Toxics Use Reduction Institute Science Advisory Board Meeting Minutes
November 18, 2021
Virtual Zoom Meeting
12:30 PM

Members Present: Dave Williams (Chair), Robin Dodson (Vice Chair), Christy Foran, Heather Lynch, Helen Poynton, Wendy Heiger-Bernays, Lisa Cashins, Denise Kmetzo

Members not present: Amy Cannon, Christine Rioux, Rich Gurney

Program staff present: Liz Harriman (TURI), Heather Tenney (TURI), Hayley Hudson (TURI), Michael Ellenbecker (TURI), Tiffany Skogstrom (OTA), Caredwen Foley (OTA), Sandy Baird (MassDEP), Kari Sasportas (OTA)

Others present: Carol Holahan (Foley Hoag ACC), Christina Bramante (Nano-C), Tom Lada (Nano-C), Jerome Lang (Nano-C), Raza Ali (ACC), John Monica (Offit Kurman), Laura Spark (Clean Water Action), Tricia McCarthy (Coyne PC for ACC)

Welcome & Introductions

Board members introduced themselves, program staff were announced and attendees were asked to put their name and affiliation in the chat.

Approve September Meeting Minutes

A motion was made to approve the September meeting minutes as written, and there was a second. After a roll call vote the minutes were unanimously approved by the eight members present.

Program Updates

- TURI has a new director, Baskut Tuncak. He previously served as the United Nations Special Rapporteur on toxics and human rights, is an attorney, chemist and researcher specializing in minimizing the use of toxic chemicals and preventing pollution. The announcement is on TURI's website and was sent out in TURI's newsletter.
- TURI had its annual Fall Continuing Education conference with sessions on PFAS, water policy and conservation, metal finishing, and lean manufacturing. All those presentations can be found on the TURI website. For those interested there will be a training on Resource Conservation planning this winter.
- The Northeast Waste Management Officials' Association (NEWMOA) has moved their PFAS conference originally scheduled for March 2020 to April 2022.
- Draft regulations which added a PFAS Not Otherwise Listed category based on the SAB recommendation and also added a definition of the term "substance" were made available in late September. Public comment was accepted until October 15th. There will be an administrative council meeting in early December where they can discuss the comments received and the program's response to comments. We received two new papers on QACs from David Jones from Lonza, and we will be adding those to the next meeting's LibGuide for Board members' information. They are not required reading for the meeting, but we wanted to share them with you as they are papers that were mentioned several times during our discussion on QACs. We will be starting the QAC Policy Analysis next year.

- EPA released four draft documents with revised toxicity values for PFOA and PFOS and they are three to four magnitudes lower than the last values. They have determined PFOA likely to be carcinogenic to humans.

Carbon Nanotubes and Fibers Petition: Continued work focused on Multi-walled Carbon Nanotubes

Heather gave an update of where the board is at with the nanomaterials discussion and the information that has been collected and received from board members. There is quite a bit of information on each endpoint. We ran a literature search on each endpoint for MWCNT and the resulting spreadsheets are available in each endpoint box on the LibGuide. Today the plan is to go through each endpoint, discuss and identify the best way to proceed.

Carcinogenicity

Board members tasked with this endpoint summarized the information and research they each reviewed.

- Rahman (2017) – attempted to identify mechanisms for cancer of MWCNT-7, which is the most studied, as well as NM-401. They looked at genotoxicity, inflammatory response, and development of fibrosis. While DNA damage may be happening to some degree, chronic inflammation and fibrosis are more important drivers.
- Be cognizant of the different exposure routes used and how to evaluate inhalation studies versus intraperitoneal studies?
- Lu (2019) was mentioned as an interesting paper related to breast cancer cascades and MWCNT exposure where the researchers found an increased likelihood of metastatic disease.
- IARC has announced they want to reevaluate the MWCNT classification in the next 5 years
- Carcinogenesis studies led to issues of chronic inflammation and other pathways; need to look at other studies such as pulmonary and genotoxicity first to get sense of mechanisms.
- Dong Ma (2015) paper is useful for good figures but doesn't characterize between pathways.

