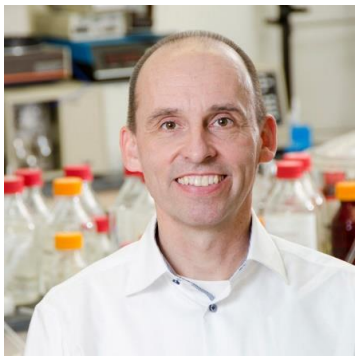
Markus Obkircher, Ph.D, MBA
Director, R&D - Reference Materials and Proficiency Testing Division
Millipore Sigma / Merck KGaA Darmstadt (Germany)

Markus Obkircher is Director R&D heading Merck's Reference Materials and Proficiency Testing division with teams in the US and Switzerland. He is responsible for the in-house development of new analytical standards and certified reference materials under ISO/IEC 17025 and ISO 17034 double accreditation with a strong focus on quantitative NMR. Prior to this position he was R&D Manager in Buchs, Switzerland, with a strong focus on synthesis, characterization and certification of reference materials. He joined Merck / Sigma-Aldrich eight years ago after heading the development unit for a custom API manufacturer. He completed his post-doctoral studies at Harvard in Boston and his PhD thesis in Basel, and further holds an executive MBA degree from the University of Zurich.

Presentation: Day 2 - Micro qNMR - Certification of Marine Toxins
ABSTRACT: Since the presence of marine toxins in shellfish and sea food is an emerging worldwide problem, fast and sensitive LC-MS methods were established for food safety testing.[1] Therefore, the access to well characterized reference materials for a precise and accurate quantitation of these different toxins has become an increased need in the market. These reference materials should be characterized and prepared according to ISO/IEC 17025 and ISO 17034. In order to achieve certification of such small batches according to this double accreditation at the highest metrological level, a combined setup of quantitative NMR (qNMR)[2],[3] and Isotope Dilution MS (IDMS)[4],[5] was successfully established.[6]

The most critical cornerstone in this process is the application of qNMR to accurately determine the low concentration of a dissolved toxin before further dilution. For this micro qNMR approach, the original ISO 17034 workflow had to be adopted to develop several paralytic shellfish toxins (PST), for example the well-known Neosaxitoxin or Saxitoxin and their stabile isotope labeled analogs 15N7-Neosaxitoxin and 15N7-Saxitoxin. In

addition, other toxins like Okadaic acid, PTX11, GTX-6, Gymnodimine, Pinnatoxin E, F and G as well as several Brevetoxins could be made available to testing laboratories as certified reference materials (CRMs).



Guido Pauli, Dr. rer. nat., FAPA
Norman R. Farnsworth Professor of Pharmacognosy, Department of Pharmaceutical Sciences
Director, Pharmacognosy Institute
Associate Director, Institute for Tuberculosis Research
University of Illinois at Chicago, UIC College of Pharmacy

Trained as a pharmacist with specialization in pharmaceutical analysis, Dr. Pauli holds a doctoral degree (Dr. rer. nat.) in pharmacognosy. He is currently the Norman R. Farnsworth Professor of Pharmacognosy, Director of the Pharmacognosy Institute, and Associate Director of the Institute for Tuberculosis Research (ITR) at the University of Illinois at Chicago College of Pharmacy. His basic and translational research project involve bioactive natural products (NPs) from diverse sources, particularly plants and actinomycetes, NP technologies, dietary supplements, clinical and dental intervention materials, drug discovery, the NAPRALERT database, and institutional training programs. Main research interests encompass bioanalytical methodology and interdisciplinary evaluation of plant-derived natural health products, anti-TB hit-to-lead development, dental biomodifiers, and pharmaceutical analysis. He has pioneered the development of innovative approaches including quantitative NMR and countercurrent separation, to advance rigor and reproducibility as well as identification of bioactive principles, respectively. Dr. Pauli seeks to enhance the understanding of natural products as health products and sources of new drugs. He is dedicated to the advancement of pharmacopoeial methods through volunteer work at the United States Pharmacopoeia (USP), where he serves as Chair of the Non-botanical Dietary Supplements Expert Committee and the Modernization of Analytical Methods Joint Subcommittee. His academic track record includes mentoring of 20 Ph.D. students, 27 postdocs, 17 visiting scientists, and ongoing international collaborations. His 250+ peer-reviewed publications have received 10,000+ citations (Scopus) and earned an h-index of 51 in Scopus and 63 in Google Scholar.

