



Biomarker Sub-Group (BMK)

2021 Annual report

Coordinator: Mohamadi Sarkar (Altria Client Services)

Secretary: Kirk Newland (Celerion)

Scientific Commission Liaison: Paul Harp (RAIS/BAT)

Virtual Smoke-Techno Conference (SSPT2021)

October 2021



Review of the Vision and Objectives

- **To align the Vision and Objectives with**
 - **CORESTA Strategy**
 - **Evolving marketplace and**
 - **Regulatory environment**
- **SG reviewed and unanimously approved the simplified Vision statement and revised Objectives.**
- **We submit to the Scientific Commission for review and approval.**



CORESTA BMK Sub-Group: Vision

From

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



**Simplify
&
Broaden**

To

“Identify and assess fit-for-purpose biomarkers for tobacco product research.”



CORESTA BMK Sub-Group: Objectives CURRENT

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



CORESTA BMK Sub-Group: Objectives – New

- 1. Develop robust understanding of mechanistic pathways and clinical outcomes for smoking-related diseases to better identify fit-for-purpose biomarkers.**
- 2. To review and summarize published literature on biomarkers that are fit-for-purpose in the assessment of potential reduced risk tobacco products (PRRPs).**
- 3. Evaluate and recommend guidelines and best practice for utilizing fit-for-purpose biomarkers in studies assessing PRRPs.**



BMK Sub-Group Meetings 2021

No	Date	Meeting	Time (EST)	Chair
1	05 May 2021	BMK sub-group spring meeting	8:00 – 12:00	GL Prasad & K Newland
2	11 Oct 2021	BMK sub-group fall meeting	8:00 – 12:00	M Sarkar & K Newland

The details of the topics discussed, timelines and plan of action are documented in the meeting minutes prepared by Kirk Newland.

Several other virtual meetings were held by the respective NWIP leaders and significant progress has been made towards the projects



Outline: 2021 Activities

1. **Tobacco Data standards; Team Update and discussion – Active**
2. **BMK-NWIP161: Biomarkers of Harm/Effect for Tobacco Regulatory Research: Opportunities and Challenges- A Literature Review – Complete**
3. **BMK-NWIP249: Meta-analysis of biomarkers of exposure – Urinary Total NNAL – Complete. Publication combining results from BMK-NWIP186 (CO and NE) and BMK-NWIP249. – Complete to be submitted after MRB reviews.**
4. **BMK-NWIP273: Status Update. Definition of use behavior and exposure terminology across product categories – Complete**
5. **Biomarker Reference Standards – Complete**
6. **BMK-NGTX-IVT Subgroup Collaborative Project – Active**
7. **Next steps**



Tobacco Data Standards: Team Update

❖ Sub-Group Objective 3

Action	Result
Data Standards. Team Lead - Brian Nordskog,	<ul style="list-style-type: none">• CDISC has applied for a grant from CTP for the development of modules specifically related to tobacco research• If the grant is awarded, CDISC anticipates initiating the project in December 2021• Completion of the modules, and review process is expected by Q4 2023 <p>SG has put together a team to begin assist in the development of the project scope</p>

Attendees

- Peg Becker
- Leanne Campbell
- Jeff Edmiston
- Stacy Fiebelkorn
- Lesley Giles
- Beth Groeber
- Paul Harp
- Christopher McNamee
- Sarah Merlet
- Kirk Newland
- Brian Nordskog
- Mohamadi Sarkar
- Max Scherer
- Neelu Sharma
- Alexandre Soulan
- Anissa Tilli
- Dai Yuki



Tobacco Data Standards: Team Update

Meeting Agenda

1. Overview
2. Discuss the types of studies and what data collected in tobacco studies (Focus Clinical)
 - a. Data cross-cutting across all tobacco studies
 - b. Data specific to certain types of studies.
3. Types of analyses performed on the data (CDISC will include analysis concepts in the project)
4. Next Meeting – Oct 18th – Revisit Scoping Effort from 2019
5. Any other Business



Biomarkers of Potential Harm/Effect Review

❖ Sub-Group Objective 2

➤ BMK NWIP161 Biomarkers of Potential Harm/Effect review (Lead, Jeff Edmiston)

