PROGRAM BOOKLET AND ABSTRACTS
Volume 77

77th Tobacco Science Research Conference

September 8-11, 2024

Atlanta, Georgia USA

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Hosted by: SWM International

GENERAL PROGRAM

Sunday, September 8, 2024

2:00PM – 6:00PM	Registration	Ballroom Foyer
2:00PM – 6:00PM	Speaker Ready Room	Planner Office
2:00PM – 3:00PM	Contemporary waterpipes, waterpipe accessories, and waterpipe tobaccos. (W1-3, listing on page 31) John Lauterbach; Lauterbach & Associates	Oakwood
3:00PM – 5:00PM	The University of Kentucky Center for Tobacco Reference Products Workshop. (W4-7, listing on page 31) Huihua Ji, Stacey Slone, Ruth McNees; University of Kentucky	Maplewood
4:00PM – 6:00PM	Ownit Reception	Ballroom Foyer
6:30PM – 9:30PM	Welcome Reception *Hosted by SWM International*	The Backyard

Monday, September 9, 2024

7:15AM – 8:30AM	U.S. TAG: ISO/TC 126 Breakfast	Maplewood
7:30AM – 5:00PM	Registration	Ballroom Foyer
7:30AM – 5:00PM	Speaker Ready Room	Planner Office
8:00AM – 8:45AM	Session Chairs Breakfast	Oakwood A
8:30AM – 9:00AM	Morning Coffee	Ballroom Foyer
9:00AM – 11:30 AM	Symposium: Tobacco Harm Reduction: What Have We Learned and How Do We Move Forward?	Ravinia Ballroom
10:15AM – 10:35AM	Break	Ballroom Foyer
11:30AM – 1:00PM	Lunch	Dunwoody
12:30PM – 2:00PM	Poster Session (#7-38)	Ballroom Foyer
2:00PM – 3:30PM	Panel Discussion: Weight of the Evidence: Assessing the Benefits of Smokefree Alternatives to Adults who smoke and the Risk of Underage Initiation.	Ravinia D
3:30PM – 4:00PM	Break	Ballroom Foyer
4:00PM – 5:45PM	Session A: Regulatory and Public Health	Ravinia D
1:55PM – 4:00PM	Session B: Consumer Reported Outcome Measures	Ravinia A-C

Tuesday, September 10, 2024

7:30AM – 5:00PM	Speaker Ready Room	Planner Office
8:00AM – 8:45AM	Morning Coffee	Ballroom Foyer
8:45AM – 10:10AM	Panel Discussion: Advancing Science-Based Consensus Standards for Nicotine Pouches in the US: Pathway to Regulatory and Public Heath Synergy.	Ravinia D
8:45AM – 10:10AM	Session B: Agronomy	Ravinia A-C
10:10AM – 10:30AM	Break	Ballroom Foyer
10:30AM – 12:15PM	Session A: ENDS Use Behavior	Ravinia D
10:30AM – 12:15PM	Session B: Method or Process Development	Ravinia A-C
12:15PM – 1:30PM	Lunch	Dunwoody
12:15PM – 2:00PM	Policy Committee Lunch	Azalea
1:00 PM – 2:30PM	Poster Session (#39-70)	Ballroom Foyer
2:30PM – 4:15PM	Panel Discussion: Tobacco Harm Reduction Success Stories: How Countries are embracing Smokeless Alternatives and Their Impact on Smoking.	Ravinia D
2:30PM – 5:15PM	Session B: Product Characterization	Ravinia A-C
4:15PM – 4:35PM	Break	Ballroom Foyer
5:15PM – 6:00PM	TSRC Business Meeting	Ravinia A-C
6:30PM – 10:00PM	Social Hour and Award Banquet	Ballroom Foyer

Wednesday, September 11, 2024

7:30AM – 12:00PM	Speaker Ready Room	Planner Office
8:00AM – 8:45AM	Morning Coffee	Ballroom Foyer
8:45AM – 10:10AM	Session A: Clinical Studies & Biomarkers	Dunwoody
8:45AM – 10:10AM	Session B: Method or Process Development	Ravinia A-C
10:10AM – 10:30AM	Break	Ballroom Foyer
10:30AM – 12:15PM	Session A: Toxicology	Dunwoody
10:30AM – 12:15PM	Session B: HTP Use Behavior	Ravinia A-C
12:15PM – 1:15PM	Lunch (take away available)	Ballroom Foyer
1:15PM – 2:00PM	Session A: Product Characterization	Dunwoody
1:15PM – 2:40PM	Session B: Agronomy	Ravinia A-C

ADJOURN

LIFETIME ACHIEVEMENT AWARD

Linda Crumpler

Linda Phillips Crumpler was born in Albuquerque, New Mexico and her path to a career in tobacco science was perhaps very different from previous Lifetime Achievement recipients. Linda's parents were not educated people. Her Father was an electrician and her mother, the daughter of a Welsh coal miner was taken out of school quite young and put to work. Following the death of her Father when Linda was four years old, her mom moved with Linda and sister Myra to Miami, Florida where their older sister lived. Linda's Mom imparted one very important life lesson to her children, "there is only one thing no one can ever take away from you, and that is your education".

In an interview for a Professional Woman of the Year Award in 2015, Linda said the following, "I didn't really pick my career, it picked me." She started her professional career at Miami Heart Institute while obtaining a degree in Medical Laboratory Technology. In 1978, Linda and her husband Mike moved to Mike's home state of NC. After a brief stint in the Lipid Lab at Baptist Hospital, Linda went to work as a Lab Technician at R.J. Reynolds Tobacco Company. In 1980 the Head of R&D, Dr. Roy Morse offered R&D employee's an opportunity to return to school for degrees in Chemistry which Linda gladly accepted. She attended Salem College and graduated Suma cum laude with a BS in Chemistry in 1984. Between the years of 1984 to 2007 Linda held numerous management positions at RJRT including Sr. Director Tobacco and Smoke Chemistry; and Sr. Director Regulatory Compliance. During her work career she has demonstrated a proven ability to engage and lead large, diverse international scientific groups in collaborative and productive work as well as engage regulators and external organizations such as Tobacco Institute of Japan (TIOJ), American Society for Testing and Materials, National Institute of Standards and Technology, FDA, CDC, and ISO in cooperative collaborative work. During her tenure with RJRT Linda developed, implemented and successfully accredited the entire Analytical division to ISO 17025 with zero deficiencies. She was selected to the American Association of Laboratory Accreditation Life Science Advisory Council. She represented RJRT as Technical Expert to the TIOJ and successfully proposed modifications to the TIOJ Tar and Nicotine Standards to accommodate "A Cigarette Which Primarily Heats Tobacco", which were vital to the company's introduction of a new product to the Japanese market.

Linda chaired the CORESTA Routine Analytical Chemistry Sub-Group from 2002 - 2008. This sub-group developed several new industry analytical methods, as well as identifying flaws in a revised rotary smoking machine design. She also served on the CORESTA Sidestream Task Force, Ignition Propensity Task Force, Special Analytes, E-cig & Smokeless Tobacco Sub-groups. Linda served four terms on the CORESTA Scientific Commission and was Secretary of the Smoke Science Study Group and President of the Product Technology Study Group.

In 2008 Linda retired from RJRT and joined Cerulean as a contractor and then as Director of Business Development. Throughout her career Linda has promoted the sharing of good science through contributions to CORESTA working groups, the CORESTA scientific commission, ISO, organizing TSRC conferences, presenting at the China Collaborative conference and being a leading contributor at the Asia Collaborative Study meetings. In her role at Cerulean, she was instrumental in examining the fundamentals of how we obtain information about smoked products and has been joint author on 10 presentations and posters given at TSRC and CORESTA over the years that have dealt with instrumental effects. She also worked on paper diffusivity of banded papers and obtained a patent for a novel system and calibration. She leveraged her deep understanding of the laboratory process to make better equipment and so share her knowledge amongst her peers.

Linda credits her success to the extraordinary mentors and scientists she had the privilege to work with, including Dr. Mary Stowe, Mrs. Brenda Hodge, Mrs. Janet Wheeler, Dr. David Townsend, Dr. Bill Coleman, and Dr.'s Bert Gordon and Luis Dominguez. As well as the most remarkable and supportive staff ever." And of course, her supportive family.

MONDAY, SEPTEMBER 9, 2024
SYMPOSIUM

9:00 AM	**Welcome Remarks** Zahia Ouar Naye, SWM International 77th TSRC Conference Chair
9:05 AM	**Tobacco Harm Reduction: What Have We Learned and How Do We Move Forward?** Karl Wagner, Altria Client Services 77th Symposium Chair
9:10 AM	Jasjit S Ahluwalia; Brown University, Providence, RI, USA
9:20 AM	Matthew Farrelly; U.S. Food and Drug Administration, Washington, DC, USA
9:35 AM	Maria Gogova; Altria Client Services, Richmond, VA, USA
9:45 AM	Chris Junker; RAI Services Company, Winston-Salem, NC, USA
9:55 AM	Derek Yach; Global Health Strategies, New York, NY, USA
10:05 AM	Brian Yagi; University of Michigan, Ann Arbor, MI USA
10:15 AM	***BREAK***
10:35 AM	Jasjit S Ahluwalia; Brown University, Providence, RI, USA
10:45 AM	Panel Discussion & Audience Q&A
11:30 AM	***LUNCH***
12:30 PM	**Poster Session:** 7-40 (listing on page 22)

Panel Discussion
Session Chair: Elizabeth Becker

2:00 PM 71 **WEIGHT OF THE EVIDENCE: ASSESSING THE BENEFITS OF SMOKEFREE ALTERNATIVES TO ADULTS WHO SMOKE AND THE RISK OF UNDERAGE INITIATION.**

Elizabeth BECKER; Altria Client Services, Richmond, VA, USA

Benjamin Apelberg; CTP FDA, Washington, DC, USA

Tiffany Parms; RAI Services Company, Winston-Salem, NC, USA

Kate Vergara; Altria Client Services, Richmond, VA, USA

Agustin Rodriguez; Troutman Pepper, Richmond, VA, USA

3.30 PM ***BREAK***

	Session A: Regulatory & Public Health *Session Chair: Candi Cunningham*	**Session B: Consumer Reported Outcome Measures** *Session Chair: Jessica Zdinak*
4:00 PM	Welcome Remarks	Welcome Remarks
4:05 PM	72 **TOBACCO IMPLEMENTATION GUIDE (TIG) V1.0: A NEW STANDARD TO SUPPORT REGULATORY REVIEW AND DECISION MAKING.** Chrissie CAI[1], Christine Connolly[2]; [1]US Food and Drug Administration, Beltsville, MD, USA, [2]CDISC, Austin, TX, USA	77 **CHARACTERIZING TOBACCO PRODUCT USE PATHWAYS LEADING TO AND FLOWING FROM REGULAR USE OF NICOTINE POUCHES.** Gavin O'DOWD[1], Jon Laucirica[1], Jasmin Alipour[1], Luke Dubery[1], Marta Esposti[1], Christopher Russell[2]; [1]Haypp Group AB, Stockholm, Sweden, [2]Russell Burnett Research & Consultancy, Glasgow, UK

4:25 PM 73 **"IT'S GOOD NEWS": CASE STUDIES IN THE FACT-CHECKING OF STATISTICAL BIAS IN THE SCIENTIFIC LITERATURE AND ITS TRANSLATION BY THE NEWS MEDIA.** Gal COHEN; Rose Research Center, Raleigh, NC, USA

78 **TRENDS IN SMOKING CESSATION AND TOBACCO PRODUCT TRANSITIONS: INSIGHTS FROM THE PATH STUDY.** Mark CROSSWHITE; Consulticx Sciences Corp, Statesville, NC, USA

4:45 PM 74 **PREVENTING YOUTH ACCESS AND USE BY OUTFITTING E-CIGARETTES WITH NEAR-FIELD COMMUNICATION (NFC) TECHNOLOGY.** Martin STEINBAUER[1], Kylie Halperin[1], David Lawson[2], Christopher Russell[3]; [1]SkyX Group, New York, NY, USA, [2]Inter Scientific, Liverpool, UK, [3]Russell Burnett Research and Consultancy, Glasgow, UK

79 **IDENTIFYING PREDICTORS OF SMOKING SWITCHING BEHAVIORS BASED ON THE POPULATION ASSESSMENT OF TOBACCO AND HEALTH STUDY DATA: A MACHINE LEARNING ANALYSIS.** Xiaona LIU[1], Yue Cao[1], Jiaxuan Li[1], Xi Chen[1], Yuming Xiong[1], Fangzhen Zheng[1], Jianqiang Zhang[1], Xiaona Liu[1], Xuxi Zhang[2], Xinying Sun[2], Ian M. Fearon[3]; [1]Smoore Research Institute, Shenzhen, Guangdong, China, [2]Peking University, Beijing, China, [3]whatIF? Consulting, Harwell, UK

5:05 PM 75 **AWARENESS, SUSCEPTIBILITY, AND USE OF NICOTINE POUCHES AMONG A PROBABILITY-BASED SAMPLE OF UNDERAGE SUBJECTS IN THE UNITED STATES.** Andrea PATTON, Gabriel Barnard, Neil Mckeganey; Centre for Substance Use Research, Glasgow, UK

80 **THE EFFECTS OF ELECTRONIC CIGARETTE USE PATTERNS ON HEALTH RELATED SYMPTOM BURDEN AND QUALITY OF LIFE: ANALYSIS OF US PROSPECTIVE LONGITUDINAL COHORT STUDY DATA.** Xiaona LIU[1], Yue Cao[1], Jiaxuan Li[1], Xi Chen[1], Yuming Xiong[1], Fangzhen Zheng[1], Jianqiang Zhang[1], Xiaona Liu[1], Xuxi Zhang[2], Xinying Sun[2], Ian M. Fearon[3]; [1]Smoore Research Institute, Shenzhen, Guangdong, China, [2]Peking University, Beijing, China, [3]whatIF? Consulting, Harwell, UK

5:25 PM 76 **DERIVATION OF EXCESS LIFETIME CANCER RISK FOR NON-COMBUSTIBLE NICOTINE PRODUCTS.** Ramez LABIB; Consilium Sciences, Glen Allen, PA, USA

ADJOURN

TUESDAY, SEPTEMBER 10, 2024
TECHNICAL PROGRAM

		Panel Discussion *Session Chairs: Rachael Schmidt & Lillian Ortega*		**Session B: Agronomy** *Session Chair: Collin Fisher*
8:45 AM		Welcome Remarks		Welcome Remarks
8:50 AM	81	**ADVANCING SCIENCE-BASED CONSENSUS STANDARDS FOR NICOTINE POUCHES IN THE U.S: PATHWAY TO REGULATORY AND PUBLIC HEALTH SYNERGY.** Cliff Watson; CDC, Atlanta, GA USA Donna Smith; Altria Client Services, Richmond, VA USA Salome Bhagan; CTP/ Office of Science, Washington, DC, USA Johan Lindholm; Swedish Match, Stockholm, Sweden Markus Lindblad; HayPP Group, Stockholm, Sweden	82	**THE ROOTS OF LOW ALKALOID TOBACCO PROBABLY DETERMINE ITS POOR LEAF QUALITY.** Barunava PATRA, C. Fisher, SK. Singh, J. Kinney; University of Kentucky, Lexington, KY, USA
9:10 AM		**Panel Discussion & Audience Q&A (continue)**	83	**STACKING A NOVEL LOW NICOTINE GENE WITH THE LA NIC1NIC2 MUTANTS LOWERS NICOTINE TO ULTRA-LOW LEVELS.** Anne FISHER[1], Stacey Slone[1], Barunava Patra[1], Colin Fisher[1], Huihua Ji[1], Jeffrey Kinney[1], Shengming Yang[2]; [1]University of Kentucky, Lexington, Kentucky, USA, [2]US Dep. of Agriculture, Fargo, ND, USA

9:30 AM		**Panel Discussion & Audience Q&A (continue)**	84	**UNDERSTANDING THE MOLECULAR MECHANISM UNDERLYING LOW ALKALOID ACCUMULATION IN A MUTANT BURLEY BREEDING LINE WITH NOVEL SPONTANEOUS MUTATION(S).** Barunava PATRA, A. Fisher, S.K. Singh, J. Kinney; University of Kentucky, Lexington, KY, USA
9:50 AM		**Panel Discussion & Audience Q&A (continue)**	85	**POST TRANSLATIONAL REGULATION OF NICOTINE BIOSYNTHESIS BY MAP KINASE CASCADE NTMEKK1B-NTMKK2A-NTMPK4.** Yan ZHOU, Yongliang Liu, Sitakanta Pattanaik, Barunava Patra, Ruiqing Lyu, Huihua Ji, Sanjay Singh, Ling Yuan; University of Kentucky, Lexington, KY, USA
10:10 AM		***BREAK***		
		Session A: ENDS Use Behavior *Session Chair: Josh Karelitz*		**Session B: Method or Process Development** *Session Chair: Jesse Phillips*
10:30 AM		Welcome Remarks		Welcome Remarks
10:35 AM	86	**ACTUAL EXPERIENCE CONDUCTING ACTUAL USE STUDIES: NOTES FROM THE FIELD ON EFFECTIVE LONGITUDINAL TRIALS.** Christopher FLEURY, Victoria Hoverman; Ipsos-Insight, Washington, DC, USA	91	**DETERMINATION OF ORGANIC ACIDS IN ENDS PRODUCTS BY GC-MS USING ALKYL CHLOROFORMATE DERIVATIZATION IN AQUEOUS SOLUTION.** Andrew CHEETHAM; Mckinney Specialty Labs, Richmond, VA, USA

10:55 AM 87 **PERSON-CENTERED APPROACHES TO UNDERSTAND CIGARETTE SWITCHING AND CIGARETTE REDUCTION RATES IN ACTUAL USE STUDIES.** Ian JONES, Jessica Zdinak, Kiri Li Stauch; Applied Research and Analysis Company, Richmond, VA, USA

92 **DETERMINATION OF NICOTINE IN OTDN AND LIQUID PRODUCTS BY UV-VIS SPECTROPHOTOMETRY.** Seok Chan PARK, Fadi Aldeek; Altria Client Services, Richmond, VA, USA

11:15 AM 88 **A RANDOMIZED EXPERIMENTAL STUDY TO ASSESS THE EFFECTS OF FLAVORED E-LIQUID PRODUCTS ON ADULT SMOKERS SWITCHING CIGARETTE CONSUMPTION BEHAVIORS.** Jessica ZDINAK[1], Ian Jones[1], Kiri Li Stauch[1], Willie McKinney[2]; [1]Applied Research and Analysis Company, Richmond, VA, USA, [2]McKinney Regulatory Science Advisors, Richmond, VA, USA

93 **GAS PHASE INFRARED SPECTROSCOPY ENABLES PUFF-BY-PUFF PROFILING OF A NOVEL HEATED TOBACCO CAPSULE (HTC) PROTOTYPE.** Frank HIGGINS, Michael B. Brown, Zack W. Blackmon, Matt Melvin, Weiling Li, Yezdi B. Pithawalla; Altria Client Services, Richmond, VA, USA

11:35 AM 89 **MENTHOL, BLUEBERRY, AND WATERMELON NJOY ACE PROMOTES SIGNIFICANTLY GREATER COMPLETE SWITCHING COMPARED TO TOBACCO-FLAVORED NJOY ACE.** Kate VERGARA, Elizabeth Becker, Hui Chen; Altria Client Services, Richmond, VA, USA

94 **NON-TARGETED CHEMICAL ANALYSIS - TRANSITIONING FROM RESEARCH TO ROUTINE APPLICATIONS.** Mark CROSSWHITE, Roxana Weil, Willie McKinney; McKinney Regulatory Science Advisors, Richmond, VA, USA

11:55 AM 90 **SIX-WEEK ACTUAL USE STUDY TO EVALUATE THE EFFECT OF THE JUUL2 SYSTEM ON CIGARETTE SMOKING AND TOBACCO PRODUCT USE BEHAVIORS AMONG ADULTS WHO SMOKE CIGARETTES IN THE UNITED STATES.** Nicholas GOLDENSON[1], Saul Shiffman[2], Ryan Black[1]; [1]Juul Labs, Inc, Washington, DC, USA, [2]PinneyAssociates, Pittsburgh, PA, USA

95 **ANALYSIS OF THE FULL COMPOSITION OF HEATED TOBACCO AEROSOLS BASED ON LARGE VOLUME THERMAL INJECTION-COLUMN INTERNAL EVAPORATION CONCENTRATION.** LI Junjie, Fei Ting, Qi Dawei, Cheng Qian, Zhang Wei, Wu Da; Shanghai Tobacco Group of CNTC, Shanghai, China

12:15 PM ***LUNCH***

1:00 PM **POSTER SESSION:** 41-70 (listing on page 22)

		Panel Discussion *Session Chair:* *Mark Forster*		**Session B: Product Characterization I** *Session Chair:* *Andrew Cheetham*
2:30 PM		Welcome Remarks		Welcome Remarks
2:35 PM	96	**TOBACCO HARM REDUCTION SUCCESS STORIES: HOW COUNTRIES ARE EMBRACING SMOKELESS ALTERNATIVES AND THEIR IMPACT ON SMOKING.** Karl Fagerström; Fagerström Consulting, Stockholm, Sweden Marewa Glover; Centre of Research Excellence: Indigenous Sovereignty & Smoking, Auckland, New Zealand Derek Yach; Global Health Strategies, Connecticut, USA	97	**A PRACTICAL FRAMEWORK FOR NOVEL ENDS EVALUATION: CHEMICAL AND TOXICOLOGICAL CHARACTERIZATION OF JUUL2 AEROSOL AND COMPARISON WITH REFERENCE CIGARETTES.** David COOK, Michael J. Oldham, Jiaming Wang, Austin Bates, Christina Sulaiman, Karen Carter, Candice Jongsma, I. Gene Gillman; Juul Labs, Inc, Washington, DC, USA
2:55 PM		**Panel Discussion & Audience Q&A (continue)**	98	**TARGETED CHARACTERIZATION OF THE CHEMICAL COMPOSITION OF NOVEL JUUL SYSTEM'S AEROSOL AND COMPARISON WITH KENTUCKY REFERENCE CIGARETTES AND ENDS.** Karen CARTER, D.K. Cook, J. Wang, A.L. Bates, C. Smith, I.G. Gillman; Juul Labs, Inc, Washington, DC, USA

3:15 PM	**Panel Discussion & Audience Q&A (continue)**	99	**EXPANDED TARGETED CHARACTERIZATION OF THE CHEMICAL COMPOSITION OF JUUL SYSTEM'S AEROSOL AND COMPARISON WITH KENTUCKY REFERENCE CIGARETTES.** Candice JONGSMA, Karen Carter, David K. Cook, Jiaming Wang, I. Gene Gillman; Juul Labs, Inc, Washington, DC, USA
3:35 PM	**Panel Discussion & Audience Q&A (continue)**	100	**ACCELERATED AGING OF PROPYLENE GLYCOL AND GLYCEROL IN THE PRESENCE OF ORGANIC ACID AND NICOTINE.** Norman FRALEY, Anastasia Lioubomirov, I. Gene Gillman; Juul Labs, Inc, Washington, DC, USA
3:55 PM	**Panel Discussion & Audience Q&A (continue)**	101	**EVALUATION OF NICOTINE DEGRADANTS IN TOBACCO PRODUCTS INTENDED FOR ORAL CONSUMPTION.** Joseph JABLONSKI, Andrew G. Cheetham; Mckinney Specialty Labs, Richmond, VA, USA
4:15 PM	***BREAK***		

4:35 PM		102	**THE IMPACT OF PRINTED CIGARETTE PAPER ON PERMEABILITY AND DIFFUSION CHARACTERISTICS.** Michael LINDNER; Tann Holding, Traun, Austria
4:55 PM		103	**A CHALLENGE FOR ROUTINE SENSORY EVALUATION: INSTRUMENTATION AND DATA ANALYTICAL MODELS FOR SENSORY PREDICTIONS.** Ian TINDALL, Reddy Selvan, Laimon Hamzah; Cerulean, Milton Keynes, Buckinghamshire, UK
5:15 PM	**BUSINESS MEETING (SESSION B, RAVINIA A-C):** All conference attendees are encouraged to attend.		
6:00 PM	***ADJOURN***		
6:30 PM	**COCKTAIL HOUR AND AWARDS BANQUET**		

WEDNESDAY, SEPTEMBER 11, 2024
TECHNICAL PROGRAM

		Session A: Clinical Studies & Biomarkers *Session Chair: Ian Fearon*		**Session B: Agronomy II** *Session Chair: Anne Fisher*
8:45 AM		Welcome Remarks		Welcome Remarks
8:50 AM	104	**APPLICATION OF BIOMARKERS OF EXPOSURE AS COMPLIANCE MEASURES IN LONG-TERM AND EPIDEMIOLOGICAL STUDIES OF NEW NICOTINE AND TOBACCO PRODUCTS.** Max SCHERER; Abf Analytisch-Biologisches Forschungslabor, Planegg, Bavaria, Germany	108	**SULFUR AND CHLORIDE FERTILIZATION IMPACT ON BURLEY TOBACCO GROWTH, YIELD AND LEAF CHEMISTRY.** Bob PEARCE, Tara Valentine, Natalia Martinez, Magdalena Ricciardi; University of Kentucky, Lexington, KY, USA
9:10 AM	105	**ENDS-INDUCED HEAVY METAL EXPOSURE AND OXIDATIVE INJURY IS MEDIATED BY VAPING BEHAVIOR.** Maureen MEISTER[1], Xiaojia He[2], Jennifer Jeon[2], Patrick Chepaitis[2], Qian Zhang[2], Mark Wilson[2], Marilyn Black[2], Christa Wright[2], Akshanda Shinde[3], Jonathan Shannahan[3], Pam Cushenan[4], Scott Weaver[4], Ruiyan Luo[4]; [1]UL Research Institutes, Marietta, GA, USA, [2]Chemical Insights Research Institute, Marietta, GA, USA, [3]Purdue University, West Lafayette, IN, USA, [4]Georgia State University, Atlanta, GA, USA	109	**DISTRIBUTION OF TOBACCO CONSTITUENTS PON AND NNK IN CURED BURLEY TOBACCO LEAF TISSUE.** Ying WU, Huihua Ji; University of Kentucky, Lexington, KY, USA

9:30 AM 106 **POTENTIAL INSIGHTS FROM REVERSE DOSIMETRY FOR IN VITRO ENDS TESTING.** Michael OLDHAM; Juul Labs, Inc, Washington, DC, USA

110 **RESEARCH AND APPLICATION OF KEY TECHNOLOGY FOR NEW MODEL OF SAFETY AND ENVIRONMENTAL PROTECTION STORED-TOBACCO PEST CONTROL IN HIGH-RACK WAREHOUSE.** QU Yongbo[1], Yin Dafeng[1], Xiao Fei[1], Fu Qiuping[1], Zhang Hui[1], Dai Lin[1], Liu Shiwei[2], Liu Xiaoqing[2]; [1] Technology Center Of Hunan Tobacco China Industry Co, Changsha, China, [2] Hunan Huawang Fumigation And Disinfection Co, Changsha, China

9:50 AM 107 **ASSOCIATIONS OF E-CIGARETTE USE PATTERNS WITH THE PREVALENCE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) AND HEART DISEASE AMONG ADULT TOBACCO USERS IN THE UNITED STATES.** Xiaona LIU[1], Yue Cao[1], Jiaxuan Li[1], Xi Chen[1], Yuming Xiong[1], Fangzhen Zheng[1], Jianqiang Zhang[1], Xiaona Liu[1], Ian M. Fearon[2], Xuxi Zhang[3], Xinying Sun[3]; [1]Smoore Research Institute, Shenzhen, China, [2]whatIF? Consulting, Harwell, UK, [3]Peking University, Beijing, China

111 **TOPPING DRIVES ADAPTIVE CHANGES OF TOBACCO ROOT-ASSOCIATED MICROBIOMES.** Peng LU[1], Mengli Gu[1,2], Jingjing Jin[1], Mengmeng Kong[1], Zechao Qu[1], Lingtong Cheng[1], Jianfeng Zhang[1], Peijian Cao[1], Jiemeng Tao[1]; [1] Zhengzhou Tobacco Research Institute of CNTC, Zhengzhou, China, [2]Zhengzhou University, Zhengzhou, China

10:10 AM ***BREAK***

		Session A: Toxicology *Session Chair:* *Katarina Aleksa*		**Session B:** **HTP Use Behavior** *Session Chair:* *Jessica Zdinak*
10:30 AM		Welcome Remarks		Welcome Remarks
10:35 am	112	**IDENTIFYING POTENTIAL ACUTE HEALTH HAZARDS FROM EXPOSURES TO (S)-6-METHYLNICOTINE TO INFORM PRODUCT DEVELOPMENT.** Willie MCKINNEY[1], Marissa Smith[2], Ranulfo Lemus[3], Roxana Weil[1]; [1]Mckinney Regulatory Science Advisors, Henrico, VA, USA, [2]Arivita, Richmond, VA, USA, [3]Letox World, Xenia, OH, USA	117	**ACTUAL USE STUDY OF TOBACCO HEATING SYSTEM 3.0.** Steve ROULET[1], Pierpaolo Magnani[1], Claudia Kanitscheider[2], Chris Freehauf[2], Stacey Bell[2], Eva Jenz[3], Divine Akumo[3], Gerd Kallischnigg[4]; [1]Philip Morris Products, Neuchatel, Neuchatel, [2]Oracle Life Sciences (formerly Cerner Enviza, Munich, Germany), Austin, TX, USA, [3] ZEG - Zentrum fur Epidemiologie und Gesunheitsforschung (Center for Epidemiology and Health Research), Berlin, Germany, [4]ARGUS GmbH, Berlin, Germany
10:55 am	113	**EVALUATION OF THE GENOTOXIC POTENTIAL OF A FLAVORED ORAL NICOTINE POUCH PRODUCT USING INTEGRATED APPROACHES.** Jingjie ZHANG, Richard Morgan, Uktarsh Doshi, Chastain Anderson, Wanyoike Kangethe, Donna Smith, K. Monica Lee (formerly of); Altria Client Services, Richmond, VA, USA	118	**ACTUAL USE STUDY OF MARLBORO HEATED TOBACCO STICK PRODUCTS USED WITH THE PLOOM® HEATED TOBACCO DEVICE AMONG US ADULTS WHO SMOKE COMBUSTIBLE CIGARETTES.** Joshua KARELITZ[1], Nelly Mainy[2], Elizabeth Becker[1]; [1]Altria Client Services, Richmond, VA, USA, [2]JT International SA, Geneva, Switzerland

11:15 AM 114 **ECOTOXICITY EVALUATION OF CIGARETTE BUTTS.** Sandra DE JONGH, Diane Raverdy Lambert; SWM International, Spay, Sarthe, France

119 **PUFF TOPOGRAPHY OF MARLBORO HEATED TOBACCO STICK PRODUCTS USED WITH THE PLOOM® HEATED TOBACCO DEVICE AMONG ADULTS WHO SMOKE COMBUSTIBLE CIGARETTES.** Joshua KARELITZ[1], Kevin Ball[1], Nelly Mainy[2]; [1]Altria Client Services, Richmond, VA, USA, [2]JT International, Geneva, Switzerland

11:35 AM 115 **RESEARCH ON THE RESPIRATORY ABSORPTION PATTERN OF SMOKE AEROSOLS.** WANG Zhuo[1], Zhang Xiaoyu[1], Cui Huapeng[2], Yan Quanping[2], Wen Jianhui[1], Tuo Suxing[1], Wang Zhiguo[1], Liu Wei[1], Du Wen[1]; [1]China Tobacco Hunan Industrial Co of CNTC, Changsha, Hunan, China, [2]Zhengzhou Tobacco Research Institute of CNTC, Zhengzhou, Henan,China

120 **ACTUAL USE OF A HEATED TOBACCO PRODUCT AND CHANGES IN CIGARETTE SMOKING BEHAVIOUR AMONG ADULTS WHO SMOKE IN CZECHIA.** Christopher RUSSELL[1], Gabriel Barnard[2], Neil Mckeganey[2], Venus Marza[2], Sophie Notley[2], Martin Fitzpatrick[3], Matthew Stevenson[3], Layla Malt[3], Thomas Nahde[4]; [1]Russell Burnett Research & Consultancy, Glasgow, UK, [2]Centre For Substance Use Research, Glasgow, UK, [3]Imperial Brands, Bristol, UK, [4]Imperial Brands Reemtsma, Hamburg, Germany

11:55 PM 116 **IN VITRO TOXICOLOGICAL EVALUATION OF CIGARETTE BASED ON AIRWAY ORGANOIDS.** TIAN Yushan[1], Lu Peng[1], Li Xiao[1,2,3], Wang Xianglong[1,2,3], Wang Hongjuan[1,2,3], Fu Yaning[1,2,3], Han Shulei[1,2,3], Chen Huan[1,2,3], Hou Hongwei[1,2,3], Hu Qingyuan[1]; [1]China National Tobacco Quality Supervision & Test Center, Zhengzhou, China, [2]Beijing Life Science Academy, Beijing, China, [3]Key Laboratory of Tobacco Biological Effects, Zhengzhou, China

121 **STRUCTURAL EQUATION MODELING FOR ADVANCED INSIGHT FROM BEHAVIORAL SURVEYS.** Ryan SELTZER; Safety in Numbers, Tucson, AZ, USA

12:15 PM ***LUNCH***

Session A: Product Characterization II
Session Chair: Clarissa Tatum

Session B: Agronomy III
Session Chair: Huihua Ji

1:15 PM Welcome Remarks

Welcome Remarks

1:20 PM 122 **ANALYSIS OF HEATED BOTANICAL SUBSTRATE AEROSOL EMISSIONS COMPARED TO A HEATED TOBACCO PRODUCT.** Stéphane DEJOIE, C. Rigoulay, N. Durot, O. Brenner, D. Raverdy-Lambert; SWM c/o LTR Industries, Allonnes, France

124 **TIME SERIES TRANSCRIPTIONAL LANDSCAPE OF TOBACCO LEAVES IN RESPONSE TO HERBIVORE AT SINGLE-CELL RESOLUTION.** Huan SU[1] Lingtong Cheng[1], Jiemeng Tao[1,2], Peng Lu[1,2], Jianfeng Zhang[1,2], Peijian Cao[1,2], Jingjing Jin[1,2]; [1]Zhengzhou Tobacco Research Institute of CNTC, Zhengzhou, China, [2]Beijing Life Science Academy, Beijing, China

1:40 PM 123 **ACCELERATED SHELF-LIFE METHOD FOR HEATED BOTANICAL SUBSTRATE CONTAINING NICOTINE.** Nathalie DUROT, D. Raverdy-Lambert, S. Dejoie, C. Rigoulay, O. Brenner; Ltr Industries C/O Swm Usine Le Mans France

125 **THE INTERACTIONS BETWEEN ETHIOPIAN TOBACCO BUSHY TOP VIRUS AND ITS SATELLITE RNA OR AN UNRELATED SATELLITE RNA.** MO Xiaohan[1], Zhao Xingneng[1,2,3], Zhang Wei[1,4], Zhang Lifang[1,2], Xu Ping [1,2], Li Yanqiong[1,2], Yu Qing[1], Yu Min[4], Chen Hairu[2]; [1]Yunnan Academy of Tobacco Agricultural Science, Kunming, Yunnan, China, [2]Yunnan Agricultural University, Kunming, Yunnan, China, [3] Wenshan Branch of Yunnan Tobacco Company, Wenshan. Yunnan, China, [4]College of Life Sciences, Yunnan University, Kunming, Yunnan, China

