

NEWSLETTER

Issue 61 - December 2021



2021 CORESTA VIRTUAL CONFERENCES

Rob STEVENS

A word from the President of the CORESTA Scientific Commission, Dr Rob Stevens:

First and foremost, I hope you and your families are safe, healthy, and looking forward to an exciting Holiday Season. As President of the CORESTA Scientific Commission, I wanted to take the opportunity to congratulate everyone for making the 2021 "virtual" CORESTA Agronomy & Leaf Integrity and Phytopathology & Genetics (AP) Study Group and the Smoke Science and Product Technology (SSPT) Study Group Conferences a huge success. Despite the worldwide limitations on travel and the safety measures in place due to COVID-19, CORESTA demonstrated a clear commitment to drive forward and provide a forum to allow scientists the

opportunity to openly share credible science and best practices related to tobacco and its derived products.

Throughout the month of October CORESTA featured over 129 presentations covering a range of relevant and important scientific topics associated to tobacco and tobacco-related products. For example, key topics such as cigar tobaccos, genetic tools & technologies, crop production & sustainability, leaf nicotine, and conventional & biocontrol of pests and diseases were highlighted in the AP program. In SSPT, the Symposium on "Advancing New Alternative Methods (NAMs) for Tobacco Harm Reduction" was extremely well received and attended. The SSPT program included a diverse array of presentations on topics including perception & behavior, nicotine science, analytical methods, product chemistry, biomarkers, statistical modeling, and in vitro & in vivo toxicology. Product categories presented and discussed included combustible cigarettes and emerging tobacco products such as e-vapor products, heated tobacco products (HTP), and nicotine pouches.

Engagement was a critical goal for the CORESTA team, and I am extremely proud to report that we had 4,393 connections during the conferences with a total of 190 and 538 participants estimated for the AP and SSPT Conferences, respectively. I am honored to serve as the President of the Scientific Commission and on behalf of the Scientific Commission, I would like to again thank you for all your continued support and contributions to CORESTA. While we reflect on the amazing conferences in 2021, we also look forward with hope and promise to a great CORESTA Congress in 2022.

2021 Agro-Phyto Virtu@l



pole rot on flue-cure

SCIENTIFIC PROGRAMME

AP2021

The Agronomy & Leaf Integrity and Phytopathology & Genetics Conference (AP2021) consisted of 52 papers organised into nine daily sessions covering the current major agricultural topics.

Tobacco production still necessitates agronomical studies to improve yield and plant protection. The session on production featured papers on the evaluation of the plant boron needs, the investigation into the effects of topping on the potassium flux in tobacco roots, suggestions for improving nutrient deficiencies, and studies on the effects of chemical drift on flue-cured tobacco, specifically glufosinate, 2,4-D and dicamba.

Plant production is heavily dependent on the effective management of pests and diseases. Papers on tobacco susceptibility to angular leaf spot and control through spray programmes were presented together with papers on the use of antivirus agents to control various other diseases, assessment of several fungicides to control *R. solanacearum*, the interaction of nematodes and black shank in some tobacco varieties, and the trapping of tobacco moth using an effective light device.

Safeguarding the planet is a key topic these days with diligent efforts being made to improve pest and disease control from an environmentally friendly perspective. Biocontrol methods are key to future pest and disease management – presentations were made on "green" nematicides, "green" manure to control soil-borne diseases, the effect of "liquid" smoke on collar rot, the use of novel bacteria to manage angular leaf spot, biological control of pole rot, and further work on *Bacillus thuringiensis*.

Continuing the environmental theme, the session on sustainability covered climate change impacts, the use of biological suckercides, the production of compressed charcoal produced from tobacco stalks, vermicompost used to improve plant growth, yield and leaf quality and wheat straw residue to improve soil properties. Similar soil improvements were shown by a study on biochar and nitrogen fertilizer addition to different soil types.



Enormous progress continues to be made in the study of genetics with numerous tools becoming available to facilitate plant breeding. The genetics session talked about molecular markers used for rapid screening of pathogen resistant plants and those related to nematode resistance. The session also focused on the genetic analysis of a major disease resistance quantitative trait loci, a transcription factor that enhances resistance and tolerance, and the agronomic performance and yield potential of different tobacco breeding lines.

While genetics is one aspect of technological breakthrough, other technological developments play a major role in furthering tobacco plant knowledge. The technology session featured presentations on high quality assembly of the tobacco genome, identification and functional characterization of tobacco genes, the use of chlorophyll fluorescence imaging, investigation of the dynamics of molecular leaf senescence processes during tobacco curing, and the use of non-destructive photonic sensing.

Genetics and production practices are an important research area when it comes to studying TSNAs, which still features prominently in the tobacco research spectrum. The TSNA section covered the consequences of molecular genetic alteration of leaf nitrate levels on TSNAs, genetic mapping of a gene mutation and the impact of potassium levels and fermentation temperature. Nitrogen being a precursor of TSNA, also covered in the session were the effects of salicylic acid on nitrogen metabolism of tobacco under drought stress and the potential role of tobacco leaf endophytic fungal communities.

To anticipate possible future regulation of nicotine by authorities, much research is being undertaken to study nicotine level reduction. Papers were presented on a novel low alkaloid gene, the functional characterization of a locus regulating nicotine biosynthesis, the impact of genotype, cultural practices and management on nicotine concentration and plant growth.

Cigar tobacco production is in a niche of its own as the customer requirements are different to traditional cigarettes. The session on cigars covered the development of production requirements for cigar fillers, binders and wrappers response to nitrogen fertilizer rates, the evaluation of experimental hybrids, and the characterization of microbial communities in the processing of leaves.

Alternative uses of tobacco are always of much interest – one of the papers presented the extraction of oil from tobacco seed. Also of interest was a paper on the adaptability of hemp production in tobacco growing systems.



SSPT2021

Challenges in analysing contem

INFLUENCES

tobacco

The Smoke Science and Product Technology Conference (SSPT2021) had 70 papers organised into 15 sessions spanning eight days. An additional session consisted of a symposium on new alternative methods featuring seven papers (explained in more detail in the interview with the organisers – see page 6).

The conference opened with a session on perception and behaviour that covered consumer-reported outcome measures' methodology, scope and definitions – work being done within the CORESTA CROM Task Force. The psychometric validation of new scales for perceived social and practical risk was discussed together with risk perceptions and likelihood of use, the impact of next generation products on population health through population modelling and statistical methodology.

Next generation products featured prominently in the conference programme. Sessions on heated tobacco products (HTPs) covered the modelling and numerical simulation of electromagnetic heating sets, electric heating non-combustion sets, heated tobacco sticks and smoke flow field characteristics and temperature distribution. HTP analysis method development continued with HTP aerosols studies that included the determination of TSNAs by ASE and LC-MS/MS analysis and various method adjustments, the determination of aromatic amines and a study on reduction of harmful and potentially harmful constituents (HPHCs).

