

**Toxics Use Reduction Institute Science Advisory Board Meeting Minutes**  
**May 26, 2022**  
**Virtual Zoom Meeting**  
**9:30 PM**

**Members Present:** Robin Dodson (Chair), Christine Rioux (Vice Chair), Christy Foran, Lisa Cashins, Denise Kmetzo, Helen Poynton, Heather Lynch, Wendy Heiger-Bernays, Rich Gurney

**Members not present:** Amy Cannon, Dave Williams

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

**Others present:** Carol Holahan (Foley Hoag ACC), Christina Bramante (Nano-C), Raza Ali (ACC), John Monica (Offit Kurman), Tom Lada (Nano-C), David Jones (Arxada LLC), Katherine Robertson (MCTA), Laura Spark (Clean Water Action)

***Welcome & Introductions***

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 July 15, 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."

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

***Approve April Meeting Minutes***

A motion was made to approve the April meeting minutes as written, and there was a second.

There was discussion around the wording of a sentence under "Additional Effects". The sentence will be changed, and the minutes will be voted on at the next meeting.

***Single Walled Carbon Nanotubes***

At the March meeting the board made a recommendation **to list MWCNTs based on the evidence of pulmonary toxicity, lung cancer, mesothelioma, and environmental persistence. There are additional concerns for genotoxicity and toxic environmental degradation products.**

The nano petition also asked us to consider CNF and SWCNT. The Board discussed CNF at the April meeting yet did not come to a conclusion. This meeting focused on SWCNT including the following endpoints:

- **Pulmonary toxicity**
- **Cancer**
- **Reproductive/developmental effects**
- **Genotoxicity**
- **Environmental effects**
- **Other**

### ***Pulmonary toxicity***

Board members summarized studies they reviewed and thought to be helpful in understanding the pulmonary endpoint. There was further discussion on any relevant details.

- Ema (2016) was noted as a helpful review paper.
- Chang (2011) mechanistic and intratracheal study that saw biomarkers of lung toxicity – granuloma and fibrotic changes.
- Many of the studies found some level of fibrosis, inflammation and cytokine production.
- Similarities in the inhalation and intratracheal studies, but intratracheal studies showed more effects as you bypass the nose and throat.
- Agglomerates were seen to not cause as many effects.
- Overall, four or five studies had strong and consistent evidence of inflammatory markers and sustained fibrosis in mice and rats.
- There was discussion around the dose relevant to humans and the impacts of functionalization.
- Members discussed the need to go back and review all the different test conditions in a matrix or table to have as much data as possible.

### ***Cancer***

Board members summarized the key studies they reviewed on the cancer endpoint and there was discussion on any relevant details.

- In the Shvedova studies they did not purify the CNTs - about 18% iron in the nanotubes. They felt the iron was contributing to toxicity and the purpose of the study was to differentiate inhalation vs aspiration.
- They looked at human relevant dose and acknowledged a non-pure substance.
- Pacurari (2008) looked at diameter of SWCNT but didn't include length. Noted ROS generation, cell death, and these cell events are similar to those seen in mesothelioma so animal studies are warranted.
- Wang (2011) lung epithelial cell study saw morphological changes. At 24 weeks of exposure, there was increased cell proliferation; those transformed cells were subcutaneously injected into mice resulting in tumor generation.
- Wang (2021) DNA methylation changes and higher ROS levels in cells exposed for 60 days; after 60 day recovery period, cells retained their DNA methylation status. Cells injected into mice and tumors developed.
- Overall, what we are seeing is suggestive data with support of inflammatory response.

### ***Reproductive/developmental effects***

Board members summarized and discussed key studies they reviewed for the reproductive/developmental endpoint.

- Those studies that had injection of SWCNT could see effects on the placenta and fetal malformation. Could be due to inflammatory response, saw increased levels of ROS.
- Farshad 2020 – oral study looked at a range of biomarkers for sperm toxicity. Results included effects on sperm viability, changes in testes; again, ROS is key.

- There are not many well conducted studies for this endpoint, board members would like to see more studies, particularly inhalation studies.
- Tang (2009) looked at zebrafish embryos and did note that there were hatching delays, but they could have been due to metals associated with the SWCNT.

### ***Genotoxicity***

Board members summarized the key studies they reviewed for the genotoxicity endpoint.

- Many of the studies saw less or very little response. Mutagenicity does not seem to be an issue, and most are in vitro studies. ROS is a major factor, and seen in dose-response manner.
- Evidence for genotoxicity is not well supported, but there is evidence for ROS and DNA damage.
- Jiang (2020) was noted as a well done study and helpful for this endpoint.
  - Molecular toxicity of SWCNTs is characterized well and they are concentration and structure dependent. Materials were well characterized with varying lengths and functionalization, and all except a semiconducting SWCNT exhibited positive genotoxicity.
- DNA damage and stress categories were useful to predict genotoxicity.