2:00 PM 126 **PREPARATION OF PH-RESPONSIVE DSRNA DELIVERY SYSTEM BASED ON BOVINE SERUM ALBUMIN FOR PEST CONTROL WITH HIGH RNAI EFFICIENCY.** Chuantao XU[2], Chenyu Su[1], Meixue Sun[1], Jingfang Cun[1], Robert I. Graham[3], Zhang Yonghui[2], Xie Qiang[2], Xiufang Wang[1], Hao Zong[4], Yingjie Liu[5]; [1]Tobacco Research Institute of Chinese Academy of

			Agricultural Sciences, Qingdao, China, [2]Luzhou City Company of Sichuan Province Tobacco Company, Luzhou, China, [3]SRUC, Aberdeen, UK, [4] Shandong Tobacco Company, Linyi, China, [5] Staff Development Institute of China National Tobacco Corporation, Zhengzhou, China
2:20 PM		127	**EFFECTS OF ACTIVE COMPOUNDS EXTRACTED FROM CITRUS FRUITS ON THE QUALITY OF CIGAR TOBACCO LEAVES DURING FERMENTATION.** HU Wanrong, Yang Zhen, Cao Yu, Jia Yun, Liu Lulu, Li Dongliang; China Tobacco Sichuan Industrial Co, Chengdu, Sichuan, China

CONFERENCE ADJOURNS

POSTERS

7. **DISSOLUTION AND PHYSICAL CHARACTERIZATION OF ORAL NICOTINE PRODUCTS.** Akchara SRIRAM, Sean P. Platt, Christa Gonzales, Pashupati Pokharel, Seok Chan Park, Steven B. Thorpe, Abaigeal Ritenthler, Fadi Aldeek; Altria Client Services, Richmond, VA, USA

8. **AN EFFICIENT ROUTINE METHOD FOR THE DETERMINATION OF OXIDES OF NITROGEN IN SIDESTREAM SMOKE OF CIGARETTES BY ONLINE CHEMILUMINESCENCE MEASUREMENT.** Thomas SCHMIDT, Frank Kraemer, Katrin Schade, Beata Kowalski; Körber Technologies Instruments Gmbh, Hamburg, Hamburg, Germany

9. **A SIMPLIFIED MEASUREMENT METHOD FOR CLASSIFICATION OF E-CIGARETTES.** Thomas SCHMIDT, Frank Kraemer, Katrin Schade, Alexander Kitta; Körber Technologies Instruments Gmbh, Hamburg, Hamburg, Germany

10. **PERCEPTIONS OF RISK OF THE MARLBORO HEATED TOBACCO STICK PRODUCTS USED WITH THE PLOOM® HEATED TOBACCO DEVICE AMONG US ADULTS.** Jennifer LEWIS[1], Nelly Mainy[2], Elizabeth Becker[1]; [1]Altria Client Services, Richmond, VA, USA, [2]JT International SA, Geneva, Switzerland

11. **BEHAVIORAL INTENTIONS FOR USING MARLBORO HEATED TOBACCO STICK PRODUCTS WITH THE PLOOM® HEATED TOBACCO DEVICE AMONG US ADULTS.** Jennifer LEWIS[1], Jonathan Gallegos[1], Nelly Mainy[2], Elizabeth Becker[1]; [1]Altria Client Services, Richmond, VA, USA, [2]JT International SA, Geneva, Switzerland

12. **A RANDOMIZED STUDY EVALUATING THE IMPACT OF ENDS ADVERTISING AND PROMOTIONAL MATERIALS ON USE INTENTIONS AMONG ADULTS WHO SMOKE AND NON-TOBACCO USERS.** Nicholas GOLDENSON[1], Stacey A. McCaffrey[1], Saul Shiffman[2]; [1]Juul Labs, Inc, Washington, DC, USA, [2]Pinney Associates, Bethesda, MD, USA

13 **STABILITY OF CERTIFIED REFERENCE CIGARS DURING LONG-TERM STORAGE.** Huihua JI, Zhenyu Jin, Laura Fenton; University Of Kentucky, Lexington, KY, USA

14 **EXTRACTABLES TESTING OF FLEECE MATERIAL USED IN MODERN ORAL NICOTINE POUCHES.** Ed CARMINES[1], Chris Woodruff[1], Lise Fraissinet[1], Scott Crekmur[2], Tom Barrett[2]; [1]Chemular, Scottsdale, AZ, USA, [2]Legend Technical Services, St Paul, MN, USA

15 **WHITE FOX 4 MG NICOTINE POUCH PRODUCTS ARE BIOEQUIVALENT TO 4 MG NICORETTE GUM.** Ed CARMINES[1], Karen Carmines[1], Lise Fraissinet[1], Naama Levy-Cooperman[2], Ryan Seltzer[3]; [1]Chemular, Scottsdale, AZ, USA, [2]Altreos Research Partners Inc, Toronto, Canada, [3]Safety in Numbers, Tucson, AZ, USA

16 **IN VITRO TOXICOLOGICAL ASSESSMENT OF WHITE FOX MODERN ORAL NICOTINE POUCH PRODUCTS.** Manoj MISRA, Ed Carmines, Chris Woodruff, Lise Fraissinet; Chemular Regulatory Consulting, Hudson, MI, USA

17 **HPHC ANALYSIS OF WHITE FOX MODERN ORAL NICOTINE POUCH PRODUCTS.** Manoj MISRA, Ed Carmines, Chris Woodruff, Lise Fraissinet; Chemular Regulatory Consulting, Hudson, MI, USA

18 **INTENTIONS TO USE DATA AND PREVALENCE ESTIMATES FOR NJOY ACE® DEMONSTRATE LOW LIKELIHOOD OF USE FOR ADULT NEVER SMOKERS AND UNDERAGE INDIVIDUALS.** Kate VERGARA, Nadja Richter, Andrea Vansickel; Altria Client Services, Richmond, VA, USA

19 **RISK PERCEPTIONS AND MISPERCEPTIONS OF NJOY ACE® 2.0 BLE ENDS PRODUCTS AMONG ADULTS 21+ WHO SMOKE COMBUSTIBLE CIGARETTES.** Kate VERGARA, Brandon Newmyer; Altria, Richmond, VA, USA

20 **ASSESSMENT OF THE ADVERSE EFFECTS OF REPEATED 28-DAY HEATED TOBACCO PRODUCTS (HTPS) EMISSION INHALATION EXPOSURE IN RATS.** Jinhee KIM[1], Su-Hyun Choi[1], Mi Jin Yang[1], Kyung-Chul Choi[2], Dohee Ahn[2], Bumseok Kim[3], Min-Seok Kim[1]; [1]Korea Institute of Toxicology, Jeongeup, Jeonbuk, Korea, [2]Chungbuk National University, Cheongju, Chungbuk, Korea, [3]Jeonbuk National University, Iksan, Jeonbuk, Korea

21 **EVALUATION OF NICOTINE, ACETALDEHYDE, CROTONALDEHYDE, AND FORMALDEHYDE LEVELS IN SMOKELESS TOBACCO PRODUCTS OBTAINED AT DIFFERENT PROCUREMENT TIMES.** Selvin EDWARDS[1], Matthew D. Hassink[1], An T. Vu[1], Kenneth M. Taylor[2]; [1]Center for Tobacco Products, Food and Drug Administration, Silver Spring, Maryland, USA, [2]Center for Veterinary Medicine, Food and Drug Administration, Laurel, MD, USA

22 **ACTUAL USE STUDY OF THE P4M3 GEN 2.0 CLOSED-END ELECTRONIC NICOTINE DELIVERY SYSTEM.** Steve ROULET[1], Claudia Kanitscheider[2], Pierpaolo Magnani[1], Aurelie Formey-Leichti[1], Alexandre Soulan[1], Felix Marckzykowski[2], Laura Marquis[2], Kelly Peters[3], Gerd Kallischnigg[4]; [1]Philip Morris Products, Neuchatel, Neuchatel, Switzerland, [2]Oracle Life Sciences, Munich, Germany (formerly Cerner Enviza), [3]Oracle Life Sciences, Austin, TX, USA (formerly Cerner Enviza), [4]ARGUS, Berlin, Germany

23 **PRODUCT PERCEPTION AND INTENTION STUDY OF THE P4M3 GEN 2.0 CLOSED-END ELECTRONIC NICOTINE DELIVERY SYSTEM.** Steve ROULET[1], Pierpaolo Magnani[1], Medy Ehtesham[1], Alexandre Soulan[1], Sarah Farnsworth[2], Eva DeJong[2]; [1]Philip Morris Products, Neuchatel, Switzerland, [2]PEGUS Research, Salt Lake City, UT, USA

24 **MODIFIED ANALYTICAL METHOD FOR THE ANALYSIS OF TOXIC METALS IN E-CIGARETTE AEROSOLS.** Naudia GRAY, R.S. Pappas; Centers for Disease Control and Prevention, Atlanta, GA, USA

25 **SWITCHING BEHAVIORS AND USE PATTERNS OF A NOVEL NICOTINE POUCH PRODUCT AMONG ADULTS WHO USE DIP OR SNUFF: RESULTS FROM AN ACTUAL USE STUDY.** Hui CHENG; Altria Client Services, Richmond, VA, USA

26 **XAD-4 RESIN AS AN ALTERNATIVE TRAPPING MATERIAL IN DETERMINATION OF SEMI-VOLATILE COMPOUNDS (SVCS) IN AEROSOL OF HEATED TOBACCO PRODUCT (HTP) USING GC-MS.** Linda ERLIA SARI, Eka Pria Utama Mulyana, Ilham Fadila Ramadhan; Filtrona Manufacturing Indonesia, Surabaya, East Java, Indonesia

27 **CHARACTERIZING AEROSOL TEMPERATURE OF ELECTRONIC NICOTINE DELIVERY SYSTEMS (ENDS) AND HEATED TOBACCO PRODUCTS (HTPS) USING WET-BULB TEMPERATURE APPROACH.** Pavel KOSACHEVSKY[1], Bonnie G. Coffa[1,2]; [1]Labstat International, Kitchener, ON, Canada, [2]Toxpharm, Mechanicsville, VA, USA

28 **COMPARATIVE ANALYSIS OF HEATED TOBACCO PRODUCTS AND 1R6F REFERENCE CIGARETTE RESPONSES IN TK6 AND CHO CELL LINES UTILIZING HIGH THROUGHPUT FLOW CYTOMETRY AND MANUAL COUNTING FOR THE IN VITRO MICRONUCLEUS ASSAY.** Katarina ALEKSA, Dong Ma, Bonnie Coffa; Labstat International, Kitchener, ON, Canada

29 **Withdrawn**

30 **EVALUATION OF ENVIRONMENTAL EMISSIONS FROM GLO HEATED TOBACCO PRODUCTS AND COMBUSTIBLE CIGARETTES.** Milly KANOBE, John Darnell, Tao Jin, Jeff Coffield, Brian M. Keyser, Patrudu Makena, Sarah A. Baxter, Kristen G. Jordan, Gary M. Dull (formerly of), Buddy Brown (retired); RAI Services Company, Winston-Salem, NC, USA

31 **LONG-TERM SAFETY SURVEILLANCE EXPERIENCE WITH TOBACCO HEATING SYSTEM PRODUCTS.** Brindusa TARANU, Virginie Schaub, Marina Suvakov; Philip Morris Products, Neuchatel, Switzerland

32 **NO MEANINGFUL EFFECT OF PROMOTIONAL MATERIALS FOR A NOVEL ORAL NICOTINE POUCH PRODUCT ON BEHAVIORAL INTENTIONS AND RISK PERCEPTIONS.** Sade JOHNS; Altria Client Services, Elkridge, MD, USA

33 **RELEASE PROFILES FROM SELECT MODERN ORAL NICOTINE PRODUCTS.** Jake HENKIE, Rebecca Cornelius, Cosmin Stoicoiu, Angel Rodriguez-Lafuente, Leona Mijangos Sirkisoon, Andy Stinson; Labstat International, Kitchener, ON, Canada

34 **HEALTHCARE PROVIDERS' AWARENESS AND TRUST OF THE UNITED STATES FOOD AND DRUG ADMINISTRATION FOR REGULATING TOBACCO AND NICOTINE-CONTAINING PRODUCTS.** Deena BATTISTA[1], Susan Martelle[2], Michael Polster[3]; [1]Womble Bond Dickinson, Winston-Salem, NC, USA, [2]RAI Services Company, Winston-Salem, NC, USA, [3]Naxion, Philadelphia, PA, USA

35 **CHARACTERIZATION OF NICOTINE PHARMACOKINETICS AND SUBJECTIVE EFFECTS DURING USE OF HEATED TOBACCO PRODUCTS IN ADULTS WHO SMOKE.** Jesse Rensch[1], Jeffery Edmiston[1], Jingzhu Wang[1], Jianmin Liu[1], Mohammad Bazargan[1], Brian Nordskog[2], Kyung Soo HONG[1]; [1]Altria Client Services, Richmond, VA, USA, [2]JT International, Geneva, Switzerland

36 **UTILIZING THE ELECTRONIC TRIAL MASTER FILE FOR CLINICAL STUDIES TO SUPPORT FDA TOBACCO PRODUCT APPLICATIONS.** Jeffrey COFFIELD, Claude Cavallo, Heather Green, Ken Szeliga; RAI Services Company, Winston-Salem, NC, USA

37 **MODELING THE POPULATION HEALTH IMPACT OF FLAVOR VARIETY AND POTENTIAL RISK OF YOUTH INITIATION RESULTING FROM THE MARKETING OF AN ORAL NICOTINE POUCH PRODUCT.** Thad HANNEL, Lai Wei, Yisha He, Raheema Muhammad-Kah, Ed Largo, Mohamadi Sarkar; Altria Client Services, Richmond, VA, USA

38 **THREE-DIMENSIONAL STRUCTURE-PROPERTY RELATIONSHIP OF REFINED FILTER MEMBRANES FROM TOBACCO EXTRACTS BASED ON HIGH-RESOLUTION CT SCANNING AND DEEP LEARNING.** Mingjing GUAN[1], Zhang Jin[1], Zhou Shun[1], Zhang Xiaoyu[1], Wang Xiaofeng[1], Cao Yun[1], Tian Huijuan[1], Ding Naihong[1], Li Yanyan[1], Chen Weijian[1], Li Lu[1], Fu Shuo[1], Yang Dahai[2], Song Xiaohui[2]; [1]China Tobacco Anhui Industrial of CNTC, Hefei, China, [2]Hefei University of Technology, Hefei, China

39 **GENERATION OF A BHAS 42 CELL TRANSFORMATION ASSAY HISTORICAL DATABASE.** Shannon W. BRUCE, Michelle L. Klug LaForce, Sandra D. Springer, Amanda Fernandez, Wannie Madraymootoo; Inotiv, Rockville, MD, USA

40 **MARKET MAP SURVEY OF HEATED TOBACCO PRODUCTS FOR HARMFUL AND POTENTIALLY HARMFUL CONSTITUENTS.** Irfan GUNDUZ, Jerome King, Cyril Jeannet, David Gosh; Philip Morris Products, Neuchatel, Switzerland

41 **OPTIMIZATION OF EXTRACTION AND IN VITRO EVALUATION OF MARKET NICOTINE GUMS.** Sara HURTADO, Yevgeniya V. Prepelitskaya, Fadi Aldeek, Utkarsh Doshi U., John H. Miller, Kyeonghee M. Lee; Altria Client Services, Richmond, VA, USA

42 **VELO NICOTINE POUCH USE BEHAVIORS AND SMOKING REDUCTION AMONG US ADULT SMOKERS WITH AND WITHOUT INTENTIONS TO QUIT SMOKING.** Tiffany PARMS, Sarah Ayoku, Patrudu Makena; RAI Services Company, Winston-Salem, NC, USA

43 **TOPOGRAPHY STUDY OF GLO HYPER, A TOBACCO HEATED PRODUCT.** Brian KEYSER, Tiffany A. Parms, Robert Underly, Tao Jin, Kristen Prevette, Meghan De Young, John Darnell, Kristen Jordan, Sarah Baxter-Wright; RAI Services Company, Winston-Salem, NC, USA

44 **Withdrawn**

45 **Withdrawn**

46 **AWARENESS AND USE PATTERNS OF ORAL NICOTINE POUCHES AMONG REPRESENTATIVE UNDERAGE SAMPLES IN THE UNITED STATES.** Evan WINIGER, Nadja Richter, Pavel Lizhnyak; Altria Client Services, Richmond, VA, USA

47 **DEVELOPMENT OF METHODS TO ASSESS PUFF TOPOGRAPHY OF HEATED TOBACCO STICK PRODUCTS USED WITH THE PLOOM® HEATED TOBACCO DEVICE AMONG US ADULTS WHO SMOKE COMBUSTIBLE CIGARETTES.** Kevin BALL[1], Nelly Mainy[2], Brian Nordskog[2], Jianmin Liu[1], Kyung Soo Hong[1], Jeffery Edmiston[1], Joshua Karelitz[1]; [1]Altria Client Services, Richmond, VA, USA, [2]JT International, Geneva, Switzerland

48 **ANALYSIS AND COMPARISON OF NICOTINE PHARMACOKINETICS OF MODERN ORAL NICOTINE POUCHES.** Kara KEETON, Alex Blanchette, Stacey M. Benson, Amy K. Madl; Valeo Sciences, Ladera Ranch, CA, USA

49 **CHARACTERIZATION AND COMPARISON OF TOBACCO-FREE POUCHES AGAINST TRADITIONAL TOBACCO REFERENCE PRODUCTS.** Andy STINSON, Leona Mijangos Sirkisoon, Angel Rodriguez-Lafuente, Hongxia Li, Rana Tayyarah; Labstat International, Kitchener, ON, Canada

50 **CHANGES IN BIOMARKERS OF EXPOSURE AMONG ADULT CIGARETTE SMOKERS WHO TRANSITIONED TO ENDS USE OR QUIT SMOKING: THE POPULATION ASSESSMENT OF TOBACCO AND HEALTH STUDY, 2013-2019.** Paul LIZHNYAK, Hui Cheng, Mingda Zhang; Altria Client Services, Richmond, VA, USA

51 **Withdrawn**

52 **Withdrawn**

53 **CHARACTERIZATION OF VOLATILES FROM HEATED REFERENCE CIGARETTES 3R4F USING THERMAL SEPARATION PROBE-GC/MS.** Antoaneta MIHAYLOVA-KROUMOVA, George J. Wagner, Victor D. Korenkov; University of Kentucky, Lexington, KY, USA

54 **COMPARISON OF POLYCYCLIC AROMATIC HYDROCARBON QUANTITIES AND YIELDS IN FILLER AND SMOKE AMONG SELECT CIGAR PRODUCTS.** Aireen ROMU, Rachel Lerebours, Mimy Young, Tricia Johnson, Charles Feng; Food and Drug Administration, Silver Spring, MD, USA

55 **PHARMACOKINETICS, PHARMACODYNAMICS, AND NICOTINE EXTRACTION IN A NOVEL NICOTINE POUCH PRODUCT COMPARED TO TRADITIONAL MOIST SNUFF.** Mikael STAAF, Camilla Pramfalk, Anna Masser, Tryggve Ljung, Robert Pendrill, Johan Lindholm; Swedish Match, Stockholm, Sweden

56 **A CROSS-SECTIONAL SURVEY OF HEALTHCARE PROVIDER AWARENESS AND PERCEPTIONS OF TOBACCO AND NICOTINE-CONTAINING PRODUCTS.** Susan MARTELLE[1], Deena Battista[2], Michael Polster[3]; [1]RAI Services Company, Winston-Salem, NC, USA, [2]Womble Bond Dickinson, Winston-Salem, NC, USA, [3]Naxion, Philadelphia, PA, USA

57 **EVALUATING THE IMPACT OF FEDERAL ENFORCEMENT ON THE ILLEGAL ELECTRONIC NICOTINE DELIVERY SYSTEMS (ENDS) MARKET.** Lillian ORTEGA[1], Joslynn Watkins[2], Kevin Burd[3], Bryan Burd[3]; [1]Chemular, Gaithersburg, MD, USA, [2]WOW Solutions, Gaithersburg, MD, USA, [3]Chemular, Hudson, MI, USA

58 **DISSOLUTION TESTING OF WHITE FOX BRAND MODERN ORAL NICOTINE POUCHES.** Ed CARMINES[1], Chris Woodruff[1], Lise Fraissinet[1], Mengliang Bao[2]; [1]Chemular, Hudson, MI, USA, [2]Labstat International, Kitchener, ON, Canada

59 **BLOCKCHAIN TECHNOLOGY – THE SOLUTION TO ILLICIT PRODUCTS AND AGE VERIFICATION.** Ed CARMINES, Bryan Burd, Kevin Burd, Jason Carrigan; Chemular, Scottsdale, AZ, USA

60 **SPECIATION ANALYSIS OF CR(III) AND CR(VI) IN AGED E-LIQUIDS CONTAINING BENZOIC ACID USING IC-ICP-MS.** Prasad LAVISETTY, Darybelle Collins, Alex Pennington, Kathy Humphries, I. Gene Gillman; Juul Labs, Inc, Washington, DC, USA

61 **A SENSITIVE GC–MS/MS METHOD FOR THE QUANTIFICATION OF BENZO[A]PYRENE TETROL IN URINE.** Max SCHERER, F. Pilz, A. Gärtner, G. Scherer, N. Pluym; Abf Analytisch-Biologisches Forschungslabor, Planegg, Bavaria, Germany

62 **DETERMINATION OF AFLATOXINS AND OCHRATOXIN A IN TOBACCO, TOBACCO-FREE PRODUCTS, AND EMISSIONS FROM HEATED TOBACCO PRODUCTS USING A LC-MS/MS.** Hongxia LI, Rebecca Cornelius, Andy Stinson; Labstat International, Kitchener, ON, Canada

63 **ASSESSING AEROSOL PARTICLE SIZE DISTRIBUTION MEASUREMENTS IN ELECTRONIC NICOTINE DELIVERY SYSTEMS.** Brittany MOORE; Reynolds, Winston-Salem, NC, USA

64 **NICOTINE ANALYSIS OF COMMERCIAL FOOD PRODUCTS USING GC-MS-MS AND LC-MS-MS.** Robert Owen BUSSEY, III[1], Joe Kennaday[2]; [1]Reynolds American, Winston-Salem, NC, USA, [2]Eurofins Professional Scientific Services, Winston-Salem, NC, USA

65 **CHANGES IN E-VAPOR HARM PERCEPTION AND RELATED TRANSITION BEHAVIORS AMONG US ADULTS WHO SMOKE: LONGITUDINAL ANALYSIS OF POPULATION ASSESSMENT OF TOBACCO AND HEALTH (PATH) STUDY WAVES 1 TO 6 DATA.** Lai WEI, Raheema Muhammad-Kah, Edward Largo, Maria Gogova, Mohamadi Sarkar; Altria Client Services, Richmond, VA, USA

66 **THE HEATED TOBACCO PRODUCT MARKET.** Phil SAUNDERS, Malcolm Saxton; Broughton Life Sciences, Earby, Lancashire, UK

67 **TOMOGRAPHIC ANALYSIS AND COMPUTER SIMULATION FOR DIFFERENT CIGARETTE FILTERS.** Oxana CHERKAS[1], Diane Raverdy-Lambert[2], Thomas Blin[2]; [1]SWM International, Allonnes, France, [2]SWM, c/o LTR, Usine Le Mans, Allonnes, France

68 **COMPARISON OF METALS CONTENT IN ENDS USING ICP-MS WITH TWO SEPARATE AEROSOL COLLECTION METHODS: ACID WASHED QUARTZ PADS AND FRITTED IMPINGERS.** Donald STOGNER, Emma Willis, Jamil Gray, Cynthia Rohrer; Eurofins Professional Scientific Services, Winston-Salem, NC, USA

69 **APPLICABILITY OF ISO 10993-17:2023 TO EXTRACTABLES AND LEACHABLES FOR THE TOXICOLOGICAL RISK ASSESSMENT OF ENDS PRODUCTS.** Harish CHEVVA, Felix Ayala-Fierro; Juul Labs, Inc, Washington, DC, USA

70 **OPTIMIZATION OF A GC-MS METHOD FOR THE DETERMINATION OF ETHYLENE OXIDE IN HEATED TOBACCO PRODUCT (HTP) AEROSOLS.** Jacqueline COLLINS, Alexandra M. Martin; Mckinney Specialty Labs, Richmond, VA, USA

WORKSHOPS

W1 **CONTEMPORARY WATERPIPES, WATERPIPE ACCESSORIES, AND WATERPIPE TOBACCOS.** John LAUTERBACH; Lauterbach & Associates, Deland, FL, USA

W2 **W2. MIXING DIFFERENT FLAVORED WATERPIPE TOBACCOS: CONSUMER PREFERENCE, MARKETING GIMMICK AND/OR REGULATORY CONUNDRUM?** John LAUTERBACH; Lauterbach & Associates, Deland, FL, USA

W3 **USE OF HEAT MANAGEMENT DEVICES IN CONJUNCTION WITH ELECTRIC HEATERS FOR THE GENERATION OF EMISSIONS FROM WATERPIPE TOBACCOS**. John LAUTERBACH; Lauterbach & Associates, Deland, FL, USA

W4 **ANALYSIS OF COMMERCIAL CIGARS FOR DEVELOPMENT OF DESIGN PARAMETERS FOR REFERENCE CIGARS.** Huihua JI; University of Kentucky, Lexington, KY, USA

W5 **THE HISTORY OF THE CENTER FOR TOBACCO REFERENCE PRODUCTS AND THE ADDITION OF CERTIFIED REFERENCE CIGARS.** Ruth MCNEES; University of Kentucky, Lexington, KY, USA

W6 **DETERMINATION OF CERTIFIED VALUES AND UNCERTAINTIES FOR REFERENCE CIGARS.** Stacey SLONE; University of Kentucky, Lexington, KY, USA

W7 **LONG-TERM SUSTAINABILITY AND FUTURE PLANS FOR THE CENTER FOR TOBACCO REFERENCE PRODUCTS.** Ruth MCNEES; Univesity of Kentucky, Lexington, KY, USA

ABSTRACTS

SYMPOSIUM: TOBACCO HARM REDUCTION: WHAT HAVE WE LEARNED AND HOW DO WE MOVE FORWARD?

In December 2023, FDA CTP published its strategic plan "…which outlines the center's programmatic and workforce initiatives for the next 5 years" (Strategic Plan (fda.gov)). The second goal of CTP's Plan is "Ensure Timely, Clear, and Consistent Product Application Review"" and goes on to state the CTP will develop information for the public and industry about how the appropriate for the protection of the public health (APPH) standard is evaluated by CTP in product review. The fourth goal of CTP's Plan is to "Enhance Knowledge and Understanding of the Risks Associated with Tobacco Product Use", which highlights educating youth and adults who smoke about the risks and relative risks of tobacco product use. During this symposium, we will hear from a diverse range of experts to better understand the potential for FDA authorized smoke free tobacco products in reducing the harm associated with cigarette smoking.

7. DISSOLUTION AND PHYSICAL CHARACTERIZATION OF ORAL NICOTINE PRODUCTS. Akchara SRIRAM, Sean P. Platt, Christa Gonzales, Pashupati Pokharel, Seok Chan Park, Steven B. Thorpe, Abaigeal Ritenthler, Fadi Aldeek; Altria Client Services, Richmond, VA, USA

Oral tobacco derived nicotine (OTDN) pouches have gained popularity in recent years due to their reduced risk potential. A study was conducted to provide a comprehensive analysis of seven commercially available nicotine pouch products, including on!®, Zyn®, Velo®, Dryft®, Rogue™, Volt™, and Loop® nicotine pouches. The assessment parameters include nicotine content, nicotine dissolution rate, particle size, bulk density, solubility, crystallinity, and extract viscosity. The nicotine dissolution profiles showed a faster and equivalent release profile for on!, Zyn, and Rogue, while Velo, Dryft, and Volt nicotine pouches exhibited slower nicotine release profiles. Loop nicotine pouches showed the slowest release among the seven products. Particle size analysis revealed Gaussian-like distributions for on!, Rogue and Zyn and . However, the remaining

products displayed bimodal particle size distributions for the remaining products. Tapped and untapped bulk densities were measured to assess the flowability of the filler in all seven nicotine pouches. Rogue and Loop nicotine pouches exhibited the highest and lowest flowabilities, respectively. Solubility data indicated that Zyn nicotine pouches had the highest percentage of soluble components, whereas Rogue nicotine pouches had the lowest. Rheology results of the nicotine pouches extracted in artificial saliva showed high viscosity for Loop and low viscosity for Volt and Rogue nicotine pouches. All products were found to have crystalline structures with both high and low temperature melting points. The aim of this study was to provide a comprehensive analysis of commercially available OTDN pouch products using a variety of analytical techniques. Results indicate differences and similarities between products, contributing to a better understanding of their physicochemical properties. This study provides valuable insights to enhance knowledge toward the development of OTDN pouch products.

8. AN EFFICIENT ROUTINE METHOD FOR THE DETERMINATION OF OXIDES OF NITROGEN IN SIDESTREAM SMOKE OF CIGARETTES BY ONLINE CHEMILUMINESCENCE MEASUREMENT. Thomas SCHMIDT, Frank Kraemer, Katrin Schade, Beata Kowalski; Körber Technologies Instruments Gmbh, Hamburg, Hamburg, Germany

Currently there is no international standard method for the determination of oxides of nitrogen in sidestream smoke of conventional cigarettes available. The only method published is Health Canada Method T-208 “Determination of Oxides of Nitrogen in Sidestream Tobacco Smoke”. The method describes the consecutive testing of three single test items in three runs.

Therefore, a method for routine testing was developed under consideration of T-208 settings but modified to allow users to analyse up to five test items in a sequential manner using an analytical smoking machine equipped with fishtail chimneys according to ISO 20773 and ISO 20774 by using an online chemiluminescence measurement. The data generated shown a higher repeatability and an improved reproducibility compared to the literature values.

9. A SIMPLIFIED MEASUREMENT METHOD FOR CLASSIFICATION OF E-CIGARETTES. Thomas SCHMIDT, Frank Kraemer, Katrin Schade, Alexander Kitta; Körber Technologies Instruments Gmbh, Hamburg, Germany

The emission generation protocol (vaping regimen) of electronic cigarettes has currently only one standardized vaping regimen, ISO 24197:2022 Vapour products — Determination of e-liquid vaporised mass and aerosol collected mass that is consistent with mouth-to-lungs inhalation. A second vaping regime, prEN 17957 Vapour products - Vaping regime for products intended to be used for direct to lung inhalation is under development and will be published soon because a significant increase in the usage of the devices offering a direct to lung vaping was observed. Due to this a differentiation method is needed for its laboratory testing.

Based on the scientific work and publication of Sebastien Soulet et al. "Highlighting Specific Features to Reduce Chemical and Thermal Risks of Electronic Cigarette Use through a Technical Classification of Devices" a simplified method was developed to differentiate the design of e-cigarettes between MtL (mouth to lung) and DtL (direct to lung) vaping usage and allows the automatically selection of the required smoking regimen.

10. PERCEPTIONS OF RISK OF THE MARLBORO HEATED TOBACCO STICK PRODUCTS USED WITH THE PLOOM® HEATED TOBACCO DEVICE AMONG US ADULTS. Jennifer LEWIS[1], Nelly Mainy[2], Elizabeth Becker[1]; [1]Altria Client Services, Richmond, VA, USA, [2]JT International, Geneva, Switzerland

FDA marketing authorization of new tobacco products is informed by understanding how users and nonusers of tobacco products perceive the risks of the new tobacco products, and how the marketing of the new tobacco products may impact those perceptions. To examine the effect of promotional materials on risk perceptions of the Ploom system (i.e., Marlboro heated tobacco sticks used with the Ploom® heated tobacco device), adults who either currently smoked cigarettes, currently used other tobacco products, or who did not currently use any

tobacco products (target n=6,975) were randomly assigned to one of three conditions. Participants viewed either: 1) a Ploom system concept (Control condition); 2) the Ploom system concept along with a portfolio of promotional materials (Test 1 condition); or 3) the Ploom system concept with a portfolio of promotional materials that included modified risk claims (Test 2 condition; not discussed). After viewing their assigned stimuli, participants completed Consumer Reported Outcome Measures that assessed perceptions of general harm, absolute risk of specific health outcomes, and risk of using the Ploom system relative to smoking cigarettes, using nicotine replacement therapies, and quitting use of all tobacco and nicotine products. The study oversampled for ages 21-24 and included a cohort of adults aged 18-20 who were under the legal age to purchase tobacco. Analyses will examine the effects of promotional materials on risk perceptions, between the Control and Test 1 conditions. Results will also discuss whether adults who use and adults who do not use tobacco products vary in risk perceptions after viewing promotional materials related to the Ploom system. Results are intended to inform tobacco regulatory submissions.

11. BEHAVIORAL INTENTIONS FOR USING MARLBORO HEATED TOBACCO STICK PRODUCTS WITH THE PLOOM® HEATED TOBACCO DEVICE AMONG US ADULTS. Jennifer LEWIS[1], Jonathan Gallegos[1], Nelly Mainy[2], Elizabeth Becker[1]; [1]Altria Client Services, Richmond, VA, USA, [2]JT International, Geneva, Switzerland

FDA marketing authorization of new tobacco products is informed by understanding how the marketing of the new tobacco products may affect tobacco product use behavior among users and nonusers of tobacco products. To examine the effect of promotional materials on behavioral intentions for the Ploom system (i.e., Marlboro heated tobacco sticks used with the Ploom® heated tobacco device), adults who either currently smoked cigarettes, currently used other tobacco products, or who did not currently use any tobacco products (target n=6,975) were randomly assigned to one of three conditions. Participants viewed either: 1) a Ploom system concept (Control condition); 2) the Ploom system concept along with a portfolio of promotional materials (Test 1 condition); or 3) the Ploom system concept with a portfolio of promotional materials that included modified

risk claims (Test 2 condition; not discussed). After viewing their assigned stimuli, participants completed consumer-reported outcome measures that assessed intention to try and intention to use the Ploom system, intention to switch to the Ploom system from cigarettes, and intentions to quit smoking and/or quit all tobacco products, as appropriate. The study oversampled for ages 21-24 and included a cohort of adults aged 18-20 who were under the legal age to purchase tobacco. Analyses will examine the effects of promotional materials on behavioral intentions, between the Control and Test 1 conditions. Results will also discuss whether adults who use and adults who do not use tobacco products vary in behavioral intentions after viewing promotional materials related to the Ploom system. Results are intended to inform tobacco regulatory submissions.

