



Biomarker Sub-Group 2019 Report

Hamburg, Germany

October 09, 2019

**Coordinator: G. L. Prasad
Secretary: Kirk Newland
Scientific Liaison: Paul Harp**



Approved by the Biomarker Sub-Group delegates at the Geneva meeting in April 2018

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

❖ 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
- Context and the purpose are highly relevant

- **Two types are in scope for the Biomarker Sub-Group (BMK SG)**
 - Biomarkers of exposure
 - Nicotine, HPHCs
 - 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**
- **For Biomarkers of Effect/ Potential Harm:**
 - Biology - Effect of the product on the consumer and potential relevance to smoking-related disease(s).
 - Measurement – Bioanalyses



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.*



The Biomarker (BMK) and Product Use Behavior (PUB) Sub-Groups hold joint meetings.

❖ 2019 Spring meeting

- **May 23, 2019 Montreal, hosted by Altasciences**
- **30 delegates attended the meeting**

❖ 2018 Fall meeting

- **October 05, 2019 Hamburg, Germany**
- **31 delegates attended the meeting**



Biomarkers of Effect Review

❖ Sub-Group Objective 1

- **BMK Project # 161 Biomarkers of Effect review (Lead, Erin Beatte). ST 44, presentation by Patrudu Makena**

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">• Goal: Critically assess the available biomarkers of harm/effect for potential use in evaluation of the effects of tobacco use.• Develop a position paper on lung biomarkers of effect• Focus: lung-related biomarkers• Jeff Edmiston gave an update at the Hamburg meeting	<p>Project work completed.</p> <ul style="list-style-type: none">• Focus on recent 10-year literature• Smoking vs non-smoking• Preferably association of the biomarker with smoking cessation• Initial search yielded 1171 papers• A presentation at the 2019 SSPT will follow• Technical report and publication delayed	<ul style="list-style-type: none">• Draft report 2019. Manuscript submission- 2Q 2020



Meta-analysis Project

❖ Sub-Group Objective 1

➤ BMK Project #186 Meta-analysis of biomarker data (Lead, Felix Ayala-Fierro)- ST45, presentation by Thomas Verron

Project No.	Activity	Status	Projected Timeline
186	<p>Meta-analysis of published biomarker data</p> <ul style="list-style-type: none">• Establish a population level for biomarkers of cigarette smoke exposure to serve as baseline for comparisons against changes in exposure for reduced-risk products• Focus on urinary NNAL, urinary nicotine equivalents and blood carboxyhemoglobin• Conduct a meta-analysis• Mohamadi Sarkar reviewed the project and shared a vision for next steps	<p>NWIP approved May 2018</p> <ul style="list-style-type: none">• Focus on recent 10-year literature• Established criteria for assessment of literature	<ul style="list-style-type: none">• Finalized Report December 2019• Anticipated draft manuscript 3Q 2020



Review of the Vision and Objectives

- ❖ **A subteam was formed to review the Vision and Objectives of the BMK SG**
 - **Jeff Edmiston, Mike McEwan and Erika Pfaunmiller**
 - **Revised vision and objectives were provided (work in progress)**
Purpose was to align the BMK SG workstreams with the evolving marketplace and regulatory environment.
- ❖ **The BMK SG is expected to prioritize and work on projects that help advance quality tobacco science in an efficient manner**
 - **The subteam will also revise/update the CORESTA BMK SG webpages accordingly**



Leveraging Strengths

❖ Potential Collaborations with other SGs and TFs within CORESTA

Lead	Purpose/topic	Action Planned
GL Prasad, Kei Yoshino and Marianna Gaca	<ul style="list-style-type: none">• Increase awareness and collaboration between BMK, In Vitro Sub-Groups and NGTX Task Force.• Representative delegates attend each other's meetings to foster collaboration.<ul style="list-style-type: none">• Mike McEwan, Kei Yoshino, GLP and Leon Stankowski provided updates for the BMK and IVT SGs• Leverage knowledge from the SGs/TF and work on inter-disciplinary project(s).• Kei Yoshino and Marianna Gaca gave updates at the Hamburg meeting	<p>Explore opportunities to integrate biomarker knowledge with regulatory toxicology and 21st Century toxicology tools to inform potentially reduced health effects of NGPs</p> <p>Once a potential path is identified, create a subteam from the three groups to execute the project once NWIP is approved</p>