E-cigarettes had sessions devoted to analytical methodology, product analyses and product chemistry. Organic acids were analysed using GC-FID and ion chromatography, quartz filter collection and electrostatic precipitation were studied for the analysis of trace metals and two GC-MS methods were investigated for determination of glycidol. Product analyses included papers on the capability of SIFT-MS to measure volatile carbonyl compounds, key parameters affecting the release of aldehydes, compound identification processes for GC-MS non-targeted





analysis using a custom mass spectral library, and machine based learning to develop new chemicals for e-cigarette vaping. E-vapour chemistry focussed on e-liquid stability studies, the effect of pH and storage temperature on e-liquid metal concentrations, collection strategies for the analysis of targeted compounds, yield comparisons between aerosols and cigarettes.

The session on nicotine pouches featured a set of five related presentations covering the nonclinical toxicity assessment of oral tobacco-derived nicotine products and described the framework, ingredient evaluation, extraction and test material characterization, *in vitro* regulatory testing and *in vitro* mechanistic assays. An additional paper described a market survey of oral nicotine products to determine selected constituents compared to smokeless products.

The nicotine science session reported on a literature review of nicotine pharmacokinetics, a study of the effects of various forms of nicotine delivery on the nervous system and hormones, and the inhibitory effect of nicotine on Parkinson's disease.

Research is still being carried out on conventional tobacco products and a session on analytical methods covered a quicker method for ammonia analysis in cigarette smoke, a chemometric approach for the development of flavour compound analysis, and the use of a charcoal cartridge trap system to identify volatile and semi-volatile organic compounds by GC-MS in cigarette smoke. The cigarette modelling and design session included presentations on the development of a prediction model for lip sticking force of cigarette tipping paper, the analysis of volatile compounds in tipping glue, the effects of cigarette circumference on ventilation rate, and cigarette packaging designs to ensure maximum moisture retention and flavour retention.

Work is also being carried out on water pipes and two presentations discussed the technical challenges of water pipe transfer studies and analysis of contemporary flavoured shisha tobaccos.

Aromas and flavours are important components of tobacco and tobacco derived products. Presentations were made on the release of natural tobacco flavourants and nicotine at heat-not-burn and vaping temperatures, the interaction of aroma components and taste characteristics of cigarettes, the saliva components of cigarette smokers, and the simultaneous detection of organosulfur compounds in cigarette smoke.

A key factor in all research and product development is the assessment of exposure for which biomarkers play a significant evaluatory role. The biomarker session addressed this major topic with papers on the analysis of NNN using an alternative method to the urinary determination method, the analysis of a biomarker for BaP exposure in smokers and users of potentially reduced risk products, a study to establish population level estimates on NNAL in smokers and non-smokers, and studies on the levels of biomarkers of exposure following transition to ENDs product use.

Cytotoxicity studies are important in appraising the potential toxicity of tobacco and tobacco derived products. In addition to the NAM Symposium, sessions were dedicated to work done on *in vitro* and *in vivo* methods and toxicological assessments of nicotine products. Papers presented included an investigation of approaches to assess ENDS vapour induced toxicity and health impacts, a study on the influence of antioxidant capacity on micronucleus induction by cigarette smoke on cells, the identification of a novel mode of action to induce micronuclei, an alternative ENDS collection method for *in vitro* testing and the development of an *in vitro* waterpipe air-liquid interface exposure system method. Toxicological assessment papers featured a study to assess alternative cell lines for cytotoxicity determination, *in vivo* genotoxicity testing of aerosols and *in vitro* evaluation of tobacco free nicotine pouches.

The conference ended with a session on statistics and laboratory operations that included a paper on a statistical approach to estimate method precision followed by a presentation discussing the elimination or accommodation of outliers. A presentation on how lab productivity is affected by the outsourcing of asset management services and an overview of tobacco reference material for monitory alkaloids and sugar closed the session and the event.

CORESTA thanks all the presenters who prepared papers and were present "live" during the sessions to comment and answer questions from the participants.

Access to the pre-recorded videos has been extended until 31 December and can be viewed by CORESTA members via the "Member Content" tab on the CORESTA website.

Abstracts and the PDFs of presentations have been published in the "Abstracts" section of the CORESTA website and can be accessed publicly when authorisation has been granted by the author(s).

CONFERENCE STATISTICS



9 sessions

16 sessions

52 presentations

77 presentations

>190 participants

>500 participants

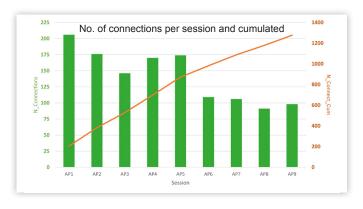
1276 connections

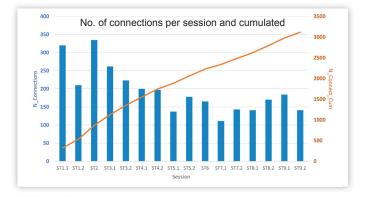
3117 connections

52 presentations made out of the original 54 initially planned.Only three presenters had difficulties joining (two due to poor internet connection, and 1 using incompatible equipment).All other presenters were present live from all over the world.

Each presenter was asked, on average, two questions by participants.

- ♦ 77 presentations made out of the original 79 initially planned.
- All presenters were present live from all over the world except for one who had indicated that he would not be able to join.
- Each presenter was asked, on average, two questions by participants.





Presenter and Participant World Distribution

AP:

Presenters from 13 countries, 24 organisations; Registered participants from 41 countries, 131 organisations

SSPT:

Presenters from

12 countries, 37 organisations; Registered participants from 34 countries, 142 organisations



POST-CONFERENCE SURVEY

85 % of presenters and 82 % of participants felt the conferences were very good to excellent.

Presenters who replied to the survey unanimously agreed that they were easily able to submit their abstract, they received sufficient preparatory information, and they found the pre-event rehearsals useful. Most found that being able to answer questions live gave added value to the conferences, although one presenter felt email correspondence was more flexible.

Of the participants who replied to the survey, most were satisfied with the registration process and the access to the conferences via the invitation links, but some expressed disappointment that questions asked via the chat box were not always answered.

In general presenters and participants enjoyed the convenience of the online conference format, but many hoped that in-person meetings would soon be back on track.

SSPT2021 - NAM SYMPOSIUM

The SSPT2021 Conference included a Symposium on "Advancing New Alternative Methods (NAMs) for Tobacco Harm Reduction" on 19 October. NAMs represent *in vitro* and *in silico* or computational methodologies, an emerging set of chemical safety assessment tools, without needing additional *in vivo* animal testing.