Presentation: Day 1 - Opening: CENAPT/UIC Introduction
Presentation: Day 3 - qNMR Stimuli: Observations & Opportunities

ABSTRACT: After much of the scientific groundwork for qNMR has been laid starting in the 1980s until the early 2010s, the recent development and implementation of qNMR methods is paralleled by a rapid growth of qNMR literature and evidence that sometimes is not publicly accessible. Established in 2016, the qNMR Summit series of events has gained global acceptance as a platform for scientific exchange on and capacity building for qNMR methodology. Key contributors to the 2019 qNMR Summit have compiled the current status and challenges of qNMR in a 2021 publication in Analytical Chemistry, which is freely accessible at DOI:10.1021/acs.analchem.1c02056.

This presentation seeks to identify both strength and weaknesses of qNMR methodology and emphasize their perspective in health and chemical research, pharmacopoeial, and regulatory environments. Covered topics involve reference and calibration, terminology, and aspects of best practices such as quantitative measures, reproducibility, and raw data sharing. The intent is to provide stimuli for the qNMR community at large and inspire both discussion and new developments that can help raise the profile of qNMR's ultimate contribution to global human health.

John Price, Ph.D.
Prof. Emeritus of Physics, Univ of Colorado, Boulder
Chief Scientist, Q Magnetics, LLC

As a physics professor at the Univ. of Colorado, John developed scientific instruments for diverse applications including millimeter-scale gravity, dielectric spectroscopy, and mesoscopic electronics. In 2008-2012, he led the design of the picoSpin benchtop NMR spectrometers. In 2020 he retired from academia to work full-time on benchtop NMR technology at Q Magnetics, LLC.

Panelist: Day 3, Session IV: Panel Discussion

Ravi Reddy, Ph.D.
Sr. Director, Reference Standards Development
USP

Ravi Reddy is Senior Director of Reference Standards Development (RSD) at USP, where he is responsible for Reference Standards Evaluation, Reference Materials Procurement and Synthetic Lab teams in the US and India. He holds both a M.Sc. and Ph.D. in chemistry from the Indian Institute of Technology, India. From 1991 to 1995, he was a Post-Doctoral Research Fellow in the US at various institutions. His research activities included isolation and purification of proteins, capillary electrophoretic methods for the process monitoring, etc. Before joining USP, from 1995 to 2017, he worked as Scientist, Manager and Director of Analytical Development in major pharmaceutical companies in the New Jersey and New York area. He has been extensively involved in all activities related to Pharmaceutical Development of both drug substance and drug product, reference standards development, analytical technology transfer, supporting projects during pre-clinical and clinical studies, methods development, methods validation, stability studies, pre-formulations, leading CMC teams, and supporting regulatory filings from Phase I through NDA.

At USP, his group is responsible for driving the development of reference standards by working in close collaboration with scientific liaisons, synthetic lab, procurement, production, reference standards labs, planning, technical service, USP expert committees, etc.

Presentation: Day 3 - Use of qNMR in Reference Standards Development
ABSTRACT: The presentation provides information about different types of reference standards and the process for development of USP reference standards. Brief details are included with respect to type of testing conducted. In addition, a few case studies are provided on the use of qNMR during the life cycle of Reference Standards. The qNMR case studies provide brief details about the usefulness of qNMR.

Alexander Rück, Ph.D.
Manager R&D Reference Materials
Millipore Sigma / Merck KGaA Darmstadt (Germany)

Alex Rueck is working for Sigma-Aldrich Production GmbH (a subsidiary of Merck KGaA, Darmstadt, Germany) since 17 years in the R&D-department in Buchs (CH). Since 2009, he is working on the development of certified reference materials (CRM) for organic molecules using quantitative NMR. The labs are accredited according to ISO/IEC 17025 and ISO 17034. In his current role, he is leading a team of experts and technicians in NMR and Mass Spectrometry, and he is signing CRM-certificates for organic neat materials.

Presentation: Day 2 - Assurance of qNMR Results by Use of Suitable qNMR Standards, Performance Qualification, and Proficiency Testing

ABSTRACT: Certified Reference Material (CRM) is characterized by specific requirements, such as traceability, measurement uncertainty, homogeneity-assessment, stress- and stability-tests, expiry date, certificate and others. All these items are defined in ISO/IEC 17025 and ISO 17034 [1,2]. Through the last years, we have been working on the development of neat CRM for use in 1H, 31P and 19F qNMR [3,4]. Traceability to the SI is achieved using primary reference material from the National Institute of Standards and Technology (NIST) or the National Metrology Institute of Japan (NMIJ). Another group of CRM comprises ready-to-use solutions that can be time saving for particular qNMR applications working either with internal or external standard.

