



# **Biomarker Sub-Group 2016 Report**

**Berlin**

**October 10, 2016**

**Coordinator: G. L. Prasad**

**Secretary: Kirk Newland**

## ❖ Biomarker

➤ Generally refers to a measurable indicator of some biological state or condition (Wikipedia)

## ❖ FDA/CTP Conducted two workshops on biomarkers (2015 Aug & 2016 April).

- “...to open the discussion on how to identify and implement the use of biomarkers for the purposes of tobacco product regulation“
- Biomarkers have broad application at FDA/CTP, including the potential to inform product reviews.

- ❖ **Objective 1: To review present knowledge of tobacco and smoking-related biomarkers of exposure and effect, and to document these in meeting minutes, CORESTA reports and scientific publications where appropriate**
- ❖ **Objective 2: To undertake ring trials / proficiency tests for selected biomarkers as agreed by SC**
- ❖ **Objective 3: To source and develop reference materials to support biomarker analysis for those biomarkers selected for ring trials / proficiency tests**



# Recent two meetings

- ❖ **October 04, 2015: Jeju Island, Korea**
  - 23 delegates attended the subgroup meeting
- ❖ **May 11, 2016: Paris**
  - 21 delegates attended the subgroup meeting
  - Meeting was hosted by Imperial Tobacco and Sodim SAS
- ❖ **As always, Biomarker SG and Tobacco Smoking Behaviour SG held joint meetings**
  - TSB SG (morning)
  - BMK SG (afternoon)

## ❖ Objective 1

- **To optimize ESI-Q-TOF Mass parameters in the Target analysis- Liu Tong**
  - Overview of efforts to perform targeted biomarker analysis using ESI-Q-TOF mass spectrometric detection
  - Potential applications include target metabolite analysis, metabolite profiling, fingerprinting and metabolomics
  - Nicotine was used as an example
  - Target analysis pipeline for unknown compounds was presented

## ❖ Objective 1

### ➤ Summary of FDA/CTP workshop on biomarkers of exposure (August 3 and 4, 2015) - Kirk Newland

- Strategies for identifying potential biomarkers for CTP regulatory use
- Biomarkers of exposure and relationship with disease risk
- Identifying biomarkers of tobacco exposure for CTP regulatory use
- Biomarkers of exposure in smokeless tobacco and electronic nicotine delivery systems
- Speakers and participants were from Government, academia and industry

## ❖ Objective 1

- Biomarkers of electronic cigarette exposure - Nicola Pluym
- A critical status review on the background on e-cigarettes that included history, composition of e-liquids and bioanalysis.
- Presented data from a pilot vapor behavior study on the detection of nicotine, Propylene Glycol and Glycerin in body fluids
- Limited methods available for detection of thermal degradation products of e-liquids and flavor ingredients
- Need to improve methods for detection of toxicants and biomarkers of effect



# Jeju Meeting (2015 October)

## ❖ Objective 2

- **Two different topics related to ring trials/proficiency tests**
  - Publication of 3-HPMA ring trial data
    - Discussion on finalizing the report as suggested by Scientific Commission
    - Publication of the work under the auspices of the BMK SG
  - Proficiency Testing of NNAL, a biomarker of NNK
    - Lots of discussion on how to proceed with proficiency testing
    - Inclusion of non-CORESTA laboratories



## ❖ Objective 2

### ➤ Stability of NNAL at room temperature - Max Scherer

- As an action item from a previous SG meeting, ABF reported that NNAL was stable in urine for 7 days
- Celerion indicated in the ensuing discussion that similar results were obtained at ambient and elevated temperatures
- The reported stability of this important biomarker of exposure enables international shipment of samples for planned international comparison studies in the event dry ice runs out

## ❖ Objective 3

- **Reference Standards: Science vs Regulations - Frank Deschamps**
  - Discussion on the possibility of generating a publication of standard expectations for reference materials to be used for analytical quantitation
  - Formed a writing committee to be lead by Frank. Max Scherer agreed to be part of the committee.



# Jeju Meeting (2015 October)

## ❖ Additional activities

- Paul Harp (SC Liaison) provided an overview of updated CORESTA vision
- Paul Nelson briefly reviewed data standards, which will be used for submission of data. FDA requires all data submissions to be in CDISC format.
  - A workshop relating to this topic was planned by FDA for November of 2015

## ❖ Objective 1

- **A presentation of CORESTA BMK SG at the FDA /CTP workshop on biomarkers of potential harm (April 4-5 2016)**
  - Abstract/request was submitted for presentation during the public comment session. “CORESTA Biomarkers Sub-Group. A platform for scientific collaboration on tobacco-related biomarkers”
  - Paul Nelson gave the BMK SG presentation at the FDA workshop; summarized the proceedings for CORESTA Newsletter 44, April 2016; and reviewed for the BMK SG meeting in Paris.
  - Lots of follow up discussion on potential collaborative studies within the BMK SG

## ❖ Objective 1

- **Five sessions in the FDA/CTP workshop on biomarkers of potential harm**
  - Overview of biomarkers of potential harm
  - Three sessions on the major smoking-related diseases
    - Cardiovascular diseases, COPD and Cancer
  - Final session on New areas of research
- **Smoking behaviour System - Krishna Prasad**
  - Discussed Vas et al publication
  - Discussed a potential collaborative project between TSB and BMK SG
  - No specific follow up/action item was identified

## ❖ Objective 1

### ➤ Long-term Assessment of Urine and Urine Extract Stability at -70°C for Urine Mutagenicity Analysis - Eckhardt Schmidt

- Ames test used as toxicological assessment of urine samples from humans exposed to tobacco products such as smoking
- Purpose of this study: Evaluation long term cryo-storage, freeze/thawing and dilution on mutagenic activity
- Results from a RJRT-sponsored clinical study were presented
- Compared to fresh urine, no significant differences were observed in Ames evaluations of urine samples stored frozen for 12 months



# Paris meeting (2016 May)

## ❖ Objective 2

### ➤ 3-HPMA interlab comparison study

- Final report was approved by the Scientific Commission
  - 3-HPMA Interlaboratory Comparison Study 2012  
(2016-07-05)
  - Referenced in Newsletter 45, August 2016
- Dr. Gerhard Scherer submitted the approved manuscript to Beitrage journal

## ❖ Objective 2

### ➤ NNAL interlaboratory comparison study: Significant progress

- Celerion agreed to serve as the central laboratory
- Study cost (reagents, shipping and other miscellaneous expenses) would be shared by RAI, BAT, Imperial Tobacco, PMI, PM USA and JT
- Dr. Steve Hecht (U. Minnesota) agreed to participate in the study
- Eight laboratories agreed to participate in the interlab comparison study
- Study to begin July-August, and hope to have preliminary data in October-November 2016



## ❖ Objective 3

### ➤ Reference Standards: Science vs Regulations - guideline

- Summarizes the testing requirements for the certification of analytical reference standards used in the BMK SG.
- Describes the minimum content of a Certificate of Analysis (CoA) for a reference standard used by analytical and bioanalytical laboratories
- The first draft of the document was generated by Frank Deschamps, and reviewed by Krishna Prasad, Mark Bentley, Max Scherer and Eckhardt Schmidt
- Revised guidelines were generated by Frank, sent for comments to the team, and will be finalized in October 2016, and sent to Scientific Commission's review

Sincere thanks to the members of the BMK SG for their contributions