12. A RANDOMIZED STUDY EVALUATING THE IMPACT OF ENDS ADVERTISING AND PROMOTIONAL MATERIALS ON USE INTENTIONS AMONG ADULTS WHO SMOKE AND NON-TOBACCO USERS. Nicholas GOLDENSON[1], Stacey A. McCaffrey[1], Saul Shiffman[2]; [1]Juul Labs, Inc, Washington, DC, USA, [2]Pinney Associates, Bethesda, MD, USA

Objectives: This study evaluated the impact of advertising and promotional materials (APM) on intentions to try and to use tobacco and menthol flavored JUUL ENDS products among adults who smoke (AWS) and adults who do not use tobacco (AWDNUT).

Methods: In this survey-based study, participants (3,045 AWS, 3,527 AWDNUT) were randomized to view an image of the ENDS products and health information (Control), or to additionally view APM (promotional fliers and information about an available App associated with the ENDS products) (Test). Outcome measures were openness to try (OTT), reasons for OTT, and openness to use (OTU), assessed separately by flavor.

Results: OTT was largely flavor-specific; very few participants were open to trying both tobacco and menthol flavors. AWS' OTT each flavor was strongly related to the flavor of cigarettes smoked; significantly more adults who smoke menthol cigarettes were OTT menthol than tobacco and vice versa. Compared to

AWS, very few AWDNUT were open to trying or using the ENDS products. Exposure to APM (i.e., Test vs Control) did not affect OTT or OTU among AWDNUT. Conversely, exposure to APM significantly increased OTT and OTU among AWS. The App was rarely cited as the only reason for participants' OTT, including among young adults, and the App was not differentially cited as a reason for OTT among AWDNUT compared to AWS.

Implications: The JUUL APM tested were not significantly appealing to adult non-tobacco users, but did significantly increase OTU among adults who smoke. OTT was largely flavor-specific, and the tobacco and menthol flavors tested in this study appealed to different segments of adults who smoke. The JUUL App was not differentially appealing to adult non-tobacco users.

13. STABILITY OF CERTIFIED REFERENCE CIGARS DURING LONG-TERM STORAGE. Huihua JI, Zhenyu Jin, Laura Fenton; University Of Kentucky, Lexington, KY, USA

In 2020, the University of Kentucky, Center for Tobacco Reference Products (CTRP) was awarded a Cooperative Agreement with the US Food and Drug Administration (FDA) to produce three certified reference cigars; a large cigar (1RLC), a cigarillo (1RSC), and a filtered cigar (1RFC). These reference cigars were manufactured in May 2022, January 2023, and April 2023, respectively. The objective of this study was to evaluate the stability of the reference cigars during long-term storage. The 1RLC, 1RSC, and 1RFC cigars were stored at room temperature (~22°C), 4°C, and -20°C for 0, 1, 2, 3, 6, 9, and 12 months. At each sampling time, the three cigar types from each storage condition were sampled and used for analysis of the unburned cigar tobacco and the smoke. The unburned cigar tobacco analyses included moisture contents (oven volatiles), pH, nicotine, and tobacco-specific nitrosamines (TSNAs), while the smoke analyses included TNCO (tar, nicotine, and carbon monoxide), TSNAs, and total particulate matter (TPM) in cigar mainstream smoke, and puff counts. Prior to analysis, the reference products stored at -20˚C were transferred to a refrigerator for 24 hours and then moved to room temperature until they reached temperature equilibrium. The study results indicated that all three reference cigar products were stable for

most of the parameters we measured; the single exception was that the moisture contents of the cigars stored at room temperature decreased with increased storage time during one year of storage.

14. EXTRACTABLES TESTING OF FLEECE MATERIAL USED IN MODERN ORAL NICOTINE POUCHES. Ed CARMINES[1], Chris Woodruff[1], Lise Fraissinet[1], Scott Crekmur[2], Tom Barrett[2]; [1]Chemular, Scottsdale, AZ, USA, [2]Legend Technical Services, St Paul, MN, USA

Modern oral nicotine pouch products are made by forming a paper like fleece material into a tube, heat sealing the bottom of the tube, filling with the granulate material containing nicotine and then heat sealing the top. This fleece material has the potential to leach chemicals into the granulate materials and also be extracted by saliva during use. The fleece material is similar to a teabag. The fleece material is considered the primary packaging for the product. The Product Quality Research Institute ("PQRI") Leachables and Extractables Working Group's recommended approach was followed to evaluate different sizes of sealed empty pouches made from Dynatec 117/8/CFW material. Specifically, the pouch material was tested using the USP 1663 method (Assessment of Extractables Associated with Pharmaceutical Packaging/Deliver Systems). Samples were extracted with aqueous solutions at pH 5.2 and 9.5 and a 50/50% solution of isopropanol and deionized water. The solutions were analyzed by GC/MS (volatiles and semi-volatiles), LC/MS (non-volatiles) and ICP/MS (metals). The fleece did not appear to have the potential to leach materials of toxicological concern above the Safety Concern Threshold (SCT) or Toxicological Threshold of Concern (TTC). Under the conditions of use, the fleece was deemed acceptable for its intended use.

15. WHITE FOX 4 MG NICOTINE POUCH PRODUCTS ARE BIOEQUIVALENT TO 4 MG NICORETTE GUM. Ed CARMINES[1], Karen Carmines[1], Lise Fraissinet[1], Naama Levy-Cooperman[2], Ryan Seltzer[3]; [1]Chemular, Scottsdale, AZ, USA, [2]Altreos Research Partners Inc, Toronto, Canada, [3]Safety in Numbers, Tucson, AZ, USA

White Fox brand (GN Tobacco Sweden AB) tobacco free nicotine pouches were tested to determine if the release and absorption of nicotine was equivalent to

Nicorette lozenges. The pharmacokinetics of nicotine absorption from White Fox All White Slim portion and Full Charge All White Regular portion pouches were assessed and compared to a 4 mg Nicorette mint flavor lozenge. A randomized, open label, crossover, in-patient clinical study was performed in 27 subjects to evaluate the nicotine plasma levels. Each study day, subjects used one of the test pouches or one Nicorette lozenge under controlled conditions for 60 minutes. Blood was collected for up to 12 hours. Geometric Least Square (LS) mean Cmax values were similar for White Fox Slim and White Fox Regular when compared to Nicorette lozenge and the 90% confidence interval of the geometric mean ratio of the difference was within the predefined margin of 80% to 125%, indicating bioequivalence. Geometric LS mean AUC0-t values were similar for White Fox Regular when compared with Nicorette lozenge. The 90% confidence interval of the geometric mean ratio of the difference for AUC0-t was within the predefined margin of 0.80 to 1.25, indicating bioequivalence. Geometric LS mean AUC0-t values were also similar for White Fox Slim when compared with Nicorette lozenge; however, for the AUC value, the lower bound of the 90% confidence interval of the geometric mean ratio of the difference was slightly below the predefined margin of 0.80, indicating slightly lower overall exposure for the White Fox Slim product compared with Nicorette lozenge, Since this is a consumer product that is used as desired, any small differences in the bioavailability are not likely to be clinically significant.

16. IN VITRO TOXICOLOGICAL ASSESSMENT OF WHITE FOX MODERN ORAL NICOTINE POUCH PRODUCTS. Manoj MISRA, Ed Carmines, Chris Woodruff, Lise Fraissinet; Chemular Regulatory Consulting, Hudson, MI, USA

In vitro toxicological assessment of Modern Oral Nicotine Products (MONP) is an essential part of the US FDA's premarket tobacco product application (PMTA) process. The in vitro toxicological assessment of a MONP pouch product was conducted using a battery of well-established regulatory assays, including the Bacterial Reverse Mutation (Ames), In Vitro Micronucleus (IVMN) and Neutral Red Uptake (NRU) assays to assess mutagenicity, genotoxicity, and cytotoxicity, respectively.

The GN Tobacco White Fox Pouches are made by mixing nicotine polacrilex and nicotine in glycerol with inert substrates and adding flavors. The principal difference between the tested products is the amount of nicotine. The tested products contained different nicotine levels (12-20 mg/pouch).

The MONP pouch products were extracted with dimethyl sulfoxide (DMSO) and extracted samples were used for toxicological assessment within the time frame of established extract stability by nicotine analysis. For toxicology assays, the dose-dependent effect of extract was conducted with the product with highest amount of nicotine per pouch and other products with lower amount of nicotine per pouch was tested only at the top dose.

Under the experimental conditions and based on the established criteria for evaluation of various assays, no cytotoxicity, mutagenicity nor genotoxicity was observed for any of the GN Tobacco White Fox pouch MONP products.

17. HPHC ANALYSIS OF WHITE FOX MODERN ORAL NICOTINE POUCH PRODUCTS. Manoj MISRA, Ed Carmines, Chris Woodruff, Lise Fraissinet; Chemular Regulatory Consulting, Hudson, MI, USA

FDA guidance is intended to assist in submitting premarket tobacco product applications (PMTAs) under section 910 of the FD&C Act which include reporting of HPHCs in tobacco and nicotine products and tobacco smoke under section 904(a)(3) of the FD&C Act.

The GN Tobacco White Fox Pouches are made by mixing synthetic nicotine with polacrilex and glycerol with inert substrates and adding flavors. The use of these products is similar to snus, the consumer places the product between the cheek and gum. The product belongs to the Category Other and subcategory Other. The FDA has not defined an appropriate list of HPHCs for products of this type. In the absence of guidance, GN Tobacco has chosen to follow the required list for portioned smokeless tobacco products. FDA recommends that companies analyze nine (9) chemicals.

The HPHC analysis were conducted on per pouch and estimated daily consumption basis. Among tested HPHCs, acetaldehyde, crotonaldehyde, cadmium, NNK or NNN levels were either not detected or below quantitative limits. Non-significant levels of formaldehyde and arsenic was found in White Fox products. The estimated daily use levels of formaldehyde and arsenic was compared with the oral no significant risk levels (NSRL) by OEHHA-Cal-EPA) and minimum risk level (MRL) by ASTDR. For all White Fox pouch products, the potential daily formaldehyde and arsenic exposure are significantly lower than the NSRL and MRL values thus presents minimal risk to the consumers.

18. INTENTIONS TO USE DATA AND PREVALENCE ESTIMATES FOR NJOY ACE® DEMONSTRATE LOW LIKELIHOOD OF USE FOR ADULT NEVER SMOKERS AND UNDERAGE INDIVIDUALS. Kate VERGARA, Nadja Richter, Andrea Vansickel; Altria Client Services, Richmond, VA, USA

In assessing Premarket Tobacco Applications, FDA considers the risks of initiation by nonusers, including youth, against the benefit of switching among adults who smoke (AS). NJOY ACE PMTAs included evidence regarding AS who completely switched to NJOY ACE. Results from two recent studies related to intentions to use and prevalence of use of NJOY ENDS among Adult Never Smokers and underage individuals, demonstrate low likelihood of use in these populations. Intentions: We conducted a cross-sectional online survey among Adult 18+ Current, Former, and Never Smokers and Youth (age 13-17) participants recruited from a probabilistic research panel to assess risk perceptions and intentions to use NJOY ACE 2.0 BLE Products with age-gated access restrictions (NJOY ACE Products). Intention to Try Soon or in the Next Year was low among Adult Never Smokers (range 1.19%-3.00%) and the vast majority of Youth (at least 95% across the NJOY ACE Products) did not Intend to Try the NJOY ACE Products Soon or in the Next Year. Also, Youth did not indicate statistically significantly greater Intention to Try the flavored NJOY ACE Products Soon or in the Next Year than Tobacco-flavored NJOY ACE or combustible cigarettes.

Prevalence: Results from the Altria Client Services Underage Tobacco Use Survey, a repeated, probability-based cross-sectional study among U.S. individuals aged 13-20 years, revealed consistently low prevalence for NJOY as usual brand, from 2021 to 2023 among both Youth (13-17 years; ranging from 'undetected' to 0.2%) and Young Adults (18-20 years; remaining stable at around 0.2%). Taken together, there is a low likelihood of use of NJOY ENDS among Adult Never Smokers and underage individuals and this has remained consistently low over time.

19. RISK PERCEPTIONS AND MISPERCEPTIONS OF NJOY ACE® 2.0 BLE ENDS PRODUCTS AMONG ADULTS 21+ WHO SMOKE COMBUSTIBLE CIGARETTES. Kate VERGARA, Brandon Newmyer; Altria, Richmond, VA, USA

A recent publication has shown that adults who currently smoke cigarettes (AS) and that perceived electronic nicotine delivery systems (ENDS) were "less harmful" than combustible cigarettes (CC) were two-fold more likely to switch from CC to ENDS (OR 2.24; CI 1.89-2.65) for PATH Wave 2-5. Results from "An Online Survey Assessment of Perceptions and Intentions to Use NJOY ACE Products in National Probability Samples of U.S. Youth and Adult Current, Former, and Never Smokers" (N=2119) inform AS perceptions of absolute and relative harm for NJOY ACE 2.0 BLE ENDS (NJOY Products).

The vast majority of AS (n=521) perceived the absolute harm of NJOY Products as harmful [97.72%; CI (96.41-99.03)]. The majority of AS perceived the relative harm of NJOY Products to be "about the same" or "more harmful" than Nicotine Patch, Gum, or Lozenges [93.65%; CI (84.83-100)] as well as "more harmful" than Quitting All Tobacco Use [53.95%; CI (49.43-58.48)]. Furthermore, AS perceived the relative harm of NJOY Products "about the same" as other ENDS [86.20%; CI (82.99-89.40)].

Notably, the majority of AS perceived the relative harm of NJOY to be "about the same" or "more harmful" than CC [81.05%; CI (73.54-88.56)]. Indeed, only 18.95% (CI 15.45-22.45) of AS perceived NJOY Products as "less harmful" than

CC. Our results demonstrate that AS do not perceive NJOY Products as risk-free, although they misperceive the harm of these products relative to CC. Given the scientific consensus that CCs are the most harmful type of tobacco product, there is a clear opportunity to address misperceptions which may promote a greater likelihood of complete switching.

20. ASSESSMENT OF THE ADVERSE EFFECTS OF REPEATED 28-DAY HEATED TOBACCO PRODUCTS (HTPS) EMISSION INHALATION EXPOSURE IN RATS. Jinhee KIM[1], Su-Hyun Choi[1], Mi Jin Yang[1], Kyung-Chul Choi[2], Dohee Ahn[2], Bumseok Kim[3], Min-Seok Kim[1]; [1]Korea Institute of Toxicology, Jeongeup, Jeonbuk, Korea, [2]Chungbuk National University, Cheongju, Chungbuk, Korea, [3]Jeonbuk National University, Iksan, Jeonbuk, Korea

Tobacco use remains a significant global public health concern, claiming around 8 million lives annually. Despite lacking definitive safety evidence, heated tobacco products (HTPs) have gained popularity among adult smokers seeking a perceived safer alternative. Hence, here we investigated the adverse effects of HTP in Sprague-Dawley (SD) rats. HTP emissions were inhalation-exposed to 7-week-old male rats for 28 days at concentrations of 50, 150, and 300 mg/m3 daily for 4 hours. The study included various evaluations such as measurements of body/organ weight, blood chemistry, total/differential cell counts and biochemical analyzes in bronchoalveolar lavage fluid (BALF). Additionally, gene expression analysis and histopathological changes were conducted. Five days after HTP inhalation, weight loss was observed in the HTP-exposed group compared to the control group. HTP also reduced the weights of the liver, heart, and kidney. Rats exposed to HTP emissions exhibited increased total cell count in BALF and elevated levels of macrophages and neutrophils. Blood analysis showed a tendency of increased BUN and CREA levels and a significant decrease in TG levels, along with a statistically significant decrease in basophil count in the HTP-exposed group. Additionally, analysis of gene expression changes in lung and liver tissues revealed the most prominent alterations in genes involved in metabolic pathways. In the histopathological examination of nasal cavity, mucous cell hyperplasia was observed in the HTP exposure group. Overall, these results suggest that HTP emissions may influence pulmonary inflammatory responses and metabolism. In this study, a 28-day subacute exposure trial was conducted, and as a result,

adverse effects due to HTP exposure were observed. Further research is considered necessary to evaluate the chronic effects of exposure to HTP emissions.

21. EVALUATION OF NICOTINE, ACETALDEHYDE, CROTONALDEHYDE, AND FORMALDEHYDE LEVELS IN SMOKELESS TOBACCO PRODUCTS OBTAINED AT DIFFERENT PROCUREMENT TIMES. Selvin EDWARDS[1], Matthew D. Hassink[1], An T. Vu[1], Kenneth M. Taylor[2]; [1]Center for Tobacco Products, Food and Drug Administration, Silver Spring, MD, USA, [2]Center for Veterinary Medicine, Food and Drug Administration, Laurel, MD, USA

Smokeless tobacco products expose adult and youth tobacco users to various addictive and carcinogenic constituents that can cause long-term nicotine dependence and oral cancers. The present study evaluated the total and unprotonated nicotine, acetaldehyde, crotonaldehyde, and formaldehyde quantities in four sets of 16 commercial smokeless tobacco products to determine content variability as a function of procurement time and location. The total nicotine content varies from 5.7 to 42.5 mg/g and the amount of nicotine in the unprotonated form ranges from 0.1 to 5.6 mg/g. The acetaldehyde quantities vary from 0.3 µg/g to 7.5 µg/g and formaldehyde content ranges from 0.16 µg/g to 4.5 µg/g. For all 16 smokeless tobacco products, the crotonaldehyde levels are below the detection or quantitation limits of the test method. All tested smokeless tobacco products exhibit statistically significant internal set-to-set content variability ($p < 0.05$) but there is no definitive correlation between analyte content and procurement time or location. The small absolute differences in set-Keto-set content may be due to differential formation of various carbonyls during product storage or the presence of high fire-cured tobacco content in the product.

22. ACTUAL USE STUDY OF THE P4M3 GEN 2.0 CLOSED-END ELECTRONIC NICOTINE DELIVERY SYSTEM. Steve ROULET[1], Claudia Kanitscheider[2], Pierpaolo Magnani[1], Aurelie Formey-Leichti[1], Alexandre Soulan[1], Felix Marckzykowski[2], Laura Marquis[2], Kelly Peters[3], Gerd Kallischnigg[4]; [1]Philip Morris Products, Neuchatel, Switzerland, [2]Oracle Life Sciences, Munich, Germany (formerly Cerner Enviza), [3]Oracle Life Sciences, Austin, TX, USA (formerly Cerner Enviza), [4]ARGUS, Berlin, Germany

The P4M3 Gen 2.0 closed-end electronic nicotine delivery system (ENDS) was developed as a better alternative for adults who would otherwise continue smoking. Complete switching to smoke-free products (SFPs), such as P4M3 Gen 2.0 ENDS, and substantial reduction in cigarette consumption are important measures to assess the impact of SFPs on public health. This 10-week actual use study examined 1) how daily cigarette smokers used the P4M3 Gen 2.0 and 2) how P4M3 Gen 2.0 availability impacted cigarette consumption. The multi-site, prospective cohort study comprised a 1-week baseline period, an 8-week observational period, and a 1-week close-out period. Subjects recorded cigarette and ENDS consumption in an e-diary. The study population comprised U.S. adults aged 21–64 years who smoked cigarettes (regular and/or menthol) daily, including dual users (cigarettes and ENDS), with no intention to quit tobacco or nicotine product use within the next 30 days. The study enrolled 821 participants; 720 (male/female: 42.6%/57.4%; mean age: 45.6) were included in the analysis (353 exclusive smokers, 367 dual users). At study completion, 4.0% of exclusive smokers and 4.1% of dual users had completely switched to P4M3 Gen 2.0 and stopped smoking cigarettes. Moreover, 25.8% of exclusive smokers and 28.1% of dual users reduced their cigarette consumption by ≥50%. This proportion was higher among those who used the menthol flavor variant only (31.3% and 28.7%, respectively) compared to the regular variant only (17.8% and 21.4%, respectively). These results suggest that the marketing of the P4M3 Gen 2.0 ENDS in the U.S. is likely to result in a large proportion of adult daily cigarette smokers switching to P4M3 Gen 2.0 ENDS and using it exclusively or substantially reducing their cigarette consumption.

23. PRODUCT PERCEPTION AND INTENTION STUDY OF THE P4M3 GEN 2.0 CLOSED-END ELECTRONIC NICOTINE DELIVERY SYSTEM.

Steve ROULET[1], Pierpaolo Magnani[1], Medy Ehtesham[1], Alexandre Soulan[1], Sarah Farnsworth[2], Eva DeJong[2]; [1]Philip Morris Products, Neuchatel, Switzerland, [2]PEGUS Research, Salt Lake City, UT, USA

The P4M3 Gen 2.0 closed-end electronic nicotine delivery system (ENDS) was developed as a better alternative for adult smokers who would otherwise continue

smoking. This randomized, parallel, two-arm, online product perception and intention study evaluated comprehension of a reduced exposure claim and its effect on intention to use and health risk perception of P4M3 Gen 2.0. The study population (n=3852) comprised U.S. adult (21+) tobacco users (current smokers with/without intention to quit and e-cigarette users) and non-users (former smokers and never tobacco users [including 18–20 years old]). Subjects were randomly assigned to a single exposure of communication material with (n=1926) or without (n=1926) the reduced exposure claim. Over 95% of subjects (both arms) understood that the product is a nicotine-containing e-cigarette. In the claim arm, >90% correctly understood that "switching completely…significantly reduces exposure to harmful chemicals," and that there are health risks associated with using the product. Tobacco users had high positive intention to use, and non-users had low intention to use the product. Claim exposure positively impacted intention to use among tobacco users while having limited or no impact on non-users. Tobacco users and non-users perceived the health risk of using the product to be lower than smoking cigarettes and higher than quitting all tobacco products. Claim exposure decreased the product's health risk perception across all groups. These results show that U.S. adult tobacco users and non-users understand that switching completely from cigarettes to the product significantly reduces exposure to harmful chemicals but is not risk free, and that a reduced exposure claim associated with the product is likely to facilitate tobacco users switching from cigarettes to the product.

24. MODIFIED ANALYTICAL METHOD FOR THE ANALYSIS OF TOXIC METALS IN E-CIGARETTE AEROSOLS. Naudia GRAY, R.S. Pappas; Centers for Disease Control and Prevention, Atlanta, GA, USA

The analysis of electronic nicotine delivery system (ENDS) aerosols for toxic metals requires the use of ultrahigh purity materials to avoid contaminating the aerosols with metals during collection and sample preparation. We continue to collect aerosols using our high purity fluoropolymer condensation tube following the ISO Standard 20768 puff regimen. We have modified our previously validated and published method with the addition of new metal analytes of interest and an improved calibration matrix match that now includes propylene glycol and

glycerol close to concentrations observed in diluted aerosols. Analytes now include aluminum, chromium, iron, cobalt, nickel, copper, arsenic, cadmium, tin, and lead. Some analytes represent metals that are constituents of various ENDS device components that were detected using scanning electron microscopy with energy dispersive X-ray spectroscopy and which have also been detected in aerosols. Other analytes are unlikely to be component materials and therefore are not expected to be detected in the aerosol. We have nevertheless added them to the method because other labs have reported detectable levels that we believe are from sample contamination. The additional analytes required replacing the previously used Apex™ HF desolvating system with a standard peltier-cooled PFA spray chamber. This requirement was due to difficulty determining an ideal heated spray chamber temperature that was appropriate for volatile complexes of all metals included in the method that also produced good calibration linearity, precision, and accuracy. The modified method was fully validated with evaluation of residuals, precision, accuracy, and verification of method limits of detection.

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

25. SWITCHING BEHAVIORS AND USE PATTERNS OF A NOVEL NICOTINE POUCH PRODUCT AMONG ADULTS WHO USE DIP OR SNUFF: RESULTS FROM AN ACTUAL USE STUDY. Hui CHENG; Altria Client Services, Richmond, VA, USA

Objectives: The study characterized tobacco use patterns and behaviors among adults who use dip or snuff (AD), with and without cigarette smoking, when provided with on!® PLUS nicotine pouches (NPs) for actual use in their natural environment.

Methods: This longitudinal observational study involved a one-week trial period and a subsequent five-week ad libitum use period when AD were provided with nine varieties of NPs, consisting of three flavor varieties (i.e., mint, wintergreen, tobacco flavor) in three nicotine strengths (i.e., 6mg, 9mg, 12mg). Participants were allowed to consume other tobacco products throughout the study.

Participants reported their use of NPs and other tobacco products via daily diaries.

Results: Among participants who completed the study (n=917), virtually all participants started using NPs. During the five-week ad libitum use period, participants used NPs almost daily. The number of pouches used increased over time. By the end of the study, 72% of participants behaviorally switched to the NPs from dip/snuff. Among participants who used both dip/snuff and smoked cigarettes, 37.5% switched from both products to the NPs; an additional 34% reduced their cigarette consumption by at least 50%. During the last week of the study, 78% of participants used mint and/or wintergreen varieties only; 13% used both mint/wintergreen and tobacco varieties; <and 9% used tobacco varieties only. Among those who switched completely to NPs, the majority used mint and/or wintergreen varieties.

Implications: The NPs can potentially facilitate switching from dip/snuff among AD as well as switching from cigarettes to the NPs among those who use dip/snuff and cigarettes. Mint and wintergreen varieties were much more commonly used than tobacco varieties, including among those who switched completely from dip/snuff or dip/snuff and cigarettes.

26. XAD-4 RESIN AS AN ALTERNATIVE TRAPPING MATERIAL IN DETERMINATION OF SEMI-VOLATILE COMPOUNDS (SVCS) IN AEROSOL OF HEATED TOBACCO PRODUCT (HTP) USING GC-MS.
Linda ERLIA SARI, Eka Pria Utama Mulyana, Ilham Fadila Ramadhen; Filtrona Manufacturing Indonesia, Surabaya, East Java, Indonesia

Objective: To establish a method for determining three semi-volatile organic compounds (Pyridine, Quinoline and Styrene) in aerosol of Heated Tobacco Product (HTP) using XAD-4 resin as an alternative trapping material and gas chromatography mass spectrometry (GC-MS) as instrument determination.

Methods: Aerosol samples were collected using a HTP linear smoking machine and Teflon Cambridge filter holders containing XAD-4 resin under Health Canada

Intense regimes. Aerosol yields in Teflon holders were extracted using methanol, and internal standards (Pyridine d5, Ethylbenzene and Quinoline d7) were added for selected semi-volatile compounds. The extract was shaken on a mechanical shaker and transferred to a 1.5 mL vial for analysis using Gas Chromatography-Mass Spectrometry

Results: The method demonstrated good sensitivity, stability, accuracy and precision. The limit of quantification was 0.04 µg/stick for Pyridine and Styrene, and 0.004 µg/stick for Quinoline. The recovery was 92-102%, and the relative standard deviation ranged from 2.6% to 5.5%.

Conclusion: This method is simple, rapid, highly accurate, and reliable, hence it suitable for detecting semi-volatile organic compounds (Pyridine, Quinoline, and Styrene) in the aerosol of Heated Tobacco Products.

27. CHARACTERIZING AEROSOL TEMPERATURE OF ELECTRONIC NICOTINE DELIVERY SYSTEMS (ENDS) AND HEATED TOBACCO PRODUCTS (HTPS) USING WET-BULB TEMPERATURE APPROACH.

Pavel KOSACHEVSKY[1], Bonnie G. Coffa[1,2]; [1]Labstat International, Kitchener, ON, Canada, [2]Toxpharm, Mechanicsville, VA, USA

Understanding the temperature characteristics of aerosols generated by Electronic Nicotine Delivery Systems (ENDS) and Heated Tobacco Products (HTPs) may be critical factors in product development and quality and regulatory requirements. While, FDA has not established standards for delivered aerosol temperature, these measures are included in PTMA guidance recommendations for reporting. This study introduces a methodology for aerosol temperature testing at multiple points using a wet-bulb temperature approach, drawing upon NIOSH (National Institute for Occupational Safety and Health) standards for heated inhalation medical devices. The configuration of the mouthpiece diffuser plays a role in defining aerosol airflow dynamics, whether laminar or turbulent. Consequently, the results of aerosol temperature testing are contingent upon the positioning of the testing probe along the x and y axes from the mouthpiece. Measurements of temperature and relative humidity were conducted at the air stream inlet of the tested device,

and at the exit aerosol temperature, utilizing miniature thermocouples. Sixteen probes were used to measure and demonstrate the temperature distribution within the aerosol stream. Five probes distributed along the y-axis direction were employed to measure aerosol temperature at four distinct locations along the x-axis direction at 1mm, 10mm, 20mm, and 100mm from the mouthpiece. Various commercially available ENDS and HTP devices, alongside 1R6F cigarettes, were evaluated under intense and non-intense regimes. Conversion to wet-bulb temperature was accomplished by converting recorded dry-bulb temperature data from thermocouples and humidity levels using the Stull conversion method. This comprehensive approach provides a robust framework for evaluating aerosol temperature characteristics and contributes to our understanding of the thermal profiles of ENDS and HTPs.

28. COMPARATIVE ANALYSIS OF HEATED TOBACCO PRODUCTS AND 1R6F REFERENCE CIGARETTE RESPONSES IN TK6 AND CHO CELL LINES UTILIZING HIGH THROUGHPUT FLOW CYTOMETRY AND MANUAL COUNTING FOR THE IN VITRO MICRONUCLEUS ASSAY. Sean OH, Dong Ma, Bonnie Coffa, Katarina Aleksa; Labstat International, Kitchener, ON, Canada

This study aims to compare the responses between heated tobacco product (HTP) aerosol and 1R6F smoke using two distinct cell lines, TK6 and CHO. Following exposure, cells were subjected to in vitro micronucleus testing to assess genotoxic effects. Flow cytometry and manual slide scoring were employed as complementary approaches for result validation. Briefly, KR-1R6F, was smoked using a rotary smoking machine and the particulate phase (PP) was extracted with DMSO and applied to CHO cells or TK-6 cell using 5 different concentrations and 3 treatment schedules as per OECD 487, three commercial heat-not-burn products (HnB) were tested with both cell lines and both the scoring methods. Manual counting, although time consuming, served as a reliable benchmark for validating the flow cytometry results.

Preliminary findings indicate differential genotoxic responses in TK6 and CHO cell lines following exposure to HTP aerosol and 1R6F cigarette smoke. Flow

cytometry demonstrated enhanced sensitivity in detecting micronuclei, providing a rapid and objective quantification of genotoxic events. Manual scoring consistently indicated 1.5% micronuclei across all schedules with TK6 cells, this was complemented by flow cytometry, revealing higher values. At the highest 1R6F dose (200 ug/mL), manual scoring showed 1.2%, 1.2%, and 1.5% micronuclei for schedules 1, 2, and 3, respectively, while flow cytometry detected 3.2%, 5.1%, and 10.1% micronuclei for each schedule. Solvent controls were consistently below 1.5% for both manual and flow cytometry.

A similar trend was observed in CHO cells as well, where the micronucleus (MN) percentage was statistically higher in flow cytometry than in manual scoring. Additionally, flow cytometry detected higher cytotoxicity across the three schedules. Specifically, in schedule 3, flow cytometry recorded 70% cytotoxicity at the highest dose (100 ug/mL), whereas manual scoring showed 42% cytotoxicity.

This study indicates that adaptation of flow cytometry as a more objective and efficient method for in vitro micronucleus assay, provides comparable data to the classical manual scoring method while increasing sample throughput and reducing the subjectivity. Furthermore, these findings encourage the wider adoption of flow cytometry in in vitro micronucleus assays, leading to improved accuracy and efficiency in genotoxicity testing.

29. Withdrawn

30. EVALUATION OF ENVIRONMENTAL EMISSIONS FROM GLO HEATED TOBACCO PRODUCTS AND COMBUSTIBLE CIGARETTES.

Milly KANOBE, John Darnell, Tao Jin, Jeff Coffield, Brian M. Keyser, Patrudu Makena, Sarah A. Baxter, Kristen G. Jordan, Gary M. Dull (formerly of), Buddy Brown (retired); RAI Services Company, Winston-Salem, NC, USA

Compared to cigarette smoke, heated tobacco product (HTP) aerosol contains significantly fewer and lower levels of harmful and potentially harmful constituents (HPHCs). However, the impact on environmental air is relatively unexplored. Therefore, this study compared levels of secondhand aerosol (SHA)

constituents in air following glo HTP use with secondhand smoke (SHS) constituents following cigarette smoking, in an environmental test chamber (ETC). Extracted ETC air samples following product use sessions were analyzed for 27 SHS/SHA constituents, including HPHCs. The use of glo HTPs resulted in significantly lower SHA HPHC levels in the ETC air relative to SHS HPHC levels from cigarette smoking. Some aerosol constituents (benzene, CO, formaldehyde, nicotine, respirable suspended particles, toluene, ethylbenzene, fine particulate matter, m- and p-cresol, o-cresol, pyridine, styrene, and ultraviolet particulate matter) were either below the limit of detection in ETC air or at significantly lower levels following glo HTP use relative to cigarette smoking. Mean concentrations of the assessed constituents were generally reduced by at least 90% following use of glo HTPs compared to smoking combustible cigarettes. These results suggest that glo HTP use would not contribute significantly to indoor air contamination and would reduce non-user exposure to HPHCs and other harmful constituents relative to combustible cigarettes. Such reductions in non-user exposure should be considered when assessing the tobacco harm
reduction potential of glo HTPs.

31. LONG-TERM SAFETY SURVEILLANCE EXPERIENCE WITH TOBACCO HEATING SYSTEM PRODUCTS. Brindusa TARANU, Virginie Schaub, Marina Suvakov; Philip Morris Products, Neuchatel, Switzerland

With the 2014 launch of Tobacco Heating System (THS) products, Philip Morris International (PMI) established a worldwide post-market safety surveillance system, the first tobacco company to do so. Health-related adverse events are collected globally from multiple sources (e.g., call centers, literature screens, clinical studies, market research surveys, poison centers, and social media) to monitor the THS safety profile. These adverse events are logged into the safety database (LifeSphere MultiVigilance System) and processed in several defined steps starting with case intake and translation, followed by medical review, quality review, and assessment for potential submission to regulatory authorities. In addition to collecting and evaluating adverse events, PMI performs signal detection activities, implements risk minimization measures for identified risks, and submits periodic reports to regulatory authorities to communicate any safety

findings. The long-term post-marketing experience with THS products showed a stable safety profile of PMI's THS products. The most frequently reported events (in >5% of THS users) were cough (10.02%), headache (5.98%), thermal burn (5.60%), and oropharyngeal pain (5.05%). PMI will continue to collect and evaluate all safety information to ensure adequate monitoring of the safety profile of THS products and the potential impact on public health.

32. NO MEANINGFUL EFFECT OF PROMOTIONAL MATERIALS FOR A NOVEL ORAL NICOTINE POUCH PRODUCT ON BEHAVIORAL INTENTIONS AND RISK PERCEPTIONS. Sade JOHNS; Altria Client Services, Elkridge, MD, USA

Objective: This study evaluated the effect of promotional materials on behavioral intentions and risk perceptions for a novel oral nicotine pouch (ONP) product among adults who use and do not use tobacco.

Methods: We conducted an online, quantitative experimental study with 4,723 U.S. adults, who currently used snuff/dip and no cigarettes (AD), used snuff/dip and cigarettes (ADU), used other tobacco products (OTP), or did not use any tobacco product (NU). The study sample included a group of underage adults (18-20 years) and an oversample of young adults aged 21-24 years. Participants were randomly assigned to view either the ONP concept with promotional materials (Test) or the ONP concept only (Control).