Especially in regulated environments, also the performance of the NMR instrument has to be demonstrated continuously according to the requirements given e.g. by the authorities or guidelines. Through a collaboration between Bruker and Sigma-Aldrich, a new CRM solution has been developed for its use as qNMR performance qualification test (qPQ). It is a binary mixture, which consists of two common CRM for qNMR, dissolved in DMSO-d6 and delivered in ampules. The certified mass fraction values result from a combination of gravimetry and qNMR according to ISO/IEC 17025 and ISO 17034.

While there is a comprehensive portfolio of (certified) reference materials available for qNMR calibration and method validation from various producers and vendors, up to now, there have only been limited possibilities for laboratories to participate in proficiency testing (PT) schemes. In order to ensure easy worldwide availability of interlaboratory comparisons in the field of qNMR, a PT material for performance evaluation of qNMR analysis has been developed [5]. The product is set up as a quick-turn study material, which means that it can be ordered any time. This leads to the advantage that the laboratory does not have to wait for a Proficiency Testing campaign to start. Analytical results can be submitted online by the user, and the result will be provided shortly thereafter. The PT material is produced and sold under ISO/IEC 17043, ISO/IEC 17025 and ISO 17034 accreditations [6].

Holger Stark, Ph.D.
Managing Director Institutes of Pharmacy
Heinrich Heine University Düsseldorf (Germany)

Holger Stark is pharmacist by education and made his PhD in Medicinal Chemistry at the Free University of Berlin, Germany, in 1991 on newly designed prodrugs (BF2.94). Then, he worked on neurotransmitter ligands, mainly at dopamine and histamine receptor subtypes for the central nervous system. In 2000 he became full professor at the Goethe University in Frankfurt, Germany and went in 2013 to the Heinrich Heine University in Düsseldorf, Germany where he has his actual position. He is founded some start-up companies on cancer therapeutics (Warburg Glycomed, PSites Pharma) and has received several prices for his successful research as well as for teaching, e.g., honorary doctorate from the University of Nis, Serbia, in 2017. On more than 380 book contributions, original papers, reviews and patents he has focused on neurotransmitter as well as on lipid signaling research. He is co-inventor of pitolisant (Wakix®), the first

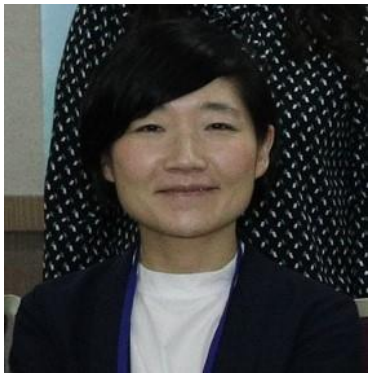
histamine H3 receptor antagonist with market approval, and has prepared several back-up candidates in different leads for various targets. From 2004 to 2019 Holger Stark has been editor-in-chief of the Archiv der Pharmazie – Chemistry in Life Sciences, one of the oldest journals on Medicinal Chemistry.

Presentation: Day 2 - Teaching Basics of 1H-qNMR in Life Sciences

ABSTRACT: Nuclear magnetic resonance spectroscopy is one of the most important techniques in chemical and pharmaceutical research and, as such, is a focus in chemistry courses. In 2008 adverse effects associated to impurities with the use of heparin were leading to the introduction of the NMR-based analytical identification into the European Pharmacopeia (Eur.Ph.), and therefore also in pharmaceutical courses. In contrast to the >200 MHz instrumentation, the availability of the low-field benchtop NMR instruments allowed us to develop practical student experiments as a part of an interactive scientific puzzle where each element supports the complex understanding of a set of information obtained from 1H-NMR measurements for students in life sciences. In teaching, we focused on both qualitative and quantitative measurements.

Here, we focus on two of the experiments: relative quantitative determination of the therapeutically active ingredients of well-known marketed pain relief drugs (acetyl salicylic acid, acetaminophen, caffeine, and vitamin C)1 as well as the logP value determination (the partition coefficient between octanol-water) of solvents and a few drugs.2,3 Comprehensive practical sessions combining those two experiments, which cover various key aspects of 1H-NMR spectroscopy, have been developed. Multiple probes have been analyzed within an undergraduate laboratory.

