Secretaries' Science Advisory Board

MEETING SUMMARY
Archdale Building, Ground Floor Hearing Room, Raleigh, NC
Monday, June 3, 2019
10:00 AM-12:30 PM

The Department of Environmental Quality (DEQ) and the Department of Health and Human Services (DHHS) Secretaries' Science Advisory Board (SAB) met on Monday, June 3, 2019 at the Ground Floor Hearing Room of the Archdale Building in Raleigh, NC. SAB members in attendance were: Tom Augspurger, PhD (Chair), Viney Aneja, PhD, Richard DiGiulio, PhD, Elaina Kenyon, PhD, Detlef Knappe, PhD, Jaqueline MacDonald Gibson, PhD, Thomas Starr, PhD, Phillip Tarte, MPH, and John Vandenberg, PhD. In attendance by telephone were: Gina Kimble, PhD, and Betsey Tilson, MD, MPH. Also in attendance were Sandy Mort, PhD, Michael Abraczinskas and Michael Pjetraj (DAQ), DEQ and DHHS support staff.

I. Call to Order (Chairman Tom Augspurger)

Chairman Augspurger called the meeting to order at 10:04 am. He welcomed attendees and outside presenters. He explained that Dr. Dorman was out of the country, and Drs. Kimble and Tilson planned to attend via telephone.

II. Ethics Statement

Chairman Augspurger read the ethics statement and reminded the members that if anyone had any conflict of interest to indicate so. No one expressed any conflict.

III. Approval of Meeting Minutes for April 1, 2019

The meeting minutes were circulated to all members on May 3. Chairman Augspurger asked if everyone had any additional comments on the minutes; there were none, so he asked for a motion to approve and adopt the minutes; Dr. Vandenberg so moved, and Dr. Starr seconded. The April minutes were approved and adopted unanimously by verbal vote.

IV. Hexavalent Chromium (Cr6)

Chairman Augspurger reviewed the charge of the Secretaries to the NCSSAB regarding hexavalent chromium. The Board has been asked to advise the state, has heard six (6) presentations, shared more than 15 papers regarding mode of action, and a was provided a table of groundwater standard value calculations from DEQ staff, which was sent via email by Dr. Mort. Dr. Dorman offered input; he is overseas, so Chairman Augspurger will convey his input.

He then asked the other Board members present for their input on the advice the Board should offer to the Secretaries.

Dr. Starr said there has been extensive toxicology research done with tumor data provided; however, there are data available which has not been considered by the Board. He explained in detail the data and the EPA 2005 risk assessment guidelines, and recommended the Board strongly consider the alternative non-linear approach which the guidelines allow, as the approach the Board should recommend.

Dr. Kenyon asked that Chairman Augspurger share Dr. Dorman's perspective, as he is very familiar with bioassays and how they are conducted. Chairman Augspurger read from Dr. Dorman's email: "I found Thompson et al. (2017) to be informative - this study evaluated several gastrointestinal tract (GIT) carcinogens including Cr(VI) and their results suggest that the tumor response is linked to a threshold effect. The Cr(VI) mutagenicity data is mixed (as reviewed by IARC and others). I would lean towards a threshold approach for GIT tumors."

Dr. Kenyon said that default approaches are conservative when information is unavailable, but metals (such as hexavalent chromium) behave uniquely pharmacokinetically, which makes it a very complex problem. Based on her reading of the literature, there is a change in the way carcinogenic effects are looked at, and when dealing with portal of entry effects, such as inhalation on humans, then pharmacokinetics becomes important. She recommended looking at dose-response analysis, taking into careful consideration the pharmacokinetics at the tumor site.

Dr. MacDonald-Gibson asked if there is a policy option to consider Dr. Starr's recommendation of the standard non-cancer approach allowed by the guidelines. Dr. Starr replied there is a policy option for such an approach, but non-linear modeling has not been done yet, and he would like to see the state consider this alternative approach.

Dr. Vandenberg shared his perspectives, indicating it is pretty clear that Cr6 is mutagenic through inhalation exposures; for our task on oral exposures there could be more than one mechanism of action. One cannot prove Cr6 is not causing cancer by the oral route (he referenced Dr. Stern's presentation to the SAB) and we need to ask whether the Big Blue® rat study is the definitive study.

Chairman Augspurger then read the charge to the Board regarding Cr6:

DEQ and DHHS request the SAB review the current hexavalent chromium toxicological science related to a linear versus a non-linear exposure response and provide recommendations to the appropriate science to be used for development of regulatory standards protective of public health and the environment for groundwater and surface water.

Then he stated the path forward is to craft a recommendation. There was more discussion of how many groundwater drinking water sources in the state may be above the 0.07 µg/L groundwater level (a provisional estimate calculated using the cancer potency factor), DEQ responded they did not have that information, noting that the geology in some areas of the state contributes to hexavalent chromium levels above this value. Chairman Augspurger asked if the Board was comfortable with the discussions on this subject; Dr. Tilson said she was and there was general consensus with Chairman Augspurger's suggestion to flesh out a recommendation.

