AGENDA

4:00 p.m. - 4:05 p.m.	Introduction to the Symposium	**Christelle Chrea**, PhD CROM Consortium Coordinator

Part I: Abuse Liability Assessment of New Tobacco Products

4:05 p.m. - 4:35 p.m.	Tobacco Product Abuse Liability	**Lynn Hull**, PhD **Megan Schroeder**, PhD Office of Science, CTP US FDA
4:35 p.m. - 5:05 p.m.	Challenges and Considerations Related to Human Abuse Liability Testing for Tobacco Products: Opportunities to Establish Tobacco-Specific Methods, Measures, and Evaluation Criteria	**Andrea Vansickel**, PhD Altria Client Services LLC **Sarah Baxter-Wright**, PhD RAI Services Company
5:05 p.m. - 5:25 p.m.	Assessment of the Exposure to Selected Smoke Constituents in Adult Smokers Using In-market Heated Tobacco Products: A Randomized, Controlled Study	**Dai Yuki**, PhD Japan Tobacco Inc.
5:25 p.m. - 5:35 p.m.	**Break**	

Part II: Abuse Liability Assessment of Other Substances

5:35 p.m. - 5:55 p.m.	Abuse Liability Assessment of CNS-active Drugs in Development: History and Overview	**Ryan Lanier**, PhD Pinney Associates
5:55 p.m. - 6:15 p.m.	The Development of Testing-Based Approaches to Screen for Hazardous Ingredients and Formulations Used in Heated Inhalation Devices with Particular Emphasis on Cannabis Products	**Rob O'Brien**, PhD Supra Research and Development
6:15 p.m. - 6:30 p.m.	Building a Consumer Technical Model for Cannabis Products – Insights & Considerations	**Martha Bajec**, PhD HCD Research

Q&A and Panel Discussion

6:30 p.m. - 7:00 p.m.	All presenters Chaired by **Lesley Giles**, PhD, JT International, and moderated by **Nicholas Goldenson**, PhD, JUUL Labs	

ABSTRACTS AND BIO SKETCHES

Tobacco Product Abuse Liability

***Lynn Hull**, PhD and **Megan Schroeder**, PhD, Office of Science, Center for Tobacco Products, U.S. Food and Drug Administration*

FDA regulates tobacco products based on a public health standard that considers the risks and benefits of the tobacco product on the population as a whole. A part of this consideration includes the evaluation of a tobacco product's abuse liability, or the ability for a product to promote continued use and lead to addiction and dependence. Abuse liability also directly informs whether one product may be acceptable as a substitute for another product, whether using a product is likely to result in a pattern of continued use, and the likelihood of an individual being able to quit using a product successfully. Tobacco product abuse liability assessments are multifaceted and rely on many different measures, including behavioral and clinical pharmacology outcomes. Many product characteristics can influence abuse liability and an understanding of these product specific characteristics is important when designing studies to inform tobacco product abuse liability evaluations.

Lynn Hull, PhD, is a pharmacologist with expertise in nicotine and tobacco regulatory science. Dr. Hull received her BS in Biochemistry from Worcester Polytechnic Institute in 2002, and then went on to receive her PhD in Pharmacology and Toxicology from Virginia Commonwealth University in 2009. She completed a Postdoctoral Fellowship at VCU and was an AAAS Science and Technology Policy Fellow in NCI's Office of Nanotechnology Cancer Research from 2012-2014. Dr. Hull joined the Center for Tobacco Products in 2014 and has been the Deputy Director of the Division of Individual Health Science since 2021.

Megan Schroeder, PhD, is a pharmacologist with expertise in abuse liability and tobacco regulatory science. Dr. Schroeder completed her BS in Biochemistry from Susquehanna University in 2006. She then went to Georgetown University to start her PhD work in Pharmacology with an emphasis in neuroscience and graduated in 2010. After completing a post-doc fellowship at the National Institutes of Health (NIH), she started at the U.S. Food and Drug Administration's Center for Tobacco Products in 2012. Since 2019, she has been the branch chief to the Office of Science's behavioral and clinical pharmacology branch which reviews premarket tobacco product applications (PMTAs), conducts clinical research on the abuse liability of tobacco products, and supports tobacco product standards and public health policy.