Project No.	Activity	Status	Projected Timeline
BMK 161 Team Members: Jeffery Edmiston, ALCS Liz Mason, Imperial Tobacco Mike McEwan, BAT Krishna Prasad, BAT Patrudu Makena, RAIS	Biomarkers of Harm/Effect for Tobacco Regulatory Research: Opportunities and Challenges - A Literature Review <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/Potential Harm• Jeff Edmiston, on behalf of the writing committee, submitted the draft manuscript to the SC	Project work and draft manuscript completed <ul style="list-style-type: none">• Initial search yielded 1171 papers• A presentation was given at the 2019 SSPT meeting• Technical report were reviewed by SC. <u>The Technical Report</u> is now published on CORESTA BMK SG website (Sept 2020)	<ul style="list-style-type: none">• Manuscript submitted to F1000 – Editor revisions update



Meta-analysis of Biomarkers of Exposure - NNAL

❖ Sub-Group Objective 2

➤ BMK NWIP279 Meta-analysis of biomarkers of exposure – Urinary Total NNAL (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">• Establish a population level for biomarkers of cigarette smoke exposure to serve as baseline for comparisons against changes in exposure for reduced-risk products• Scope modified to include only urinary nicotine equivalents and blood carboxyhemoglobin• Conduct a meta-analysis	<p>The <u>technical report</u> was reviewed by the SC and published in December 2019.</p> <ul style="list-style-type: none">• The report covered two biomarkers- carboxyhemoglobin and nicotine equivalents levels	<p>Anticipated draft manuscript will include data from NWIP-249</p>



Meta-analysis of Biomarkers of Exposure - NNAL

❖ Sub-Group Objective 2

➤ BMK NWIP279 Meta-analysis of biomarkers of exposure – Urinary Total NNAL (Lead, Felix Ayala-Fierro)

Project No.	Activity	Status	Projected Timeline
279	<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• Scope modified to include only urinary nicotine equivalents and blood carboxyhemoglobin• Conduct a meta-analysis	<p>Final manuscript involving all three biomarkers of exposure – COHb, NEQ and NNAL completed</p> <p>Internal manuscript review board reviews ongoing</p>	<p>Anticipate submitting to Biomarkers by Dec. 2021</p>



Meta-analysis of Biomarkers of Exposure - NNAL

❖ Sub-Group Objective 2

- **BMK NWIP279 Meta-analysis of biomarkers of exposure – Urinary Total NNAL (Lead, Felix Ayala-Fierro)**

Population estimates of biomarkers of exposure to carbon monoxide, nicotine and NNK in smokers and nonsmokers.

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Elamin A^e Prasad GL^d and M. Sarkar^e

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❖ Sub-Group Objective 2

- **BMK NWIP273 Definition of use behavior and exposure terminology across product categories (Co-lead, Dai Yuki)**

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



Biomarker Reference Standards

❖ Sub-Group Objective 3

➤ Biomarker Reference Standards (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



BMK-NGTX-IVTSG Collaborative Project

Item	Current state
Collaboration between BMK SG, NGTX and In Vitro sub-groups.	<ul style="list-style-type: none">• Start with simple projects<ul style="list-style-type: none">• Human relevance and biological impact of experimental models: e.g., 3D models• What is human relevance?• In vitro assays for clinical biomarkers• Consider a meta analysis project- common denominator exposure?• Adverse Outcome Pathways, can we build one?• Alternative methods, SOT workshop May 28• Symposium organized by Monica Kyeonghee Lee (ALCS)

TUESDAY 19 OCTOBER

SYMPOSIUM

Advancing New Approach Methods (NAMs) for Tobacco Harm Reduction

- ❖ Review WHO Study Group Report 1029 and consider the implications on BMK sub-group activities
- ❖ Align BMK sub-group long term plans with CORESTA strategy
 - 2-year plan
 - Develop robust understanding of mechanistic pathways for smoking-related disease outcomes
 - COPD, CVD and Cancer
 - Quality of Life
 - Build comprehensive knowledgebase of biomarkers that are sensitive and specific for adult smokers switching to PRRPs (e.g. ENDS, HTPs and Oral Nicotine Products)
 - 5-year plan
 - Develop guidelines and best practices for utilizing fit-for-purpose biomarkers for assessing PRRPs
- ❖ Selection of Potential Research Projects and Team Assignments



Any Questions?

A huge thank you to all the members for their contribution

If you have any questions regarding this report, please contact
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