



Agenda

Peer Review of Draft NTP Approach to Genomic Dose-Response Modeling Expert Panel Meeting

Rodbell Auditorium, Rall Building
National Institute of Environmental Health Sciences
Research Triangle Park, NC
October 23–25, 2017

Day 1: Monday, October 23

| Time | Agenda Item | Presenter |
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| 8:30 a.m. | Welcome and introductions | Dr. Carole Yauk (Panel Chair) <i>Health Canada</i> |
| | Conflict of interest statement | Dr. Mary Wolfe, DFO <i>NIH/NIEHS/DNTP</i> |
| 8:45 a.m. | Meeting format | Dr. Yauk |
| 9:00 a.m. | Background on NTP's proposed approach to genomic dose-response modeling and panel charge | Dr. Scott Auerbach <i>NIH/NIEHS/DNTP</i> |
| 9:15 a.m. | Public comment | |
| Session 1: Approaches to Genomic Dose-Response Analysis | | |
| 9:45 a.m. | Genomic Dose Response: The Big Picture | Dr. Russell Thomas <i>U.S. EPA/ORD/NCCT</i> |
| 10:15 a.m. | Overview of the NC State approach to genomic dose-response modeling | Dr. Fred Wright <i>NC State University</i> |
| 10:45 a.m. | Break | |
| 11:00 a.m. | Overview of the US Army approach to genomic dose-response modeling | Dr. Lyle Burgoon <i>U.S. Army</i> |
| 11:30 a.m. | An automated method to identify dose-responsive genes and quantitate points of departure (PODs) from transcriptomic data | Dr. David Gerhold <i>NIH/NCATS</i> |
| 12:00 p.m. | Lunch | |
| 12:45 p.m. | Overview of NTP's proposed approach to genomic dose-response modeling | Dr. Auerbach |
| 1:00 p.m. | Public comment (ad hoc) | |
| 1:15 p.m. | Panel discussion of strengths and weaknesses of the different approaches and comparison to NTP's approach | Dr. Yauk |
| 2:15 p.m. | Break | |



Session 2: Filtering of Measured Features

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| 2:30 p.m. | Some pertinent findings from MAQC related to reproducibility of gene expression | Dr. Pierre Bushel <i>NIH/NIEHS/Biostatistics & Computational Biology Branch</i> |
| 3:00 p.m. | NTP's proposed approach to filtering unresponsive genes | Dr. Auerbach |
| 3:15 p.m. | Public comment (ad hoc) | |
| 3:30 p.m. | Panel discussion on filtering of unresponsive genes | Dr. Yauk |
| 4:30 p.m. | Recap Day 1 | Dr. Yauk |
| 4:45 p.m. | Adjourn | |



Day 2: Tuesday, October 24

| Time | Agenda Item | Presenter |
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| 8:30 a.m. | Welcome and introductions | Dr. Carole Yauk (Panel Chair) <i>Health Canada</i> |
| | Conflict of interest statement | Dr. Mary Wolfe, DFO <i>NIH/NIEHS/DNTP</i> |
| Session 3: Fitting Features to Dose-Response Models | | |
| 8:45 a.m. | Interpreting the results of EPA dose-response models | Dr. Jeff Gift <i>U.S. EPA/ORD/NCEA</i> |
| 9:15 a.m. | Fitting curves using non-parametric approaches | Dr. Keith Shockley <i>NIH/NIEHS/Biostatistics & Computational Biology Branch</i> |
| 9:45 a.m. | NTP's proposed approach to curve fitting | Dr. Scott Auerbach <i>NIH/NIEHS/DNTP</i> |
| 10:00 a.m. | Public comment (ad hoc) | |
| 10:15 a.m. | Break | |
| 10:30 a.m. | Panel discussion on fitting curves and determining potency | Dr. Yauk |
| Session 4: Gene Set-Level Potencies | | |
| 11:30 a.m. | When is a pathway changed? | Dr. Sorin Draghici <i>Wayne State University</i> |
| 12:00 p.m. | Deriving points of departure using toxicogenomics for chemical risk assessment | Mr. Andrew Williams <i>Health Canada</i> |
| 12:30 p.m. | Lunch* | |
| 1:30 p.m. | NTP's proposed approach to estimating gene set-level potency | Dr. Auerbach |
| 1:45 p.m. | Public comment (ad hoc) | |
| 2:00 p.m. | Panel discussion on approaches to pathway-/gene set-level potency values | Dr. Yauk |
| 3:00 p.m. | Break | |

*A Lunch and Learn session on BMDExpress is available during lunch in the Rall Lake View Conference Room.



Session 5: Study Design

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| 3:15 p.m. | Improving study designs for quantifying biological potency with genomics data | Dr. Woodrow Setzer <i>U.S. EPA/ORD/NCCT</i> |
| 3:45 p.m. | NTP's proposed approach to study design for genomic dose-response analysis | Dr. Auerbach |
| 4:00 p.m. | Panel discussion on study design | Dr. Yauk |
| 4:30 p.m. | Public comment (ad hoc) | |
| 4:45 p.m. | Recap Day 2 | Dr. Yauk |
| 5:00 p.m. | Adjourn | |



Day 3: Wednesday, October 25

| Time | Agenda Item | Presenter |
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| 8:30 a.m. | Welcome and introductions | Dr. Carole Yauk (Panel Chair) <i>Health Canada</i> |
| | Conflict of interest statement | Dr. Mary Wolfe, DFO <i>NIH/NIEHS/DNTP</i> |
| Session 6: Biological Interpretation | | |
| 8:45 a.m. | Using the AOP framework to aid in gene set identification | Dr. Stephen Edwards <i>U.S. EPA/ORD/NHEERL</i> |
| 9:15 a.m. | Interpreting dose-dependent biological responsiveness through the lens of gene co-expression networks | Dr. James Stevens <i>Eli Lilly</i> |
| 9:45 a.m. | NTP's proposed approach to biological interpretation of genomic dose-response results | Dr. Auerbach |
| 10:00 a.m. | Break | |
| 10:15 a.m. | Public comment (ad hoc) | |
| 10:30 a.m. | Panel discussion on biological interpretations | Dr. Yauk |
| 11:00 a.m. | Panel discussion on development of recommendations on the proposed NTP approach | Dr. Yauk |
| 12:30 p.m. | Next steps | Dr. Auerbach |
| 12:45 p.m. | Adjourn | |