SYMPOSIUM

Advancing New Alternative Methods (NAMs) for Tobacco harm reduction

The Symposium was organised and led by Dr K. Monica Lee (ML) from Altria Client Services, and Dr Shannon Bell (SB) from Integrated Laboratory Systems.

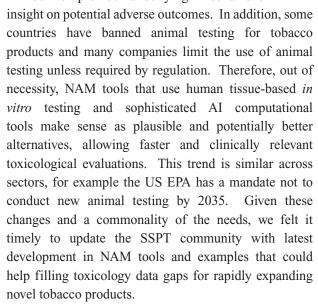
Interviewed after the event by the CORESTA Secretariat, Monica and Shannon shared some comments on their experience.

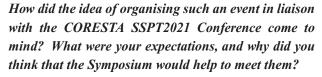
Monica, Shannon,

You organised a Symposium on new alternative approaches for tobacco harm reduction during the CORESTA SSPT Conference and it proved to be a great success with up to 335 connections for the live session.

Why is the theme of the Symposium of importance in our current environment?

ML & SB: The toolbox for toxicological assessment is rapidly changing. Traditional tools like *in vivo* animal testing are still being used but they are slow, resource intensive, yet limited to provide underlying mechanistic





ML: This topic of NAMs or alternatives to *in vivo* testing is something that has been on my mind throughout my career in toxicology. This is a bit ironic as I started out as an *in vivo* toxicologist and am fully aware that animal



K. Monica LEE Altria Client Services



Shannon BELL Integrated Laboratory Systems

data are often critical in standard risk assessments. At the same time, for tobacco products we already have a lot of human data (mostly from conventional cigarettes and smokeless products) but the standard risk assessment often relies on, among other things, data from animal studies. With rapid development in NAM tools, it becomes plausible that we could fill data gaps for reduced-risk (RR) alternative products using non-animal methodologies. With this mindset, when an opportunity came for a potential CORESTA session early this year, I thought "why not use the SSPT platform and start the discussion". I knew that NAMs are well suited to CORESTA's pursuit of 3Rs (Reduce/

Replace/Refine animal testing) and would support nonclinical activities of several Sub-Groups (*In Vitro* Tox and Biomarkers SGs and Next Generation TF). The SSPT2021 organizers (Rob, Stéphane, and Karl) and the Sub-Group leads were fully supportive of the proposal and all the coordination and technical support (Stéphane and Natacha) were exceptional throughout the process.

The presenters were internationally recognised experts and the content of the programme was impressive. How did you contact and convince the presenters to participate? Was it difficult?

ML: Thank you - To make a symposium like this work, desirably involving distinguished experts from diverse external groups, I needed to first map out the overall story with potential topics of interest. With the outline drafted and to ensure the content is representing the current status in the wider NAM community, I sought a co-chair who is immersed in external NAM activities with various stakeholders, Shannon at ILS. I have worked with Shannon on my IVIVE modelling work and she graciously agreed to serve as co-chair. We sought to identify candidate speakers using peer-review publications and professional networking, and in the end, put together an impressive set of experts from both

regulatory and private entities. I add - some speakers would have difficulty participating if it involved international travel and the fact that this year's SSPT conference was virtual and free to the public definitively helped.

Overall, what were the main challenges you had to face, and how did you tackle them?

ML & SB: The biggest challenge, when we had the fortune of getting a panel of internationally recognised experts, was that they are extremely busy! Since we are preparing this symposium as "101" to NAMs, it was important that the speakers' contents are general enough and relevant to CORESTA participants. We were most grateful for the discretionary time the speakers gave to the symposium, including many late day/early morning meetings and back and forth of materials. Pre-recoding the presentations and delivering the recorded talks without the real-time feedback from the audience and ability to build off other speakers was also a challenge to The CORESTA organizers were some speakers. incredibly helpful, providing us with check-ins to test the technology and troubleshoot connections and showed immense patience throughout and also with speakers' clearance timelines. All this led to a very smooth live symposium with very effective Team tools set up by CORESTA, allowing speakers to share information with participants real-time in the chat something that would be hard to do in person.

What main conclusion can you draw after this Symposium?

ML & SB: "NAMs are here!", already being used as you have heard from speakers' case examples in environmental chemical risk assessment. I'd like to note that the tobacco community is not too far off either, many of us using the tools whether calling a method a NAM or not, for instance the air-liquid-interface (ALI) in vitro system for inhalation toxicity testing. One of the learnings from the symposium is the confirmation that many SSPT members are interested in further application of NAMs beyond screening but as a group we are not sure how to best build and evaluate its applicability in risk assessment. Considering another learning from the symposium, the availability of various public/free tools and database, one does not need to, or

should not, start from scratch as it is simply too much to incorporate and develop all the aspects of NAMs in silo on their own. So, the parting message is, let's keep the momentum, continue the discussion, and identify a common area of interest for a case application through multi-party CORESTA activities.

Would you encourage other CORESTA members to organise similar events? What are your next steps now?

ML: Yes — I'd say not only for this but other emerging topics as well. It is challenging to keep track of rapidly expanding scientific developments and symposiums like this allow an open platform to share learning between CORESTA and external communities. I appreciate the Scientific Commission's current effort to break down the top-to-bottom mindset and structure, fostering horizontal interactions among all members and beyond. On this topic of NAMs, we received lots of positive feedbacks and interests to be involved in possible follow-ups. For instance, among nonclinical and clinical Sub-Groups, we are considering a NAM-II workshop to share and highlight tested NAM cases from member companies.

Any concluding comments? A last message to deliver to our readers?

ML: I believe that CORESTA members have a common goal of tobacco harm reduction, which has become more real in recent years with expanding introduction of a variety of smoke-free alternatives. As the leader in tobacco sciences, we are uniquely situated to learn and foster the use of novel scientific tools such as NAMs to substantiate the THR. I look forward to our continued discussions, challenging each other! Lastly, I thank all the SSPT participants with great questions, each of the speakers, the co-chair Shannon, and the Scientific Commission for making this first all external SME symposium successful. And I encourage those interested in exploring a follow-up NAMs workshop to reach out to me, thank you.

CORESTA would like to thank Monica and Shannon for their engagement with the international scientific community, for their contribution to the dissemination of important scientific knowledge, and for their commitment to CORESTA.







A PEEK BEHIND THE SCENES

When the CORESTA Board once again made the decision to organise the 2021 conferences virtually, there was a strong feeling of 'déjà vu' among the Secretariat team, a sensation of something already experienced, or at least partly experienced, in 2020.

Considering the global pandemic situation, the basic requirements for events were to be safe, secure and to comply with internationally accepted meeting standards. All these seemed quite easily attainable.