❖ 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"> • Previously considered as NWIP. However not pursued as CDISC-led consortium was chosen as a better platform • Renewed discussion within BMK SG at the Montreal meeting due to the disengagement by CDISC with tobacco industry • Followed up phone call with a subteam in September. Focus on clinical biomarkers • Informal dialog at TSRC indicates FDA/CTP appears to be interested in having common data standards 	<p>Renewed discussions within the SG on a path forward to develop a NWIP</p>

❖ Potential new projects

Lead	Topic/Title	Status/ next steps
Max Scherer and Kirk Newland	Potential interlab comparison study of a new biomarker <ul style="list-style-type: none"> • Biomarkers of exposure or Biomarker of Potential Harm? 	Planning
Frank Deschamps	Reference standards <ul style="list-style-type: none"> • Revise the previously developed guidance 	Initiated
TBD	Revisit NNAL biomarker population level estimates, a literature review and publication <ul style="list-style-type: none"> • Several scenarios exist 	Planning



❖ Potential new projects

Lead	Topic/Title	Status/ next steps
GL Prasad/ (M. Sarkar)	<p>Follow up from Biomarker Workshop –Kunming Fall 2018. Several thoughts</p> <ul style="list-style-type: none">• Tease out link to and path for a BoPH to be accepted as “clinical risk marker”• Co-develop an Adverse Outcome Pathway	Likely collaborations with NGTF



Montreal Meeting Spring 2019

❖ Scientific presentations and discussion

Presenter	Topic	Potential benefit
Mike McEwan	<p>An overview of a one year study on the effects of switching from cigarette smoking to using a Tobacco Heating Product on health effect indicators in healthy subjects</p> <ul style="list-style-type: none">• BAT clinical research project evaluates the effect of glo product on changes in Biomarkers of Exposure and Biomarkers of Potential Harm	Opportunity for delegates to incorporate learnings into their studies
Ashraf Elamin	<p>Intervals, a platform facilitating transparent data sharing. An update</p> <ul style="list-style-type: none">• Contained 22 studies published (from PMI, Altria, JTI) about aerosol chemistry, pre-clinical, and clinical assessment of heat-not-burn and e-cigarette platforms• The Intervals contained 75 protocols and 162 datasets• The Intervals included some published CORESTA protocols (methods 35, 36, 38, 72)	Opportunity to collaborate



Hamburg Meeting Fall 2019

❖ Scientific Présentations**

Lead	Topic	Potential Benefit
Patrudu Makena	<p>Urinary Leukotriene E4 And 2,3-dinor Thromboxane B2: Potential Biomarkers of Effect for Tobacco Product Evaluations</p> <ul style="list-style-type: none">• Development two BoPH that are useful for tobacco products• The two arachidonic acid metabolites change rapidly in response to smoking cessation and switching to non-combustible tobacco products	Dissemination of knowledge



For consideration

- ❖ **Valuable non-competitive science that is beneficial to the CORESTA community is possible**
 - **Cross collaboration between SGs/TFs is important**
 - **Prioritization necessary to show impact**

- ❖ **Scope for improvement**
 - **Limited active participation**
 - **Delegates encouraged to “honor commitments”**
 - **Limited number of laboratories exist to allow robust interlab comparison studies**



Looking forward

- ❖ **Next BMK SG meeting will be held in Belfast, Ireland, in May 2020**
 - **Host: Celerion**
 - **As customary, PUB and BMK hold joint meetings on May 5th, 2020**
 - **CROM and NGTX Task Forces meet on May 6th, 2020.**

Thanks