Results: Overall, AD and ADU had high intention to try and moderate to high intention to use and switch to the ONP product. NU and underage individuals had low intention to try or use the ONP product. The promotional materials had no effect on behavioral intentions among AD, ADU, OTP, and NU. The promotional materials did not have any effect on quit intentions in any study groups.

AD, ADU, and OTP accurately perceived using ONP as less risky than using cigarettes, using snuff/dip, or dual-use and riskier than using nicotine replacement therapies (NRTs) or quitting altogether. NU perceived using ONP as similar in risk to using cigarettes and snuff/dip and riskier than using NRTs and

completely quitting all tobacco.

Implications: These results suggest that the ONP can facilitate AD and ADU transition to the ONP while not increasing risk of initiation among nonusers. Tobacco users and nonusers understand that the ONP is not risk-free.

33. RELEASE PROFILES FROM SELECT MODERN ORAL NICOTINE PRODUCTS. Jake HENKIE, Rebecca Cornelius, Cosmin Stoicoiu, Angel Rodriguez-Lafuente, Leona Mijangos Sirkisoon, Andy Stinson; Labstat International, Kitchener, ON, Canada

The modern oral nicotine product category is quite diverse and includes tobacco-free (plant and fiber-based) pouches, gums, lozenges, pastes, and strips, among others. Products may contain natural or synthetic nicotine, various flavors and sweeteners, and other ingredients unique to the matrix. Consequently, for this multitude of product subtypes, there may be unique rates of nicotine release when consumed, even for products containing similar total nicotine amounts. To our knowledge, a direct comparison of nicotine release profiles for these products has not been published previously. Thus, the aim of this study was to compare the in-vitro release rates of nicotine from several different product subtypes using mastication and or dissolution.

A purpose-built chewing gum tester (DRT3 from Erweka) was employed for gums and a USP Type IV dissolution apparatus (CE7Smart from Sotax) for lozenges and pouches, both using artificial saliva as the extraction medium. Nicotine concentration in collected fractions was quantitatively determined by a validated HPLC-UV method.

In general, each product subtype displayed distinct release windows. For example, the release profiles for nicotine gums plateaued after approximately 30 minutes of chewing, whereas modern oral pouches released nicotine at a slower rate and required up to 1 hour for full release.

34. HEALTHCARE PROVIDERS' AWARENESS AND TRUST OF THE UNITED STATES FOOD AND DRUG ADMINISTRATION FOR

REGULATING TOBACCO AND NICOTINE-CONTAINING PRODUCTS.
Deena BATTISTA[1], Susan Martelle[2], Michael Polster[3]; [1]Womble Bond Dickinson, Winston-Salem, NC, USA, [2]RAI Services Company, Winston-Salem, NC, USA, [3]Naxion, Philadelphia, PA, USA

The United States Food and Drug Administration (FDA) acknowledges that no tobacco product is safe; however, evidence shows that cigarettes are the most harmful with other tobacco products existing lower on the continuum of risk. Nonetheless, research has demonstrated that there is a pervasive misperception in the US that tobacco and nicotine-containing products (TNPs) are associated with similar levels of risk. Unfortunately, these misperceptions are also widespread among healthcare providers.

An online survey of 700 physicians, nurse practitioners and physician assistants in five medical specialties—family and general practice, internal medicine, obstetrics and gynecology, cardiology, and pulmonology assessed healthcare providers' (HCPs) awareness of TNP regulation, and their confidence in government and medical organizations to provide accurate information about risks associated with TNPs.

Only 56% of HCPs select FDA as the government agency that regulates TNPs, with 30% purporting that other government agencies regulated such products, and 14% claiming that they do not know. Analysis reveals four tiers of trust in organizations to provide accurate information. The American Heart Association (mean rating of 8.8 on a 1–10 scale), American Cancer Society (8.7), and American Lung Association (8.7) are most trusted, followed by HCP's specialty-affiliated organizations (8.5), then the American Medical Association and Centers for Disease Control and Prevention (both 8.1). Finally, the FDA (7.4) is trusted the least.

Findings indicate that many HCPs are not aware that the FDA is responsible for regulating TNPs and trust the FDA less than other regulatory bodies. Lack of awareness and relatively lower trust in the FDA to provide accurate information must be addressed to reduce misperceptions among HCPs and the relaying of such information to patients.

35. CHARACTERIZATION OF NICOTINE PHARMACOKINETICS AND SUBJECTIVE EFFECTS DURING USE OF HEATED TOBACCO PRODUCTS IN ADULTS WHO SMOKE. Jesse Rensch[1], Jeffery Edmiston[1], Jingzhu Wang[1], Jianmin Liu[1], Mohammad Bazargan[1], Brian Nordskog[2], Kyung Soo HONG[1]; [1]Altria Client Services, Richmond, VA, USA, [2]JT International, Geneva, Switzerland

Heated tobacco products (HTPs) are a smoke-free alternative for legal age adults who smoke (AS). Thus, AS switching to HTPs may reduce their smoking-related diseases risks. In this study, we characterized the nicotine pharmacokinetics (PK) and subjective measures in AS using Ploom® HTPs (Test) and comparators and to assess the switching potential of these products. The HTP systems consist of hand-held battery-operated devices and consumables (heated tobacco sticks [HTS]), inserted into the device which heats but does not burn the tobacco. The HTPs included were non-menthol and menthol Test (two each) and comparators (1 each). We conducted a two group (menthol [n=24] and non-menthol products [n=23]), randomized, within group, crossover study characterizing nicotine PK of these products, relative to the subject's usual brand cigarette (UBC). To facilitate acclimation with the HTPs, subjects were allowed to use assigned products during a product trial and a 4-hour ad libitum product use episode the day prior to the PK session. PK assessments were conducted during a single 5-minute ad libitum use session of the HTP or UBC. Subjects completed questionnaires on Tobacco/Nicotine Withdrawal, Direct Effects of Product, Use the Product Again, and a Modified Cigarette Evaluation Questionnaire. The baseline adjusted average plasma nicotine Cmax (ng/ml) were: menthol products - 11.7 and 14.3(Test) and 12.8(HTP comparator); non-menthol products: 17.4 and 18.7(Test) and 16.8(HTP comparator). Cigarette comparator Cmax values were 23.8(menthol) and 21.2(non-menthol). For subjective measures, the Ploom® HTPs reduced cravings, urges to smoke, and were rated pleasant and satisfying; these scores were generally lower, compared to cigarette comparator. Overall, based on the nicotine uptake and the subjective responses, the Ploom® HTP products may be acceptable switching products for AS.

36. UTILIZING THE ELECTRONIC TRIAL MASTER FILE FOR

CLINICAL STUDIES TO SUPPORT FDA TOBACCO PRODUCT APPLICATIONS. Jeffrey COFFIELD, Claude Cavallo, Heather Green, Ken Szeliga; RAI Services Company, Winston-Salem, NC, USA

Clinical studies are often lengthy endeavors with potentially large numbers of subjects and study conditions conducted across multiple study sites. These studies produce vast quantities of documentation including every record associated with each subject's trial participation. This information must be tracked, verified, stored, and easily accessible upon request, as per FDA regulatory requirements. An electronic Trial Master file (eTMF) system is a secure database that ensures all records associated with the clinical trial are managed in compliance with FDA regulations promulgated under good clinical practice (GCP), HIPPA and FDA 21 CFR Part 11. Upon inspection, some common deficiencies that a sponsor, contract research organization (CRO), or monitor may experience in clinical studies include inadequate monitoring, failure to bring investigators into compliance, inadequate accountability for the investigational product, protocol deviations, inadequate subject protection, inadequate investigational product accountability, and failure to obtain IRB approval before study initiation activities. An accurate and complete eTMF decreases the likelihood of deficiencies. Best practices related to submitting documents into the eTMF in a timely fashion, evaluating the quality of the documents and reconciling the eTMF is key to quality documentation. If discovered, the details surrounding issues should be documented to provide rationale for handling concerns exhibiting oversight and resolution of those issues. The eTMF helps clearly document how our company adheres to the rigorous quality standards for clinical research studies within the tobacco industry and has provided substantiation of clinical evidence supporting applications that have resulted in receipt of FDA Marketing Granted Orders for various new tobacco products. In conclusion, the efficacy of an archived eTMF is demonstrated in the retrieval-ready electronic documents available for regulatory applications, inspections, or review.

37. MODELING THE POPULATION HEALTH IMPACT OF FLAVOR VARIETY AND POTENTIAL RISK OF YOUTH INITIATION RESULTING FROM THE MARKETING OF AN ORAL NICOTINE

POUCH PRODUCT. Thad HANNEL, Lai Wei, Yisha He, Raheema Muhammad-Kah, Ed Largo, Mohamadi Sarkar; Altria Client Services, Richmond, VA, USA

on! PLUS™ products are new oral tobacco-derived nicotine pouch products (NP) that have substantially reduced HPHCs and offer an alternative for adults who use smokeless tobacco (ST) products. A marketing determination of a new product by the FDA considers the risks of nonuser initiation against the benefit of users switching to a potentially lower risk product.

We used a validated agent-based model to evaluate the impact of marketing the NPs and the contribution of non-tobacco flavor varieties on morbidity and mortality in the U.S. population. Importantly, we assessed the risk to youth using tipping point analyses to predict their hypothetical initiation rates that would offset any benefit from switching by adults who use ST.

Marketing the NP resulted in a benefit to the population with a 0.40 percentage point reduction in ST prevalence and prevention of 74,000 premature deaths over a 75-year period. Limiting the NP portfolio to tobacco flavored products reduced the projected benefit by 73%. Tipping point analyses indicated that youth (ages 12-17) initiation rates specific to these NPs would have to increase more than 40 times from 0.04% and 0.03% to over 1.64% and 1.23% for males and females, respectively, resulting in underage prevalence more than 3.46% before the population benefit would reduce to zero. While no youth should use tobacco, prevalence trends approaching this level may provide early signals of population health risks. Understanding the role of flavors and the risk to youth is important in regulatory decision-making. While all models have limitations, these simulations provide a methodology for quantifying the risks of potential initiation vs the benefit of switching to potentially lower risk products, including benefits associated with flavored products.

38. THREE-DIMENSIONAL STRUCTURE-PROPERTY RELATIONSHIP OF REFINED FILTER MEMBRANES FROM TOBACCO EXTRACTS BASED ON HIGH-RESOLUTION CT SCANNING AND DEEP LEARNING. Mingjing GUAN[1], Zhang Jin[1], Zhou Shun[1], Zhang Xiaoyu[1], Wang

Xiaofeng[1], Cao Yun[1], Tian Huijuan[1], Ding Naihong[1], Li Yanyan[1], Chen Weijian[1], Li Lu[1], Fu Shuo[1], Yang Dahai[2], Song Xiaohui[2]; [1]China Tobacco Anhui Industrial of CNTC, Hefei, China, [2]Hefei University of Technology, Hefei, China

Membrane separation is an important method for the refinement of tobacco extracts, but existing research focuses primarily on its engineering applications, leaving the quantitative relationship between the three-dimensional structural parameters of filtration membranes and the targeted refinement of tobacco extracts unclear. In this study, we aim to quantify the structural changes of typical membranes before and after filtration and in conjunction with the analysis of the effective components in tobacco extracts, to dissect the microstructure of the membranes and their mechanisms in the separation and refinement of tobacco extracts. [Methods] Dynamic light scattering (DLS) and gas chromatography/mass spectrometry (GC/MS) analyses are used to characterize the changes in particle size and composition of tobacco extracts before and after separation. High-resolution CT scanning tomography is used for structural characterization of the filtration membrane. In addition, deep learning technique using the U-Net neural network algorithm is applied to quantitatively calculate membrane parameters. [Results] (1) Compared with PA membranes, PTFE membranes can retain more solid-phase materials and nicotine from tobacco extracts. (2) Intelligent segmentation calculations show that after filtration, the porosity of the PA membrane decreases by 4.4%, the thickness increases by 0.6 mm, and there is a slight decrease in both the average length and diameter of individual fibers. This is attributed to fiber compression due to pore blockage. (3) PTFE membranes with a pore size of 0.22 μm have an average fiber diameter of 1694.0 μm and a porosity of 42.7%, which are smaller than those of PA membranes. The dense fiber alignment of PTFE membranes results in greater retention of solid-phase materials. [Conclusion] This study provides a quantitative method for analyzing the three-dimensional structure of filtration membranes. By integrating membrane microstructure characterization with deep learning and correlating it with changes in sample composition before and after membrane separation, it provides theoretical support for targeted membrane separation of tobacco extracts.

39. GENERATION OF A BHAS 42 CELL TRANSFORMATION ASSAY HISTORICAL DATABASE. Shannon W. BRUCE, Michelle L. Klug LaForce, Sandra D. Springer, Amanda Fernandez, Wannie Madraymootoo; Inotiv, Rockville, MD, USA

The Bhas 42 cell transformation assay (CTA) is a sensitive short term system for predicting chemical carcinogenicity. Bhas 42 cells were established from BALB/c 3T3 cells by the transfection of v-Ha-*ras* gene and postulated to be initiated in the two-stage carcinogenesis theory. The Bhas 42 CTA measures the induction of morphologically transformed (MT) foci that show invasive growth into the monolayer of surrounding contact-inhibited cells. The assay protocol consists of two parts, the initiator assay (Sasaki, *et.al.* 1988, 1990, Asada, et.al. 2005) and promoter assay (Ohmori, *et.al.* 2004, 2005) to detect tumor-initiating and promoting activity, respectively, of chemical carcinogens. The positive control used for the initiator arm is 3-methylcholanthrene (3MCA) at 1.0 μg/mL and for the promoter arm is 12-O-tetradecanoylphorbol-13-acetate (TPA) at 50 ng/mL. Vehicle controls selected for database were deionized water, dimethyl sulfoxide (DMSO) and ethanol. In the Bhas 42 assay initiator arm, the mean MT foci values are 5.17, 5.24, and 4.53 for the vehicle controls (aqueous, dimethyl sulfoxide, and ethanol) and 16.17 for the positive control. In the Bhas 42 assay promoter arm, the mean MT foci values are 5.25, 6.67, and 5.63 for the vehicle controls (aqueous, dimethyl sulfoxide, and ethanol) and 31.23 for the positive control. Thus, we have established a historical database for the most commonly used vehicles and positive control along with 95% control limits for both the initiator and promoter arms of the Bhas 42 CTA.

40. MARKET MAP SURVEY OF HEATED TOBACCO PRODUCTS FOR HARMFUL AND POTENTIALLY HARMFUL CONSTITUENTS. Irfan GUNDUZ, Jerome King, Cyril Jeannet, David Gosh; Philip Morris Products, Neuchatel, Switzerland

Heated tobacco products (HTPs) are smoke-free alternatives to cigarettes that heat tobacco instead of burning it, thus avoiding combustion. The generated aerosol contains fewer and lower levels of harmful and potentially harmful constituents (HPHCs) than cigarette smoke, resulting in reduced consumer

exposure. Absence of combustion is one of the key indicators that differentiate HTPs from cigarettes. This study was performed to conduct a market map survey of HTPs; analyze their aerosols for HPHCs typically found in cigarette smoke; and verify that the yields of CO, NO, and NOx are below thresholds defined by the British Standards Institution (BSI) for HTPs. Ten HTP consumables with their respective five devices were collected from various markets (including Japan, Italy, Korea, and Greece) and tested for HPHCs. Data analysis indicated that all sampled products 1) demonstrated the absence of combustion based on the criteria defined by publicly available BSI specification 8850:2020 and 2) yielded substantially lower HPHC levels than reference cigarette 1R6F smoke. These results confirm that testing for the absence of combustion is a key criterion for determining reduced levels of HPHCs compared to cigarette smoke other than those that directly transfer from tobacco and/or are formed from a tobacco precursor.

41. OPTIMIZATION OF EXTRACTION AND IN VITRO EVALUATION OF MARKET NICOTINE GUMS. Sara HURTADO, Yevgeniya V. Prepelitskaya, Fadi Aldeek, Utkarsh Doshi U., John H. Miller, Kyeonghee M. Lee; Altria Client Services, Richmond, VA, USA

The European Pharmacopoeia describes the use of mastication apparatuses to simulate chewing for in vitro dissolution testing of gum products. While these apparatuses can also be used to prepare test material for in vitro toxicity testing, they lack throughput and scalability. In this study, we evaluated alternative approaches to generate test materials with high-throughput and sufficient volume for in vitro testing of nicotine gum products.

We evaluated various sample preparation procedures including cutting, grinding, and freeze grinding using 2 commercial nicotine gum products. The resulting samples were further processed in artificial saliva with different sample weights and extraction times. The final extracts were evaluated for nicotine recovery relative to the product label's nicotine expressed as %Recovery. The mastication method (Aldeek et al. 2022) was also used for comparison. The freeze-grinding method with one gum product extracted in 10 mL of artificial saliva (or cell media) for 3 hours was selected as the most optimal based on comparable %Recoveries (66-90%) to those from the mastication method (55-86%).

Using the selected method, we processed three market gum products (MP-1, MP-2, and MP-3) and the resulting extracts were subjected to in vitro toxicity testing using standardized battery of bacterial mutagenicity (Ames, 5 strains), cytotoxicity (Neutral Red Uptake-NRU, BALB/c 3T3 cells), and genotoxicity (Micronucleus-MN, human TK6 cells) assays. MP-1 and MP-2 were found to be non-mutagenic, non-cytotoxic, and non-genotoxic. MP-3 was non-mutagenic but showed 35% cytotoxicity and genotoxicity (positive MN responses observed for ST+S9 and LT-S9).

In summary, the optimized extraction method provides high-throughput, is scalable and is suitable for in vitro toxicological assessment of nicotine-gum products.

42. VELO NICOTINE POUCH USE BEHAVIORS AND SMOKING REDUCTION AMONG US ADULT SMOKERS WITH AND WITHOUT INTENTIONS TO QUIT SMOKING. Tiffany PARMS, Sarah Ayoku, Patrudu Makena; RAI Services Company, Winston-Salem, NC, USA

Objective: To evaluate product use behaviors and reduction in cigarettes smoked per day (CPD) between actual use study participants who indicated low-moderate intention to quit smoking cigarettes (selected 6 or less on a 10-point scale) compared to those who indicated high intention to quit smoking cigarettes (selected 7 or greater on a 10-point scale), on a baseline assessment questionnaire (self-reported).

Methods: Current cigarette smokers aged 21-60 were recruited into a multi-site, open-label, prospective observational study and provided a selection of Velo products in multiple sizes, nicotine strengths, and flavors for use in their naturalistic environment. Velo products are portioned oral nicotine pouches made of tobacco-derived, pharmaceutical-grade nicotine, cellulose, and flavors, as applicable. Post-hoc analyses were conducted on existing study data.

Results: Neither product use behaviors (i.e., number of days of Velo used per week, number of Velo flavors used per week, and number of Velo nicotine levels

used per week), nor average number of CPD differed among study participants regardless of quit intention at baseline. Irrespective of quit intentions, study participants used Velo on average 5.3 days per week, and used approximately 3 flavors and 2 different nicotine levels per week. Further, overall, CPD consumption among all study participants decreased by nearly 3 CPD on average at the end of the study period (mean 12.5 CPD consumption at baseline).

Conclusion: Velo use and CPD reduction were not impacted by expressed quit intention at baseline. Results suggest that Velo products are viable alternatives of nicotine delivery, which are vital to tobacco harm reduction strategies. Further, despite consumers' preconceived intentions to quit smoking, availability of viable non-combustible nicotine products contribute positively to public health by decreasing cigarette consumption.

43. TOPOGRAPHY STUDY OF GLO HYPER, A TOBACCO HEATED PRODUCT. Brian KEYSER, Tiffany A. Parms, Robert Underly, Tao Jin, Kristen Prevette, Meghan De Young, John Darnell, Kristen Jordan, Sarah Baxter-Wright; RAI Services Company, Winston-Salem, NC, USA

Topography is useful in assessing the health risk of a tobacco product by measuring how a user consumes a product. User puffing behaviors can impact the level of harmful and potentially harmful constituents (HPHCs) consumers are exposed to when using heated tobacco products (HTPs). A total of 194 US adults aged 21 years and older who used combustible cigarettes or HTPs as their primary source of nicotine were enrolled in a 28-day ambulatory topography study designed to evaluate puffing patterns after switching to glo Hyper. Study participants were assigned to use one of four HTP consumables ("neo sticks") based on their self-reported usual brand cigarette or HTP. Three menthol neo stick variants, including one with a crushable menthol capsule, and one non-menthol variant were assessed. Topography parameters including puff duration, number of puffs per day, inter-puff interval duration, and number of glo Hyper device activations per day were captured using the Product Use Behavior (PUB) instrument. On average, participants took 57.5 puffs per day and used an estimated average of five neo sticks per day. The overall mean puff duration was 1.66 seconds, overall mean inter-puff interval was 17.7 seconds, and study participants activated the device on average 4.9 times a day. Participants had similar puffing patterns regardless of neo stick variant used. Importantly, participants' puffing patterns aligned with the Health

Canada Intense machine puffing regimen utilized in chemistry studies of glo HTP that demonstrated substantial overall reductions in HPHCs compared to combustible cigarettes. The findings of this topography study suggest that as actually used by consumers, the use of glo HTP reduces exposure to tobacco smoke constituents.

44. Withdrawn

45. Withdrawn

46. AWARENESS AND USE PATTERNS OF ORAL NICOTINE POUCHES AMONG REPRESENTATIVE UNDERAGE SAMPLES IN THE UNITED STATES. Evan WINIGER, Nadja Richter, Pavel Lizhnyak; Altria Client Services, Richmond, VA, USA

Oral nicotine products have been marketed for several years, yet research on their utilization is in its infancy. The few research studies that have investigated underage use of nicotine pouches thus far suggest that these products have limited use among youth and underage adults.

The objective of this research was to estimate awareness, ever use, and current use of oral nicotine pouches by examining data from the National Youth Tobacco Survey (NYTS), Monitoring the Future (MTF), and the Altria Client Services Underage Tobacco Use Survey (UTUS) spanning from 2019 to 2023.

Recent nationally representative survey data sources show moderate awareness of nicotine pouches, with NYTS reporting 40.9% for high schoolers and middle schoolers in 2022 and UTUS reporting 40.6% for youth (13-17) and 53.9% for underage young adults (18-20) in the first half of 2023. Evidence from all three studies converge and show a low prevalence of ever use of nicotine pouches, with NYTS reporting 3.1% for high schoolers, MTF reporting between 1.2% and 3.6% for 8th, 9th, and 12th graders in 2023, and UTUS reporting 1.5% for youth and 4.5% for underage young adults. Similarly, current use of nicotine pouches was low, with NYTS reporting 1.7% for high schoolers and MTF reporting between 0.4% and 1.4% for 8th, 9th, and 12th graders in 2023.

Oral nicotine products have been in the US market for several years. Recent nationally representative data demonstrate there is moderate awareness of nicotine pouches and a low prevalence of underage ever- or current-use. Still, underage monitoring and prevention efforts should focus on novel oral nicotine products in the youth and underage adult space.

47. DEVELOPMENT OF METHODS TO ASSESS PUFF TOPOGRAPHY OF HEATED TOBACCO STICK PRODUCTS USED WITH THE PLOOM® HEATED TOBACCO DEVICE AMONG US ADULTS WHO SMOKE COMBUSTIBLE CIGARETTES. Kevin BALL[1], Nelly Mainy[2], Brian Nordskog[2], Jianmin Liu[1], Kyung Soo Hong[1], Jeffery Edmiston[1], Joshua Karelitz[1]; [1]Altria Client Services, Richmond, VA, USA, [2]JT International, Geneva, Switzerland

Puff topography (PT) methodologies are established for combustible cigarettes but not heated tobacco sticks (HTS). We conducted a study among adults who smoke cigarettes (aged 21-64) to develop and validate methods assessing PT of HTS used with the Ploom® device (collectively, Ploom system). We aimed to identify and address logistical barriers and characterize and assess consistency of PT across repeated assessments. We also assessed product use experience via Consumer Reported Outcome Measures.

Prior to study conduct, initial testing identified the need to support the SODIM SPA/M measurement device mouthpiece during PT assessment, addressed by a bespoke adjunct-brace designed to bolster the PT device without affecting flow rate or draw resistance.

The study involved seven visits on separate days. After Screening Visit, participants (n=61) were randomized to one of four HTS varieties (two menthol-flavored, two tobacco-flavored), matched on preference for menthol or tobacco cigarettes. Participants used their assigned HTS during Topography Visits 1-5, switching to the other variant within menthol/tobacco category for Visit 6. Topography Visits included four product use periods (PUP)—5 minutes of ad libitum use (i.e., device-limited period for one HTS) and 55 minutes of rest. PT measurements occurred during the final PUP only, using SODIM SPA/M attached

via tight-fit adjunct-brace. Participants completed the Modified Cigarette Evaluation Questionnaire (adapted for HTS) after PUP 3-4. PT outcomes included number of puffs, puff duration, per-puff volume, total volume, inter-puff interval, and flow rate. Descriptive statistics of puffing behavior and self-reported outcomes, and analyses assessing within-subject consistency of PT outcomes across visits will be presented. Methods for assessing PT of the Ploom system proved logistically feasible and provide an initial assessment of consumer product use behavior.

48. ANALYSIS AND COMPARISON OF NICOTINE PHARMACOKINETICS OF MODERN ORAL NICOTINE POUCHES. Kara KEETON, Alex Blanchette, Stacey M. Benson, Amy K. Madl; Valeo Sciences, Ladera Ranch, CA, USA

Nicotine delivery from modern oral nicotine (MON) products is influenced by various factors, including product characteristics (e.g., pouch mass, moisture content, pH, total nicotine content, % free nicotine), user experience, and clinical study design. This study aims to compare pharmacokinetic (PK) parameters, specifically peak plasma nicotine concentration (Cmax) and the total nicotine dose as area under the curve (AUC), from MON pouches under controlled use conditions. PK studies from peer-reviewed and gray literature were reviewed, and data were extracted for product and user characteristics, study methods, and PK results.

Available PK studies differed in product use durations, blood sampling timepoints, and AUC calculations. To directly compare across studies, analyses were conducted to calculate the product-specific elimination rates for 55 product strength + flavor combinations and to predict the Cmax and AUC0→240 for a standardized 30-minute product use session. Nicotine elimination, modeled using linear regression, demonstrated consistency across studies and products (mean=0.00585, SD=0.00134, range=0.00237-0.00916 min-1), with no significant differences by product strength, flavor, or user experience ($p>0.05$). However, significant differences were observed for Cmax (mean=6.28, SD=3.00, range=1.60-14.3 ng/mL) and AUC0→240 (mean=823, SD=409, range=195-1987 ng/min*mL) across product strengths (all p's<0.05), with AUC also significantly different by user experience ($p<0.05$). Product flavor did not have a statistically significant influence over any of the assessed parameters.

In conclusion, while the direct comparability of reported PK study results in the literature is limited by study design variations, analytical methods were leveraged to predict Cmax and AUC0→240 associated with a 30-minute product use session. These findings underscore the importance of standardizing certain methods for MON product PK studies to improve comparability of results and provide valuable data to inform regulatory decision-making.

49. CHARACTERIZATION AND COMPARISON OF TOBACCO-FREE POUCHES AGAINST TRADITIONAL TOBACCO REFERENCE PRODUCTS.

Andy STINSON, Leona Mijangos Sirkisoon, Angel Rodriguez-Lafuente, Hongxia Li, Rana Tayyarah; Labstat International, Kitchener, ON, Canada

The recent rise in popularity and diversity of modern oral products has brought greater attention to this category from consumers and regulators alike. The U.S. Food and Drug Administration (FDA) has published an abbreviated list of 9 harmful and potentially harmful constituents (HPHCs) in smokeless products. We analyzed select brands in this market for these 9 HPHCs and other compounds of interest. In order to ensure method robustness, products were chosen based on market volume and major variables, such as nicotine content, ingredients (flavors and sugars), and base matrices for the product category. Samples were analyzed for nicotine, minor alkaloids, nicotine degradants, tobacco-specific nitrosamines (TSNAs), benzo[a]pyrene (B[a]p), carbonyls, trace metals, aflatoxins, water activity, and water. Preliminary results show that aflatoxin levels (B1, B2, G1, G2) and ochratoxin were below quantitation limits (4.00 ng/pouch), consistent with the low water activity levels. Surprisingly, Karl Fisher titrations revealed that the water levels varied more than expected. Also, there were challenging matrix affect to overcome. As expected, HPHC levels were substantially lower in modern oral products compared to a reference tobacco pouch product and traditional reference cigarettes.

50. CHANGES IN BIOMARKERS OF EXPOSURE AMONG ADULT CIGARETTE SMOKERS WHO TRANSITIONED TO ENDS USE OR QUIT SMOKING: THE POPULATION ASSESSMENT OF TOBACCO

AND HEALTH STUDY, 2013-2019. Paul LIZHNYAK, Hui Cheng, Mingda Zhang; Altria Client Services, Richmond, VA, USA

Transitioning from cigarette smoking to electronic nicotine delivery systems (ENDS) or lowering cigarette consumption can reduce exposure to harmful constituents. This research examines changes in biomarkers of exposure (BOEs) among adults who exclusively smoked cigarettes at baseline (AS, n=6,112), using data from the Population Assessment of Tobacco and Health (PATH) Study (2013-2019). We estimated changes in BOEs (representing exposure to tobacco-specific nitrosamines, nicotine, heavy metals, and volatile organic compounds) between baseline and follow-up within wave pairs (W1-W2, W2-W3, W3-W4, W4-W5) using weighted generalized estimating equation models among AS who continued exclusive cigarette smoking (CS; n=5,178), switched to exclusive ENDS use (AE; n=79), smoked cigarettes and used ENDS (ADU; n=311), or reported no past 30-day tobacco use (AQ; n=544) at follow-ups. ADU were further subdivided based on self-reported changes in cigarette consumption (CPD) from the previous wave – substantive (≥50%; n=73) and moderate (up to 50%, n=64) reducers, no change in CPD (n=96), and substantive (≥50%; n=44) and moderate (up to 50%; n=34) increasers. Significant reductions in a majority of BOEs were seen among ADU (13/21), AE (16/21), and AQ (18/21) compared to CS. BOEs were significantly lower among substantive (16/21) and moderate reducers (10/21). There is a clear correlation between BOE levels and CPD. Comparable reductions in BOEs are observed between AE and AQ. These results demonstrate that even a moderate reduction in CPD among AS and ADU can significantly decrease exposure to harmful constituents.

51. Withdrawn

52. Withdrawn

53. CHARACTERIZATION OF VOLATILES FROM HEATED REFERENCE CIGARETTES 3R4F USING THERMAL SEPARATION PROBE-GC/MS. Antoaneta MIHAYLOVA-KROUMOVA, George J. Wagner, Victor D. Korenkov; University of Kentucky, Lexington, KY, USA

Tobacco harm reduction is a significant goal of the tobacco industry. Numerous studies have found a substantial reduction in harmful compounds released from heated and other non-combusted tobacco products compared to burning cigarettes. The devices designed to work with heated tobacco sticks generate temperatures between 50°C and 350°C.

In this study, the volatiles from the filler of reference cigarettes 3R4F were characterized using a thermal separation probe (TSP) attached to a gas chromatography-mass spectrometry (GC/MS) system. The TSP was set to temperatures of 200°C, 275°C, and 325°C. Volatiles were detached from the matrix before entering the column, and samples were analyzed in triplicate for each temperature. The focus of the work was on the potential flavor and fragrance compounds rather than the harmful chemicals.

Reference cigarettes were chosen to exclusively characterize natural compounds, avoiding interference from additives. While many volatiles matched those reported in a published tobacco flavor library (Krusemann et al., 2018), our approach revealed additional compounds, including potential natural flavor compounds and natural substances with uncharacterized flavor properties.

Notably, the number of detected volatiles from the heated reference tobacco material increased with rising temperature, suggesting a link between heating temperature and the overall volatiles. Although heating rods are designed to reach temperatures as high as 350°C, the gradual temperature increase might contribute to a more complex and potentially more satisfying organoleptic experience for users.

54. COMPARISON OF POLYCYCLIC AROMATIC HYDROCARBON QUANTITIES AND YIELDS IN FILLER AND SMOKE AMONG SELECT CIGAR PRODUCTS. Aireen ROMU, Rachel Lerebours, Mimy Young, Tricia Johnson, Charles Feng; Food and Drug Administration, Silver Spring, MD, USA

Available chemical analysis research of cigars has largely focused on tar and a limited number of harmful and potentially harmful constituents (HPHCs) (e.g., nicotine, carbon monoxide, tobacco-specific nitrosamines, selected carbonyls). To

date, very limited data exist on polycyclic aromatic hydrocarbon (PAH) yields in cigar products, and therefore, the differences in PAH yields across cigar types (i.e., little cigars, cigarillos, large cigars) are under evaluated. In this study, eight PAHs in tobacco filler and 10 PAHs in smoke were quantified and compared in a selected number of commercially available cigar products (29 little cigars, 19 cigarillos, and 10 large cigars) using the Canadian Intense smoking regimen (i.e., 55 mL puff volume, 30 sec puff frequency, 2 sec puff duration) in International Organization for Standardization (ISO) 17025 accredited laboratories. PAH quantities/yields were analyzed using a linear regression plot and coefficients of determination (r2) were calculated using the linear regression analysis function. The relationship between individual PAH and total PAH yields was evaluated. Our analysis shows that the average yield of each PAH in cigar filler and smoke have similar trends among these three cigar categories and chemical constituents. In addition, strong correlations ($r2 \geq 0.9$) were observed for most PAHs in filler and some of the individual PAHs in smoke yields in all cigar categories.

55. PHARMACOKINETICS, PHARMACODYNAMICS, AND NICOTINE EXTRACTION IN A NOVEL NICOTINE POUCH PRODUCT COMPARED TO TRADITIONAL MOIST SNUFF. Mikael STAAF, Camilla Pramfalk, Anna Masser, Tryggve Ljung, Robert Pendrill, Johan Lindholm; Swedish Match, Stockholm, Sweden

Nicotine pouches (NPs) are oral products that are packaged in permeable material and placed under the lip to deliver nicotine via the oral mucosa. Unlike snus and moist snuff, NPs contain no tobacco leaf, and the nicotine meets pharmaceutical standards. On the proposed risk continuum of nicotine-containing products, cigarettes are associated with the most risk, while NPs and other non-combustible products are on the other end of the spectrum. A product's nicotine delivery profile is probably one of the main determinants of its acceptability as an alternative to more harmful combustible products. However, few commercially available NP products have undergone scientific evaluation. This multi-center, open-label, randomized, cross-over, single-dose administration study assessed pharmacokinetics (PK), pharmacodynamics (PD), and nicotine extraction in two unflavored NPs (3 and 6 mg nicotine) of a new moist format compared to a

commercially available portioned moist snuff product (18 mg) in daily users of oral tobacco/NPs. The PK parameters maximum plasma nicotine concentration (C_{max}) and total nicotine exposure (AUCinf) were higher for moist snuff than the two NPs. In addition, the extracted nicotine amount—but not the extracted fraction—was higher for moist snuff than the two NPs. For PD parameters, moist snuff showed the median largest decrease in "craving" and increase in "satisfaction," followed by NP 6 mg and NP 3 mg. The findings show that compared to the moist snuff comparator, NP products did not lead to higher nicotine exposure in the study participants. Administration of all products was well tolerated by the subjects, with no safety concerns raised.