Yet something new was added to the specifications this time: the 2021 Conferences had also to be interactive. Quite a challenging novelty – based on the feedback collected from the 2020 Congress.

All event organisers know that every event has its unique set of challenges and goals. As for "live" events, those who had already experienced them whispered some serious doubts about their successfulness. However, for the Secretariat team there was no room for second thoughts or hesitations as time was of the essence.

The team reacted rapidly and knew from former experience that work well planned was work half done. A solid planning phase was established and a risk assessment was done. What platform should be used? What problems might occur? How could problems be minimised or solved?

Firstly, the event platform was selected. The CORESTA team settled on using MS Teams Live Event as it covered all the functional needs of the conferences and was the most accessible to the largest number of people.

Addressing the request for interaction was quite a challenge not only for the Secretariat team and the presenters, but also to the members of the Scientific Commission who were to chair and/or co-chair the various conference sessions. Each presentation had to be followed by an approximate 5-minute Question & Answer session where presenters could answer live. This required active involvement by the chairpersons.

Although many of us are now familiar with virtual environments having often had to work remotely since the pandemic began, things can still be tricky. Who does what and when? All the roles had to be well defined and interchangeable. What about internet connections? They do not always work, sometimes they are difficult to access or unreliable, or for some other unknown reason everything goes wrong. These fears and doubts were addressed over the several weeks of the planning phase.

One of the main concerns for the Secretariat team was to sort out how to minimize risks knowing that CORESTA does not have ready access to IT professionals. The first step was to find supplementary office space in case internet connection issues should occur at the CORESTA office. Fortunately, space was found in the building right next door (and included an attractive rooftop terrace from which to admire the Paris rooftops).

The second precaution concerned the scheduling of presentations and the Question & Answer sessions, audio, and technical issues. One had to find a time suitable for Europeans, Asians, Americans and Africans, so that it was neither too late at night nor too early in the morning for anyone.

It was essential that not only the Secretariat team but also the speakers (presenters and chairpersons) be involved in the preparations. Training was needed for the different roles. The first rehearsal session was not a huge success with presenters experiencing connection issues and failing to join. This did not bode well and caused quite some worry for the organisers. Nevertheless, time passing by and the conferences fast approaching, the rehearsal sessions began to fill up. Everyone had to handle the very basics, such as to join in, to hear, to be heard and to be seen – easier said than done. The initial 26 planned rehearsals spanned out to become 40 rehearsals that covered the whole month of September. These were tirelessly carried out by two persons from the Secretariat who made sure that all the presenters, the chair- and co-chairpersons received a detailed checklist of their roles and understood the logistics. In the end, all the speakers had the chance to test their connections, address their concerns, and prepare for their presentations.

Meanwhile, two other persons from the team were sweating the details of each individual PowerPoint presentation that was submitted for both conferences. These were scrutinized for audio and visual quality, and timing checked before being converted into video format.

Finally, on 4 October, the 2021 Agronomy & Leaf Integrity and Phytopathology & Genetics Virtual Conference began and was broadcast daily until the 14 October. It was followed by the 2021 Smoke Science and Product Technology Virtual Conference from the 18 to 28 October.



Presenter checklists and invitation reminders were sent, and depending on the schedule, one or two daily conference sessions were broadcast from the CORESTA premises every afternoon by a member of the Secretariat team acting as producer and backed up by a co-producer operating from the extra office space in case of problems. At the beginning of each session there was a short moment when the presenters, chairpersons and the organisers had to make sure their cameras were on to say hello and had a moment of (semi)



relaxed chatting. The organisers then switched off cameras and began managing from the background, all microphones were switched off, and tension built up as "go live" approached.

"Fivesecondstillyouarelive" and all setto go—the chairperson opened thesession by welcoming the participants and introducing the first presenter, the video was broadcast, the presenter went live and the co-chair asked questions raised by participants in the Q&A chat box. There was maximum concentration as the sequence was repeated, unexpected problems were sorted, instructions were given, until all breathed a sigh of relief as the chairperson closed the session after the final presentation.

Unquestionably an interactive virtual meeting places a different kind of strain on the brain than traditional in-person meetings. During every session cognitive skills were under pressure for each speaker, not to mention the organisers!

What was the feeling in CORESTA Office when the month of conferences was over?

The overall sensation was that of a great relief that finally all had gone well with only a few minor glitches. Connection issues had usually been solved the common IT way: log off and log back in. The live interaction with presenters finally went smoothly without any major blunders. For the Secretariat team, the overall impact of these conferences was much work in advance, during and after the event. As well as presenters, chairpersons and co-chairs, the team had to adapt to new work realities and the value of a physical work- or meeting place was assessed in a new way.

What did we learn from organizing interactive events for the second time?

The most obvious lesson was probably the fact that the initially slowly progressing digital transition actually became a leap with a steep learning curve.

Virtual events are here to stay, they have changed our vision of the future in many ways. The added value for CORESTA members is undeniable – they are safe, there is low carbon footprint, they give the opportunity for new participants from around the world to participate who would not have been able to do so otherwise. All this is true and positive. What is also true is the sensation of void and the strange feeling of being disconnected with reality after you close your laptop and go for a coffee-break in the kitchen.

The Secretariat has established long lasting connections with many members of the association and it is doing its best, even in the virtual world, to continue to foster a sense of community and welcome to newcomers.

The CORESTA Secretariat's focus has always been to offer opportunities to its members to cooperate and share science against all odds. When members cannot participate in physical conferences or congresses, we do our best to provide virtual ones, whatever the situation.

No-one knows when life as we knew it will be "normal" again, but perhaps we need to get used to a new normality and in practice it may sadly mean that there is no longer any need to go back to the way things used to be? Let us however hope for a better and brighter future and try to stay positive ...



UPCOMING CORESTA MEETINGS (2021 / 2022)

With in-person meetings remaining a challenge, the CORESTA Sub-Group and Task Force meetings continue to be held virtually, often with short prior notice. The CORESTA website lists the latest schedule in the "Meetings/Upcoming" section at www.coresta.org/meetings/upcoming.

The second Virtual Symposium organised by the Consumer Reported Outcome Measures Task Force has been scheduled for 9 December 2021. This year's event will focus on Survey Methodology and features a number of high-profile presenters. More information is available on the CORESTA website.





The Board and host of the 2022 Congress planned in Washington D.C. have evaluated the situation and, in view of the uncertainties surrounding Covid19 and related travel issues, they have decided that the event will once again be a virtual one. Further details in the next Newsletter ...

CORESTA Scientific Commission and Board Meetings

The CORESTA Board and Scientific Commission continued to meet virtually over the last months to administrate the association and to manage scientific activities, respectively.

The **BOARD** has met three times since last July with the participation of the President and Vice-President of the Scientific Commission.