Challenges and Considerations Related to Human Abuse Liability Testing for Tobacco Products: Opportunities to Establish Tobacco-Specific Methods, Measures, and Evaluation Criteria

***Andrea Vansickel**, PhD, Altria Client Services LLC and **Sarah Baxter-Wright**, PhD, RAI Services Company*

The U.S. Food and Drug Administration (FDA) recommends that tobacco product manufacturers provide information regarding the abuse liability of tobacco and nicotine-containing products to support pre-market tobacco, modified risk tobacco product and substantial equivalence applications. While many methods exist, no standard tobacco product abuse liability assessment methodology has been established and no formal guidance document for such testing has been issued. The CORESTA Product Use Behavior subgroup previously reviewed the FDA's recommendations in the context of published literature and information from authoritative bodies related to the abuse liability of tobacco and pharmaceutical products, and identified, summarized, and published a review of the most promising approaches for abuse liability assessment of tobacco products. The recommended approaches apply traditional abuse liability testing methods for pharmaceutical products to tobacco and nicotine-containing products and have been implemented for testing of tobacco products, some of which have received FDA marketing granted orders. However, current data reveals opportunities to enhance methods and measures employed in these tobacco abuse liability studies and interpretation of results. We will highlight these opportunities and discuss considerations for establishing standard measures and methods that may better account for unique aspects of tobacco and nicotine-containing products. Special emphasis will be placed on considerations for how information from tobacco abuse liability studies can be used to evaluate whether the marketing of a product is appropriate for the protection of public health.

Andrea Rae Vansickel, PhD, serves as a Senior Principal Scientist in the Population Sciences function within Regulatory Sciences for Altria Client Services in Richmond, VA. In this role, she leads a team responsible for postmarket surveillance studies and scientific support for Altria's underage prevention and cessation initiatives, FDA engagement, and advocacy efforts toward tobacco harm reduction. Dr. Vansickel is a classically trained behavioral pharmacologist, educated in experimental psychology-behavioral neuroscience, and psychopharmacology at the University of Kentucky and in the clinical pharmacology of tobacco at Virginia Commonwealth University. She has published many papers and book chapters related to human behavioral pharmacologic models, human abuse liability testing, and the clinical pharmacology of e-vapor and oral nicotine products, among others. Dr. Vansickel has been building programs and infrastructure to support regulatory research and engagement efforts for Altria since January of 2012. These programs relate to tobacco abuse liability testing, e-vapor topography, cross-sectional surveys, actual use trials and prospective cohort studies, among others.

Sarah Baxter-Wright, PhD, Vice President – Scientific and Regulatory Affairs is responsible for driving the development of regulatory science for RAI Services Company (RAIS) (RAIS is a wholly owned subsidiary of Reynolds American Inc.). In this role she leads a team responsible for statistics and nonclinical, clinical, and population effects research in support of FDA and external science engagement, and for advancing discussions on tobacco harm reduction. Dr. Baxter holds a Ph.D. in Biochemistry from Vanderbilt University, Nashville, TN, with training in biomarkers and systems biology, focusing on proteomics and metabolomics. Since joining RAIS in 2016, Dr. Baxter has held responsibilities for overseeing clinical science and clinical research data dissemination as part of the regulatory science team. Prior to joining RAIS, Dr. Baxter held scientific research positions in several organizations focusing on cancer research, agriculture, health and nutrition, pharmaceutical testing, and biodefense.

Assessment of the Exposure to Selected Smoke Constituents in Adult Smokers Using In-market Heated Tobacco Products: A Randomized, Controlled Study

***Dai Yuki**, PhD, Japan Tobacco Inc.*

The objectives of this clinical study were to demonstrate a reduction in exposure to selected harmful and potentially harmful constituents (HPHCs) in Japanese healthy adult smokers who switched to four in-market heated tobacco products. Eighty-nine smokers were randomly assigned for five days to one of six study groups: four groups who switched to one of the commercially available heated tobacco products; a group who continued to smoke their own brand of combustible cigarettes; or a group who stopped smoking. Fifteen biomarkers of exposure to 14 HPHCs and pyrene were measured at baseline, Day 3 and Day 5 in 24h urine and breath, under clinical confinement. Product consumption, nicotine uptake and subjective effects were also measured before and after product switching.

In this presentation, for heated tobacco products, I will explain the reduced exposure potential from the present study and will summarize the current thinking on the abuse liability by assessing the subjective effects measures before and after product switching and referring to related available information.

Dai Yuki, PhD, is a research scientist in the field of human clinical studies within Scientific & Regulatory Affairs at Japan Tobacco Inc. in Japan. He is a pharmacological scientist with technical expertise in the design, development, and testing of physiological and behavioural assessments in clinical research. He has 15+ years international experience in human research on tobacco products and contributes to regulatory submissions for non-combustible tobacco products by JT Group. He also participates in the CORESTA Biomarkers and Product Use Behaviour Sub-Groups and contributes to international collaborative industry activities.