### ***Environmental effects***

Board members summarized the key studies they reviewed for the environmental endpoint.

- The GreenScreen noted low acute toxicity due to high EC50 and LC50, with high persistence and low bioaccumulation.
- Some studies support GreenScreen's determination and some don't.
- Some studies reviewed found effects at very low and environmentally relevant concentrations.
- Many studies didn't measure metal contents or exposure concentrations. Ali 2014 freshwater snail study results showed LC50 of 0.61 mg/L. and saw effects at 0.05 mg/L; metals weren't measured.
- Arndt 2013 multi-generational daphnid study saw effects on reproduction at high concentrations.
- Several studies show SWCNT staying in gut and being excreted, but not crossing epithelial wall. That could result in trophic transfer or could inhibit uptake of food and nutrients.
- Kotchey (2012) was an interesting study about enzymes being able to break SWCNTs down, but not very environmentally relevant. Unsure how much of this kind of degradation you would see in the natural environment.
- Images were shared from the Zhu (2014) study as you can actually see the CNT piercing the wall.
- Rodrigues 2012 showed bacterial soil community was impacted but recovered, as opposed to fungal community which did not recover. The carbon and phosphorus biogeochemical cycle could be adversely affected.

### ***Other***

- TURI agreed to put together a table for the next meeting organizing all the key physiochemical characteristics from each of the studies.

### ***Visitor Questions/Comments***

There was an opportunity for visitor comments at this time.

We did receive information and comments from two industry groups Nano-C and the NIA.

Tom Lada from Nano-C commented on the density of the material they make (30 mg/L) which is helpful in thinking about how doses translate to volumes.

### ***Remote Meeting Update***

The Governor's order for remote meetings has been extended until July 15<sup>th</sup>. We will need to vote on remote participation for when we do begin in person meetings. Remote participation is allowed under certain conditions if a public body has voted to adopt it. When we vote on remote participation, we should set guidelines (e.g., members should identify if they need to participate remotely when responding to the meeting date poll, as a quorum must be present at the meeting site).

### ***Next Meeting***

Heather will send out a WhentoMeet for the end of June. This will be our last meeting before we break for the summer, and we hope to wrap up SWCNTs and CNFs.

### ***Visitor Comments (inserted verbatim from zoom chat)***

From David Jones to Everyone 09:33 AM

David Jones, Arxada LLC,

From Katherine Robertson to Everyone 09:33 AM

Katherine Robertson, MCTA

From iPhone to Everyone 09:33 AM

John Monica, Offit Kurman on iPhone

From Christina Bramante to Everyone 09:33 AM

Christina Bramante, representing Nano-C

From chris to Everyone 09:33 AM

Christine Rioux - Environmental Health Scientist

From Raza Ali to Everyone 09:33 AM

Raza Ali, American Chemistry Council

From Carol Holahan to Everyone 09:33 AM

Carol Holahan, Foley Hoag LLP

From Tom L to Everyone 09:34 AM

Tom Lada, Nano-C

From Rich Gurney (Simmons University) to Everyone 09:34 AM

Rich Gurney (Simmons University) Chair of the Chemistry and Physics Department

From Tiffany Skogstrom to Everyone 09:35 AM

July 15th is when the remote meeting is extended to

From chris to Everyone 09:41 AM

<https://www.cdc.gov/niosh/docs/2013-145/pdfs/2013-145.pdf>

Although data from animal studies with CNF are more limited [Murray et al. 2012; DeLorme et al. 2012], physical-chemical similarities between CNT and CNF and findings of acute pulmonary inflammation and interstitial fibrosis in animals exposed to CNF [Murray et al. 2012] indicate the need to also control occupational exposure to CNF at the REL of 1 µg/m<sup>3</sup> EC. Because of uncertainties in the risk estimates some residual risk for adverse lung effects may exist at the REL; therefore, efforts should be made to reduce airborne concentrations to CNT and CNF as low as NIOSH CIB 65 • xi Carbon Nanotubes and Nanofibers possible. Until the results from animal research studies can fully explain the mechanisms (e.g., shape, size, chemistry, functionalized) that potentially increase or decrease their toxicity all types of CNT and CNF should be considered a respiratory hazard and occupational exposures controlled at the REL of 1 µg/m<sup>3</sup>.

From Clean Water Massachusetts Office to Everyone 11:15 AM

Laura Spark, Clean Water Action

From Tom L to Everyone 11:40 AM

The density of our as produced material is typically 0.03 kg/L. I'll double check whether this number was included in our submission. Hoping that it's a helpful metric to evaluate the size of various doses mentioned in exposure studies.

From Christina Bramante to Everyone 11:53 AM

This is Christina Bramante, representing Nano-C, may I also suggest documenting the dose used in the pulmonary studies, as adverse effects may be related to lung overload due to excessive dose administration. Thank you.