



Biomarker Sub-Group 2018 Report

Kunming, China

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❖ 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



Tobacco Biomarkers

- **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
- **Biomarkers of Effect can be very complex, diverse and present unique challenges**



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”



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

❖ 2018 Spring meeting

- April 10, 2018 Geneva, hosted by JTI
- 36 delegates attended the meeting

❖ 2018 Fall meeting

- October 21, 2018 Kunming, China
- 31 delegates attended the meeting

❖ As always, the Biomarker (BMK) and Product Use Behavior (PUB) Sub-Groups hold joint meetings.



NNAL interlab comparison study

❖ Sub-Group Objective 2

➤ NNAL interlab comparison study, BMK Project 092

Project No.	Activity	Status	Projected Timeline
092	Inter-laboratory Comparison: Bioanalytical Assay to Measure Total NNAL in Human Urine	Draft submitted to the Scientific Commission, and now with the Board <ul style="list-style-type: none">• Study Summary will be presented as a platform presentation at the Kunming meeting	September 2018 (completed)



Biomarkers of Effect Review

❖ Sub-Group Objective 1

➤ BMK Project # 161 Biomarkers of Effect review (Lead, Erin Beatte)

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	<p>Project work in progress.</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	<ul style="list-style-type: none">• June 2019 to generate a final version



Meta-analysis Project

❖ Sub-Group Objective 2

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

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	<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 2018• Anticipated draft manuscript April 2010



New Opportunities

❖ Potential Collaborations with other Sub-Groups

Lead	Activity	Action
GL Prasad and Kei Yoshino	<ul style="list-style-type: none">• Increase awareness and collaboration between BMK and In Vitro Sub-Groups.• Representative delegates attend each other's meetings to foster collaboration.• Leverage knowledge from both SGs and develop multi-disciplinary project(s).	<p>Future joint meeting of BMK, PUB and In Vitro SGs.</p> <p>Mike McEwan, GL Prasad and G Wood attended IVT SG meetings and Kei Yoshino attended BMK SG meeting.</p>
GL Prasad and Kei Yoshino	Kei Yoshino proposed to incorporate the principles/concepts from Tox 21 initiatives into CORESTA work streams for risk assessment. Few examples of potential projects were put forth.	An organizing committee for planning next steps will be formed with a few delegates from BMK and IVT SGs.

❖ Scientific presentations and discussion

Lead	Topic	Potential action
Max Scherer	Analysis of urinary eicosanoids by LC-MS/MS revealed alterations in the metabolic profile after smoking cessation	Opportunity for delegates to incorporate into their studies
Liu Tong	Intraday fluctuation profile of salivary cotinine and exhaled carbon monoxide levels	None.
Stephanie Bouie	INTERVALS a platform facilitating transparent data sharing (a demonstration)	Opportunity to collaborate
Mike McEwan	Updates from the In vitro Toxicology Sub-Group meeting, Southampton, January 2018	Opportunity to learn and collaborate
Takuya Suzuki	A study to investigate the reduction in exposure to selected HPHCs in healthy smokers who switched to a novel tobacco vapor product.	None. Dissemination of knowledge
Nicola Plyum	Analysis of urinary eicosanoids by LC-MS/MS revealed alterations in the metabolic profile after smoking cessation	Opportunity for delegates to incorporate into their studies



Kunming meeting Fall 2018

❖ Scientific Presentations

Lead	Topic	Potential action
Chikako Sakaguchi	Changes in biomarkers of potential harm due to reduced exposure to cigarette smoke in adult smokers	None. Dissemination of knowledge. Opportunity for others to incorporate learnings
Gang Li	Analysis Cotinine and NNAL in Urine by Heart Cutting Two Dimensional Liquid Chromatography Tandem Mass Spectrometry	None. Dissemination of knowledge. Opportunity for others to incorporate learnings
Kei Yoshino	In vitro Toxicology Sub-Group meetings	To foster collaboration and develop inter-disciplinary projects
Ashraf El Amin	Exposure Response Study	None. Dissemination of knowledge



- ❖ **Next BMK SG meeting will be held in Montreal in May 2019**
 - **Host: Altasciences**



Thanks



PUB-BMK Sub-Group Delegates