56. A CROSS-SECTIONAL SURVEY OF HEALTHCARE PROVIDER AWARENESS AND PERCEPTIONS OF TOBACCO AND NICOTINE-CONTAINING PRODUCTS. Susan MARTELLE[1], Deena Battista[2], Michael Polster[3]; [1]RAI Services Company, Winston-Salem, NC, USA, [2]Womble Bond Dickinson, Winston-Salem, NC, USA, [3]Naxion, Philadelphia, PA, USA

Aims: Healthcare providers (HCP) should be key sources of accurate information about tobacco use because they provide primary care or treat the respiratory and cardiovascular diseases that can result from cigarette smoking. Therefore, HCP perceptions about the risks of different types of combustible and non-combustible tobacco and nicotine-containing products (TNPs) are important to understand as they may impact interactions/conversations with patients who smoke, and consequently affect potential patient TNP use behavior.

Methods: An online survey was conducted with 700 physicians, nurse practitioners, and physician assistants in five medical specialties —family and general practice, internal medicine, obstetrics and gynecology, cardiology, and pulmonology to quantify:

- HCP awareness of different TNP types and perceived health-related risk potential for each of these products
- Frequency with which HCPs engage with patients about quitting cigarette smoking, comfort with having those conversations, and frequency with which various methods to help patients quit smoking are recommended

Results:

- HCPs assign less than 40% of the risk associated with cigarettes to the smoke in burned tobacco (whereas independent estimates suggest it represents close to 90% of the risk)
- HCPs estimate that e-cigarettes are associated with roughly 80% of the health risks of cigarettes (whereas a multi-criteria decision analysis model places the maximum relative harm of e-cigarettes as 4% of that of cigarettes)
- Half of HCPs do not believe that quitting smoking completely and switching to e-cigarettes reduces health risks

Conclusions: The findings suggest that the surveyed HCPs are unable to provide patients with accurate information about TNPs generally, and the continuum of risk specifically, and highlight the critical need for medical education to help correct widespread misperceptions about the health risks of nicotine.

57. EVALUATING THE IMPACT OF FEDERAL ENFORCEMENT ON THE ILLEGAL ELECTRONIC NICOTINE DELIVERY SYSTEMS (ENDS) MARKET. Lillian ORTEGA[1], Joslynn Watkins[2], Kevin Burd[3], Bryan Burd[3]; [1]Chemular, Gaithersburg, MD, USA, [2]WOW Solutions, Gaithersburg, MD, USA, [3]Chemular, Hudson, MI, USA

The illegal marketplace for electronic nicotine delivery systems (ENDS), poses substantial public health risks due to substandard manufacturing, evasion of federal regulatory requirements and the use of unknown ingredients. This abstract evaluates federal enforcement actions from January 2021 to January 2024, assessing the effectiveness of the actions taken by the Food and Drug Administration (FDA), the Bureau of Alcohol, Tobacco, Firearms and Explosives (ATF), the Department of Justice (DOJ), and Customs and Border Protection (CBP) on the illegal ENDS products. The study approach analyzed the metrics through a lens of regulatory timelines and enforcement priority policies, comparing types of enforcement actions, entities issued actions and impact of the actions. Since January 2021, the FDA has issued over 700 warning letters and filed civil money penalties to manufacturers and retailers. The DOJ filed

permanent injunctions against seven e-cigarette manufacturers. CBP and FDA have conducted seizures at ports and international mail facilities of shipments ranging from thousands to millions of dollars in illegal ENDS products. Despite the use of the range of enforcement tools, driven primarily by the FDA and DOJ, the illegal ENDS are still making it to the retail shelves and into consumers' hands. Enforcement actions by a single agency alone are insufficient to transform the illegal ENDS marketplace into a compliant and regulated one; a comprehensive, multipronged, whole-of-government approach is required. Leveraging the efforts and insights from all federal agencies that have developed strategies to combat illicit markets for other commodities can be highly beneficial. Enhanced inter-agency collaboration among federal and state partners is crucial to ensure comprehensive compliance with all tobacco-related laws which supports the broader goal of tobacco harm reduction.

58. DISSOLUTION TESTING OF WHITE FOX BRAND MODERN ORAL NICOTINE POUCHES. Ed CARMINES[1], Chris Woodruff[1], Lise Fraissinet[1], Mengliang Bao[2]; [1]Chemular, Hudson, MI, USA, [2]Labstat International, Kitchener, ON, Canada

White Fox is an oral tobacco-derived nicotine pouch product that does not contain cut, ground, powdered or leaf tobacco. The nicotine source is synthetic. Dissolution testing was performed as part of a PMTA development program in order to demonstrate that the products are appropriate for the protection of public health (APPH). The nicotine release profiles for the portfolio of White Fox brand nicotine pouches were characterized using the U.S. Pharmacopeia flow-through cell dissolution apparatus 4 (USP-4). Samples of all the study products were placed in the apparatus flow-through cells at a constant temperature of 37°C. A pump delivered a constant flow of artificial saliva for 100 minutes. The flow was sampled throughout the release period. The method followed the approach of Miller et al. 2020. Nicotine release profiles were compared by calculating the difference factor (f1) and similarity factor (f2) by adopting methodology referenced in Guidance for Industry from FDA's Center for Drug Evaluation and Research (CDER). The tested products varied in size, flavor, and nicotine content. The excipients are the same in all of the products. About 20% of the nicotine was

released over the first 30 minutes for all of the products. By 100 minutes the release was about 40%. The dissolution rate was about 0.4% per minute. All of the products were considered statistically equivalent to each other. The release rates were markedly slower than market comparators ZYN and VELO.

59. BLOCKCHAIN TECHNOLOGY – THE SOLUTION TO ILLICIT PRODUCTS AND AGE VERIFICATION. Ed CARMINES, Bryan Burd, Kevin Burd, Jason Carrigan; Chemular, Scottsdale, AZ, USA

Modern oral nicotine pouch products are made by forming a paper like fleece material into a tube, heat sealing the bottom of the tube, filling with the granulate material containing nicotine and then heat sealing the top. This fleece material has the potential to leach chemicals into the granulate materials and also be extracted by saliva during use. The fleece material is similar to a teabag. The fleece material is considered the primary packaging for the product. The Product Quality Research Institute ("PQRI") Leachables and Extractables Working Group's recommended approach was followed to evaluate different sizes of sealed empty pouches made from Dynatec 117/8/CFW material. Specifically, the pouch material was tested using the USP 1663 method (Assessment of Extractables Associated with Pharmaceutical Packaging/Deliver Systems). Samples were extracted with aqueous solutions at pH 5.2 and 9.5 and a 50/50% solution of isopropanol and deionized water. The solutions were analyzed by GC/MS (volatiles and semi-volatiles), LC/MS (non-volatiles) and ICP/MS (metals). The fleece did not appear to have the potential to leach materials of toxicological concern above the Safety Concern Threshold (SCT) or Toxicological Threshold of Concern (TTC). Under the conditions of use, the fleece was deemed acceptable for its intended use.

60. SPECIATION ANALYSIS OF CR(III) AND CR(VI) IN AGED E-LIQUIDS CONTAINING BENZOIC ACID USING IC-ICP-MS. Prasad LAVISETTY, Darybelle Collins, Alex Pennington, Kathy Humphries, I. Gene Gillman; Juul Labs, Inc, Washington, DC, USA

Electronic Nicotine Delivery Systems (ENDS) contain an e-liquid and wicking material that contacts a resistive heating element that may be based on alloys such as nichrome or kanthal. Currently, there are concerns about potential leaching of chromium (Cr) species

into the e-liquid if the heating element is under a relatively acidic environment. Chromium ions could exist in two oxidation states, Cr(III) state, which is considered pharmacologically active, and Cr(VI) state, which is hazardous with mutagenic and carcinogenic effects at low levels. The potential impact of these different oxidation states highlights the importance of quantitation for the speciation of chromium. In this study, we developed and validated a quantitative analytical approach using IC-ICPMS with an anion exchange column for simultaneous Cr(III) and Cr(VI) speciation analysis. Linearity, accuracy, and precision during validation met all acceptable limits in determining the method being "fit-for-purpose". Linearity was established from 0.1-60 ng/mL with an R2 of 0.995, accuracy was found to have recoveries of 94-105% over four different spiking levels, and precision and intermediate precision showed not more than 20% and 25% RSD respectively, for both species of chromium. Additionally, the method detection limit for Cr(III) and Cr(VI) was found to be 1.0 and 3.6 ng/g respectively while the quantitation limit for both species was found to be 10 ng/g. Standards and samples were freshly prepared to avoid any potential transitions of the chromium species including conversion of Cr(VI) to Cr(III) at low pH due to increased redox potential. During this study, a range of ENDS liquids containing benzoic acid were analyzed and no Cr(VI) was detected using this validated method.

61. A SENSITIVE GC–MS/MS METHOD FOR THE QUANTIFICATION OF BENZO[A]PYRENE TETROL IN URINE. Max SCHERER, F. Pilz, A. Gärtner, G. Scherer, N. Pluym; Abf Analytisch-Biologisches Forschungslabor, Planegg, Bavaria, Germany

Polycyclic aromatic hydrocarbons (PAHs) are ubiquitous pollutants formed during the incomplete combustion of organic matter such as tobacco. Among these, benzo[a]pyrene (BaP) has been classified as a known carcinogen to humans. It unfolds its effect through metabolic activation to BaP-(7R,8S)-diol-(9S,10R)-epoxide (BPDE), the ultimate carcinogen of BaP. Here we present a simple and highly sensitive GC–NICI–MS/MS method for the quantification of urinary BaP-(7R,8S,9R,10S)-tetrol ((+)-BPT I-1), the hydrolysis product of BPDE. The method was validated and showed excellent results in terms of accuracy, precision, and sensitivity (lower limit of quantification (LLOQ): 50 pg/L). In urine samples derived from users of tobacco/nicotine products and non-users, only

consumption of combustible cigarettes was associated with a significant increase in BPT I-1 concentrations. Levels of users of potentially reduced-risk products as well as non-users were all below the LLOQ. In addition, the urine levels of six occupationally exposed workers were analyzed and showed the highest overall concentrations of BPT I-1 (844.2 ± 336.7 pg/L). Moreover, correlation with 3-hydroxybenzo[a]pyrene (3-OH-BaP), the major detoxification product of BaP oxidation, revealed higher levels of 3-OH-BaP than BPT I-1 in almost all study subjects. Despite the lower levels, BPT I-1 can provide more relevant information on an individual's cancers susceptibility since BPDE is generated by the metabolic activation of BaP. In conclusion, BPT I-1 is a suitable biomarker to distinguish not only cigarette smokers from non-smokers but also from users of potentially reduced-risk products.

62. DETERMINATION OF AFLATOXINS AND OCHRATOXIN A IN TOBACCO, TOBACCO-FREE PRODUCTS, AND EMISSIONS FROM HEATED TOBACCO PRODUCTS USING A LC-MS/MS. Hongxia LI, Rebecca Cornelius, Andy Stinson; Labstat International, Kitchener, ON, Canada

Many species of microorganisms, such as the food-borne mold Aspergillus flavus, produce aflatoxins which are acutely toxic. Regulatory reporting needs for microbial analysis in tobacco products requires more specific and sensitive techniques for the analysis of aflatoxins in tobacco and tobacco products.

In the present study, we developed and validated a sensitive liquid chromatography–tandem mass spectrometry method for the quantitation of aflatoxins (B1, B2, G1 and G2) and ochratoxin A in tobacco, pouches, and, due to non-combustion temperatures, emissions from HTP (heated tobacco products). The samples were quantified using matrix-matched curves. The sample was extracted with acetonitrile, and then injected on LC-MS/MS after dilution without further sample cleanup. A Poroshell Phenyl-hexyl column and EC-C18 column were used for the separation of the tobacco samples and HTP/pouches samples, respectively. The mobile phases utilized were 5 mM ammonium formate and 0.1% formic acid in water as mobile phase A, and 0.1% formic acid in methanol-acetonitrile mix (90:10) as mobile phase B. The detection was performed in MRM mode using an ESI source in positive mode. The method showed good linearity

(R2 >0.99), precision (CV <15%), and recoveries (70-120%) over the calibration range of 0.02-4 ng/mL for all the target analytes. The recoveries ranged from 75-120% at three fortified levels (low-, medium-, and high-fortification levels). The method quantitation limits for all aflatoxins and ochratoxin A were 2.0 ng/g, 4.0 ng/pouch, and 0.32 ng/cig for tobacco, tobacco-free (i.e., modern oral) pouches and HTP emissions, respectively. This simple, efficient, cost-effective, and sensitive method can be applied in the monitoring of tobacco and other plant or food matrices.

63. ASSESSING AEROSOL PARTICLE SIZE DISTRIBUTION MEASUREMENTS IN ELECTRONIC NICOTINE DELIVERY SYSTEMS. Brittany MOORE; Reynolds, Winston-Salem, NC, USA

The Final Guidance for Industry, Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems (ENDS), issued by the FDA in March 2023 recommends evaluating particle size distribution (PSD) to gain insights into aerosol emissions from ENDS products. The objective of this study was to analyze PSD of four ENDS products utilizing a low-flow cascade impactor known as the MSP 135 Mini-MOUDI. Each product was evaluated utilizing two puffing regimens (non-intense and intense), in addition to assessing any potential impact of flavor variances. The mass median aerodynamic diameter (MMAD) ranged from 0.70 to 0.98 µm for each product. The geometric standard deviation (GSD), which is indicative of particle size distribution spread, was between 1.5 and 1.7. MMADs and GSDs remained consistent with respect to puffing regimen, flavor, and nicotine strength. Understanding particle size distribution (PSD) helps assess potential tobacco harm reduction of ENDS products although further research is needed to fully understand their long-term effects. The aim of this work is to provide valuable data for regulatory decisions and public health considerations related to ENDS.

64. NICOTINE ANALYSIS OF COMMERCIAL FOOD PRODUCTS USING GC-MS-MS AND LC-MS-MS. Robert Owen BUSSEY, III[1], Joe Kennaday[2]; [1]Reynolds American, Winston-Salem, NC, USA, [2]Eurofins Professional Scientific Services, Winston-Salem, NC, USA

The Final Guidance for Industry, Premarket Tobacco Product Applications for Electronic Nicotine Delivery Systems (ENDS), issued by the FDA in March 2023 recommends evaluating particle size distribution (PSD) to gain insights into aerosol emissions from ENDS products. The objective of this study was to analyze PSD of four ENDS products utilizing a low-flow cascade impactor known as the MSP 135 Mini-MOUDI. Each product was evaluated utilizing two puffing regimens (non-intense and intense), in addition to assessing any potential impact of flavor variances. The mass median aerodynamic diameter (MMAD) ranged from 0.70 to 0.98 μm for each product. The geometric standard deviation (GSD), which is indicative of particle size distribution spread, was between 1.5 and 1.7. MMADs and GSDs remained consistent with respect to puffing regimen, flavor, and nicotine strength. Understanding particle size distribution (PSD) helps assess potential tobacco harm reduction of ENDS products although further research is needed to fully understand their long-term effects. The aim of this work is to provide valuable data for regulatory decisions and public health considerations related to ENDS.

65. CHANGES IN E-VAPOR HARM PERCEPTION AND RELATED TRANSITION BEHAVIORS AMONG US ADULTS WHO SMOKE: LONGITUDINAL ANALYSIS OF POPULATION ASSESSMENT OF TOBACCO AND HEALTH (PATH) STUDY WAVES 1 TO 6 DATA. Lai WEI, Raheema Muhammad-Kah, Edward Largo, Maria Gogova, Mohamadi Sarkar; Altria Client Services, Richmond, VA, USA

Despite the overwhelming scientific evidence that e-vapor products (EVPs) are less harmful than cigarettes, many adults in the U.S. who smoke (AS) perceive EVPs as being equally or more harmful than cigarettes and these misperceptions are increasing over time. We analyzed PATH Wave 1 (2013-14) to Wave 6 (2021) data to determine changes in e-vapor harm perception among AS over time and associated behavioral transitions. The proportion of AS that perceived EVPs to be the same or more harmful than smoking cigarettes increased greatly from Wave 1 [45.6% (95%CI 44.4-46.7%)] to Wave 6 [87.7% (95%CI 86.5-88.8%)]. Similar trends were observed when we further segmented AS and adults who use EVPs (AV) based on their tobacco use status (i.e., never, current or former use of cigarettes and/or EVPs). The AS subgroups with the correct harm perception of

EVPs (i.e., EVPs being less harmful than cigarettes) were more likely to transition to exclusive EVP use or dual use. Similarly, AV subgroups with the correct harm perception were more likely to transition to or remain using EVPs exclusively. For example, adults who both vape and smoke with the correct perception transitioned to exclusive EVP use at a rate of 6.1% (Wave 1 to 2, 95%CI 4.7-7.9%) to 22.5% (Wave 5 to 6, 95%CI 18.2-27.5%) compared to those with misperceptions who transitioned at a rate of 2.9% (Wave 1 to 2, 95%CI 1.7-4.7%) to 11.9% (Wave 5 to 6, 95%CI 9.5-14.8%). In conclusion, accurate and timely messages are needed to correct misperceptions of EVPs relative to cigarettes and help facilitate AS transitions away from cigarette smoking.

66. THE HEATED TOBACCO PRODUCT MARKET. Phil SAUNDERS, Malcolm Saxton; Broughton Life Sciences, Earby, Lancashire, UK

A strong and growing body of evidence shows that switching from conventional, combustible cigarettes to alternative nicotine products significantly reduces a user's exposure to harmful and potentially harmful constituents (HPHCs). There are currently three main categories of consumer-reduced-risk nicotine products: e-cigarettes, heated tobacco products (HTPs), and oral nicotine pouches (ONPs).
While e-cigarettes are now a relatively mature category with established requirements for launching products in most parts of the world, both HTPs and ONPs are rapidly developing categories with diverse and often unclear routes to market globally.
This review focuses on the current state of the HTP market, including the products available, current development trends such as HTP nicotine delivery systems using non-tobacco substrates (HxP) such as veo™ designed for glo™ from British American Tobacco, global regulatory status and potential risks to the category, and the current analytical strategies recommended by manufacturers, regulators, and health bodies to assess the efficacy, safety, and appropriateness for the protection of public health (APPH) of these products.

In conclusion, this presentation provides an overview of the HTP market and the regulatory and technical challenges of bringing a product to market, including potential future challenges for the category.

67. TOMOGRAPHIC ANALYSIS AND COMPUTER SIMULATION FOR DIFFERENT CIGARETTE FILTERS. Oxana CHERKAS[1], Diane Raverdy-Lambert[2], Thomas Blin[2]; [1]SWM International, Allonnes, France, [2]SWM, c/o LTR, Usine Le Mans, Allonnes, France

Considering that 80% of marine litter is made of plastic and that cellulose acetate cigarette butts are among the top ten pollutants, there is an interest in replacing cellulose acetate filters by non-plastic alternative like for instance a cellulose based non-woven filter media.

It is important to have a comprehensive characterization method allowing to understand the differences between cigarette filters. One approach is to visually study the internal structure of the filters. The cigarette filter 3D structure can be figured out with X-Ray tomography which shows the distribution of the filtering media inside the filter. We presented the 3D structures of cellulose acetate and paper cigarette filters at CORESTA in 2022. These results were complemented with the addition of a non-woven airlaid, filter material.

Computer simulation through 3D filters helps understanding the aerosol retention of those filtering materials. Fibre's orientation, occupied fibre volume and filter porosity indicate that an homogeneous pore distribution and a low occupied fiber volume are important parameters to achieve an acceptable smoke retention. Additionally, air flow simulation through the filter confirms similar smoke retention with the airlaid filter studied vs a cellulose acetate filter.
X-Ray tomography and computer simulation are complementary techniques which provide a visual understanding of fibers distribution inside the filters and its influence on smoke deliveries.

68. COMPARISON OF METALS CONTENT IN ENDS USING ICP-MS WITH TWO SEPARATE AEROSOL COLLECTION METHODS: ACID WASHED QUARTZ PADS AND FRITTED IMPINGERS. Donald STOGNER, Emma Willis, Jamil Gray, Cynthia Rohrer; Eurofins Professional Scientific Servies, Winston-Salem, NC, USA

Analytical evaluation of metals in Electronic Nicotine Delivery Systems (ENDS) is critical for the regulatory compliance of ENDS products. Detection of metals is difficult due to their high boiling point. Therefore, contamination, collection efficiency, and break through are all important parameters to consider when using any collection method. Previous method development work incorporated these parameters to determine the best possible method. Previous work included an ICP-MS method, evaluating quartz pads and fritted impingers. Additional work has been performed to show the comparison of these parameters using ICP-MS and two collection methods by studying various spiking as well as un-spiked samples. Chromium, nickel, zinc, and iron was studied as these are most prevalent in ENDS. Multiple replicates will be performed for these metals as much of what is detected is from leaching and to average any variability between pods. Spiked work will use cadmium and arsenic as these have the lowest boiling points of the metals of interest in ENDS. Overall, the data support the use of ICP-MS using fritted impingers as the preferred method of collection to evaluate metals in ENDS products.

69. APPLICABILITY OF ISO 10993-17:2023 TO EXTRACTABLES AND LEACHABLES FOR THE TOXICOLOGICAL RISK ASSESSMENT OF ENDS PRODUCTS. Harish CHEVVA, Felix Ayala-Fierro; Juul Labs, Inc, Washington, DC, USA

Extractables & leachables (E&L) studies are required for the chemical characterization of materials/components that are in contact with as part of the toxicological risk assessment (TRA) of consumer products including pharmaceuticals, food, medical devices, and electronic nicotine delivery systems (ENDS). The updated ISO-10993-17:2023 includes key new approaches that impact how TRAs are conducted. Some of these include the toxicological screening limit (TSL) to prioritize “critical” extractables for the risk assessment and the calculation of their worst-case total quantity (TQ) and estimated exposure dose (EED). Early identification is key to identify compounds that may require targeted testing.

Herein we describe the approach for the evaluation of one ENDS component that results in different consumer exposure scenarios. Even though no concerns were identified in the preliminary analysis, non-targeted semi-quantitative extractable and simulated leachable analysis were conducted. The extracted compounds were evaluated for their potential hazards and overall risks based on the product specific exposure scenario using the updated ISO 10993-17:2023. A scaling factor (SF) was used to differentiate materials that may result in limited contact.

The SF is the component surface area in contact with the body divided by the component area extracted and is important to calculate the "total quantity" (^{TQmax}). This approach helps in real estimation of extracted compounds with respect to consumer exposure scenarios considering the placement of the component in the device. This concept in conjunction with the derivation of the TSL for the extracted chemical compounds when compared to the calculated T^{Qmax} for all the compounds are herein explored. Overall, the new guidance principles can be effectively applied to differentiate components associated with ENDS products specific to the exposure scenario.

70. OPTIMIZATION OF A GC-MS METHOD FOR THE DETERMINATION OF ETHYLENE OXIDE IN HEATED TOBACCO PRODUCT (HTP) AEROSOLS. Jacqueline COLLINS, Alexandra M. Martin; Mckinney Specialty Labs, Richmond, VA, USA

This presentation will describe the challenges of expanding a validated method for the analysis of volatile organic compounds (VOCs) in Electronic Nicotine Delivery Systems (ENDS), to evaluate VOCs in heated tobacco product (HTP) aerosols.

In 2023, we successfully validated a method for VOCs in ENDS e-liquid and aerosol for 1,3-butadiene, vinyl chloride, ethylene oxide, isoprene, propylene oxide, acrylonitrile, benzene, and toluene. This method was based upon CRM No 70 and ISO 21330; ISO 23923, with expected modifications to the analysis (different column, ion source, and calibration range).

In 2024, we applied the new method to VOCs in HTP aerosol. While levels of VOCs in ENDS aerosol were typically near, or below, the limit of quantitation (LOQ), all analytes, except vinyl chloride, were detected in the HTP aerosol

samples at or above the LOQ. The chromatograms for the HTP aerosol were more complex than for the ENDS aerosol and changes to the GC method were required to resolve some interferences from the analytes of interest. However, the biggest challenge was a large interference coeluting with ethylene oxide. Additional investigation determined the interfering compound to be acetaldehyde, which is present at a level 1000-times that of ethylene oxide in HTP aerosols. To aid in ethylene oxide selectivity, a derivatization method was adopted and incorporated into the method for HTP aerosols.

The validation of the new ethylene oxide method was conducted according to FDA/ICH Guidelines, and included selectivity, linearity and range, LOD/LOQ, accuracy, precision, stability, and robustness. The extract LOQ was 100 ng/mL, equivalent to 1 µg/collection, recoveries ranged from 91.5 to 102.8%, and method precision was 2.9%.

71. WEIGHT OF THE EVIDENCE: ASSESSING THE BENEFITS OF SMOKEFREE ALTERNATIVES TO ADULTS WHO SMOKE AND THE RISK OF UNDERAGE INITIATION. Elizabeth BECKER; Altria Client Services, Richmond, VA, USA

The objective of this session is to discuss how to evaluate and interpret the benefits of smokefree alternatives to adults who smoke and the risk of those products to underage populations, as well as the evolving and litigious landscape surrounding this risk/benefit equation. The panel will include perspectives of tobacco manufacturers, FDA, and policy experts. The panel will review and discuss the latest regulatory decisions including new guidance, market denials, market authorizations, and pending litigation. FDA will speak to the applicable study designs and approaches for PMTAs. Manufacturers will share data and analyses submitted as part of Premarket Tobacco Product Applications. These data will demonstrate how adults who smoke transition to smokefree products. Further, national data sets and intentions data among underage populations will be highlighted. The panel will also discuss how flavor may change the risk/benefit evaluation and what data may be most useful to the FDA. Finally, we will review

the current litigation environment and potential impacts to the regulatory decisions.

72. TOBACCO IMPLEMENTATION GUIDE (TIG) V1.0: A NEW STANDARD TO SUPPORT REGULATORY REVIEW AND DECISION MAKING. Chrissie CAI[1], Christine Connolly[2]; [1]US Food and Drug Administration, Beltsville, Maryland, USA, [2]CDISC, Austin, TX, USA

This presentation will describe the culmination of work from a collaborative project commenced by the FDA Center for Tobacco Products with the Clinical Data Interchange Standards Consortium (CDISC) to develop data standards for tobacco studies to support regulatory review and decision making. CDISC standards are required for regulatory submission of clinical drug trial data in the US, Japan and are accepted in EU and China. With publication planned in 2024, the Tobacco Implementation Guide (TIG) v1.0 provides an initial set of data standards including dataset specifications, controlled terminology, and conformance rules for nonclinical and clinical use cases.

Why is this Research/Study Important to Tobacco and Nicotine Product Regulation?

The FDA CTP mission is to protect the public health of the U.S. population from tobacco-related death and disease by comprehensively regulating the manufacture, distribution, and marketing of tobacco products; educating the public, especially youth, about the dangers of using tobacco products; and promoting and supporting strategies that ensure an equitable chance at living a healthier life for everyone. To achieve this mission CTP conducts scientific review of tobacco product applications, provides public education campaigns and resources, develops regulations and guidances, and takes compliance and enforcement actions when appropriate. Data standards in the Tobacco Implementation Guide (TIG) v1.0, planned for publication in 2024, will facilitate the quality and consistency of data submissions received by FDA-CTP and will further enable the use of tools to aid in review and policy decisions.

73. "IT'S GOOD NEWS": CASE STUDIES IN THE FACT-CHECKING OF STATISTICAL BIAS IN THE SCIENTIFIC LITERATURE AND ITS TRANSLATION BY THE NEWS MEDIA. Gal COHEN; Rose Research Center, Raleigh, NC, USA

As of 2020, 52% of US adults believed that combusted cigarettes are definitely or possibly harm-reduced products. The perception that e-cigarettes are not harm-reduced thus represents a pre-existing belief which may foster confirmation bias. Case studies (including those below) will be reviewed, identifying cases of mistranslation of study publication results by the press, or invalid statistical approaches which survived the fact-checking process.

Patel et al. evaluated stroke incidence in NHANES and concluded that aOR were higher for e-cigarettes than cigarettes, and that strokes happened earlier. This became the basis for an ad campaign by the California Department of Public Health. GC and Floe Foxon (Pinney Associates) raised several concerns, including lack of accounting for imbalances in ages of subgroups when determining stroke onset, and improbable sample sizes and confidence intervals. Other concerns were highlighted in an investigation by Retraction Watch and Science.

Bene-Alhasan et al. presented an abstract which evaluated heart failure incidence in the All of Us database, with wide press coverage. A partial enumeration of concerns have been mentioned in an interview of GC by Filter. Notably, Fox News celebrated "let's be honest, it's good news," because it provided an opportunity to highlight the harms of e-cigarettes, and an unsubstantiated media interpretation arose that "vaping, just once, could put you at risk for heart failure."

74. PREVENTING YOUTH ACCESS AND USE BY OUTFITTING E-CIGARETTES WITH NEAR-FIELD COMMUNICATION (NFC) TECHNOLOGY. Martin STEINBAUER[1], Kylie Halperin[1], David Lawson[2], Christopher Russell[3]; [1]SkyX Group, New York, NY, USA, [2]Inter Scientific, Liverpool, UK, [3]Russell Burnett Research and Consultancy, Glasgow, UK

Background: Youth use of e-cigarettes remains unacceptably high in the United States (US). Applying strategies that are effective in preventing youth access to e-cigarettes is crucial for both protecting youth from the health risks of vaping and preserving retail access to e cigarettes for adults who smoke. Near-Field Communication (NFC) technology enables e cigarettes to be 'locked' at the point of manufacture and 'unlocked' by a point-of-sale NFC reader following age verification of the customer's photo ID by a licensed retailer. This study modelled the potential US youth access prevention impact of fitting e cigarettes with NFC chips.

Methods: Model input parameters were literature based estimates of the number of US youth current e-cigarette users (YCEU) in 2023, and the proportions of YCEU obtaining e cigarettes from retail versus social sources, including underage social sources who obtained e-cigarettes from retail. The number of 2023 YCEU that may be prevented access to e cigarettes was estimated under different scenarios of future adoption of NFC technology by e cigarette manufacturers and point of sale success of the NFC system.

Results: In an "optimistic" scenario in which NFC chips are fitted into 10% of all e-cigarettes sold in the US in 2024, between 289,009 and 389,833 (13.6-18.3%) 2023 YCEU may be prevented access to e-cigarettes between 2024 and 2026. In an "ambitious" scenario (25% NFC chip adoption), between 671,721 and 881,578 (31.5-41.4%) 2023 YCEU may be prevented access to e-cigarettes.

Conclusions: In addition to existing proven policies and strategies, fitting e-cigarettes with NFC chips is a simple, inexpensive step that manufacturers can take to substantially reduce youth access to e-cigarettes without inconveniencing, discouraging, or otherwise deterring adults who smoke from accessing and using e cigarettes.

75. AWARENESS, SUSCEPTIBILITY, AND USE OF NICOTINE POUCHES AMONG A PROBABILITY-BASED SAMPLE OF

UNDERAGE SUBJECTS IN THE UNITED STATES. Andrea PATTON, Gabriel Barnard, Neil Mckeganey; Centre for Substance Use Research, Glasgow, UK

Objectives: Nicotine pouches are small, discrete, and available in a range of flavors. Along with the emergence of slang nicotine pouch use terminology ("Zynning") and increased presence of "Zynfluencers" on social media, there are heightened concerns about the impact this may have on underage appeal and use of nicotine pouches. Consequently, it is crucial to not only continually monitor underage use of nicotine pouches, but also the stages preceding use including awareness and susceptibility to nicotine pouches.

Methods: This study examined awareness, susceptibility, ever use, and current (past 30-day) use of nicotine pouches among a probability-based sample of underage (13 to 20 years) individuals (n = 4,603) in the United States who participated in Wave 3 (June-July 2023) of the Tobacco Product Prevalence Study.

Results: Main findings indicate that 39.2% [95%CI: 37.2-41.3] of underage individuals reported awareness of nicotine pouches, 6.9% [95%CI: 5.9-8.0] were susceptible to future nicotine pouch use, 3.0% [95%CI: 2.4-3.8] reported ever use, and 1.7% [95%CI: 1.2-2.3] reported current use. Susceptibility to nicotine pouches was lowest among tobacco-naïve subjects and highest among subjects who were currently using another tobacco product.

Conclusions: Despite concerns that nicotine pouches are small, discrete, and available in flavors, this study's findings indicate that the potential increased appeal of nicotine pouches has not had an impact on underage use of nicotine pouches, as current use remains low. Continued monitoring of the nicotine pouch uptake continuum and deeper insights into underage use of nicotine pouch brands, including the flavors and nicotine strengths used, will

be crucial in assisting regulatory decisioning on the net public health impact of these products.

76. DERIVATION OF EXCESS LIFETIME CANCER RISK FOR NON-COMBUSTIBLE NICOTINE PRODUCTS. Ramez LABIB; Consilium Sciences, Glen Allen, PA, USA

The United States Food and Drug Administration (US FDA) has raised concerns that assessment of individual constituents in electronic nicotine devices (ENDs) does not provide relative assessment of carcinogenicity. To address this, the Center for Tobacco Product (CTP) is proposing to evaluate cancer risk of ENDs constituents using Excess Lifetime Cancer Risk (ELCR) analysis using Inhalation Unit Risk (IUR) consistent with methodology used by EPA. The ELCR is the estimated probability that an individual's exposure to a substance could result in cancer. When IUR does not exist, the FDA is proposing to use alternative sources of risk or use a Threshold of Toxicological Concern (TTC) value of 1 in 100,000 (1.5 ug/day). The ELCR will be calculated for each “carcinogenic” constituent and then summed to determine a cumulative ELCR. This estimate of cancer risk in new products (ENDs) can then be compared to other tobacco products. The final determination of cancer risk of an ENDS product to appropriate comparators is one aspect considered in the appropriate for protection of public health (APPH) determination. In this case study, we will present a calculation of ELCR for various Non-Combustible Nicotine products and use it in a comparative risk assessment with cigarette smoke.

77. CHARACTERIZING TOBACCO PRODUCT USE PATHWAYS LEADING TO AND FLOWING FROM REGULAR USE OF NICOTINE POUCHES. Gavin O'DOWD[1], Jon Laucirica[1], Jasmin Alipour[1], Luke Dubery[1], Marta Esposti[1], Christopher Russell[2]; [1]Haypp Group AB, Stockholm, Sweden, [2]Russell Burnett Research & Consultancy, Glasgow, UK

Background: The potential for nicotine pouches (NP) to benefit population health depends on how they are used in relation to other, potentially more harmful tobacco products (TP). Characterizing TP use pathways leading to and flowing from NP can inform their public health impact.

Methods: A cross-sectional online questionnaire was completed (August 2023) by a self-selecting sample of 1,409 U.S. adult (21+) regular NP users who purchased NP through two e-commerce marketplaces, Nicokick and Northerner. Participant characteristics, current TP use behavior, and chronology of first and last use of a spectrum of TP were assessed.

