



# **Biomarker (BMK) Sub-Group 2020 Report**

**Virtual Congress**

**October 2020**

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Secretary: Kirk Newland  
Scientific Liaison: Paul Harp**

## ❖ Biomarkers

- Generally refer to measurable indicators of some biological state or a condition (Wikipedia)
- Examples of biomarkers
  - Blood pressure
  - Hemoglobin A1C
  - Prostate Specific Antigen (PSA)
- Important decision-making tools
- Several different types of biomarkers exist
- Context of use and the purpose are highly relevant



**“Identify and evaluate biomarkers of exposure and potential harm that are fit-for-purpose for tobacco product research”**

- **Two types are currently in scope for the Biomarker Sub-Group (BMK SG)**
  - Biomarkers of exposure
    - Nicotine and other Harmful and Potentially Harmful Constituents
  - Biomarkers of effect / potential harm- inform of the effect of exposure
    - Markers of DNA damage, oxidative stress and inflammation
- **Biomarkers of Effect / Potential Harm can be measures of individual risk**
  - Biology - Effect of the product on the consumer and potential relevance to smoking-related disease(s).
  - Measurement – Bioanalyses
- **To align with the evolving science, the SG may consider other “types” of Biomarkers**



# Objectives of the BMK SG

- ❖ *To review new studies and analytical methods of tobacco and smoking-related biomarkers of exposure and effect*
- ❖ *To undertake ring trials / proficiency tests for selected biomarkers, as agreed by the Scientific Commission*
- ❖ *To source and develop reference materials to support biomarker analysis for those biomarkers selected for inter-laboratory comparisons.*



# Recent Meetings

## The Biomarker (BMK) SG has switched to virtual meetings for 2020

### ❖ 2020 Spring meeting - Virtual

- May 05 2020
- 43 delegates attended the meeting

### ❖ 2020 Fall meeting - Virtual

- October 08, 2020
- 32 delegates attended the meeting



# Biomarkers of Effect Review

## ❖ Sub-Group Objective 1

### ➤ BMK Project #161 Biomarkers of Effect review (Lead, Jeff Edmiston).

Project No.	Activity	Status	Projected Timeline
BMK 161	<p>Biomarkers of Harm/Effect for Tobacco Regulatory Research: Opportunities and Challenges - A Literature Review</p> <ul style="list-style-type: none"><li>• Goal: Critically assess the available biomarkers of harm/effect for potential use in evaluation of the effects of tobacco use</li><li>• Develop a position paper on lung biomarkers of effect/Potential Harm</li><li>• Jeff Edmiston, on behalf of the writing committee, submitted the draft manuscript to the SC</li></ul>	<p>Project work and draft manuscript completed</p> <ul style="list-style-type: none"><li>• Initial search yielded 1171 papers</li><li>• A presentation was given at the 2019 SSPT meeting</li><li>• Technical report were reviewed by SC. <u>The Technical Report</u> is now published on CORESTA BMK SG website (Sept 2020)</li></ul>	<ul style="list-style-type: none"><li>• Manuscript submission to follow - now 4Q 2020</li></ul>



# Meta-analysis Project

## ❖ Sub-Group Objective 1

### ➤ BMK Project #186 Meta-analysis of biomarker data (Lead, Felix Ayala-Fierro)

Project No.	Activity	Status	Projected Timeline
186	<p>Meta-analysis of published biomarker data</p> <ul style="list-style-type: none"><li>• Establish a population level for biomarkers of cigarette smoke exposure to serve as baseline for comparisons against changes in exposure for reduced-risk products</li><li>• Scope modified to include only urinary nicotine equivalents and blood carboxyhemoglobin</li><li>• Conduct a meta-analysis</li></ul>	<p>The <u>technical report</u> was reviewed by the SC and published in December 2019.</p> <ul style="list-style-type: none"><li>• The report covered two biomarkers- carboxyhemoglobin and nicotine equivalents levels</li></ul>	<p>Anticipated draft manuscript will include data from NWIP-249</p>





# Meta-analysis Project-2

## ❖ Sub-Group Objective 1

### ➤ BMK Project #249 Meta-analysis of cigarette smoke exposure biomarkers – Urinary Total NNAL (Lead, Felix Ayala-Fierro)

Project No.	Activity	Status	Projected Timeline
249	Establish a population level estimate for the biomarker of exposure, urinary total NNAL, which can be used for comparisons against changes in exposure when switching to candidate modified risk products or evaluation of new products	<ul style="list-style-type: none"><li>• Literature review completed</li><li>• Data elements captured</li><li>• Anticipated manuscript will combine data from NWIP-186 to include data on carboxy hemoglobin, nicotine equivalents and NNAL</li></ul>	Anticipated report and draft manuscript 2Q2021



# Biomarker Terms Project

## ❖ Sub-Group Objective 1

- **BMK Project #273 Definition of use behaviour and exposure terminology across product categories (Co-lead, Dai Yuki)**