With these applications and based on the experimental design, the students were highly motivated on deeper understanding of multiple aspects of 1H-NMR (spectra interpretation, data processing, chemical properties, chemical shift connections etc.).



Nahoko Uchiyama, Ph.D.
Section Chief, Division of Pharmacognosy, Phytochemistry and Narcotics
National Institute of Health Sciences (NIHS), Japan

I received my Ph.D. in Pharmaceutical Sciences from Kyoto University, Japan in 2004. After completing my Ph.D., I worked as Junior Assistant Professor at the Department of Pharmacognosy, Faculty of Pharmaceutical Sciences, Doshisha Women's College of Liberal Arts in Kyoto (Japan). In 2006, I moved to National Institute of Health Sciences (NIHS) in Tokyo, Japan as Researcher in the Narcotics Section of the Pharmacognosy, Phytochemistry and Narcotics Division, and was promoted to Senior Researcher at the same Division in 2009. I investigated chemical analysis of abused drugs, especially designer drugs. Since 2016, I have been working as Section Chief in the Pharmacognosy Section of the same Division of NIHS. My current research is mainly focused on chemical evaluation of herbal medicines along with chemical analysis of unregulated drugs and counterfeit medicines. I am also contributing to the development of Japanese Pharmacopoeia (JP) standards for crude drugs and Kampo extracts as a member of JP expert committee on crude drugs.

Presentation: Day 1 - Utilization of qNMR for assay in Japanese pharmacopoeia

ABSTRACT: Quantitative NMR (qNMR) was implemented in the Japanese Pharmacopoeia (JP) since the release of JP16 Supplement II published in 2014. This presentation details the following topics: 1) Nineteen reagents evaluated by qNMR as the HPLC reference standards in the assay of crude drug section; 2) development of the optimal preparation method for qNMR of hygroscopic reagents; 3) utilization of relative molar sensitivity (RMS) coupled with qNMR and HPLC for assay of perillaldehyde, an unstable compound in Perilla Herb; 4) qNMR description in the guideline for drafting the JP; 5) a comparison of descriptions related to qNMR among the three pharmacopoeias (JP, USP, EP). 6) utilization of 31P-qNMR absolute determination method as a further approach in qMNR for organophosphorus pharmaceuticals.

Aaron Urbas, Ph.D.
Research Chemist
National Institute of Standards and Technology (USA)
Aaron Urbas has been a research chemist in the Chemical Sciences Division at NIST since 2007. There he has been involved in the development of applications and reference materials for vibrational and nuclear magnetic resonance (NMR) spectroscopies and his past and current research efforts are in a diversity of areas including polymers, metabolomics and forensics.

Presentation: Day 1 - Benchtop NMR for Forensic Drug Analysis
ABSTRACT: Forensic laboratories commonly encounter new psychoactive substances, such as fentanyl analogues, that can be difficult to definitively identify. High-field NMR can be quite useful in the analysis of these compounds but is not practical in many forensic laboratories due to instrument and maintenance costs among other considerations and benchtop NMR systems represent an attractive alternative. In this talk the application of benchtop NMR for the differentiation of a wide variety of fentanyl analogs and related substances, including various types of positional isomers, using 1H and 19F NMR spectra will be discussed. In addition, the use of quantum mechanical spectral analysis (QMSA) will be discussed for the purposes of translating experimental high-field NMR data to lower field strengths including examples with fentanyl analogs and other designer drugs. QMSA offers the potential to generate field-strength independent NMR spectral libraries that can enable reference material data dissemination across forensic drug laboratories.