Results: Participants were predominantly (70%) exclusive NP users, with smaller proportions reporting occasional (15%) or regular (15%) dual/polyuse of NP and other TP. A total of 234 unique TP use pathways were identified. The ten most common pathways, reported by 62% of participants, all ended with NP (i.e., no further TP initiation). Cigarettes (51%) and dip/chew (36%) were the most commonly reported 'first TP ever used'; 8% reported NP as the first TP ever used and 6% reported NP as the only TP ever used. Approximately 66% initiated cigarette use prior to NP, with 13% reporting a direct cigarettes to NP path. In contrast, 1% initiated cigarette use after NP. Exclusive NP users were most likely to arrive at NP directly from dip/chew (35%), e cigarettes (26%), and snus (15%).

Conclusions: In this sample of regular NP users, the most common TP use pathways started with cigarette smoking and/or dip/chew use and ended with exclusive use of NP, often via an intermediate TP. Initiation of any TP use through NP, and initiation of further TP use following NP, were both uncommon.

78. TRENDS IN SMOKING CESSATION AND TOBACCO PRODUCT TRANSITIONS: INSIGHTS FROM THE PATH STUDY. Mark CROSSWHITE; Consulticx Sciences Corp, Statesville, NC, USA

In this presentation we present PATH (Population Assessment of Tobacco and Health) data regarding combustible cigarette smoking cessation trends and transitions of combustible cigarette smokers to other tobacco products. The PATH study is conducted by the National Institute on Drug Abuse and the Food and Drug Administration (FDA) Center for Tobacco Products and is designed to inform the FDA's regulatory decisions and actions related to tobacco products. This is a large-scale (>50,000 participants), longitudinal study conducted in the United States to assess tobacco use and its effects on public health and to understand patterns of tobacco product use, transition behaviors, and health outcomes.

After a thorough evaluation of Waves 1–6 of the PATH data, we found that the prevalence of combustible cigarette smoking dropped from about 42% to approximately 20% (from around 13,500 to about 6,300 participants). During the same period, e-cigarette use showed a slight decline, decreasing from 11.2% to 10.8% (from about 3,500 to around 3,300 participants). However, within the group of approximately 3,500 e-cigarette users, there has been a significant demographic shift towards younger adults aged 18-24. The 28 – 24 age demographic represented 30% of e-cigarette users in Wave 1 and 50% by Waves 5 and 6. This contributed to the dramatic reduction of combustible cigarette smoking in participants aged 18-24. The reduction in this demographic contributed to the overall decline in smoking rates among the aggregate adult group, but has consistently contributed to the largest most dramatic reductions in smoking of any age group (from about 3500 participants to about 800).

79. IDENTIFYING PREDICTORS OF SMOKING SWITCHING BEHAVIORS BASED ON THE POPULATION ASSESSMENT OF TOBACCO AND HEALTH STUDY DATA: A MACHINE LEARNING ANALYSIS. Xiaona LIU[1], Yue Cao[1], Jiaxuan Li[1] , Xi Chen[1] , Yuming Xiong[1], Fangzhen Zheng[1], Jianqiang Zhang[1], Xiaona Liu[1], Xuxi Zhang[2], Xinying Sun[2],

Ian M. Fearon[3]; [1]Smoore Research Institute, Shenzhen, Guangdong, China, [2]Peking University, Beijing, China, [3]whatIF? Consulting, Harwell, UK

Completely abstaining from combustible cigarette (CC) smoking or fully switching to e-cigarette (EC) may be beneficial to reduce the global burden of smoking-related diseases. This study aimed to identify and compare the top 10 prospective predictors of smokers switching away from smoking CCs in the United States. Data from adult exclusive CC smokers at Wave 4 (2016-2017) of the US Population Assessment of Tobacco and Health (PATH) Study, who were followed up at Wave 6 (2021), were analysed. Using all eligible 396 variables from the Study, a Xgboost-based machine learning (ML) approach, evaluated via a nested cross-validation scheme, was utilized to develop a multiclass predictive model to classify smokers' behavioral changes from W4 to W6, including smoking cessation, full and partial switching to EC, and CC non-switching. The SHapley Additive exPlanations (SHAP) algorithm was deployed to identify and examine the top 10 predictors of each switching behavior. Among the 5,039 participants, 18.5% (weighted) reported stopping smoking, 4.4% completely switched to EC use, 7.2% partially switched to EC use, and 69.9% continued smoking exclusively, within 5 years. The top 3 predictors of smoking cessation were prior regular EC use, age, and household rules about non-combusted tobacco products; of full switching to EC use were age, type of current living space, and frequency of social media visits; of partial switching to EC use were daily consumption of CCs, time interval from waking up to smoking the first CC and living with tobacco users. ML is a promising technique to provide comprehensive information for predicting smokers' behavioural changes. Public health interventions aimed at assisting adults in switching away from CC should consider the predictors identified in this study.

80. THE EFFECTS OF ELECTRONIC CIGARETTE USE PATTERNS ON HEALTH RELATED SYMPTOM BURDEN AND QUALITY OF LIFE: ANALYSIS OF US PROSPECTIVE LONGITUDINAL COHORT

STUDY DATA. Xiaona LIU[1], Yue Cao[1], Jiaxuan Li[1], Xi Chen[1], Yuming Xiong[1], Fangzhen Zheng[1], Jianqiang Zhang[1], Xiaona Liu[1], Xuxi Zhang[2], Xinying Sun[2], Ian M. Fearon[3]; [1]Smoore Research Institute, Shenzhen, Guangdong, China, [2]Peking University, Beijing, China, [3]whatIF? Consulting, Harwell, UK

Electronic cigarette (EC) use is rising, and evidence increasingly supports that ECs are helpful in smoking cessation. However, evidence concerning the health effects of EC use, especially on changes in health related symptoms and quality of life (QoL), are lacking. This study aimed to examine the association between e-cigarette (EC) use patterns and health related symptoms (fatigue, pain, and emotional problems) as well as general QoL. Data were analysed from 7,225 adults across Waves 1-6 of the US Population Assessment of Tobacco and Health (PATH) Study. Current combustible cigarette (CC) or EC use patterns included non-current use of CC or EC, exclusive EC use, and dual CC/EC use, with exclusive CC smoking used as a reference. Linear mixed effects models controlling for age, gender, race/ethnicity, educational attainment, employment status, household income, health insurance coverage, visit to an emergency room, and PATH wave investigated the longitudinal associations between EC use patterns and symptom burdens/QoL scores, over periods spanning two waves. Those who were not currently smoking or vaping reported the lowest fatigue, pain, and emotional problems, and the best QoL, among the four groups. Compared to exclusive CC smoking, exclusive EC use was significantly associated with a decrease of approximately 0.065 units in average fatigue (95% confidence interval [CI]: -0.121, -0.009), a decrease of approximately 0.206 units in average pain (95% CI: -0.355, -0.058), and a decrease of approximately 0.103 units in average QoL scores (95% CI: -0.155, -0.051), with emotional problems similar over time. Exclusive EC users had less health related symptoms and better QoL than those who were exclusive CC smokers. This should be taken into account when assessing the harm reduction potential of ECs.

81. ADVANCING SCIENCE-BASED CONSENSUS STANDARDS FOR NICOTINE POUCHES IN THE U.S: PATHWAY TO REGULATORY AND PUBLIC HEALTH SYNERGY. Rachael SCHMIDT, Lillian Ortega; Chemular, Hudson, MI, USA

Nicotine pouches, a rapidly emerging category in the tobacco and nicotine market, present a unique regulatory challenge. As consumer demand for alternatives to traditional tobacco products increases in popularity, there is a pressing need for coherent, science-based standards. Establishing a science-based consensus standard enhances consumer safety by setting quality benchmarks and manufacturing protocols. Specifying permissible levels of nicotine, toxicants and other constituents, a consensus standard ensures product consistency and reduces health risks associated with manufacturing variability. Additionally, a consensus standard offers regulatory agencies a clear framework for oversight and enforcement. Aligned with scientific principles, it enables efficient evaluation of product compliance and streamline marketing authorization to protect public health.

Moreover, the development of a U.S. consensus standard propels innovation and industry collaboration in tobacco harm reduction. By establishing a level playing field, it incentivizes manufacturers to invest in research and development, driving nicotine product improvement and differentiation of products lower on the continuum of risk.In conclusion, establishing a science-based U.S. consensus standard for nicotine pouches is essential for advancing public health objectives, enhancing regulatory oversight, and fostering industry innovation. By aligning stakeholder interests and scientific expertise, this standardization initiative has significant potential to positively influence the rapidly evolving landscape of nicotine harm reduction products.

The proposed workshop will explore the development of a U.S. consensus standard for nicotine pouches and discuss its potential impacts. Panelists will

examine the scientific evolution of smokeless tobacco products including dissolvables and novel products, the current status of the science in regard to developing a consensus standard for nicotine pouches, as well as the appropriate regulatory framework needed to ensure consumer safety and enhance public health. Each panelist brings their unique perspectives from diverse regulatory, scientific and industry backgrounds, enriching the discussion and ensuring a comprehensive approach.

82. THE ROOTS OF LOW ALKALOID TOBACCO PROBABLY DETERMINE ITS POOR LEAF QUALITY. Barunava PATRA, C. Fisher, SK. Singh, J. Kinney; University of Kentucky, Lexington, KY, USA

Nicotine comprises heterocyclic pyridine and pyrrolidine rings, each of which is derived from two independent primary metabolic pathways, the NAD pathway, and the polyamine (PA) pathway respectively. Low-nicotine (LA) tobacco varieties lack the two NICOTINE (NIC) loci containing major regulators of nicotine biosynthesis. LA plants have delayed leaf maturation and poor cured leaf quality. It is also more susceptible to insect herbivory compared to the regular high alkaloid (HA) variety. To investigate the factors associated with poor leaf quality of LA lines, we did a reciprocal grafting experiment where the shoot (scion) of LA was grafted onto normal HA stock, and vice versa. The typical characteristics of the LA line disappeared and cured leaf quality was acceptable when this was grafted on the HA root system, and conversely, the leaves of the HA line showed the typical characteristics of LA lines and produced poor quality cured leaves when grafted on the LA roots. These changes were associated with the concomitant reversal in nicotine concentration. These results suggest that tobacco roots, besides being the source of nicotine biosynthesis, also dictate the leaf development process. The root produces PAs, which undergo extensive transport, degradation, and conjugation throughout the plant's life cycle. PAs play a vital role in the growth and development of plants. Root also produces phytohormones, which integrate environmental signals to influence plant

development and cell division, elongation, differentiation, etc. A root growth assay indicates that the lateral root density and branching of LA plants are greater than HA roots. Transcriptomics analysis revealed expression of genes related to NAD and PA biosynthesis, phytohormone biosynthesis, and signaling are altered in the LA line suggesting that these factors are possibly responsible for poor leaf quality and different root phenotypes in LA plants.

83. STACKING A NOVEL LOW NICOTINE GENE WITH THE LA NIC1NIC2 MUTANTS LOWERS NICOTINE TO ULTRA-LOW LEVELS. Anne FISHER[1], Stacey Slone[1], Barunava Patra[1], Colin Fisher[1], Huihua Ji[1], Jeffrey Kinney[1], Shengming Yang[2]; [1]University Of Kentucky, Lexington, Kentucky, USA, [2]United States Department of Agriculture, Fargo, ND, USA

In 2012, a stable population of the burley breeding line L8 gave rise to a 2013 population segregating for alkaloid content. A single plant selection from this population produced a fairly uniform 2014 population with lower alkaloids, and alkaloid levels were similar in subsequent generations. Nic1Nic2 marker analysis showed that these low alkaloid lines (L8 LN) and their sister lines with normal alkaloid levels (L8 HI) were the same genotype, Nic1nic2, indicating the presence of a novel gene. Compared with the L8 HI sister line, alkaloids in the L8 LN lines were reduced in the leaves but not in the roots, whereas in the traditional low alkaloid (LA) lines, alkaloids are reduced in both the leaves and the roots. Segregation in the F2 (L8 LN x L8 HI) suggested a single gene. A $\chi 2$ analysis could not distinguish between complete or partial dominance, although the F1 data suggested that partial dominance is more likely. We made the cross LA x LN, anticipating that the addition of the LN gene would reduce alkaloids below the LA level. Over the last two years, the selfed lines (F3, F4) were tested in agronomic trials. In 2022, alkaloids levels in the F3 were slightly lower than in the LA line, but were further reduced in the 2023 F4 lines (nicotine + nornicotine 0.51-0.68 mg/g, 1-2% of the high alkaloid HA check), compared with the LA line (2.1-4.5

mg/g, 8-9% of the check) and a gene-edited line (0.37-0.50 mg/g, 1-2% of the check). Stacking the novel gene with nic1nic2 reduces alkaloids to ultra-low levels almost as low as the gene-edited lines, but the cured leaf quality is extremely poor.

84. UNDERSTANDING THE MOLECULAR MECHANISM UNDERLYING LOW ALKALOID ACCUMULATION IN A MUTANT BURLEY BREEDING LINE WITH NOVEL SPONTANEOUS MUTATION(S). Barunava PATRA, A. Fisher, S.K. Singh, J. Kinney; University of Kentucky, Lexington, KY, USA

Nicotine is produced in the root, transported through the vasculature, and accumulated in the leaf. Nicotine biosynthesis in tobacco is predominantly regulated by the two independent loci, Nic1 and Nic2 harboring clustered transcription factor genes of the AP2/ERF subfamily. Mutation or deletion of these loci significantly reduces nicotine biosynthesis. We have identified low alkaloid spontaneous mutant(s) in the burley line L8 line (designated as L8LN), in which nicotine accumulation is reduced in the leaf, but not in the root. In the L8LN line, the Nic2 locus is deleted, but Nic1 is present. Reduction of nicotine content in this line may be a result of misregulation of the nicotine pathway genes and/or transcription factors, or a putative mutation leading to a less efficient enzyme. Loss or mutation of putative nicotine transporters could lead to a lower nicotine accumulation in the leaf. We have employed RNA-seq to understand the molecular basis of low nicotine content in L8LN. Transcriptome analysis revealed that there are no significant differences in the expression of the nicotine biosynthesis genes and their major regulators, except for MYC2a. The analysis further revealed downregulation of the polyamine oxidase gene, leading to poor recycling of polyamines in the root, limiting the availability of putrescine for nicotine biosynthesis. While there were no significant differences in the expression of known nicotine transporter genes, two novel transporters belonging to the MATE and PUP categories are significantly downregulated in the L8LN root.

Multiple nitrate transporters are also downregulated in the L8LN root, which can alter the nitrogen uptake, metabolism, and subsequently nicotine production. These findings pave the way for identifying new candidates to manipulate nicotine biosynthesis in tobacco.

85. POST TRANSLATIONAL REGULATION OF NICOTINE BIOSYNTHESIS BY MAP KINASE CASCADE NTMEKK1B-NTMKK2A-NTMPK4. Yan ZHOU, Yongliang Liu, Sitakanta Pattanaik, Barunava Patra, Ruiqing Lyu, Huihua Ji, Sanjay Singh, Ling Yuan; University of Kentucky, Lexington, KY, USA

Nicotine is an essential specialized metabolite that tobacco produces mainly for resisting biotic stresses. The transcriptional regulation of nicotine biosynthesis has been extensively studied; however, the post-translational regulation mechanisms involved in the pathway remain unclear. The mitogen-activated protein kinase (MAPK) cascades comprise at least 3 kinases, including MAP3K, MAP2K, and MAPK. The upstream kinase (MAP3K) phosphorylates the downstream kinase MAP2K, which phosphorylates multiple protein substrates, such as transcription factors, resulting in the modification of protein activities. MAPK cascades are well-known stress-responsive regulators; however, how they are involved in specialized metabolism is poorly understood.

Our previous work has demonstrated that the tobacco MAPK, *NtMPK4*, is a positive regulator of nicotine biosynthesis. However, the upstream MAP3K and MAP2K in the signaling cascade have not been identified.

Here, we identified *NtMEKK1b* and *NtMKK2s* as the upstream kinases of *NtMPK4* in the cascade. Protein-protein interaction assays demonstrated that *NtMKK2a* and *NtMKK2b* interact with *NtMPK4* and that the *NtMEKK1b* interacts with *NtMKK2a* in yeast and plant cells. *NtMKK2a* phosphorylates *NtMPK4 in vivo*. Promoter transactivation assays demonstrated that *NtMEKK1b* and *NtMKK2*s increase the activity of a nicotine biosynthesis-related transcription factor, *NtERF221*, by 131% and 66%, respectively. The

overexpression of *NtMEKK1b* or *NtMKK2a* in tobacco hairy roots increased the expression of nicotine biosynthetic genes and nicotine contents. Knocking down *NtMEKK1b* in transgenic plants resulted in reduced expression of nicotine biosynthetic genes and nicotine contents. Knocking down *NtMKK2s* in tobacco hairy roots decreased the nicotine content and pathway gene expression significantly.

In summary, our findings indicated that the *NtMEKK1b-NtMKK2-NtMPK4* cascade plays a positive role in the post-translational regulation of nicotine biosynthesis.

86. ACTUAL EXPERIENCE CONDUCTING ACTUAL USE STUDIES: NOTES FROM THE FIELD ON EFFECTIVE LONGITUDINAL TRIALS. Christopher FLEURY, Victoria Hoverman; Ipsos-Insight, Washington, DC, USA

A recurring theme in the FDA's market denial orders to PMTA applicants has been that the predominantly crosssectional data submitted did not provide evidence of the impact that the candidate products might have on adults' tobacco and nicotine behaviors over time. This spurred industry interest in conducting longitudinal studies to fill this gap. Such studies include randomized controlled trials (RCTs) and actual use studies (AUSs) that track participants' ad libitum product usage behavior over time in a "real world" environment. Such studies are major investments, requiring careful contemplation of the study design as well as thoughtful on-the-ground planning and coordination before fieldwork begins.

Drawing on blinded data, case studies, and practical examples from longitudinal studies conducted for tobacco and nicotine companies by the Ipsos Regulatory Affairs Research Team, this presentation will discuss the special considerations and best practices for conducting this type of study. Topics will include recruitment strategies, product distribution logistics,

incentives management, fraud prevention, staff training, technical support for participants, adverse event reporting, data protection, coordination of external and internal research partners, and project management across the lifecycle of the study.

87. PERSON-CENTERED APPROACHES TO UNDERSTAND CIGARETTE SWITCHING AND CIGARETTE REDUCTION RATES IN ACTUAL USE STUDIES. Ian JONES, Jessica Zdinak, Kiri Li Stauch; Applied Research and Analysis Company, Richmond, VA, USA

In the tobacco harm reduction literature, there has been a heavy reliance on descriptive statistics such as percentages, frequencies, and means with little use of inferential statistical testing. The FDA has asked manufacturers to conduct inferential statistics using null hypothesis testing (NHST) to provide substantial evidence backing their research. Currently, we have a manuscript in preparation in this regard; however, the objective of this proposal is to provide information on an alternative inferential method for analyzing data that uses a person-centered prospective. A longitudinal experimental switching study was conducted with 602 total participants over 3 months. NHST analyses were conducted on the full sample, but person-centered analyses are considered for participants with no missing data (n = 164) across all 3 months. Person-centered approaches allow researchers to highlight key behavioral changes that might otherwise be missed when aggregating the data. Inferential person-centered analyses revealed that a greater percentage of participants using flavored e-liquids showed a reduction in their CPD over time compared to the tobacco tasting e-liquid users. The FDA stated in October 2023 at a public workshop that a 50% or more reduction of cigarettes is likely to be a "benefit" to public health. Our analyses further demonstrate that a greater percentage of tobacco tasting users increased CPD compared to the flavored e-liquid users. The present collection of findings offers an alternative method which is easier to understand by laypersons, regulators, and scientists. By using an alternative method of data analysis, more

comprehensive forms of analyses can be conducted which focus upon the individuals within a given sample. Moreover, these analyses provide a greater range of information to regulators, scientists, and consumers alike.

88. A RANDOMIZED EXPERIMENTAL STUDY TO ASSESS THE EFFECTS OF FLAVORED E-LIQUID PRODUCTS ON ADULT SMOKERS SWITCHING CIGARETTE CONSUMPTION BEHAVIORS. Jessica ZDINAK[1], Ian Jones[1], Kiri Li Stauch[1], Willie McKinney[2]; [1]Applied Research and Analysis Company, Richmond, VA, USA, [2]McKinney Regulatory Science Advisors, Richmond, VA, USA

FDA CTP has advised industry to include Randomized Control Trials or Longitudinal Cohort Studies in their product applications. This randomized longitudinal experimental study was conducted to assess the impact of e-liquid flavors and opportunity to choose from a portfolio of products on adult smokers switching, and cigarette consumption .We hypothesize that for adult smokers, 1) the availability of a portfolio of non-tobacco flavored e-liquids will result in a greater reduction in the number of cigarettes smoked per day compared to only tobacco flavored e-liquids, and 2) the ability to choose from a portfolio of multiple products will result in a greater reduction in the number of cigarettes smoked per day compared to only one product choice. The 3-month study is currently ongoing with 579 participants completing the first month. Results from baseline to month one indicates that there was a greater reduction in cigarette consumption in the non-tobacco flavor versus the tobacco flavor groups. The ability to choose from a portfolio of products resulted in a marginally greater reduction in cigarette consumption compared to no choice. The preliminary study results suggest that giving adult cigarette smokers a choice of non-tobacco flavored e-liquids may reduce cigarette use.

89. MENTHOL, BLUEBERRY, AND WATERMELON NJOY ACE PROMOTES SIGNIFICANTLY GREATER COMPLETE SWITCHING

COMPARED TO TOBACCO-FLAVORED NJOY ACE. Kate VERGARA, Elizabeth Becker, Hui Chen; Altria Client Services, Richmond, VA, USA

In 2022, the FDA authorized the Tobacco-flavored NJOY ACE Products as appropriate for the protection of public health. The PMTA included NJOY's longitudinal cohort study (LCS) (n=8002; data collection October 2019-June 2020) which prospectively assessed tobacco use behaviors among NJOY users over time and demonstrated that 16.8% of adults 21+ who smoke (AS) and initially used Classic Tobacco (CT) NJOY ACE completely switched from cigarettes at the three-month timepoint (Primary Outcome). We further analyzed the LCS data to assess Menthol (MT), Blueberry (BB), and Watermelon (WM) NJOY ACE relative to CT NJOY ACE.

Results from these analyses demonstrate that MT, BB, and WM NJOY ACE are more effective in promoting complete switching relative to CT NJOY ACE. For Per Protocol 30-day Point Prevalence Abstinence analyses, statistically significantly greater proportions of AS who initially used MT (24.2%), BB (26.3%), and WM (29.0%) reported not smoking for the past 30-days at the three-month time point compared to those who initially used CT (16.8%; all p-values<0.05). When using an Intent to Treat 30-day Point Prevalence Abstinence analysis, MT (17.5%), BB (16.1%), and WM (20.0%) also outperformed the CT (11.3%; all p-values<0.05). Furthermore, the number of AS who completely switched and initially used MT (n=135), BB (n=191), or WM (n=126) was higher than for CT (n=88). Taken together, the efficacy (rate of switching for AS who initially used flavored NJOY ACE) and reach (number of AS who initially used flavored NJOY ACE) provide a greater positive public health impact for the flavored NJOY ACE than Tobacco-flavored NJOY ACE.

90. SIX-WEEK ACTUAL USE STUDY TO EVALUATE THE EFFECT OF THE JUUL2 SYSTEM ON CIGARETTE SMOKING AND TOBACCO PRODUCT USE BEHAVIORS AMONG ADULTS WHO

SMOKE CIGARETTES IN THE UNITED STATES. Nicholas GOLDENSON[1], Saul Shiffman[2], Ryan Black[1]; [1]Juul Labs, Inc, Washington, DC, USA, [2]PinneyAssociates, Pittsburgh, PA, USA

In this six-week actual use study, US adults who smoked cigarettes every day were provided with the JUUL2 System 18 mg/mL, a next-generation electronic nicotine delivery system (ENDS) product, for *ad libitum* use. At the end of each week, participants completed electronic surveys that assessed cigarette smoking, JUUL2 product use and related constructs (e.g., dependence, respiratory symptoms).

A total of 242 participants and 239 participants who were provided with Virginia Tobacco and Polar Menthol JUUL2 products, respectively, were included in the primary analysis. Both samples consisted of US adults (mean age: 38-39) who smoked cigarettes daily, reported high levels of dependence on cigarettes and predominantly were not planning to quit smoking (0.8%-1.3% planning to quit smoking in the next 30 days). Rates of complete past 7-day switching away from cigarettes increased progressively across the six weekly actual use periods: from 27.8% at Week 1 to 38.2% at Week 6 for Virginia Tobacco and from 32.7% at Week 1 to 45.3% at Week 6 for Polar Menthol. Participants who switched completely away from smoking at Week 6 had significantly lower levels of dependence on JUUL2 products relative to their own dependence on cigarettes at baseline and reported improvements in respiratory symptoms (ps<0.01). Switch rates were higher among participants who used menthol-flavored (vs. tobacco-flavored) JUUL2 products.

The JUUL2 System can facilitate high rates of complete switching away from cigarettes among US adults who are heavily dependent on cigarettes and predominantly do not plan to quit smoking. Adoption of JUUL2 products can help substantial proportions of US adults who smoke switch completely away

from cigarettes, thereby reducing their exposure to cigarette-related toxicants and ultimately improving their health.

91. DETERMINATION OF ORGANIC ACIDS IN ENDS PRODUCTS BY GC-MS USING ALKYL CHLOROFORMATE DERIVATIZATION IN AQUEOUS SOLUTION. Andrew CHEETHAM; Mckinney Specialty Labs, Richmond, VA, USA

Organic acids are a common constituent of electronic nicotine delivery system (ENDS) liquids and aerosols. These are present either as e-liquid ingredients (e.g., use of nicotine salts, preservatives) or from the degradation of the PG-VG matrix and certain flavourants. Their presence can affect the overall user experience with regards to taste, aroma, and nicotine uptake. From a regulatory standpoint, reporting of constituents that are contained within, or emitted in ENDS products aerosols (including any reaction by-products) is required for U.S. FDA premarket tobacco product applications (PMTAs). Published methods for analysing organic acids in ENDS products include HPLC-UV, ion chromatography, and GC-FID. The first two offer simple sample preparation but can have selectivity issues for certain acids, while the latter has excellent selectivity at the cost of a more involved sample preparation. Herein, we present a GC-MS method that uses an alkyl chloroformate reagent that allows for simple derivatization of organic acids in basic aqueous solution.

To prepare samples for analysis, an aliquot of an ENDS e-liquid or aerosol sample in basic water is treated with pyridine/isobutanol/isobutyl chloroformate (3:4:3). After 5 minutes, the esterified-organic acids are extracted into hexanes and analyzed by GC-MS. Stable isotope-labelled analogues are used as internal standards. Excellent selectivity was observed for acetic, propionic, benzoic, glycolic, and lactic acids within the 21-minute run-time, both from each other and from other potential acid interferences. Across multiple flavored e-liquid products, accuracy ranged from 80 to 105% and precision was under 10%. The instrument limits of quantitation (LOQ)

were 0.75–1 μg/mL, with method LOQs of 1.9–2.5 μg/mL for e-liquid and 7.5–10 μg/collection for aerosol.

92. DETERMINATION OF NICOTINE IN OTDN AND LIQUID PRODUCTS BY UV-VIS SPECTROPHOTOMETRY. Seok Chan PARK, Fadi Aldeek; Altria Client Services, Richmond, VA, USA

In recent years, the popularity of Oral Tobacco-Derived Nicotine (OTDN) products has increased due to their non-combustible nature and the associated potential reduction in tobacco and combustion-related toxicants. In this study, we developed and validated a fast and efficient method for the determination of nicotine in OTDN pouches (e.g., on! nicotine pouches) and nicotine solutions. Nicotine from pouch products was extracted by hand mixing in Type 1 water for one minute, and in 50:50 acetonitrile/Type 1 water solution using a Geno-grinder for nicotine solutions. After centrifugation, dilution, and filtration, nicotine content was determined by UV-Vis spectrophotometry at 260 nm. Flavored zero (0) mg nicotine products were used as reference products to minimize matrix interference during UV-Vis spectral data acquisition. For method validation, we used twelve (12) on! nicotine pouch products including original, citrus, mint, and wintergreen flavors at three nicotine strengths (2 mg, 4mg, and 8mg) alongside with non-flavored nicotine solution. The method was validated according to ICH guidelines and demonstrated excellent linearity within the concentration range of 5.0 - 40.0μg/mL, with R2 values ≥ 0.999. Accuracy was confirmed through fortification recovery, with values falling within the acceptable range of 95 to 108%. The method exhibited excellent precision, with %RSD values ≤ 0.11%, 8.1%, and 8.5% for instrument precision, repeatability, and intermediate precision, respectively. The method robustness was evaluated by varying the extraction time and device, resulting in %change values ≤ 2% and ≤ 10% for the pouch product and nicotine solution, respectively. The results show that this method is suitable for rapid quantitative analysis of nicotine in

OTDN pouches and nicotine solutions, making it potentially applicable to a wide range of OTDN tobacco products.

93. GAS PHASE INFRARED SPECTROSCOPY ENABLES PUFF-BY-PUFF PROFILING OF A NOVEL HEATED TOBACCO CAPSULE (HTC) PROTOTYPE. Frank HIGGINS, Michael B. Brown, Zack W. Blackmon, Matt Melvin, Weiling Li, Yezdi B. Pithawalla; Altria Client Services, Richmond, VA, USA

Heated Tobacco Products (HTPs) heat a tobacco substrate to low temperatures (below 350°C), to produce an inhalable nicotine-containing aerosol with significantly reduced levels of harmful and potentially harmful constituents (HPHCs) compared to cigarettes. HTPs use varying heating algorithms (i.e., temperature kept constant or changed over a product use session) to provide adult consumers who smoke a consistent user experience. Analyzing HTP aerosols with real-time puff-by-puff resolution, can enhance the understanding of HPHC deliveries over a product use session and inform development of potentially lower risk HTPs. Due to inherent limitations, traditional methods for collecting and analyzing aerosols are not easily adaptable or sensitive enough for puff-by-puff quantification. We present a Fourier transform infrared spectroscopy (FTIR) technique capable of simultaneously analyzing multiple HPHCs, such as nicotine, CO and carbonyls, in a HTP aerosol with puff-by-puff resolution in real-time. The system is nitrogen purged between puffs to minimize carryover and ensure accurate puff-by-puff quantification. Chemometric calibrations are developed to quantitate concentration of constituents in parts per million, which are then converted to mass amounts (i.e., mg/capsule or mg/stick). The application of puff-by-puff analysis to a novel heated tobacco capsule (HTC) prototype will be discussed. The method's suitability will be demonstrated by showing comparability of the cumulative puff-by-puff nicotine yields to yields obtained by standard methods. Trends in HPHC delivery across a product use

session will be explored. Also, results from comparator HTPs using heated tobacco sticks (HTS) will be shared.

94. NON-TARGETED CHEMICAL ANALYSIS - TRANSITIONING FROM RESEARCH TO ROUTINE APPLICATIONS. Mark CROSSWHITE, Roxana Weil, Willie McKinney; McKinney Regulatory Science Advisors, Richmond, VA, USA

Non-targeted chemical analysis (NTA) is a sophisticated method for chemical characterization that generates comprehensive data sets crucial for monitoring complex reaction systems and understanding chemical dynamics. This technique significantly enhances our grasp of the interplay between physical and chemical process in play in a product, pivotal for advancing product development, stewardship, and safety measures.

Despite its advantages, the primary challenge of NTA is managing the vast amount of data it produces, which can be overwhelming and has often deterred its widespread adoption. To address these challenges, it is important to implement advanced strategies in experiment design, data processing, and interpretation.

This presentation outlines effective strategies for transitioning NTA data interpretation from a labor-intensive research project to a more routine workflow. Critical to this transition is the selection of reference data sources that are relevant to the specific sample type and aligned with downstream workflow. As an example, we will focus on NTA of modern oral and electronic cigarette product types and downstream toxicologic evaluations. We will draw on recent Center for Tobacco Products memos concerning toxicant yields and data on extractables and leachables for premarket tobacco product applications. We advocate for a strategic cross-referencing of NTA-detected compounds with multiple databases. These include, 1) The FDA's Substances Added to Food (formerly EAFUS) list, with the additional cross-referencing to

available JECFA and FEMA PADI values, 2) Compounds typically found in food, indicative of NFC-related substances, 3) Extractable and leachable compounds, 4) Chemicals identified in tobacco products, and 5) The FDA's list of Harmful and Potentially Harmful Constituents. Our discussion highlights our methodology for selecting relevant compound databases and aligning our analytical strategies with downstream processes, emphasizing the automation of these processes to enhance efficiency and reliability.

95. ANALYSIS OF THE FULL COMPOSITION OF HEATED TOBACCO AEROSOLS BASED ON LARGE VOLUME THERMAL INJECTION-COLUMN INTERNAL EVAPORATION CONCENTRATION.

LI Junjie, Fei Ting, Qi Dawei, Cheng Qian, Zhang Wei, Wu Da; Shanghai Tobacco Group of CNTC, Shanghai, China

Heated tobacco aerosols, generated during the heating process of tobacco sticks, are a complex system whose composition directly affects product quality, aroma, and smoking sensation. The analysis of the components of heated tobacco aerosols is of significant importance to reduce harm and improve product quality. This study presents the development of a large volume thermal desorption-column internal evaporation concentration system that overcomes the limitations of existing techniques and effectively meets the high sensitivity analysis requirements for trace components in complex matrices. The method optimizes pretreatment and solvent evaporation conditions, allowing direct analysis of the captured components of heated tobacco aerosol gas-phase and particle-phase by large volume thermal desorption-column internal evaporation concentration-gas chromatography-mass spectrometry (GC-MS) analysis. A simple and efficient analytical procedure suitable for high-throughput sample analysis is achieved. The method features high automation, simple pretreatment, high sensitivity, and good accuracy, with relative standard deviations of less than 10% for 143 aerosol components (including 13 harmful tobacco components listed by the FDA and Hoffman Inventory), of which 107 components have relative standard deviations of less than 5%. The proposed method provides a

powerful technical tool for research on heated tobacco aerosol emissions, as well as for improving the quality and reducing the harm of heated tobacco products. It can also be applied to research on puff-by-puff release of heated tobacco aerosols and the analysis of other trace components in environmental tobacco smoke.

96. TOBACCO HARM REDUCTION SUCCESS STORIES: HOW COUNTRIES ARE EMBRACING SMOKELESS ALTERNATIVES AND THEIR IMPACT ON SMOKING. Mark FORSTER; British American Tobacco, Southampton, UK

The objective of this session is to discuss how different countries have been embracing smokeless alternatives, the role regulation has played, and the impact on the smoking prevalence. The panel will present views on why different smokeless alternatives have had success in certain countries: Snus/Oral Nicotine Pouches in Sweden, Vaping Products in the United Kingdom and/or New Zealand, and Heated Products in Japan etc. The panel will review and discuss how each country has embraced smokeless alternatives through regulation and what can be learned globally with regards to these approaches. The panel will also review and discuss insights related to youth access prevention: How each country has balanced the need to provide smokers who would otherwise continue to smoke access to smokeless alternatives whilst managing potential youth uptake. The panel will provide their views on how the successes of other countries could offer insight to the FDA on regulatory changes that could further Tobacco Harm Reduction in the U.S.