Project No.	Activity	Status	Projected Timeline
273	<ul style="list-style-type: none"><li>• Joint Project with PUB SG (Leads: Lesley Giles and Dai Yuki)</li><li>• To recommend definitions that are consistent with diverse tobacco products currently exist (including products such as e-cigarettes, HTP and oral nicotine products)</li><li>• Update terms from <a href="#">Gregg et al. 2013</a></li></ul>	<ul style="list-style-type: none"><li>• Initial discussions on project scope were held in September 2020</li><li>• A team of contributors from BMK SG will jointly work with PUB SG delegates</li><li>• This project scope definition in progress (whether to expand beyond biomarkers of exposure)</li></ul>	To be established



# Biomarker Reference Standards

## ❖ Sub-Group Objective 3

➤ Lead, Frank Deschamps

Project No.	Activity	Status	Projected Timeline
Not assigned	Tobacco Biomarker Reference Standards Frank revised the previously developed guidance (CORESTA Guide N° 20 Biomarker studies - Requirements for the certification of analytical reference standards)	Addendum will be circulated within the SG for comments	Expect to finalize the revised guide by 4Q2020



# Review of the Vision and Objectives

- **To align the BMK SG workstreams with the evolving marketplace and regulatory environment, a review of the Vision and Objectives of the SG was initiated**
  - **Sub Team: Jeff Edmiston and Michael McEwan, Kirk Newland**
- **A simplified Vision statement and revised Objectives for consideration. The delegates will review the updated Vision and Objectives.**
- **Once approved by the SG, these materials will be sent to the Scientific Commission for approval**

## ❖ Data standards, a potential new project

Lead	Topic/Title	Status/ next steps
TBD	<p>Development of common industry data standards for tobacco biomarkers</p> <ul style="list-style-type: none"> <li>• The BMK SG continued deliberations into the scope and logistics of this effort</li> <li>• Generally the FDA/CTP have shown interest in biomarker data standards</li> <li>• A formal presentation on electronic submission standards was given by an external vendor, WiseDesign</li> </ul>	<p>Renew discussions with CTP, and Standards Development Organizations (CDISC and HL7) to build a consortium</p>



# Leveraging Strengths

## ❖ Potential Collaborations with other SGs and TFs within CORESTA

Lead	Purpose/topic	Action Planned
GL Prasad, Kei Yoshino, Monica Lee and Marianna Gaca	<ul style="list-style-type: none"><li>To develop collaborative joint project(s) that leverage the strengths of the BMK, IVT SG and NGTX on the principles of <u>Toxicology Testing in 21<sup>st</sup> Century</u> for better toxicity assessments</li></ul>	Will revisit after the anticipated leadership changes in IVT SG and NGTX TF.
GL Prasad / M. Sarkar	<p>Follow up from Biomarker Workshop – Kunming Fall 2018. Several thoughts</p> <ul style="list-style-type: none"><li>Tease out link to and path for a BoPH to be accepted as “clinical risk marker”</li><li>Co-develop an Adverse Outcome Pathway</li></ul>	

## ❖ Potential new projects (Sub-Group Objective 2)

Lead	Topic/Title	Status/ next steps
Max Scherer and Kirk Newland	Potential interlab comparison study of a new biomarker • Biomarkers of exposure or Biomarker of Potential Harm?	On Hold (due to limited CRO participants)

## ❖ Scientific presentations and discussion (Objective 1)

Presenter	Topic	Potential benefit
Mohamadi Sarkar	Review of Benowitz 2019: <u>Biochemical Verification of Tobacco Use and Abstinence</u> (Nicotine Tob Res. 2019 Oct 1) <ul style="list-style-type: none"> <li>• Importance of biochemical verification of tobacco biomarkers in smoking cessation and in use of ENDS discussed</li> <li>• Several potential compliance biomarkers were proposed</li> <li>• CEMA as a compliance marker appears to be a useful biomarker of compliance</li> </ul>	Dissemination of knowledge. Delegates can leverage this information for their own purposes.





## ❖ Scientific presentations and discussion (Objective 1)

Presenter	Topic	Potential benefit
Kirk Newland	<p>2,3-dinor Thromboxane B<sub>2</sub> in Human Urine</p> <ul style="list-style-type: none"><li>• New biomarker of potential harm</li><li>• Presented analytical method development and clinical samples</li><li>• The biomarker 2,3-dinor Thromboxane B<sub>2</sub> has been shown in clinical testing to successfully differentiate conventional cigarette user, heat-not-burn user, and non-smoker samples</li></ul>	<p>Exploring a NWIP for interlaboratory comparison study.</p> <p>Identification of testing labs is initiated.</p>



# Looking Forward

## ❖ Next BMK SG meeting

- **Celerion has expressed interest in hosting the Spring 2021 meeting(s), if the travel situation improves**
  - If in-person meetings are envisioned, Celerion would need confirmation
  - Based on the current travel restrictions, it is likely that the Spring 2021 will be held virtually

**Thank you**

**Contact [prasadg@rjrt.com](mailto:prasadg@rjrt.com) for any clarifications**