Abuse Liability Assessment of CNS-Active Drugs in Development: History and Overview

***Ryan K. Lanier**, PhD, Pinney Associates, Inc.*

The Controlled Substances Act (CSA) describes eight factors that need to be examined to assess the abuse potential (or liability) of drugs in clinical development that are active within the central nervous system (CNS). These factors encompass a wide range of topics regarding the drug, including the totality of its physical and behavioral effects, consequences to the individual and public health, its availability, and use patterns. The results of this analysis are a required part of any New Drug Application (NDA) submission to FDA for a product with CNS activity and is the basis for labeling and scheduling decisions. This presentation will review the history and provide an overview of the regulations surrounding the abuse potential evaluation of CNS-active drugs in the context of FDA's 2017 final guidance on the topic. This will include a review of the step-wise approach to determine whether an abuse potential assessment is needed for a new drug, the types of scientific evidence that is required and studies that need to be conducted during drug development, and the processes involved with drug scheduling if deemed necessary and consistent with the CSA by FDA during its review of a sponsor's NDA.

For the past 20 years, including 15 years in the pharmaceutical, cannabinoid, and dietary supplement industries, **Dr. Ryan Lanier**'s nonclinical and clinical research has supported the development of a range of compound classes ranging from analgesic and anti-inflammatory drugs, CNS-active dietary supplements, modified risk non-combustible tobacco products, cannabinoid-based medicines, and psychedelic medicines.

Following positions at Javelin Pharmaceuticals, Inc., and Rock Creek Pharmaceuticals, Inc., Dr. Lanier led the consulting team at Analgesic Solutions, Inc., where he spearheaded the validation and implementation of MADDERS®, a novel standardized system for prospectively identifying and assessing potentially abuse-related adverse events in clinical trials. Prior to joining Pinney Associates in 2021, Dr. Lanier counseled AusCann Group Holdings, Ltd., and served as Associate Director for Pain and Abuse Liability for Spectrum Therapeutics, a division of Canopy Growth Corporation, working on early clinical development of cannabinoid-based medicines and novel cannabinoid formulations, assessments of market opportunities, and development plans for new products. Dr. Lanier has authored or co-authored more than 30 papers and book chapters on topics such as drug development and abuse potential and has presented his research findings at numerous scientific meetings. He received his PhD in Biological Psychology from the University of North Carolina at Chapel Hill and completed a postdoctoral fellowship within the Behavioral Pharmacology Research Unit (BPRU) at Johns Hopkins University School of Medicine.

The Development of Testing-Based Approaches to Screen for Hazardous Ingredients and Formulations Used in Heated Inhalation Devices with Particular Emphasis on Cannabis Products

***Rob O'Brien**, PhD, Supra Research and Development*

Dr. Rob O'Brien is the founder and CEO of Supra Research and Development, an Analytical Service and contract research firm in Kelowna, British Columbia. Dr. O'Brien has been involved as a senior executive in a variety of companies in the Cannabis and Natural Health Product sectors. He has also founded a series of successful commercial analytical laboratories. Prior to engaging in the private sector, Dr. O'Brien held research academic positions at Okanagan University College and UBC Okanagan, where he specialised in Analytical Mass Spectrometry. He is currently an Adjunct Professor in the UBC Okanagan Biology Department and the Chemistry Department at Thompson Rivers University.

Building a Consumer Technical Model for Cannabis Products – Insights & Considerations

***Martha Bajec**, PhD, HCD Research*

Although globally prohibited for over a century, humans have been using cannabis and its multitude of extracts and preparations for many millennia. With countries and states around the world decriminalizing or legalizing cannabis for medical and/or recreational use at a rapid rate, understanding the perceptions, attitudes, and behaviors of cannabis users and non-users is essential for public health and safety during this time explosive growth in available cannabinoid-containing products on the consumer market. Here we present key insights from two years (2021 & 2022) of cross-sectional research on adult US cannabis user and non-user samples toward understanding consumer perspectives on the cannabis product landscape.

Martha Bajec (PhD) has been a scientist and leader with some of the world's largest and most influential consumer packaged goods (CPG) companies for almost 15 years. With broad academic training and experience working on subjects ranging from fruit flies and crayfish to humans of all ages, Martha brings her unique expertise, perspective, and personality to all her research endeavours. Most recently, Martha has pursued her passion for innovation and excellence as Senior Consulting Scientist with HCD Research focusing on evaluation of cannabis and other health and wellness products. Under her own consultancy practice, Bajec Senseworks, Martha enjoys contributing to numerous diverse research projects on a wide range of topics and considerations, including harm reduction, risk perception, and the value of our senses.