97. A PRACTICAL FRAMEWORK FOR NOVEL ENDS EVALUATION: CHEMICAL AND TOXICOLOGICAL CHARACTERIZATION OF JUUL2 AEROSOL AND COMPARISON WITH REFERENCE CIGARETTES. David COOK, Michael J. Oldham, Jiaming Wang, Austin Bates, Christina Sulaiman, Karen Carter, Candice Jongsma, I. Gene Gillman; Juul Labs, Inc, Washington, DC, USA

Electronic Nicotine Delivery Systems (ENDS) are designed as a non-combustible alternative to cigarettes, aiming to deliver nicotine without the harmful byproducts of tobacco combustion. As the category evolves and new ENDS products emerge throughout the world, it is important to continually assess the levels of toxicologically relevant chemicals in the aerosols and characterize any related toxicology. Herein, we present a proposed framework for characterizing novel ENDS products (i.e., device and e-liquid formulations) and determining the reduced risk potential utilizing analytical chemistry and in-vitro toxicological studies combined with a qualitative risk assessment. To demonstrate this proposed framework, long term stability studies (12-months) analyzing relevant toxicant emissions from six formulations of a next generation product, JUUL2, were conducted and compared to reference combustible cigarette smoke under both non-intense and intense puffing regimes. In addition, in vitro cytotoxicity, mutagenicity and genotoxicity assays were conducted on aerosol and smoke condensates. In all samples, relevant toxicants under both non-intense and intense puffing regimes were substantially lower than those observed in reference combustible cigarette smoke. Furthermore, neither cytotoxicity, mutagenicity nor genotoxicity was observed in aerosol condensates generated under both intense and non-intense puffing regimes, in contrast to results observed for reference combustible cigarette smoke. Following the proposed framework, the results demonstrate that the ENDS products studied in this work generate significantly lower levels of toxicants relative to reference combustible cigarette smoke and were not cytotoxic, mutagenic, or genotoxic under these in vitro assay conditions.

98. TARGETED CHARACTERIZATION OF THE CHEMICAL COMPOSITION OF NOVEL JUUL SYSTEM'S AEROSOL AND COMPARISON WITH KENTUCKY REFERENCE CIGARETTES AND ENDS. Karen CARTER, D.K. Cook, J. Wang, A.L. Bates, C. Smith, I.G. Gillman; Juul Labs, Inc, Washington, DC, USA

The JUUL® System is a temperature regulated, electronic nicotine delivery system (ENDS) designed to provide reduced-risk alternatives to adult smokers who would otherwise continue to smoke cigarettes. In this study, the aerosol compositions of a novel tobacco flavored JUUL System (5.0% and 3.0% nicotine by weight) and commercially available ENDS (including seven closed pod, four refillable pod, two cigalike, and one disposable) were characterized and compared to aerosol of combustible cigarette mainstream smoke (Kentucky reference cigarette). Aerosol was generated using two puffing regimes (ISO 27068 and intense). Quantitative chemical analysis for the JUUL products included Harmful and Potentially Harmful Constituents (HPHCs) as specified in the Guidance on PMTAs for ENDS (U.S. Food and Drug Administration, 2019b), as well as additional constituents including metals, nicotine-related compounds, water, and benzoic acid. Across the two novel JUUL products and two puffing regimens, only 11 of the 41 targeted analytes were present at quantifiable levels. Competitor aerosol was analyzed for primary constituents, metals, carbonyls, and glycidol. Across all comparator products and two puffing regimens, 11 of the 13 targeted analytes were present at quantifiable levels. Average analyte reductions (excluding primary ingredients and water) for both JUUL System aerosols and ENDS Comparator aerosols exhibit a 37-97% reduction in toxicants when compared to mainstream cigarette smoke. In summary, chemical characterization and evaluation of JUUL and commercially available ENDS product aerosols demonstrate a reduction in toxicants when compared to mainstream cigarette smoke. This study provides additional data demonstrating the high level of reduction of HPHCs in JUUL System aerosol compared to combustible cigarettes, supporting their utility as reduced-risk alternatives for adult smokers who would otherwise continue to smoke cigarettes.

99. EXPANDED TARGETED CHARACTERIZATION OF THE CHEMICAL COMPOSITION OF JUUL SYSTEM'S AEROSOL AND COMPARISON WITH KENTUCKY REFERENCE CIGARETTES.
Candice JONGSMA, Karen Carter, David K. Cook, Jiaming Wang, I. Gene Gillman; Juul Labs, Inc, Washington, DC, USA

The JUUL® System is a temperature-regulated, electronic nicotine delivery system (ENDS) designed to provide reducedrisk alternatives to adult smokers who would otherwise continue to smoke cigarettes. In this study JUUL System aerosol for four marketed product formulations (JUUL Menthol 5.0% and 3.0%; JUUL Virginia Tobacco 5.0% and 3.0%) was thoroughly characterized by analyzing the aerosol for the potential presence of 103 constituents of interest, including 59 of 93 Harmful and Potentially Harmful Constituents (HPHCs) identified by the United States Food and Drug Administration (FDA) in the Final Guidance on Premarket Tobacco Applications (PMTAs) for ENDS (FDA; 2023) and the Final Rule on PMTAs (FDA, 2021) and 17 of 19 proposed additions to the FDA HPHC list (Federal Register Number 2019-16658; 2019). Aerosols were collected for targeted analysis using intense and non-intense puffing regimes. The quantifiable analytes were compared to combustible cigarette mainstream smoke constituent values for the 1R6F and 3R4F reference cigarettes (University of Kentucky). The JUUL System aerosols showed a reduction of more than 95% in the levels of HPHCs and targeted constituents (excluding propylene glycol, vegetable glycerin, and water) relative to cigarette smoke, irrespective of puffing regime and product formulation. The decrease in the number and levels of HPHCs in the aerosols demonstrate likely substantial reductions in toxicant exposures and the overall associated health hazards (i.e., cancer risks and noncancer hazards) compared to cigarette smoking.

100. ACCELERATED AGING OF PROPYLENE GLYCOL AND GLYCEROL IN THE PRESENCE OF ORGANIC ACID AND NICOTINE. Norman FRALEY, Anastasia Lioubomirov, I. Gene Gillman; Juul Labs, Inc, Washington, DC, USA

The Family Smoking Prevention and Tobacco Control Act empowered the FDA to protect public health by regulating the manufacturing, distribution, and marketing of tobacco products. In its guidance (FDA-2019-N-2854) for PMTAs for electronic nicotine delivery systems (ENDS), FDA recommends that applicants evaluate chemical changes in their product over its shelf-life and provide complete product characterization. Compounds commonly used

in the e-liquids of ENDS, such as propylene glycol (PG), glycerin (VG), organic acid and nicotine have the potential to degrade through oxidation, acidification, or radical processes during storage, resulting in the creation of new compounds. Because these compounds may potentially transfer into the aerosol, resulting in consumer exposure, it is desirable to identify them as part of product characterization.

Expanding upon the work presented at TSRC 2023, a semi-quantitative GC-MS based non-targeted analysis (NTA) screening method was used for chemical characterization. The aim of this work was to characterize new compounds arising from PG, VG, nicotine, and organic acid and build a custom mass spectral database, used in concert with commercial databases, to identify compounds in aged e-liquid formulations. A simplified e-liquid (60/40 PG/VG w/w 1.6% nicotine 1.2 % benzoic acid) lacking flavor ingredients was stored at high temperature (100° C) for 25 days to accelerate the potential reaction process under exaggerated sample storage condition, representing over 4+ years of room temperature storage.

This presentation will reveal how degradant compounds, such as PG acetals, dioxolanes, and hydroxyacetone are amplified or suppressed by acid and nicotine. Because PG/VG, nicotine and acid are used as e-liquid components across the ENDS industry, the results of these studies will expand foundational knowledge and improve the ease of NTA identification generally.

101. EVALUATION OF NICOTINE DEGRADANTS IN TOBACCO PRODUCTS INTENDED FOR ORAL CONSUMPTION. Joseph JABLONSKI, Andrew G. Cheetham; Mckinney Specialty Labs, Richmond, VA, USA

The landscape of nicotine delivery products intended for oral use is continually evolving with a goal of lowering the consumer's exposure to harmful or potentially harmful constituents (HPHCs). To evaluate the levels of HPHCs, standardized test methods need to be developed for both traditional smokeless tobacco (ST) products and "modern" oral nicotine products (ONP), which include both white-granular powders and plant-

based, non-tobacco leaf. Recently, the CORESTA Tobacco and Tobacco Product Analysis (TTPA) subgroup published CORESTA recommended method No. 105 (CRM-105) for the analysis of nicotine degradants and impurities in ONPs. Using CRM-105 as a basis, we validated a method for the analysis of nicotine degradants in traditional ST products. Using this method, we then examined the levels of nicotine degradants in several commercially available tobacco products intended for oral use.

For this study, eighteen tobacco products intended for oral use (four plant-based ONPs, ten traditional ST products, and four reference ST products) were assessed for seven nicotine degradants/minor alkaloids. Based on the inherent differences in these product classes, we expected nicotine degradant levels in traditional ST products to be greater than those measured in the plant-based ONPs. The only nicotine degradant consistently above the LOQ in ONPs was nicotine-N-oxide (59.6 μg/g - 242.7 μg/g). For traditional ST products, all analytes except myosmine were measured consistently above the LOQ (~ 5 μg/g), with the most abundant being nicotine-N-oxide, the main oxidation product of nicotine, measuring up to 2021 μg/g.

102. THE IMPACT OF PRINTED CIGARETTE PAPER ON PERMEABILITY AND DIFFUSION CHARACTERISTICS. Michael LINDNER; Tann Holding, Traun, Austria

Cigarette paper is a thin, low-substance and flexible wrapping material playing a highly essential role for the manufacturing of conventional filter cigarettes and heated tobacco products. Hereby, cigarette paper fully encloses the fine-cut or alternatively configured tobacco blend, provides the required roundness of the tobacco rod, controls the level of smoke deliveries through ventilation and diffusion, supports the combustion properties of smoking articles and acts as substrate for the connection with the filter plug via the tipping paper. Generally, cigarette paper is not supposed to comprise specific printing designs, as it is almost totally burnt during the consumption of combustible cigarettes. However, there is a noticeably increasing demand

from tobacco product manufacturers for individually printed cigarette paper to enhance brand characterization and security. In the present study, the influence of variously printed cigarette paper on the key parameters air permeability and diffusivity will be investigated. For this objective, cigarette paper with two different permeability levels of 75 CU and 125 CU was printed with standard rotogravure technology using particularly developed printing inks suitable for combustion and pyrolysis. In this context, the relevant printing parameters include three different color shades with respectively four intensity and four ink coverage levels related to the printed surface area. With this test matrix, the collected experimental data will trigger the following observations: (i) The different performance of the two paper grades regarding diffusivity versus permeability and (ii) the effect of colors on diffusivity yields relative to a specified threshold. The findings may serve as technically and regulatory vital basis for the creation of customized artworks for printed cigarette paper.

103. A CHALLENGE FOR ROUTINE SENSORY EVALUATION: INSTRUMENTATION AND DATA ANALYTICAL MODELS FOR SENSORY PREDICTIONS. Ian TINDALL, Reddy Selvan, Laimon Hamzah; Cerulean, Milton Keynes, Buckinghamshire, UK

The smoking industry spends hundreds of millions of dollars annually to assess the sensory characteristics of its' products. Human sensory panels form the backbone of this evaluation, reporting sensations such as "impact", "mouthful", "irritation", etc. This approach becomes problematic when considering consistency, the ethics of human testing, availability and critically, cost.

Instrumental replacement of the sensory panelist has the potential to overcome some of these problems. Using a controlled puffing mechanism and multiple sensors simultaneously collecting data, a correlation between reported panel sensations and a large data set, first been flattened using classical statistical treatments, can be established. Such equipment is described in the paper methods.

Three products under two environmental conditions were tested for a number of sensory attributes. Recording panelist response in the form of a score and then matching this to the sensor data array using mathematical models such as Random Forrest, decision tree matrix and classical machine learning, it is possible to gain correlation with an accuracy greater than 95%.

Calibrating the electronic test equipment using standard products and "standardized" panelist responses enhances the accuracy of the method, effectivity increasing by using maxima/minima of response.

To test the applicability of this decision tree matrix to sensory correlation, a predictive model was created and tested using "blind" panelist sensory attributes and sensor response test. A match of better than 95% was achieved. The potential for further expansion, both in terms of sensations and sensors, is presented. Limitations of this approach including the "language" of sensation, the concept of calibrated correlation as opposed to analytical measurement, and sensor poisoning are discussed and a method of eliminating these potential problems proposed.

104. APPLICATION OF BIOMARKERS OF EXPOSURE AS COMPLIANCE MEASURES IN LONG-TERM AND EPIDEMIOLOGICAL STUDIES OF NEW NICOTINE AND TOBACCO PRODUCTS. Max SCHERER, Nikola Pluym, Gerhard Scherer; Abf Analytisch-Biologisches Forschungslabor, Planegg, Bavaria, Germany

Over the past ten years, the tobacco landscape has undergone significant transformation, witnessing the emergence of various new product categories such as e-cigarettes (ECs), heated tobacco products (HTPs), and oral nicotine delivery products (nicotine pouches (NP)). Evaluating the potential public health benefits requires extensive, long-term studies. However, such studies face challenges due to potential non-compliance when participants self-report their use behaviour. To ensure robust risk assessment in uncontrolled settings over extended periods, there is a need for suitable biomarkers of exposure (BoE) as measures for compliance, commonly referred to as biomarkers of compliance. These BoEs should be specific to each nicotine/tobacco product

category, enabling biochemical verification of self-reported use. Historically, exhaled carbon monoxide (eCO) and cotinine have been used to confirm tobacco use or abstinence. However, with the declining prevalence of smoking and the rise of alternative tobacco and nicotine products, these two biomarkers alone are insufficient for monitoring compliance in most studies. An extensive literature review revealed several BoEs suited to assess product compliance based on their prevalence, specificity, and half-life. It proposes single BoEs and BoE patterns to ascertain the use status of the most prevalent product categories (EC, HTP, NP), as well as combustible cigarettes (CC) and smokeless tobacco products like moist snuff. Their applicability was demonstrated in a clinical study with 10 sole users of the aforementioned product categories.

This presentation may guide researchers in designing new studies aimed at robustly assessing subject compliance in long-term, epidemiological, or cross-sectional studies where subjects' use behaviour is primarily self-reported and not rigorously controlled.

105. ENDS-INDUCED HEAVY METAL EXPOSURE AND OXIDATIVE INJURY IS MEDIATED BY VAPING BEHAVIOR.

Maureen MEISTER[1], Xiaojia He[2], Jennifer Jeon[2], Patrick Chepaitis[2], Qian Zhang[2], Mark Wilson[2], Marilyn Black[2], Christa Wright[2], Akshanda Shinde[3], Jonathan Shannahan[3], Pam Cushenan[4], Scott Weaver[4], Ruiyan Luo[4]; [1]UL Research Institutes, Marietta, GA, USA, [2]Chemical Insights Research Institute, Marietta, GA, USA, [3]Purdue University, West Lafayette, IN, USA, [4]Georgia State University, Atlanta, GA, USA

Electronic nicotine delivery systems (ENDS) elicit heavy metal exposure and respiratory toxicity. The objective of this study was to utilize an integrative approach to determine how vaping behavior influences heavy metal exposures and subsequent effects on health. Recruited non-users and current ENDS users provided a saliva sample and completed a lung function assessment by spirometry. Saliva was analyzed for concentrations of heavy metals, inflammatory cytokines, and mediators of oxidative stress. Utilizing their preferred ENDS device, users completed a puffing topography

assessment. Principle component analysis (PCA) was carried out, identifying user's puff volume as a primary exposure mediator. Thus, ENDS users were subdivided into low (>90 mL/puff), medium (90-150 mL/puff), and high (>150 mL/puff) puff volume groups. One-way ANOVA with Tukey's post-hoc test was used to compare results across all groups. When parsed out by puff volume, the concentrations of heavy metals, Ag, As, Cd, Co, Pb, Ni and Zn, in saliva were higher in participants with a high puff volume in comparison to those with low puff volume and non-users. Further, inflammatory cytokine concentrations in saliva were higher in ENDS users with a high puff volume compared to non-users. Additionally, ENDS users with a high puff volume had significantly higher levels of 8-OHdG, a marker of oxidative DNA damage and increased superoxide dismutase activity compared to non-users. Further, users with a medium puff volume had significantly lower lung function compared to non-users. These results demonstrate how individual vaping behaviors influence exposures. We show that puff volume drives heavy metal exposure and oxidative stress. These findings illustrate how vaping behavior may dictate health outcomes and provide an opportunity for education and implementation of harm reduction strategies.

106. POTENTIAL INSIGHTS FROM REVERSE DOSIMETRY FOR IN VITRO ENDS TESTING. Michael OLDHAM; Juul Labs, Inc, Washington, DC, USA

Reverse dosimetry (sometimes called exposure reconstruction) is extrapolating from in-vivo data (animal or human) to inform in vitro studies and has not been used with dynamic and complex aerosols, such as ENDS. ENDS aerosols are dynamic in that they change as they are diluted and inhaled into the respiratory tract. Their complexity stems from use of volatile (e.g., some flavors), semi-volatile (e.g., some flavors, nicotine, propylene glycol) and relatively non-volatile (e.g., glycerin) e-liquid ingredients. Reverse dosimetry from in vivo data to in vitro study doses must include target organ anatomical parameters (e.g., surface area, mucus, surfactant, etc.), ENDS aerosol considerations (e.g., particle, vapor or both phases), and dynamics of

ENDS aerosol exposure (e.g., puffing and duration of exposure) among other considerations.

As an example of application of reverse dosimetry, one clinical study reported 4.0 ± 3.3 mg nicotine was inhaled during 15 minutes of ad-libitum ENDS product use by 13 participants (St Helen et al., 2016). Using a recent published aerosol dosimetry model for ENDS aerosols (CTP funded) predicted that for the nicotine vapor and particulate phase, only 5% of the inhaled nicotine would deposit in the tracheobronchial tree (TB) and approximately 50% in the pulmonary region (PUL) (Asgharian et al., 2024). Using the surface area of the TB (0.4717 m2) and PUL (70.9254 m2) regions and assuming 100% transfer through the TB mucus and PUL surfactant, resulted in a calculated dose range of 2.83 ± 2.34 ng/cm2-min and 0.187 ± 0.154 ng/cm2-min for the TB and PUL regions, respectively. These in-vivo based calculated doses are drastically lower, in some cases 100-1,000 times lower, than the doses used in most in-vitro studies.

107. ASSOCIATIONS OF E-CIGARETTE USE PATTERNS WITH THE PREVALENCE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) AND HEART DISEASE AMONG ADULT TOBACCO USERS IN THE UNITED STATES. Xiaona LIU[1], Yue Cao[1], Jiaxuan Li[1], Xi Chen[1], Yuming Xiong[1], Fangzhen Zheng[1], Jianqiang Zhang[1], Xiaona Liu[1], Ian M. Fearon[2], Xuxi Zhang[3], Xinying Sun[3]; [1]Smoore Research Institute, Shenzhen, China, [2]whatIF? Consulting, Harwell, UK, [3]Peking University, Beijing, China

Chronic obstructive pulmonary disease (COPD) and heart disease are major smoking-associated causes of morbidity and mortality. Despite the rising popularity of electronic cigarettes (EC) in recent years, limited research has examined the impact of EC use patterns on COPD and heart disease. This study aimed to assess the association between EC use patterns and COPD or heart disease diagnoses. Using data from the 2021 National Survey on Drug Use and Health, we analyzed 11,764 US adults who had smoked or vaped within the past year, including 59.5% (weighted) exclusive combustible

cigarette (CC) smokers, 15.3% exclusive EC users, and 25.2% dual users of CC and EC. Multivariate logistic regression models calculated adjusted odds ratios with 95% confidence intervals (CI) for COPD or heart disease prevalence among exclusive EC users compared to exclusive CC smokers or dual users. Crude COPD prevalence was 9.2%, 8.8%, and 2.4% among exclusive CC smokers, dual users, and exclusive EC users, respectively. Lifetime heart disease prevalence was 11.5%, 9.6%, and 5.5% among exclusive CC smokers, dual users, and exclusive EC users, respectively. After Adjusting for confounders, exclusive EC users demonstrated 0.4 times lower odds (95% CI: 0.37-0.99) of reporting COPD compared to exclusive CC smokers, while dual users had 1.7 times higher odds (95% CI: 1.09-2.66) of heart disease diagnosis relative to exclusive CC smokers. However, no significant differences were observed in adjusted heart disease prevalence between exclusive EC users and other groups. Exclusive EC use was associated with a lower cross-sectional risk of lifetime COPD compared to exclusive CC smoking and dual use. Further research is suggested to explore the causal relationship between EC use patterns and the development of COPD.

108. SULFUR AND CHLORIDE FERTILIZATION IMPACT ON BURLEY TOBACCO GROWTH, YIELD AND LEAF CHEMISTRY.
Bob PEARCE, Tara Valentine, Natalia Martinez, Magdalena Ricciardi; University of Kentucky, Lexington, KY, USA

Recent trials on potassium fertilizer sources for burley tobacco have demonstrated an interesting trend toward increased levels of Tobacco Specific Nitrosamines (TSNAs) in cured burley leaf when potassium sulfate was applied compared to potassium chloride. To better understand the role of sulfate and chloride in this response, field trials were conducted in 2022 and 2023 with different sources of chloride and sulfate. Trials were conducted on a Bluegrass-Maury silt loam soil (Fine, mixed, active, mesic Typic Paleudalfs) near Lexington, Kentucky. The trial site in 2023 was on a soil that tested marginally deficient in sulfur. During the 2022 growing season there was no observed growth or yield difference due to fertilization treatment, however TSNAs were significantly greater in all treatments where sulfate was applied

as compared to the check and chloride treatments. In 2023 a mid-season growth response was observed with sulfate treated plants showing a darker green color. Cured leaf yield was significantly greater in treatments that received sulfate fertilization. This was the first known field observed response to sulfate fertilization on burley tobacco in Kentucky. Sulfate fertilization significantly increased the sulfur and nitrogen content of the cured leaf. Alkaloid and TSNA data will be presented. Additional work is continuing to better understand the role of sulfate and chloride fertilization on burley tobacco yield and leaf chemistry.

109. DISTRIBUTION OF TOBACCO CONSTITUENTS PON AND NNK IN CURED BURLEY TOBACCO LEAF TISSUE. Ying WU, Huihua Ji; University of Kentucky, Lexington, KY, USA

NNK is a potent carcinogen that is found in tobacco smoke. Pseudooxynicotine (PON), an oxidation product of nicotine, is considered the precursor of NNK. To determine whether there is a significant correlation between the formation of NNK and PON, the distribution of PON and NNK in the tobacco leaves was evaluated. Twenty cured burley tobacco leaves collected in 2017 were divided into 84 defined leaf segments. All segments were analyzed for Free PON, matrix -bond PON and Free NNK, matrix- bond NNK using LC/MS/MS. Comparison of the free and total forms of both components was conducted based on 3D Mesh maps. The matrix - bound PON in the midrib and lamina is about 57% and 59%, respectively. The matrix - bound NNK in the midrib and lamina is about 87% and 65%, respectively. In the midrib, the concentration of PON gradually increases from the base to the tip, while the highest concentration of NNK is found in the middle of the midrib, with the lowest level at the tip compared to the middle and base. In the lamina, the edge areas have a higher concentration of PON than the middle. The highest concentration is about 350 ug/g of free PON and 1000 ng/g of total PON on the edge of a leaf. The accumulation of NNK decreases from the center to the outer periphery, with the highest concentration being

approximately 200 ng/g of free NNK and 780 ng/g of total NNK in the center. Given the formation of a small amount of NNK after curing and the distribution trend of NNK concentrations in the leaves not aligning with that of PON, we concluded that PON is not the limiting factor for NNK accumulation.

110. RESEARCH AND APPLICATION OF KEY TECHNOLOGY FOR NEW MODEL OF SAFETY AND ENVIRONMENTAL PROTECTION STORED-TOBACCO PEST CONTROL IN HIGH-RACK WAREHOUSE.

QU Yongbo[1], Yin Dafeng[1], Xiao Fei[1], Fu Qiuping[1], Zhang Hui[1], Dai Lin[1], Liu Shiwei[2], Liu Xiaoqing[2]; [1] Technology Center Of Hunan Tobacco China Industry Co, Changsha, China, [2] Hunan Huawang Fumigation And Disinfection Co, Changsha, China

The pest control method of fumigation using toxic and harmful gas, such as phosphine, will be gradually eliminated. Because of its disadvantages for damaging environment and high risk. In view of poor sealed effect of massive elevated tents and poor repeatability of stored-tobacco pest control effect by nitrogen filling technology in high-rack warehouse, the safety and environment protection new stored-tobacco pest control model had been researched in paper. The model based on nitrogen filling technology was constructed by insect-proof net barrier, deep cleaning of the environment to maintain hygiene. The effects of key factors, such as tent material, sealing method, nitrogen-filling network, nitrogen-charging process, tent volume and insecticidal effect had been systematically researched and improved.

The results showed that tents made of 0.10mm PA/PE membrane sealed floor with tape can meet requirements of air tightness for nitrogen filling technology in high-rack warehouse. And nitrogen-filling network and stack volume had significant effect on oxygen reduction rate. The oxygen reduction rate of different nitrogen-charging processes had a polynomial correlation with nitrogen filling time. The intermittent nitrogen-filling process was the best process.The death time of tobacco beetle eggs, larvae and adults

controlled by this process in sealed tents of high-rack warehouse was significantly correlated with temperature and oxygen concentration. And the mortality rate for three stages of tobacco beetle all reached 100% at 98% nitrogen concentration in tents for 30d. Compared with phosphine fumigation technology, the application results in high-rack warehouse showed that total number of tobacco beetles and tobacco moths controlled by the new pest control model had decreased by 100% in the insect-proof net, the comprehensive cost of pest control had decreased by 46.7% in the two-year period. Therefore, the safety and environment protection new pest control model of stored-tobacco high-rack warehouse will have high management efficiency and broad application prospects.

111. TOPPING DRIVES ADAPTIVE CHANGES OF TOBACCO ROOT-ASSOCIATED MICROBIOMES. Peng LU[1], Mengli Gu[1,2], Jingjing Jin[1], Mengmeng Kong[1], Zechao Qu[1], Lingtong Cheng[1], Jianfeng Zhang[1], Peijian Cao[1], Jiemeng Tao[1]; [1]Zhengzhou Tobacco Research Institute of CNTC, Zhengzhou, China, [2]Zhengzhou University, Zhengzhou, China

Topping can stimulate the development of tobacco root system and induce a large amount of nicotine synthesis in root system. However, the response mechanism of root-associated microbiomes to topping is not clear. Therefore, in this study, high-throughput sequencing analysis was carried out on the root-associated microbiomes (bulk soil, rhizosphere soil, rhizoplane, and root endosphere) in different periods before and after topping. The results showed that topping significantly affected the diversity, structure, and composition of tobacco root-associated microbiomes, and the response was the strongest on the first day after topping, and then the microbial community gradually showed adaptability to the environment. Specifically, the bacterial community in bulk soil and rhizosphere soil and the fungal community in root are more susceptible to topping. Topping caused the changes of phytohormones and alkaloids in tobacco roots. Abscisic acid and auxin increased significantly after topping, and the contents of jasmonates and nicotine increased significantly on the first day after topping, and then decreased. The results of

correlation analysis showed that the relative abundance of Thanatephorus, Nocardioides and other genera was significantly related to the nicotine content. Therefore, high-throughput separation of nicotine-degrading bacteria was carried out from the topped samples, 221 and 197 strains belonging to 55 genera were separated from rhizosphere and root endosphere, respectively. Furthermore, two strains belonging to Pantoea and Cupriavidus with high nicotine tolerance were obtained by re-screening. The research results reveal the response mechanism of tobacco root-associated microbiomes to topping, which can provide theoretical basis for the succession law of plant microbiome driven by topping.

112. IDENTIFYING POTENTIAL ACUTE HEALTH HAZARDS FROM EXPOSURES TO (S)-6-METHYLNICOTINE TO INFORM PRODUCT DEVELOPMENT. Willie MCKINNEY[1], Marissa Smith[2], Ranulfo Lemus[3], Roxana Weil[1]; [1]McKinney Regulatory Science Advisors, Henrico, VA, USA, [2]Arivita, Richmond, VA, USA, [3]Letox World, Xenia, OH, USA

Nixodine-S™ is a flavorless concentrate containing (S)-6-Methylnicotine ((S)-6-MN), a nicotinic acetylcholine receptor (nAChR) agonist, diluted in either PG or VG. Nixodine-S™ is sold by Bonguard Naturals solely through business-to-business transactions and may be used in the manufacturing of e-liquids, vape products, and oral products, among others. There are currently no guidance or regulatory requirements for putting products containing (S)-6-MN on the market, and although some data is available on potential health hazards from exposure to (S)-6-MN, these data are limited. For these reasons, we developed a product scientific evaluation program aimed to better understand the potential health hazards of Nixodine-S™ relative to nicotine. This program consists of a battery of studies to 1) evaluate the acute toxicity of the pure (S)-6-MN contained in Nixodine-S™ relative to nicotine, 2) evaluate the nAChR activation of Nixodine-S relative to nicotine, and 3) evaluate the levels of (S)-6-MN and harmful and potentially harmful constituents (HPHCs) in aerosols generated by a prototype vape product

containing Nixodine-S™. Adult male and female Sprague Dawley rats were exposed to either pure (S)-6-MN or nicotine via intravenous administration. The animals exposed to pure (S)-6-MN compound showed adverse effects, including seizures and death, at lower doses than nicotine; this informed the dilution and final concentration of (S)-6-MN in Nixodine-S™. The acute intravenous toxicity study results, nAChR activation results, and levels of (S)-6-MN and HPHCs in aerosols generated by prototype vape devices filled with a Nixodine-S™ containing liquid formulations will be presented.

113. EVALUATION OF THE GENOTOXIC POTENTIAL OF A FLAVORED ORAL NICOTINE POUCH PRODUCT USING INTEGRATED APPROACHES. Jingjie ZHANG, Richard Morgan, Uktarsh Doshi, Chastain Anderson, Wanyoike Kangethe, Donna Smith, K. Monica Lee (formerly of); Altria Client Services, Richmond, VA, USA

Oral nicotine pouch products typically contain flavor ingredients that are "GRAS" ("generally recognized as safe") in foods. While the GRAS status is not intended to apply to tobacco products, the scientific data supporting the GRAS status are relevant in characterizing toxicological profiles of the ingredients in the oral nicotine pouch products. In this feasibility study, we used integrated approaches to evaluate the genotoxic potential of a nicotine pouch product containing maltol and ethyl maltol ("maltols"). Maltols, selected as example flavor ingredients, are reported to induce in vitro genotoxicity but do not lead to in vivo sequelae. We first identified maltols as the in vitro activity driver in the in vitro micronuclei assay. We then investigated the dosimetry basis to interpret in vitro versus in vivo genotoxicity and carcinogenicity outcomes for maltols (in vitro-to-in vivo extrapolation, IVIVE). Using open-source PBPK models, we estimated the C_{max} in the target tissue (e.g., plasma) under in vivo (rodent) exposure conditions and compared to the in vitro exposure concentrations. These New Approach Methods (NAMs)-based approach was evaluated with the negative in vivo genotoxic responses of the test product based on a combined in vivo

micronuclei and comet assay in rats conducted following the ICH S2(R1) guidance. In summary, using maltols as case examples, the integrated approaches utilizing in vitro and in silico methods as well as bioassay outcomes could enable a holistic evaluation of the genotoxic potential of an oral nicotine pouch product, building a case of NAMs-based toxicological assessment without the need for confirmatory in vivo testing.

114. ECOTOXICITY EVALUATION OF CIGARETTE BUTTS. Sandra DE JONGH, Diane Raverdy Lambert; SWM International, Spay, Sarthe, France

Cigarette butts (CBs) are the most common litter found all over the world. Beside their persistence in the environment, there is a growing number of articles discussing their ecotoxicity. As the literature on the subject seems inconsistent, the objectives of this study were:

- To gain some preliminary insights on the CBs acute toxicity on the model soil organism Eisenia fetida, marine water organism Artemia franciscana and freshwater organism, Daphnia magna. For the latter, a chronic toxicity test was also performed.
- To monitor the presence of selected harmful and potentially harmful compounds (HPHCs) into environment.

Commercial cigarettes with paper and cellulose acetate filters at similar smoke deliveries were smoked in ISO smoking regime. CBs were tested for acute toxicity following existing standards OECD 202 (Daphnia magna) and ASTM E1676 (Eisenia fetida) and OWS recommendations for Artemia franciscana. A concentration of 0,1 % dry weight was used on both water environments and 1 % fresh weight for the soil environment.

Despite detecting toxicants such as nicotine, phenol and benzo(a)pyrene in soil after two weeks, no acute toxicity was observed for Eisenia. Toxicants were occasionally detected after 48h in fresh water and some acute toxicity

was observed on daphnia, especially with cellulose aetate filters. These toxicants seem to disappear quickly, and the toxicity is no longer observable in the chronic test. Similarly, with the marine water test, no toxicants were found after one week nor was any toxicity observed.

These first results show the importance of sampling and testing standardization, especially the choice of model organisms, to have representative and reproducible results allowing a fact-based comparison of the ecotoxicity of different CBs.

115. RESEARCH ON THE RESPIRATORY ABSORPTION PATTERN OF SMOKE AEROSOLS. WANG Zhuo[1], Zhang Xiaoyu[1], Cui Huapeng[2], Yan Quanping[2], Wen Jianhui[1], Tuo Suxing[1], Wang Zhiguo[1], Liu Wei[1], Du Wen[1]; [1]China Tobacco Hunan Industrial Co of CNTC, Changsha, Hunan, China, [2]Zhengzhou Tobacco Research Institute of CNTC, Zhengzhou, Henan,China

To study the absorption of tobacco smoke aerosols in the human respiratory tract, the deliveries of inhaled and exhaled aerosol components in tobacco smoke were analyzed, their respiratory absorption patterns were studied by combining with relevant theoretical calculations, and the basic method of flavoring technology based on the respiratory loss of different flavor molecules was verified. The results showed that: ① The significant loss of inhaled aerosols after passing through the human respiratory tract was demonstrated by aerosol inhalation and exhalation experiments. ② The absorption experiments using two types of aerosol capture devices showed that not only particle deposition and gas absorption occurred during the aerosol absorption process, but also particle-gas conversion absorption phenomena. ③ A model for the variation of aerosol composition in smoke after inhalation and exhalation was established by theoretical analysis, including three mechanisms of aerosol respiratory loss: particle deposition, gas absorption, and particle-gas conversion absorption. And the relevant parameters of respiratory absorption of different flavor molecules in smoke aerosols were calculated. ④ The characteristics of flavoring technology based

on aerosol respiratory absorption were verified through the olfactory evaluation and smoking sensory evaluation of flavor blending in the aerosol flavoring experiment, and the basic method was given. This study bridges the gap between the smell of flavors and the actual feeling of tobacco smoke, and lays the foundation for the innovation and enrichment of smoke flavoring theory.