On <u>27 September 2021</u>, the Board members reviewed the progress made on current actions and the Secretary General reported on the preparation of the AP and SSPT Conferences to be held in October. Discussions took place on the concept of a CORESTA Science Academy with the objective to enhance knowledge sharing via in-person or virtual training sessions covering science of tobacco and related products from seed to population studies. It was agreed to investigate further if and how such a concept should be implemented in the future.

The Board met again on 29 September 2021, which gave the four Committees (Administration/Finance IT, Strategy, Events, Science Communication) the opportunity to report.

Johan Lindholm (Chair of the Strategy Committee) reported on a virtual meeting held on 9 September 2021 and organised by Rob Stevens (President of the Scientific Commission) with his support and that of Stéphane Colard (Secretary General). **SGTF** coordinators and secretaries were invited to participate in this meeting in order to receive background information on the origin of the CORESTA Strategy House and related strategic subjects, and to explain the roles and responsibilities for creating and maintaining All SGTFs were represented. its content. objective was to fully align Board, Scientific Commission and SGTF activities via a virtuous circular process of cooperation. The participants were invited

to cascade the information to their SGTF members and to initiate discussions to answer the following questions from their groups' perspective: i) What are the workstreams in your group for each strategic subject?, ii) What are the plans for each workstream?, iii) What projects exist for each workstream?, and iv) What deliverables are expected over the next two and five years. Answers to these four questions will help to consolidate global 2-year and 5-year plans.

Steven Coburn (Chair of the Science Communication Committee) reported on the Topline Newsletter circulated recently, and on the options for post-Conference promotion considering the great quality of the scientific programmes.

On his side, Mauri Winegardner (Chair of the Events Committee) reported that his committee was working on a guideline for organising virtual events taking into account the key learnings from the 2020 and 2021 virtual events.

The Board also met on 30 September 2021 to discuss specifically the potential risks of duplicated collaborative studies with ISO to assess method performance. The consensus was that CORESTA should continue to conduct method developments and collaborative studies, and should invite ISO members to participate in CORESTA collaborative studies as Guests if they wish to do so.

The **SCIENTIFIC COMMISSION** held one virtual meeting on 21 September 2021 to monitor ongoing actions and to make sure that everything was in place to ensure that the online 2021 Conferences were successful. And they were a great success indeed (see statistics on page 5). Next meetings are planned in January 2022 to review on-going projects and to prepare the Congress.

CORESTA IN THE PRESS

Tobacco Reporter

The August 2021 issue featured an article by Stéphane Colard, the CORESTA Secretary General, entitled "Scientific Partnerships for Sustainable Change" in which he "offers suggestions for how the tobacco industry can demonstrate its responsible approach to a skeptical audience".

Although a world without tobacco does not seem to be realistically achievable in the near future, efforts continue under the auspices of the World Health Organisation Framework Convention on Tobacco Control (WHO FCTC), to reduce tobacco demand and supply. This inevitably affects the way tobacco companies envisage the future of their business. Sustainable development encompasses the corporate and social responsibility of organisations in partnership with governments and civil society and genuine transformation initiatives can only be achieved if the impacts are assessed with internationally acknowledged methods. The article argues for the need for science based assessment methods that reflect the universal principles and values of science such as "transparency on assumptions and results, honesty and clarity in interpretations, or capacity to replicate experiments". The article concludes that the CORESTA platform's neutrality puts it in a "privileged position to initiate new scientific and transparent partnerships and forge a consensus on methodologies for measuring the transformation of tobacco companies".



CORESTA PROJECTS

The following projects were approved by the Scientific Commission and launched:

- Project 310: Amendment of CRM 84 and Technical Report 2015 Collaborative Study for Determination of Glycerin, Propylene Glycol, Water and Nicotine in Collected Aerosol of E-Cigarettes SG EVAP - E-Vapour - Approved August 2021
- Project 311: In Vitro Micronucleus Assay Inter-Laboratory Proficiency Study SG IVT - In Vitro Toxicity Testing - Approved August 2021
- Project 312: Determination of Select Metals in E-Liquids by ICP-MS SG EVAP E-Vapour Approved August 2021
- Project 313: Survey on Cigarette Ignition Propensity Testing Protocol SG SA Smoke Analysis Approved September 2021
- Project 314: Update CORESTA Guide No. 1 (GRLs)
 ACAC Agrochemical Advisory Committee Approved September 2021
- Project 315: Update CORESTA Guide No. 27 (HHPs)
 ACAC Agrochemical Advisory Committee Approved September 2021
- Project 316: CRM93 Determination of Selected Metals in Tobacco Products by ICP-MS (Update) SG TTPA Tobacco and Tobacco Products Analytes Approved September 2021
- Project 317: Round Robin Test on Low Pressure Drop Calibration Standards SG PTM Physical Test Methods Approved October 2021
- Project 318: Report to CEN/TC 437 on CORESTA Activities Related to the EVAP Sub-Group CORESTA Approved October 2021
- Project 319: 2022 Collaborative Study for Nitrate and Nitrite in Tobacco and Tobacco Products SG TTPA Tobacco and Tobacco Products Analytes Approved September 2021
- Project 320: CROM Virtual 2021 Symposium on Survey Methodology December 2021
 TF CROM Consumer Reported Outcome Measures Consortium Approved November 2021

CORESTA GUIDES

All CORESTA Guides may be downloaded in PDF format at

www.coresta.org

Updates

CORESTA Guide No. 1

The Concept and Implementation of CPA Guidance Residue Levels (Seventh edition – October 2021) [ACAC-314-CTG-01]

Guide No. 1 focuses on guidance on the interpretation of CPA residue testing results to ensure good agricultural practices are being implemented. However, there is a need to more comprehensively link this document to Guide No. 27 that focuses on providing key basic information on highly hazardous pesticides with a view to mitigating risk/exposure and working towards eliminating their use. The Agrochemical Advisory Committee (ACAC) updated Guide No. 1 with the insertion of a dedicated explanatory paragraph on HHPs in order to bring clarity and avoid misinterpretations.

CORESTA Guide No. 3

Good Agricultural Practices (GAP) Guidelines (Second edition – October 2021) [ACAC-300-CTG-03]

The CORESTA Guide No. 3 on GAP was first published in 2005. Over the last 16 years, there have been many changes and new challenges to take into consideration. With an increased focus on the impact of farming practices on the environment and more emphasis on sustainable methods of crop production, this Guide has been updated to cover additional topics such as minimal tillage, personal protection equipment, social issues, carbon footprint, etc.