Genotoxicity

- Many board members feel like they need to look at different endpoints in order to better understand connections between effects seen; pulmonary toxicity was mentioned many times as a good starting point.
- Suggestions were made to parse further, consider systems and doses, ADME (absorption, distribution, metabolism, and excretion).
- We will note any key studies mentioned today.
- Fraser (2020) was mentioned as a helpful paper as it studied what physiochemical properties were important related to different MWCNTs.
- It was noted that some of the cell line work will not capture physical damage that cascades oxidative stress to cell damage.

Pulmonary Toxicity

Board members discussed the information and large number of studies on pulmonary toxicity effects of MWCNT exposure. There was further discussion on the difficulty and the different approaches in trying to compare so many multifaceted studies for just one endpoint.

- From an occupational perspective, there is evidence that workers have the potential to be exposed to CNT.
    - Four studies were mentioned as useful and summarized: Beard (2018), Vlaanderen (2017), Fatkhutdinova (2016), and Kuijpers (2016)
- Evidence summarized that showed CNT (SWCNT and MWCNT) could be harmful.
    - Studies showing that both SWCNT and MWCNT have the potential to be harmful were briefly summarized by board members.
    - MWCNT studies: Donaldson (2006) - Materials longer than 20 microns can cause fibrosis; Mercer (2010 & 2013); Muller (2005); Samiei (2020) - inhalation of <10nm negatively affected brain of rats; Porter (2010), and Boyles (2015).
- Evidence comparing CNTs to other substances with known health effects like carbon black, quartz, or asbestos.
    - Lam (2004) and Donaldson (2006) both generally conclude that CNT exposure could have similar adverse effects if not worse than these materials we already know are hazardous.
    - An in vitro study Muller (2005) showed that ground CNT induced the overproduction of TNF-alpha by macrophages, suggesting that CNTs are potentially toxic to humans.
    - Boyles (2015) in vitro study found greater response from MWCNT than asbestos
- Looking at epi/occupational studies, two studies were summarized: Vlaanderen (2017) and Fathutdinova (2016) observed early indication of adverse lung health and significant upward trends of biomarkers.
- An inhalation study Samiei (2020) evaluated adverse effects on the brains of rats and found MWCNT smaller than 10 nm caused negative effects. In contrast, asbestos is too large to penetrate the blood brain barrier.
- Does increased production of reactive oxygen species, increased inflammatory cytokines, and pulmonary toxicity potential occur in all MWCNT or just specific ones?
- Poulsen/Knudsen workgroup published several papers over the years as well as evolving Mercer group's papers. Both were mentioned as helpful in making sense of the physiochemical properties and the health effects.

Environmental Toxicity

Board members discussed the information they reviewed related to environmental toxicity, fate, transformation and breakdown for MWCNT.

- A board member summarized two papers by Zhao (2020 and 2021) that looked at MWCNT exposure in frogs.
    - Researchers observed adverse effects, but high concentrations (up to 8 mg/L) were used (Zhao 2020). Some toxicity was a result of accumulation of MWCNTs in their gills and digestive tracts, which didn't clear when survivors were placed in fresh filtered water.
- The reproductive study (Zhao 2021) evaluated effects in frogs exposed to MWCNTs.
    - Exposure for 56 days to 0.5 mg/L and 2.5 mg/L. MWCNTs were added to the water with food, CNT adhered to red worm food facilitating exposure and digestion.
    - Impacts include reduced growth and decreased gonadal organ size. Embryo survival in 2.5 mg/L exposure group was 0.