116. IN VITRO TOXICOLOGICAL EVALUATION OF CIGARETTE BASED ON AIRWAY ORGANOIDS. TIAN Yushan[1], Lu Peng[1], Li Xiao[1,2,3], Wang Xianglong[1,2,3], Wang Hongjuan[1,2,3], Fu Yaning[1,2,3], Han Shulei[1,2,3], Chen Huan[1,2,3], Hou Hongwei[1,2,3], Hu Qingyuan[1]; [1]China National Tobacco Quality Supervision & Test Center, Zhengzhou, China, [2]Beijing Life Science Academy, Beijing, China, [3]Key Laboratory of Tobacco Biological Effects, Zhengzhou, China

Organoids are a kind of tissue analogues with specific spatial structure cultured in vitro, which can best simulate the structure and function of tissues *in vivo* and can be stably cultured for a long time. According to the current toxicological studies of tobacco products, this study aims to establish a toxicological evaluation system based on organoids *in vitro*. Cigarette extract was used in our study, and the results showed that organoids were successfully cultured *in vitro*, as evidenced by the identification of characteristic markers of different cell types. Based on optimized experimental conditions and 3D cell viability analysis, the IC_{50} of cigarettes was measured. A decrease in organoid diameter was observed and the different cell types in airway organoids were induced with increasing concentrations of cigarette extract. In addition, cigarette exposure induced increased ROS production in a dose-dependent manner and caused a significant increase in pro-inflammatory factors, but no significant change in the expression of anti-inflammatory factors at high concentration exposure, thus inducing cell damage. Furthermore, the determination of γ-H2AX showed that cigarette extract exposure led to obviously DNA damage,

providing a good evaluation model *in vitro* for toxicological studies of tobacco products and other environmental pollutants.

117. ACTUAL USE STUDY OF TOBACCO HEATING SYSTEM 3.0.

Steve ROULET[1], Pierpaolo Magnani[1], Claudia Kanitscheider[2], Chris Freehauf[2], Stacey Bell[2], Eva Jenz[3], Divine Akumo[3], Gerd Kallischnigg[4]; [1]Philip Morris Products, Neuchatel, [2]Oracle Life Sciences (formerly Cerner Enviza, Munich, Germany), Austin, TX, USA, [3] ZEG - Zentrum fur Epidemiologie und Gesunheitsforschung (Center for Epidemiology and Health Research), Berlin, Germany, [4]ARGUS GmbH, Berlin, Germany

Tobacco Heating System (THS) 3.0 is an induction heating device used with specially designed tobacco sticks that was developed as a better alternative for adults who would otherwise continue smoking. Complete switching to smoke-free products (SFPs), such as THS 3.0, and substantial reduction in cigarette consumption are important measures to assess the impact of SFPs on public health. This 6-week actual use study examined the proportion of U.S. adult (21+ years) daily smokers who switched from cigarettes to THS 3.0 at the end of the observational period and determined the change in cigarette consumption. The multi-site, two-arm, mid-term, prospective cohort study comprised a 1-week baseline period, a 4-week observational period, and a 1-week close-out period. Subjects recorded cigarette and induction tobacco stick consumption in an e-diary. A total of 987 subjects (male/female: 48.8%/51.2%; mean age: 44.4) were enrolled and randomized into one of the two study arms: 1) use of the single-component (Mono) THS 3.0 (n=494) or 2) use of the dual-component (Mid) THS 3.0 (n=493). At the end of the study, 7.0% (Mono 7.1%/Mid 6.9%) of subjects switched to exclusive THS 3.0 use (completely stopped smoking cigarettes). Almost half of the subjects (Mono 45.5%/Mid 46.8%) reduced their cigarette consumption by ≥50%. Finally, about three-quarters of subjects who stated they were likely to purchase THS 3.0 (Mono 71.1%/Mid 75.1%) expressed a positive intent to gradually switch to or completely replace their cigarettes with THS 3.0. These results suggest

that the marketing of THS 3.0 in the U.S. is likely to result in a sizeable proportion of adult daily smokers switching to THS 3.0 and using it exclusively or substantially reducing their cigarette consumption.

118. ACTUAL USE STUDY OF MARLBORO HEATED TOBACCO STICK PRODUCTS USED WITH THE PLOOM® HEATED TOBACCO DEVICE AMONG US ADULTS WHO SMOKE COMBUSTIBLE CIGARETTES. Joshua KARELITZ[1], Nelly Mainy[2], Elizabeth Becker[1]; [1]Altria Client Services, Richmond, VA, USA, [2]JT International, Geneva, Switzerland

FDA marketing authorization of new tobacco products is informed by how adult tobacco consumers use such products and their use of other tobacco products. We conducted a six-week, open-label, actual use study of heated tobacco products—Marlboro heated tobacco sticks (HTS) used with the Ploom® device (collectively, the Ploom system)— among adults who smoke cigarettes (AS; aged 21-64) and were not planning to quit. Our objective was to characterize switching behavior and change in cigarette consumption among AS when provided with the Ploom system. The study consisted of an initial one-week sampling period and five weeks of ad libitum use. During the first week, participants received four HTS variants (two tobacco-flavored and two menthol-flavored) to familiarize participants with the device and HTS variants. Participants were then offered free choice of HTS variants to use ad libitum for five weeks, with no restriction on other tobacco product usage. All tobacco product use was recorded daily via a smartphone app. Participants returned to the study site at the end of each week to receive additional HTS products in their preferred variant(s). At site visits following Weeks 1, 3, and 6, participants completed Consumer Reported Outcome Measures (CROM) on Ploom system use behavior, subjective product use experience, and intention to purchase. Primary outcomes include Week 6 switching behavior (i.e., self-reporting no cigarette consumption and continued Ploom system

use), change in cigarette consumption from screening to Week 6, and CROM at Weeks 1, 3, and 6. Results will include descriptive characterization of the primary outcomes, which will inform regulatory submissions.

119. PUFF TOPOGRAPHY OF MARLBORO HEATED TOBACCO STICK PRODUCTS USED WITH THE PLOOM® HEATED TOBACCO DEVICE AMONG ADULTS WHO SMOKE COMBUSTIBLE CIGARETTES. Joshua KARELITZ[1], Kevin Ball[1], Nelly Mainy[2]; [1]Altria Client Services, Richmond, VA, USA, [2]JT International, Geneva, Switzerland

Objectives: Measuring puff topography of inhalable tobacco products generates evidence on potential toxicant exposure and product use experience for tobacco regulatory applications. We examined puff-by-puff topography and self-reported reinforcing effects of the Ploom® heated tobacco device—used with Marlboro heated tobacco sticks (HTS; collectively the Ploom system)—among adults who smoke (AS) non-menthol or menthol cigarettes.

Methods: We conducted a four-week randomized cross-over puff topography study of four HTS (two tobacco-flavored and two menthol-flavored) among AS (n=71). The study consisted of five visits (Screening Visit, four Topography Visits) and ad libitum at-home use of HTS products during each week between visits. Participants were randomly assigned to one of four HTS variant sequences that allowed all participants to use all HTS variants, regardless of their incoming preference for non-menthol/menthol cigarettes. During each Topography Visit, participants used their currently assigned HTS variant ad libitum via SODIM SPA/M topography measurement device over a two-hour period then completed the Modified Cigarette Evaluation Questionnaire (mCEQ; adapted for HTS). Usual brand cigarette topography and mCEQ were measured at screening.

Results: Puff topography outcomes included number of sticks, number of puffs, per-puff volume, total volume, puff duration, inter-puff interval, and flow rate. We will present descriptive statistics of puffing behavior and self-reported outcomes by product (i.e., by HTS variant and/or cigarette) and incoming preference for non-menthol/menthol cigarettes.

Implications: Capturing puff topography data—complemented by product experience Consumer Reported Outcome Measures—can facilitate understanding of new tobacco product use perceptions and behavior among adult tobacco consumers. Results provide insights concerning AS' product experience of four HTS variants used with the Ploom® heated tobacco device.

120. ACTUAL USE OF A HEATED TOBACCO PRODUCT AND CHANGES IN CIGARETTE SMOKING BEHAVIOUR AMONG ADULTS WHO SMOKE IN CZECHIA. Christopher RUSSELL[1], Gabriel Barnard[2], Neil Mckeganey[2], Venus Marza[2], Sophie Notley[2], Martin Fitzpatrick[3], Matthew Stevenson[3], Layla Malt[3], Thomas Nahde[4]; [1]Russell Burnett Research & Consultancy, Glasgow, UK, [2]Centre For Substance Use Research, Glasgow, UK, [3]Imperial Brands, Bristol, UK, [4]Imperial Brands Reemtsma, Hamburg, Germany

Background: There is growing interest in how adults who smoke cigarettes use heated tobacco products (HTP) in their everyday lives, or the extent to which HTP are used as a complete or partial replacement for cigarettes over time. This study assessed changes in cigarette smoking behaviour when using HTP in neartoreal world settings for six weeks.

Methods: Participants were 332 adults who smoked 5 30 cigarettes per day, living in Prague or Brno, Czechia, who did not intend to quit smoking within the next three months but reported a positive intention to use the Pulze+iD Heated Tobacco System (HTS) on a regular basis following a brief trial use period. Participants were given a pre funded personal debit card to purchase packs of consumable tobacco sticks (iD® Sticks, 'IDS') in 12 commercially

available flavours of their choice, directly from retail outlets in the community, for personal use as desired for six weeks. Participants recorded their daily consumption of cigarettes and IDS in an e diary. Data were collected between May July 2023.

Results: After using Pulze+iD HTS *ad libitum* for six weeks, 16.0% of participants had completely switched from cigarettes to Pulze+iD HTS; 33.7% reduced their daily cigarette consumption by 50 99% while continuing to use Pulze+iD HTS. Cigarette consumption reduced by 35.6% (1.9 fewer packs per participant) during Week-1 and 45.2% (2.4 fewer packs per participant) during Week-6. At Week-24, 63.6% continued to purchase IDS with their own money; 50.9% were using Pulze+iD HTS as a complete or substantial replacement for cigarettes.

Conclusions: Pulze+iD HTS has potential to help adult smokers to completely replace or substantially reduce cigarette consumption in the short to medium term in real world settings.

121. STRUCTURAL EQUATION MODELING FOR ADVANCED INSIGHT FROM BEHAVIORAL SURVEYS. Ryan SELTZER; Safety in Numbers, Tucson, AZ, USA

Demonstrations of Appropriateness for the Protection of Public Health (APPH) in Premarket Tobacco Applications (PMTAs) often entail separate comparisons of perceptions and intentions survey questions between age and tobacco user groups. Such unidimensional hypothesis tests, while useful, often do not maximize the information available to make more comprehensive and insightful inferences about APPH.

Structural Equation Modeling (SEM) is a statistical technique that explains an ecosystem of relationships among numerous variables simultaneously. Beyond

simply comparing outcomes between user groups, this method can test causal hypotheses on why and under what conditions patterns emerge.

The IQOS PMTA data were used to test how the relationship between demographic factors and intention to use the IQOS is mediated by risk perceptions. Results from 955 adult smokers revealed that those with intentions to quit ($p<0.0001$) and those who are younger ($p=0.0002$) have significantly higher perceptions of risk of cigarettes compared with adults with no intentions to quit and who are older, respectively. Risk perceptions ($p<0.0001$) and current e-cigarette use ($p=0.005$) was then associated with greater intention to use the IQOS. The overall specification of this mediation model yielded fit indices suggesting an excellent fit to the data (GFI = 0.998, CFI = 0.99, NNFI = 0.98).

This SEM approach to mapping a sequence of events among numerous variables highlights the risk motivations of why people may be interested in the IQOS and how these motivations can differ among demographic groups. Such detailed information can help manufacturers and scientists take targeted efforts to design, research, and market harm reduction products that address APPH.

122. ANALYSIS OF HEATED BOTANICAL SUBSTRATE AEROSOL EMISSIONS COMPARED TO A HEATED TOBACCO PRODUCT.
Stéphane DEJOIE, C. Rigoulay, N. Durot, O. Brenner, D. Raverdy-Lambert; SWM c/o LTR Industries, Allonnes, France

A reconstituted material (2 steps paper process) of green tea was developed with the addition of nicotine (1.4 %) and different organic acids. Commercial tobacco sticks tubes for an external heater system reaching a temperature of 240°C were filled with the reconstituted plant material cut filler replacing the tobacco substrate. An aerosol of the commercial tobacco stick and of the "botanical stick" was generated on a Borgwaldt NGX10 smoking machine and collected on a Cambridge filter. The smoking regime was an HCI modified smoking regime: 2s per puff, 30s inter puff, 55 mL puff volume and non-

blocked ventilation. In the same way, ACM, nicotine and glycerin puff-by-puff profiles of both types of sticks were measured with a smoking machine that was developed at SWM to collect automatically and successively each puff.

The comparison of the aerosol composition showed no significant difference in nicotine and glycerin emissions. Indeed, at a similar cut filler nicotine level, the botanical substrate emits 0.95+/- 0.11 mg/stick of nicotine and the commercial tobacco sticks 0.86 +/- 0.07 mg/stick. Similarly, botanical and tobacco substrates displayed comparable aerosol puff-by-puff profiles.

In conclusion, heated reconstituted botanical substrate with the addition of nicotine and an acid allows to reach the same level of nicotine emissions in the aerosol as a heated tobacco. This kind of botanical substrate can be a non-tobacco alternative with a comparable nicotine delivery profile to an HTP.

123. ACCELERATED SHELF-LIFE METHOD FOR HEATED BOTANICAL SUBSTRATE CONTAINING NICOTINE. Nathalie DUROT, D. Raverdy-Lambert, S. Dejoie, C. Rigoulay, O. Brenner; Ltr Industries C/O SWM, Usine Le Mans, France

New nicotine non-tobacco products are emerging on the market, particularly heated products. They require a botanical substrate containing nicotine that will release nicotine when undergoing heating. Botanical such as for instance food or aromatic or medicinal plant parts can be processed with a two-steps papermaking process during which nicotine or a nicotine salt will be added in a controlled manner.

The objective of this study is to develop an accelerated shelf-life method to evaluate new product stability. The pH of the botanical is likely to increase depending on the amount of nicotine added and the botanical initial pH and buffering capacity. This pH will determine the predominance of protonated nicotine and volatile neutral nicotine. An organic acid may be added to form a nicotine salt to limit nicotine loss. 30 days shelf-life was performed at

different temperatures 20°C and 40°C at 60% RH with pH measurement and determination of nicotine, humectants (GC-FID), water (GC-TCD).

Different botanicals were tested with different nicotine and organic acid levels.

- Gingko biloba with addition of 1.6 % nicotine and a pH of 5.4 is stable without addition of an organic acid.
- Green tea with addition of 1.8 % nicotine without organic acid has a pH of 7,2. 15% of the nicotine is lost in standard shelf-life conditions (20°C 60%RH,30 days) and 33% in accelerated conditions (40°C, 60% RH, 10 days). Addition of 0,5 molar equivalent malic acid or 1 molar equivalent of salicylic acid decreases the green tea pH to 5,8, stabilizing nicotine in both shelf-life conditions.

In conclusion, 10 days accelerated shelf-life allows to assess rapidly the nicotine stability across the time and to select the appropriate organic acid and nicotine levels for a given botanical substrate.

124. TIME SERIES TRANSCRIPTIONAL LANDSCAPE OF TOBACCO LEAVES IN RESPONSE TO HERBIVORE AT SINGLE-CELL RESOLUTION. Huan SU[1], Lingtong Cheng[1], Jiemeng Tao[1,2], Peng Lu[1,2], Jianfeng Zhang[1,2], Peijian Cao[1,2], Jingjing Jin[1,2]; [1]Zhengzhou Tobacco Research Institute of CNTC, Zhengzhou, China, [2]Beijing Life Science Academy, Beijing, China

Defense against herbivores and diseases is an important issue that urgently needs to be addressed in sustainable agricultural production. Massive reprogramming of the plant transcriptome occurs during herbivore responses in plants. Although lots of studies have reported a large number of key regulators induced by herbivore attacks, a systematic analysis of cell-type-specific responses and the associated transcriptional regulation is still lacking. Here we constructed single-cell transcriptional atlases for four time-series

tobacco leaves upon herbivore attack. A total of 28,318 cells were grouped into 15 different cell clusters, and finely annotated to 7 major cell types. These cells underwent extensive transcriptional reprogramming from 1 hour, most of which were recovered at 8 hour. Moreover, there was significant heterogeneity between different cell types during herbivore response, with epidermal and mesophyll cells response at an early stage by activating immune-related pathways, and vascular cells response at latter stage by repairing damage-related pathways. Herbivore attacking also induced cell-cell communication related to plant defense, especially between internal guard cells, and epidermal and vascular cells. Co-expression network analysis demonstrated the importance of jasmonic acid signaling and intracellular oxidative stress in plant defense against herbivores. During herbivore response, plant immune defense genes, particularly immune receptor genes, cooperated with the Ca^{2+} signaling pathway and MAPK cascade, were activated at 1 hour and significantly upregulated in mesophyll, epidermal and guard cells, implying that they might mediate herbivore responses in cell-specific and time-specific manners. These results provide valuable information concerning herbivore response networks at the single-cell resolution, improving our understanding of how transcriptional reprogramming occurs in plant leaves at the cell-type level. The obtained information could serve as a valuable resource for comprehensively investigating the prevention and control of agricultural pests.

125. THE INTERACTIONS BETWEEN ETHIOPIAN TOBACCO BUSHY TOP VIRUS AND ITS SATELLITE RNA OR AN UNRELATED SATELLITE RNA. MO Xiaohan[1], Zhao Xingneng[1,2,3], Zhang Wei[1,4], Zhang Lifang[1,2], Xu Ping [1,2], Li Yanqiong[1,2], Yu Qing[1], Yu Min[4], Chen Hairu[2]; [1]Yunnan Academy of Tobacco Agricultural Science, Kunming, Yunnan, China, [2]Yunnan Agricultural University, Kunming, Yunnan, China, [3]Wenshan Branch of Yunnan Tobacco Company, Wenshan. Yunnan, China, [4]College of Life Sciences, Yunnan University, Kunming, Yunnan, China

Tobacco bushy top disease affects tobacco in China, Zimbabwe, Malawi and Ethiopia, causing significant economic losses. Agrobacterium-mediated infectious clones of Ethiopian tobacco bushy top virus (ETBTV) and its satellite RNA were constructed to investigate the interactions between the virus and its satellite RNA. The results indicated that ETBTV alone could replicate and systemically infect *Nicotiana benthamiana* plants, causing mild symptoms. ETBTV satellite RNA could not replicate and infect *N. benthamiana* plants by itself. When coinfected with ETBTV and its satellite RNA, *N. benthamiana* plants developed severe symptoms, and both ETBTV and its satellite RNA could replicate and systemically infect plants. ETBTV could facilitate the replication and systemic movement of its satellite RNA, while the satellite RNA could boost the severity of the disease symptoms. We further tested whether ETBTV could act as a helper virus to support the unrelated tobacco bushy top virus (TBTV) satellite RNA from China. The results indicated that when *N. benthamiana* plants were coinfected with ETBTV and TBTV satellite RNA, ETBTV could support the replication and systemic movement of TBTV satellite RNA, which is phylogenetically unrelated to ETBTV satellite RNA, and TBTV satellite RNA could boost the severity of disease symptoms. The interchangeability of the phylogenetically unrelated satellite RNAs from different umbraviruses (ETBTV and TBTV) facilitates the understanding of interactions between plant viruses and their satellite RNAs.

126. PREPARATION OF PH-RESPONSIVE DSRNA DELIVERY SYSTEM BASED ON BOVINE SERUM ALBUMIN FOR PEST CONTROL WITH HIGH RNAI EFFICIENCY. Chuantao XU[2], Chenyu Su[1], Meixue Sun[1], Jingfang Cun[1], Robert I. Graham[3], Zhang Yonghui[2], Xie Qiang[2], Xiufang Wang[1], Hao Zong[4], Yingjie Liu[5]; [1]Tobacco Research Institute of Chinese Academy of Agricultural Sciences, Qingdao, China, [2]Luzhou City Company of Sichuan Province Tobacco Company, Luzhou, China, [3]SRUC, Aberdeen, UK, [4]Shandong Tobacco Company, Linyi, China, [5]Staff

Development Institute of China National Tobacco Corporation, Zhengzhou, China

Pest RNAi control contributes to the development of sustainable agriculture, and the single-copy genes with critical functions, such as heat shock protein 90 in lepidopterans, are ideal targets for developing novel strategies to control pests. However, with the existing application technologies, it is difficult to guarantee RNAi efficiency, which in turn impacts control efficiency. Herein, we describe the development of a nucleic acid delivery system using the biological material bovine serum albumin (BSA) to deliver dsRNA targeting HSPs 90 gene (*Hsp90*) of *Spodoptera litura*, a globally important agricultural pest causing serious economic losses of crops. The prepared BSA particle (GBSA·NPs) structure is stable and has a size of only 292 nm. The shell structure composed of BSA was able to effectively protect dsRNA from degradation. Additionally, the schiff-base formed by glutaraldehyde cross-linking is an acid-sensitive bond that easily releases dsRNA in the acidic environment inside cells, which cell-based experiments showed an RNAi efficiency increase by 43.59%. Crucially, the results of experiments on individual insects showed that the use of GBSA·NPs to deliver dsRNA increased the RNAi efficiency by nearly 3-fold and the insecticidal activity by 2.3-fold, compared to direct treatment with dsRNA. These results suggest a novel strategy for controlling pests with BSA-delivered dsRNA targeting functional single-copy genes.

127. EFFECTS OF ACTIVE COMPOUNDS EXTRACTED FROM CITRUS FRUITS ON THE QUALITY OF CIGAR TOBACCO LEAVES DURING FERMENTATION. HU Wanrong, Yang Zhen, Cao Yu, Jia Yun, Liu Lulu, Li Dongliang; China Tobacco Sichuan Industrial Co, Chengdu, Sichuan, China

Fermentation plays an important role in improving the quality of cigar tobacco leaves. In particular, fermentation with characteristic additives is an effective approach to enhance

the fermentation effects. The aim of this study was to develop new additives and investigate their effects on cigar tobacco leaves. Active compounds extracted from three types of citrus fruits were obtained by ultrasound-assisted extraction coupled with solid phase purification, and their effects as fermentation additives on the main chemical components, microbial communities, and sensory quality of cigar tobacco leaves were analyzed. The results showed that: (1) Flavonoids were the main components of the prepared citrus extracts. (2) The addition of citrus extracts decreased the contents of amino acids, oxalic acids, and unsaturated fatty acids in cigar tobacco leaves, while increasing the content of citric acid. In addition, the total amount of aroma substances in cigar tobacco leaves increased by 38.15% with the addition of citrus extracts, and the contents of D-limonene, β-dihydroionone, dihydroactiniolactone, and other representative aroma components increased. (3) The addition of citrus extracts promoted the succession of the microbial community in cigar tobacco leaves and promoted the enrichment of Pseudomonas and Corynebacterium. (4) The addition of citrus extracts effectively reduced the irritation and improved the aroma richness of cigar tobacco leaves. In this study, the influence of citrus extracts on cigar quality was systematically analyzed, which provided a reference for the development of characteristic cigar fermentation additives and the expansion of cigar quality improvement technologies.

WORKSHOPS

W1. CONTEMPORARY WATERPIPES, WATERPIPE ACCESSORIES, AND WATERPIPE TOBACCOS. John LAUTERBACH; Lauterbach & Associates, Deland, FL, USA

While many other parts of the conventional tobacco industry have suffered from declining sales for the past decade or more, the waterpipe industry has been expanding on all fronts, including waterpipes (also known as hookahs, hookah pipes), waterpipe accessories [tobacco-product-holders (also known as bowls), heat management devices, charcoals, electric heaters, foils] and waterpipe tobaccos (also known as shisha). However, there apparently has been no peer-reviewed scientific literature on such devices and products and knowledge of the supposed effects of

using such devices and products appears to be limited to reviews published on consumer-oriented websites and comments on social media. Consequently, the purpose of this workshop will be to provide experimental data derived from devices such as portable hookah pipes, all-glass waterpipes and bowels, novel heating and heat management devices, alternative apparatus and techniques for collecting the waterpipe tobacco emissions, and lab-scale preparation of waterpipe tobaccos using leaf and processes traditionally used to manufacturer such tobaccos as well as leaf and processes those that are used in other parts of the tobacco industry. Furthermore, the concept of the pH of the waterpipe aerosol will be explored with differing tobaccos and agents known to modify smoke pH.

W2. MIXING DIFFERENT FLAVORED WATERPIPE TOBACCOS: CONSUMER PREFERENCE, MARKETING GIMMICK AND/OR REGULATORY CONUNDRUM? John LAUTERBACH; Lauterbach & Associates, Deland, FL, USA

Most consumers of tobacco products use the products as intended by the manufacturers. While users of waterpipe tobacco (WPT) have always had options to chose a variety of waterpipes (WP) and accessories (e.g., charcoal, bowls, foils) that can alter smoke composition, there has been no emphasis by marketers of WPT for users to blend different flavors of WPT to get a more pleasing smoke. Now that has changed with specific mixing instructions and flavors of WPT to use on the Internet. Recommended mixing is blending the two or three WPT together, layering them in the bowl, or using virtual sections of the bowl such as 1/3 of the bowl for each flavor. Such practices may have the users buying two or three packages of product instead of one so 2X or 3X product is sold. Also, mixing can involve WPT from more than one manufacturer and/or mixing flue-cured (FC) WPT with dark-air-cured (DAC) as some flavors are only available in DAC. To study mixing, we looked at both the emissions and residues (about 70% of WPT remains after use) using liquid chromatography (LC). Using a combination of vanilla FC WPT and a fruit WPT, we evaluated all three mixing procedures. We also evaluated a mixture of a FC fruit WPT with a single-fruit flavored DAC WPT. LC of the emissions (Cogent BiD C8 column

with Agilent 1100 diode-array detector with acetonitrile/water (75/25) at 0.6 mL/min) showed that the three mixing techniques for FC WPT did not make a significant difference in emissions nor did the mixture of FC and DAC WPT. Based on the mixtures studied, mixing of flavored WPT should not raise regulatory concerns.

W3. USE OF HEAT MANAGEMENT DEVICES IN CONJUNCTION WITH ELECTRIC HEATERS FOR THE GENERATION OF EMISSIONS FROM WATERPIPE TOBACCOS. John LAUTERBACH; Lauterbach & Associates, Deland, FL, USA

Heat management devices (HMD) are used to replace the perforated aluminum foil that separates the glowing charcoal briquettes from the waterpipe tobaccos (WPT) when they are smoked in a waterpipe. In addition, HMD, can be used to modulate the heat that can be applied to the tobacco, without the need to add or remove the glowing briquettes or move them to different positions on the perforated foil. However, we have also shown that HMD can be used, with some modification, for use with electric heaters. Consequently, we have conducted a comparison the emissions using two brands of HMD versus those obtained with the use of two layers of perforated aluminum foil. This comparison has included several brand-styles of both flue-cured and dark air-cured flavored WPT. The data included in the comparisons are weight-loss of the WPT on heating 1-hour with 530/3/20 puffing regimen, liquid chromatography data on the water in the base of the glassmouth, the acetonitrile/water (85/15) washing of the glassmouth after the water was removed, and of the (WPT) residue left in the bowl. Our weight-loss results are similar to those reported in the literature for similar WPT products using charcoal heating. The main difference between use of HMD versus perforated foil is that the preheating period before puffing needs to be extended from 10 min to 20 min and the power to the heater needs to be increased by up to 50% to maintain the same WPT temperature profile as monitored with Type K thermocouples embedded in each bowl.

W4. ANALYSIS OF COMMERCIAL CIGARS FOR DEVELOPMENT OF DESIGN PARAMETERS FOR REFERENCE CIGARS. Huihua JI; University of Kentucky, Lexington, KY, USA

Abstract Omitted

W5. THE HISTORY OF THE CENTER FOR TOBACCO REFERENCE PRODUCTS AND THE ADDITION OF CERTIFIED REFERENCE CIGARS. Ruth MCNEES; University of Kentucky, Lexington, KY, USA

Abstract Omitted

W6. DETERMINATION OF CERTIFIED VALUES AND UNCERTAINTIES FOR REFERENCE CIGARS. Stacey SLONE; University of Kentucky, Lexington, KY, USA

Abstract Omitted

W7. LONG-TERM SUSTAINABILITY AND FUTURE PLANS FOR THE CENTER FOR TOBACCO REFERENCE PRODUCTS. Ruth MCNEES; Univesity of Kentucky, Lexingtion, KY, USA

Abstract Omitted

CONFERENCE HISTORY

Technical Conference on Analytical Methods for Tobacco	1947 – 1948
Research Conference on Tobacco	1949
Research Conference on the Chemistry of Tobacco	1950
Tobacco Chemists' Research Conference	1951 – 1997
Tobacco Science Research Conference	1998 – present

1	1947	Oct 22-23	Philadelphia, PA	Eastern Regional Res. Lab
2	1948	Nov 22-23	Philadelphia, PA	Eastern Regional Res. Lab
3	1949	Oct 17-18	Richmond, VA	Medical College of VA
4	1950	Sept 11-12	State College, PA	Pennsylvania State College
5	1951	Oct 25-26	Durham, NC	Duke University
6	1952	Dec 4-5	Louisville, KY	University of Louisville
7	1953	Oct 1-2	Winston-Salem, NC	Bowman Grey
8	1954	Nov 11-12	Richmond, VA	Medical College of Virginia
9	1955	Oct 6-7	Raleigh, NC	NC State College
10	1956	Nov 8-9	Washington, DC	USDA
11	1957	Oct 10-11	New Haven, CT	Connecticut Agriculture Research Station
12	1958	Oct 23-24	Durham, NC	Duke University
13	1959	Oct 29-30	Lexington, KY	University of Kentucky
14	1960	Oct 13-14	Winston-Salem, NC	Wake Forest University
15	1961	Oct 4-6	Philadelphia, PA	USDA
16	1962	Sept 26-28	Richmond, VA	Virginia Institute Scientific Research
17	1963	Sept 22-25	Montréal, Quebec	Canada Department Agriculture
18	1964	Oct 20-22	Raleigh, NC	NC State University
19	1965	Oct 26-28	Lexington, KY	University of Kentucky
20	1966	Nov 1-3	Winston-Salem, NC	Wake Forest University
21	1967	Oct 18-19	Durham, NC	Duke University
22	1968	Oct 17-18	Richmond, VA	Virginia Institute Scientific Research
23	1969	Oct 22-24	Philadelphia, PA	USDA
24	1970	Oct 28-30	Montréal, Quebec	Canada Department Agriculture
25	1971	Oct 6-8	Louisville, KY	University of Kentucky
26	1972	Oct 22-28	Williamsburg, VA	VPI & SU
27	1973	Oct 3-5	Winston-Salem, NC	Wake Forest University
28	1974	Oct 28-30	Raleigh, NC	NC State University
29	1975	Oct 8-10	College Park, MD	USDA
30	1977	Oct 18-20	Nashville, TN	University of Tennessee
31	1977	Oct 5-7	Greensboro, NC	UNC-G & NC AT&T Univ.
32	1978	Oct 30-Nov	Montréal, Canada	Canadian Tobacco Manufacturing Council
33	1979	Oct 29-31	Lexington, KY	University of Kentucky
34	1980	Oct 27-29	Richmond, VA	VPI & SU
35	1981	Oct 6-9	Winston-Salem, NC	Wake Forest University
36	1982	Oct 24-27	Raleigh, NC	NC State University
37	1983	Oct 10-13	Washington, DC	USDA & University of Maryland
38	1984	Nov 5-8	Atlanta, GA	USDA & University of Georgia

39	1985	Oct 2-5	Montréal, Canada	Canadian Tobacco Manufacturing Council
40	1986	Oct 13-16	Knoxville, TN	University of Tennessee
41	1987	Oct 4-7	Greensboro, NC	UNC-G & NC AT&T University
42	1988	Oct 2-5	Lexington, KY	University of Kentucky
43	1989	Oct 2-5	Richmond, VA	VPI & SU
44	1990	Sept 30 - Oct 3	Winston-Salem, NC	Wake Forest University
45	1991	Oct 20-23	Asheville, NC	NC State University
46	1992	Sept 27-30	Montréal, Quebec	Canadian Tobacco Manufacturing Council
47	1993	Oct 18-21	Gatlinburg, TN	University of Tennessee
48	1994	Sept 25-28	Greensboro, NC	UNC-G & NC AT&T University
49	1995	Sept 24-27	Lexington, KY	University of Kentucky
50	1996	Oct 20-23	Richmond, VA	VPI & SU
51	1997	Sept 14-17	Winston-Salem, NC	Wake Forest University & R. J. Reynolds Tobacco Co.
52	1998	Sept 13-16	Atlanta, GA	University of Georgia & Schweitzer-Mauduit
53	1999	Sept 12-15	Montréal, Quebec	Canadian Tobacco Manufacturing Council
54	2000	Sept 24-27	Nashville, TN	United States Tobacco Manufacturing
55	2001	Sept 9-12	Greensboro, NC	Lorillard Tobacco Company
56	2002	Sept 29-Oct 2	Lexington, KY	University of Kentucky
57	2003	Sept 21-24	Norfolk, VA	Virginia Tech University
58	2004	Sept 19-22	Winston-Salem, NC	R. J. Reynolds Tobacco Co.
59	2005	Sept 25-28	Atlanta, GA	Schweitzer-Mauduit Intl.
60	2006	Sept 17-20	Montréal, Quebec	Rothmans, Benson & Hedges
61	2007	Sept 23-26	Charlotte, NC	Wattenspapier
62	2008	Sept 21-24	Nashville, TN	U.S. Smokeless Tobacco Manufacturing Company
63	2009	Sept 27-30	Amelia Island, FL	Lorillard Tobacco Company
64	2010	Oct 3-6	Hilton Head, SC	Cerulean & Global Laboratory Services
65	2011	Sept 18-21	Lexington, KY	The University of Kentucky
66	2012	Sept 9-12	Concord, NC	R. J. Reynolds Tobacco Co.
67	2013	Sept 15-18	Williamsburg, VA	Borgwaldt
68	2014	Sept 28-Oct 1	Charlottesville, VA	delfort Group
69	2015	Sept 20-23	Naples, FL	ITG Brands
70	2016	Sept 18-21	Palm Beach Gardens, FL	Cerulean
71	2017	Nov 28-Dec 1	Bonita Springs, FL	Tobacco Technology Inc & eLiquidTech
72	2018	Sept 16-19	Memphis, TN	American Snuff Company & RAI Services Company
73	2019	Sept 15-18	Leesburg, VA	Altria Client Services
74	2021	Aug 29-31	Boston, MA	Imperial Brands
75	2022	Sept 11-14	New Orleans, LA	RAI Services Company
77	2023	Sept 24-27	Norfolk, VA	Juul Labs, Inc
78	2024	Sept 8-11	Atlanta, GA	SWM International

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