• CORESTA Guide No. 27

Identification and Elimination of Highly Hazardous Pesticides (HHPs) in Leaf Tobacco Production (*Third edition – October 2021*) [ACAC-315-CTG-27]

The Agrochemical Advisory Committee (ACAC) also updated the Guide No. 27 with the insertion of an "HHP Indicative Reference List" showing HHPs with GRLs and most detected HHPs without GRLs. This update more comprehensively links Guide No. 27 with Guide No. 1 (above) and provides additional clarification.

CORESTA REPORTS

The following reports have been published on the CORESTA website at www.coresta.org:

• A Review of Aerosol Exposure Systems Relative to the Analysis of Cytotoxicity

Technical Report [IVT-286-2-CTR] – July 2021 (Sub-Group In Vitro Toxicity Testing)

Given the combination of exposure parameters and biological endpoints being deployed, it was considered a high priority to assess these systems and contextualize the responses obtained. A detailed and comprehensive survey was conducted on over 40 parameters across eight geographically independent laboratories. The results from the survey provided awareness of the exposure systems, parameters and nuances, that may be of substantial benefit to scientists in intersecting fields and in the development of harmonized approaches. This Technical Report is based on the external publication *A survey of aerosol exposure systems relative to the analysis of cytotoxicity: A Cooperation Centre for Scientific Research Relative to Tobacco (CORESTA) perspective published by the same authors in the Journal Toxicology Research and Application.*

• CORESTA Reference Products - 2021 Analysis

Technical Report [TTPA-281-CTR] – September 2021 (Sub-Group Tobacco and Tobacco Products Analytes)

In October 2020, a third stability study was initiated to assess the stability of the four CORESTA Reference Products (CRPs) manufactured in 2016, and to provide repeatability (r) and reproducibility (R) results and z-scores to support laboratory accreditation. The participating laboratories reported the levels of nicotine, pH, moisture (oven volatiles), and tobacco specific nitrosamines (TSNAs) in the CRPs using CORESTA Recommended Methods (CRMs). The results from this 2021 stability analysis generally compared well to the 2016 and 2019 analyses. The only statistically significant differences from the 2016 and 2019 results were slight changes in moisture for CRP3.1 and CRP2.1. The TTPA recommends that the stability of the 2016 CRPs continues to be monitored on a biennial basis.

• University of Kentucky Cigar Reference Products - 2021 Analysis

Technical Report [TTPA-282-CTR] – September 2021 (Sub-Group Tobacco and Tobacco Products Analytes)

In October 2020, an interlaboratory study was initiated to characterize four reference cigars manufactured by the University of Kentucky Center for Tobacco Reference Products (CTRP) for unburned analytes and measures. The participating laboratories reported nicotine, tobacco-specific nitrosamines (TSNAs), moisture (oven volatiles), pH, ammonia, water activity, arsenic, and cadmium in the unburned cigars primarily using CORESTA Recommended Methods (CRMs). All analyses included the wrapper/binder and filler from the cigars. Data were statistically evaluated in basic conformance with the recommendations of ISO 13528:2015. Additionally, z-scores were calculated. The results of this study suggest that the cigar reference products tested are suitable for use in collaborative studies, except one product, which is currently not suitable for filler ammonia, pH, and TSNA.

• 2021 Nicotine Pouches Collaborative Study

Technical Report [TTPA-284-1-CTR] - October 2021 (Sub-Group Tobacco and Tobacco Products Analytes)

Nicotine pouches, or white pouches, are oral tobacco products that contain tobacco derived nicotine, but not tobacco leaf. As at October 2020, there were no standardized methods available for the analysis of nicotine pouches even though there were regulatory reporting requirements. A collaborative study was therefore carried out with the intent to update the scopes of the applicable CORESTA Recommended Methods (CRMs) to also include nicotine pouches and to provide repeatability (r) and reproducibility (R) results and z-scores to support laboratory accreditation. The results of the study demonstrated that the CRMs for the determination of nicotine, pH, moisture (oven volatiles), tobacco-specific nitrosamines (TSNAs), water activity, metals, carbonyls, and benzo[a]pyrene (B[a]P) were suitable for the analysis of nicotine pouches and it was recommended that the eight CRMs be updated to include nicotine pouches.

• 2015 Collaborative Study for Determination of Glycerin, Propylene Glycol, Water and Nicotine in Collected Aerosol of E-Cigarettes

Technical Report [EVAP-310-1-CTR] - October 2021 (Sub-Group E-Vapour)

This technical report was published in March 2017 and revised in 2021 to include r&R values for device mass loss (DML). The study compared results from multiple laboratories applying CRM81 for aerosol collection from commercial electronic cigarette products. This report supports CRM84, that was also published in March 2017 and updated in 2021.

• Long-Term Public Maintenance of Nicotiana Germplasm

Final Task Force Report [NGPC-297] – November 2021 (Task Force Nicotiana Germplasm Collection)

Genetic diversity within *Nicotiana tabacum* and related species has been essential for historical improvements in tobacco cultivars during the last 100 years. This report covers the findings and recommendations of the Nicotiana Germplasm Collection (NGPC) Task Force for the long-term public maintenance of *Nicotiana germplasm*.

CORESTA REPORTS (continued)

• 2019 Initial Collaborative Study for the Determination of Very Low Nicotine in Total Particulate Matter from the Mainstream Smoke

Technical Report [RAC-SA-244-CTR] – November 2021 (Sub-Groups Routine Analytical Chemistry / Smoke Analysis)

A collaborative study was initiated by the CORESTA Routine Analytical Chemistry (RAC) Sub-Group in October 2019 to verify the feasibility of expanding the calibration range of ISO 10315:2021 Cigarettes – Determination of nicotine in total particulate matter from the mainstream smoke – Gas-chromatographic method. The intent of the study was to provide an assessment of laboratory capability to determine very low nicotine (VLN) in total particulate matter from mainstream smoke generated under ISO 3308 smoking conditions. The results of the study demonstrate that, with modification to the calibration range, ISO 10315 is suitable for this purpose and is relevant for emerging regulations to reduce nicotine for combusted tobacco products.

 Characterization of University of Kentucky Reference Smokeless Tobacco Products - 2021 Analysis

Technical Report [TTPA-283-CTR] – November 2021 (Sub-Group Tobacco and Tobacco Products Analytes)

In October 2020, the CORESTA Tobacco and Tobacco Analytes (TTPA) Sub-Group initiated a large inter-laboratory collaborative study designed to characterize the four certified smokeless tobacco products offered by the University of Kentucky Center for Tobacco Reference Products (CTRP). The results of this study suggest that the certificates of analysis for the University of Kentucky reference products are in good agreement with the certified values.