- Another study (Falinski 2019) exposed zebrafish to MWCNT and found that aggregation led to less toxic effects. MWCNT-induced mortality of zebrafish was physical, and these characteristics may be driving the toxicity. Mortality seen at 25 mg/L and above.
- A study that was not on the LibGuide, Zhu (2016), was mentioned that observed lysosomal damage after exposure to MWCNT-7. One of the findings concluded that lysosomal damage was not related to high surface area or sharpness but the length and rigidity of the material.
- In Hu (2018) the researchers tried to characterize nano scale fragments with a carbon content up to 80% in wastewater treatment plant effluents. Rice grown in these effluents resulted in uptake and impacts on chloroplasts, increased ROS (Reactive Oxygen Species) in roots and other phytotoxicity.

Visitor Comments

At this time any visitors or guests had an opportunity to ask any questions or offer any comments.

- A visitor suggested that it would be helpful to have draft minutes or a minutes "light" version promptly after the meeting.
- Heather stated that the draft minutes from the previous meeting are posted on the TURI website a few days before each meeting. However, she will send out a short summary including highlights from today's meeting.

Path Forward

There is an extensive amount of information on the LibGuide already and what is there is not yet comprehensive. It was suggested that TURI, using SAB members comments, identify key studies on the LibGuide. Additionally, in each endpoint box there is a spreadsheet with additional current literature. SAB members committed to review these spreadsheets and identify which new papers they would like to see by December 14th.

- A board member mentioned particular interest in the neurotoxicity endpoint.
- It was suggested we focus on just the pulmonary toxicity endpoint for next meeting.
- We will see how this approach works and have a micro goal of making a decision on MWCNT in the spring.
- Board members expressed concern for how deeply we will have to go before it is enough evidence. This is a key question and something to consider as we try to get a better sense of the pulmonary endpoint.
- As we review the pulmonary toxicity information there was a suggestion to subdivide the information further into "buckets" - to think about materials with specific characteristics.
- Other board members expressed that if there is overwhelming evidence supporting a specific hazard, we should not spend too much time on the physical characteristics if they are intrinsically hazardous.
- Heather will send out dates and tasks that were discussed today to board members after the meeting.

Next Meeting

Heather will send out a doodle poll for a proposed meeting sometime in the first two weeks of January.

The chair noted that this meeting is being conducted remotely, consistent with An Act Extending Certain COVID-19 Measures Adopted during the State of Emergency. This Act includes an extension, until April 1, 2022, of the remote meeting provisions of Governor Baker's March 12, 2020, Executive Order resulting from the outbreak of the 2019 novel coronavirus, known as “COVID-19."

A motion was made to adjourn.

Visitor Comments (inserted verbatim from zoom chat)

From Tom L to Everyone: 12:37 PM
Tom Lada - Nano-C, Inc.
From Laura Spark, Clean Water Action to Everyone: 12:37 PM
Laura Spark, Clean Water Action
From Raza Ali, ACC to Everyone: 12:37 PM
Raza Ali, American Chemistry Council, Northeast Region
From Jerome Lang to Everyone: 12:37 PM
Jerome Lang, EHS Manager Nano-C
From Liz Harriman to Everyone: 12:37 PM
thanks, could you all identify yourselves in chat please!
From John Monica to Everyone: 12:37 PM
John Monica, Offit Kurman, Tysons Corner, VA
From Carol Holahan to Everyone: 12:38 PM
Carol Holahan Foley Hoag, LLP
From Carol Holahan to Everyone: 01:15 PM
if there’s something in writing, can it be shared in the chat, or otherwise circulated?
From Liz Harriman to Everyone: 01:17 PM
Carol, we will summarize what she shared, and I don't know if she has something written - we may just be checking back with her on specific references to make sure we get the studies correct.
From Helen Poynton (she/her) to Everyone: 01:40 PM
https://www.pnas.org/content/113/44/12374
From Carol Holahan to Everyone: 01:41 PM
Thank you. That would be helpful. It would also be helpful if you could share minutes, even if clearly marked as “draft” or “unofficial” following the meeting. Thank you.