Stefan Walch, Ph.D.
Executive Director
CVUA Karlsruhe

Dr Stephan G Walch is currently the Executive Director of the CVUA Karlsruhe, which is an ISO 17025 accredited Official Food and Feed Laboratory and Official Medicines Control Laboratory of the federal state of Baden-Württemberg, Germany. Dr Walch received his state examination for Pharmacy from the University of Heidelberg, Germany and Diploma in Food Chemistry and Toxicology (Dipl.-LMC) at the Karlsruhe Institute of Technology (KIT), Germany. He received his Ph.D. in Public Health from the UMIT in Hall in Tyrol (Austria). He served as a scientist and senior scientist in different governmental laboratories in Germany in the fields of food safety, food additives, analysis and evaluation of residues and contaminants in food, feed, and water. He is also a lecturer at the Technische Universität Kaiserslautern and has published over 45 peer reviewed articles. Regarding qNMR he is particularly concerned with food and medicines analysis. He is serving as an expert in the food ingredients EC of USP, the WHO/FAO JECFA, as member of the German delegation to the Codex Committee on Methods of Analysis and Sampling (CCMAS) of Codex Alimentarius and is member of the working group of food chemistry experts from the federal states and the Federal Office of Consumer Protection and Food Safety (ALS). He is also member of several national and international working groups which focus on method standardization or standard development (such as AOAC, ISO, CEN, DIN).

Presentation: Day 3 - Current Use and Opportunities for qNMR in Regulatory and Industrial Laboratories. What are the Differences?
ABSTRACT: Forthcoming

Greg Walker
Associate Research Fellow
Pfizer

Gregory S. Walker is an Associate Research Fellow at Pfizer Inc. with 30 years of experience in both pharmaceutical science and drug metabolism. Currently, he manages the drug metabolism NMR facility at Pfizer's research headquarters in Groton, CT. For the past 25 years he has worked in NMR groups at The Upjohn Company, Pharmacia and Pfizer. Greg has specialized in the structural characterization of low level unknown organic molecules originating from complex matrices using a variety of chromatographic and spectroscopic techniques. His career highlights include establishing NMR as a global analytical resource for the Pfizer drug metabolism division, developing a generalized quantitative NMR assay for qualification of bio-generated analytical standards and 50+ external publications and presentations. Greg is a member of the APA organizing committee and was chair of the SMASH 2018 NMR meeting. Greg is a recognized expert in structural elucidation of metabolites and has taught numerous short courses for such organizations as the American Chemical Society, Applied Pharmaceutical Analysis (APA) and International Society for the Study of Xenobiotics (ISSX). Greg is a two-time recipient of the Pfizer Achievement Award, most recently for his work in quantitative NMR as it pertains to drug metabolism.

Presentation: Day 3 - Weighing the Unweighable Sample: The Transformative Role of qNMR in the Discovery of New Medicines

ABSTRACT: Over the past decade NMR has become an increasingly important spectroscopic technique in drug metabolism groups within the pharmaceutical industry. This growth in influence is because of enhanced sensitivity from developments in both NMR hardware (micro cryo-probes) and in vitro techniques used to generate metabolites. Concomitant with these developments was the re-discovery of qNMR and its ability to quantify isolated materials at the low nmole level. These enhancements in hardware and the resurgence of qNMR have not only benefitted the drug metabolism scientist but also medicinal chemists working in lead diversification (LD), where sample amounts are very limited. The goal of LD is to enhance the already proven pharmacology of a molecule or to address other compound properties such as solubility or ADME related issues. Classical approaches to LD typically require tens to hundreds of milligrams of starting material to ensure weighable amounts of a single end product. Recently, we have implemented, on a microscale, a series of radical based chemistries to expand the structural space of our lead compounds. By design this approach is promiscuous and will produce multiple products at low levels (micrograms) which are then isolated via preparative HPLC and characterized by MS and NMR. Because of the low amount of product, gravimetric analysis is not possible. Instead, we have used qNMR, in conjunction with the enhanced mass sensitivity of the micro cryo-probe, to determine the structure and the solution concentration of the isolated material in the NMR sample. The levels of these isolated products preclude the routine use of room temperature and larger volume cryo NMR probes, hence, key to this entire process is the enhanced sensitivity of the micro cryo-probe. These NMR samples are then used as stock solutions for pharmacology and ADME assays. Using this process, over the last four years, we have registered 600 - 700 new leads per year.

Aleksandra Zivkovic, Ph.D.
Academic Councilor
Heinrich Heine University Düsseldorf (Germany)

Aleksandra Zivkovic is chemist by education and made her PhD in Organic Chemistry at the Goethe University in Frankfurt, in 2005 on modifed RNA. Afterwards, she did postdoc working mostly on synthesis and development of siRNA for two years. Since 2007 she is working in the field of medicinal chemistry. 2013 she started working at the Heinrich Heine University in Duesseldorf, as acedemic seniour councillor continuing her research in medicinal chemistry.

Presentation: Day 2 Teaching Basics of 1H-qNMR in Life Sciences

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