CORESTA RECOMMENDED METHODS

Update

• **CRM No. 84** – Determination of Glycerin, Propylene Glycol, Water, and Nicotine in the Aerosol of E-Cigarettes by Gas Chromatographic Analysis

(Fourth edition - October 2021) [EVAP-310-2-CRM-84]

This CRM was updated to include repeatability (r) and reproducibility (R) for device mass loss following there vision of the document's supporting Technical Report 2015 *Collaborative Study for Determination of Glycerin, Propylene Glycol, Water and Nicotine in Collected Aerosol of E-Cigarettes* [EVAP-310-1-CTR].

- CRM No. 62 Determination of Nicotine in Tobacco and Tobacco Products by Gas Chromatographic Analysis
 - (Third edition December 2021) [TTPA-284-2-CRM-62]
- **CRM No. 69** Determination of pH in Tobacco and Tobacco Products (*Third edition December 2021*) [TTPA-284-2-CRM-69]
- **CRM No. 76** Determination of Moisture Content (Oven Volatiles) of Tobacco and Tobacco Products (*Third edition December 2021*) [TTPA-284-2-CRM-76]
- **CRM No. 82** Determination of Benzo[a]pyrene in Tobacco Products by GC-MS (Fifth edition December 2021) [TTPA-284-2-CRM-82]
- **CRM No. 86** Determination of Select Carbonyls in Tobacco and Tobacco Products by UHPLC-MS/MS (Second edition December 2021) [TTPA-284-2-CRM-86]
- **CRM No. 88** Determination of Water Activity of Tobacco and Tobacco Products (Second edition December 2021) [TTPA-284-2-CRM-88]
- **CRM No. 93** Determination of Selected Metals in Tobacco Products by ICP-MS (Second edition December 2021) [TTPA-284-2-CRM-93]

The above eight CRMs were updated to include nicotine pouches in their scope. The modifications are based on the Technical Report 2021 Nicotine Pouches Collaborative Study also published in October 2021 [TTPA-284-1-CTR].

All CORESTA Recommended Methods can be downloaded in PDF format at www.coresta.org

JOURNAL PUBLICATIONS

In conjunction with the Technical Report *A Review of Aerosol Exposure Systems Relative to the Analysis of Cytotoxicity*, the *In Vitro* Toxicity Testing (IVT) Sub-Group had a report [IVT-286-1-CXP] published as an external publication as follows:

A survey of aerosol exposure systems relative to the analysis of cytotoxicity: A Cooperation Centre for Scientific Research Relative to Tobacco (CORESTA) perspective

David Thorne⁽¹⁾, Roman Wieczorek⁽²⁾, Toshiro Fukushima⁽³⁾, Han-Jae Shin⁽⁴⁾, Robert Leverette⁽⁵⁾, Mark Ballantyne⁽⁶⁾, Xiang Li⁽⁷⁾, Betsy Bombick⁽⁵⁾, Kei Yoshino⁽³⁾

(1) British American Tobacco, Group R&D, Southampton, Hampshire, UK; (2) Reemtsma Cigarettenfabriken GmbH, Hamburg, Germany; (3) Scientific Product Assessment Center, R&D Group, Japan Tobacco Inc., Yokohama, Kanagawa, Japan; (4) Korean Tobacco & Ginseng Corporation, Yuseong-gu, Daejeon, Republic of Korea; (5) RAI Services Company, Winston-Salem, NC, USA; (6) Covance Laboratories Ltd, Harrogate, UK; (7) Zhengzhou Tobacco Research Institute of China National Tobacco Corporation, Zhengzhou, PR China

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https://journals.sagepub.com/doi/10.1177/23978473211022267

DOI: 10.1177/23978473211022267

The E-Vapour (EVAP) Sub-Group also published an external publication [EVAP-088-CXP] as follows:

Machine Vaping of Electronic Cigarettes - A Comparison of Puffing Regimes

Amit Gupta⁽¹⁾, Rana Tayyarah⁽²⁾, Gene Gillman⁽³⁾, Charles Garner⁽⁴⁾, and Rob Stevens⁽⁴⁾

(1) Battelle Memorial Institute, 505 King Avenue, Columbus OH, USA; (2) ITG Brands, LLC, PO Box 21688, Greensboro NC, USA; (3) Enthalpy Analytical LLC., 800 Capitola Dr., Durham NC, USA; (4) RAI Services Company, 401 North Main Street, Winston Salem NC, USA

Contributions to Tobacco & Nicotine Research, Volume 30 • No. 3 • July 2021

https://sciendo.com/article/10.2478/cttr-2021-0009

DOI: 10.2478/cttr-2021-0009

Biomarkers (BMK) Sub-Group

The Biomarker Sub-Group (BMK SG) held a virtual meeting on October 11th, 2021, with 35 delegates in attendance. On behalf of all members of the BMK SG, we bid farewell to Dr G.L. Prasad and thanked for his contributions towards the SG. Under his leadership for the past several years the Sub-Group has made tremendous progress. We hope to continue the tradition as we align new projects to the overall CORESTA strategy.

As the SG embarks in this new phase, the group is aligning its Vision and Objective with CORESTA Strategy to make them more relevant to the evolving marketplace of tobacco products and current regulatory environment not only in the US but for the rest of the world. The revised vision and objective that will serve as the foundation for the SG will be presented for approval at the next Scientific Commission meeting early next year.

The members of the SG have been very prolific and active, with significant progress made against current projects. Specifically, a manuscript for external publication "Meta-analysis of Biomarkers of Exposure – Urinary Total NNAL" has been finalized and will be submitted for review by the Scientific Commission (BMK-249). This manuscript combines results from the BMK-186 (carbon monoxide and nicotine equivalents) and BMK-249 projects. Additionally, the BMK-161 project on "Biomarkers of Harm/Effect for Tobacco Regulatory Research: Opportunities and Challenges - A Literature Review" has been completed and BMK-273 on "Definition of Use Behavior and Exposure Terminology Across Product Categories", a collaborative project between the Product Use Behavior and BMK Sub-Groups has been completed and is undergoing final review among the Sub-Group members.

Two important workstreams have been advancing at a good pace. The first relates to collaborations between the Biomarker/Next Gen Tox and *In Vitro* Tox Sub-Groups. The focus of this workstream would be to identify clinically relevant biomarkers for smoking-related diseases informed by basic science knowledge and insights. The second project relates to Tobacco Data Standards. The objective of this workstream is to harmonize and standardize data reporting methods to regulatory agencies. The Clinical Data Interchange Standards Consortium (CDISC) has applied for funding in response to a request for proposal from FDA. The next steps for this workstream will be developed once CDISC hears back from FDA.

Finally, the BMK SG will be meeting to discuss potential projects to undertake that align with the 2-year and 5-year CORESTA strategy.



Mohamadi SARKAR BMK SG Coordinator



Kirk NEWLAND BMK SG Secretary



G.L. PRASAD Former BMK SG Coordinator

In Vitro Toxicity Testing (IVT) Sub-Group

This year Kei Yoshino (Coordinator) and David Thorne (Secretary), stepped down after several years of leading the Sub-Group (SG) and were replaced by Damian McHugh (Coordinator) and Liam Simms (Secretary). Damian has led the preclinical regulatory toxicology laboratory at PMI for the past decade and joined PMI from the pharmaceutical industry. Liam joined Imperial 20 years ago and has worked in both Product Stewardship and Preclinical Toxicology functions in his current role as Principal Toxicologist.

There have been no face-to-face meetings due to the pandemic, however the group has succeeded in holding several dynamic on-line meetings that were well attended by members, despite the horrors of the time differences between us all. Given the change of leadership, one of the initial tasks of the group was to undertake a review of the current activities and ways of working. As a result of this exercise, at the February 2021 meeting, the priorities for the group were redefined and organised into workstreams and are:

- To support the assessment of novel tobacco products with robust data and studies on trapping methodologies designed to support regulatory toxicity testing.
- To support the assessment of novel tobacco products with regulatory submission quality *in vitro* testing methodologies (e.g. 3D genetox, Toxtracker) in collaboration with NGTX.
- To continue to perform *in vitro* proficiency studies to support CORESTA member accredited laboratories. Current proficiency studies include an *in vitro* micronucleus and NRU cytotoxicity trials.
- To maintain a strong working relationship with the IIVS (Institute for In Vitro Sciences) and other participants from industry, academia and regulatory agencies in a series of workshops addressing *in vitro* testing of tobacco products.

One of our SG members, K. Monica Lee from ALCS, organised an excellent symposium at this year's CORESTA Smoke Science and Technology (SSPT) Conference entitled "AdvancingNew Alternative Methods (NAMs) for Tobacco Harm Reduction". The range of topics and the quality of speakers was truly excellent and was very well received by the attendees. Plans are afoot to repeat and extend the exercise in 2022. Reflecting this evolution of biology and toxicology within our industry, closer collaboration between the IVT SG and both the Next Generation (NGTX) Task Force and Biomarkers (BMK) SG were discussed and will be further reinforced in the new year since there is much cross over and mutual interest between the groups.

The SG reports completed this past year include Project 245 CTR Ames led by Roman Wieczorek and Project 286-CXP Whole Smoke Testing report led by David Thorne.

Finally, if you wish to get involved in the activities of this Sub-Group please forward your details to Damian (damian.mchugh@pmi.com). Notes from previous meetings will be added to the CORESTA website.



Damian McHUGH IVT SG Coordinator



Liam SIMMS IVT SG Secretary



Kei YOSHINO Former IVT SG Coordinator



David THORNE Former IVT SG Secretary

All TSRC abstracts and presentations are also accessible

via the Abstracts section of the

CORESTA website

CORESTA COMMUNICATION AT EXTERNAL EVENTS

Tobacco Science and Research Conference (TSRC 2021)

Two CORESTA working groups made presentations at the Tobacco Science Research Conference (TSRC) held in Boston, MA, USA, from 30 August to 1 September 2021.

- Presentation "Development of Recommendations of Descriptive Consumer-Reported Outcome Measures (Descriptive-CROM) and Related Definitions in Tobacco and Nicotine Research" by Lai Wei (Altria Client Services, USA) on behalf of the CORESTA CROM Task Force.
- Presentation "Human abuse liability assessment of tobacco and nicotine products: considerations to meet current regulatory recommendations" by Andrea Vansickel (Altria Client Services, USA) on behalf of the CORESTA Product Use Behaviour (PUB) Sub-Group.



European Committee for Standardization (Comité Européen de Normalisation - CEN)

CEN/TC 437 Web Meeting - 25 November 2021

Presentation "CORESTA Report to CEN/TC437" by Stéphane Colard (CORESTA Secretary General).

The above presentations can be viewed in the Information/CORESTA Communication section of the CORESTA website

Acronyms / Abbreviations used in the Newsletter		
ACAC CORESTA Agrochemical Advisory Committee AI Artificial Intelligence ALI Air Liquid Interface AP Agronomy & Leaf Integrity and Phytopathology & Genetics ASE Accelerated Solvent Extraction B[a]P Benzo[a]pyrene BMK Biomarkers CEN Comité Européen de Normalisation CET Central Eastern Time CORESTA Cooperation Centre for Scientific Research Relative to Tobacco CPA Crop Protection Agent CRM CORESTA Recommended Method CROM Consumer Reported Outcome Measures (CORESTA) CRP CORESTA Technical Guide CTG CORESTA Technical Guide CTR CORESTA Technical Report CTRP CORESTA Technical Report CTRP CORESTA External Presentation DML Device Mass Loss DOI Digital Object Identifier ENDS Electronic Nicotine Delivery System EPA Environmental Protection Agency (USA) EVAP E-Vapour (CORESTA) FCTC Framework Convention on Tobacco Control FDA Food and Drug Administration (USA) GAP Good Agricultural Practices GC-FID Gas Chromatography-Flame Ionization Detection	GC-MS Gas Chromatography–Mass Spectrometry GmbH Gesellschaft mit beschränkter Haftung (Germany) GRLs Guidance Residue Levels HHPS Highly Hazardous Pesticides HPHC Harmful and Potentially Harmful Constituents HTPS Heated Tobacco Products ICP-MS Inductively Coupled Plasma Mass Spectrometry IIVS Institute for In Vitro Sciences ISO International Organization for Standardization IT Information Technology IVIVE In Vitro to In Vivo Extrapolation IVT In Vitro Toxicity Testing (CORESTA) LC-MS/MS . Liquid Chromatography–Tandem Mass Spectrometry LLC Limited Liability Company MA Massachusetts (USA) MS Microsoft NAM New Alternative (or Approach) Methods NC North Carolina (USA) NGPC Nicotiana Germplasm Collection (CORESTA) NGTX	NRU Neutral Red Uptake OH Ohio (USA) pH percentage Hydrogen PR People's Republic PUB Product Use Behaviour (CORESTA) Q&A Question and Answer R&D Research & Development r&R repeatability & Reproducibility RAC Routine Analytical Chemistry (CORESTA) RAI Reynolds American International RR Reduced Risk RRPs Reduced Risk Products SG Sub-Group SGTF Sub-Group and Task Force SIFT-MS Selected ion Flow Tube Mass Spectrometry SME Subject Matter Expert SSPT Smoke Science and Product Technology TC Technical Committee TF Task Force THR Tobacco Harm Reduction TSNA Tobacco Specific Nitrosoamines TTPA Tobacco and Tobacco Products Analytes (CORESTA) UHPLC-MS/MS Ultra-High Performance Liquid Chromatography Tandem Mass Spectrometry UK United Kingdom US United Kingdom