Chairman Augspurger outlined the next steps: The charge is advisory guidance on mode of action and science to be used for developing water standards, not recommending a level or range, and guidance can be crafted as a memo or letter back to the Secretaries with input from supporting staff of DEQ and DHHS. As EPA is going through the same process, a more intense, systematic review of MOA, there is no need for the Board to do the same work. He then asked if anyone knew the EPA timeframe, and how it would affect the timeframe of guidance from the Board.

Dr. Mort replied that there is no specific deadline for the Board, but the agencies would like a recommendation as soon as is feasible. She noted her last update from IRIS estimated the draft RfD for public comment released during 2020, and realistically the end of 2020 for a final number; Dr. Vandenberg said that was an optimistic deadline, as after public comment and review of the comments and any changes to the draft, the draft would be subject to peer review, then presented. Dr. Starr asked why the Board is being asked to attend to this now; Dr. Mort replied that there are areas of the state with elevated levels of hexavalent chromium, and the issue has been dealt with fairly intensively over the last 5-6 years, so there is an urgency to come to a resolution. Dr. Vandenberg consulted the most recent IRIS timeline during the meeting (https://www.epa.gov/sites/production/files/2019-04/documents/iris_program_outlook_apr2019.pdf) which lists target dates for the hexavalent

chromium Public Comment Draft in the first quarter of federal fiscal year 2021 and an External Peer Review in the third quarter of that fiscal year.

Chairman Augspurger suggested a small team within the Board consider what the Board has heard, received and reviewed to draft a guidance memo or letter to be presented at the next Board meeting for full SAB review in advance of sending to the Secretaries. He asked for volunteers; Drs. Vandenberg, Kenyon and Starr volunteered. Dr. Kenyon asked that Chairman Augspurger ask Dr. Dorman to be part of the editorial group, as he had insightful input. Drs. Kimble and Tilson said they were satisfied with the path forward as proposed by the Chairman. Dr. Vandenberg wanted to convey to the presenters the Board's thanks for their time and good quality presentations.

Chairman Augspurger then opened the floor for any public comment; he recognized Chad Thompson of ToxStrategies, Inc. of Katy TX to speak. Mr. Thompson asked for clarification that the units for the 0.07 hexavalent chromium value were parts-per-billion. Dr. Mort confirmed the units were parts-per-billion for that concentration. Chairman Augspurger thanked Mr. Thompson for his question and interest in attending the meeting, and stated the Board would take a break before attending to the next item on the agenda.

V. Methyl Bromide

Chairman Augspurger reconvened the meeting at 11:25 AM, and thanked the Board members for a good discussion on the path forward for hexavalent chromium. He reviewed the action on methyl bromide to this point in time. In early April, the SAB completed its work on the methyl bromide ambient action level (AAL). At the April SAB meeting, the SAB recommended a range of values for the AAL and the document remained open for one week for 7 points of additional clarification recommended by the Board and the document was finalized in April. In early May, the EMC met and discussed the SAB's recommendations on the methyl bromide AAL. The EMC's discussions included comments prepared by the Methyl Bromide Industry Panel (and representing the National Pest Management Association (NPMA), EcoLab, Inc. and Western Fumigation, hereafter identified as the "MBIP" document) following the April 1, 2019 SAB AAL discussions and recommendations, and the 30-day public comment period for the methyl bromide AAL report to the SAB. These comments were dated April 5th and were

provided directly to the EMC by email from the MBIP. The DEQ received a copy of the April 5th comments from the EMC. The MBIP package dated April 5th included additional MBIP comments dated March 27, 2019 that were not provided to the SAB in written form. The March 27 documents were missed in collating public comment prior to the SAB meeting, but the issues raised and advice offered were similar to comments MBIP's representatives provided during the presentations at the April 1 SAB meeting. The April 1 and March 27 documents were subsequently shared with the SAB prior to the June 3rd meeting with the request for their review and discussion of their content as it related to the SAB's methyl bromide AAL recommendations. The MBIP documents included references to USEPA Office of Pesticide Programs (OPP) draft methyl bromide risk assessment reports publicly released on April 8, 2019. DAQ had shared these draft documents with the Board prior to the meeting, noting DAQ would provide a summary of the OPP documents at the June 3rd meeting, as well as DAQ's response to the April 5th MBIP document.

Mr. Michael Pjetraj, Deputy Director of Air Quality, DEQ, gave an update on the May 8th and 9th meetings of the EMC and their actions on the methyl bromide AAL. DAQ presented the log fumigation rule and suggested 0.005 milligrams per cubic meter (mg/m^3) as a 24-hour AAL value previously presented as the draft rule to the EMC. DAQ stated this value represented the upper-bound AAL range recommended by the SAB and identified as the value associated with the highest confidence. The lower-bound range value (0.002 mg/m^3) was also presented to the EMC. The DAQ also presented the fiscal note to the EMC. The Commissioners discussed the Board's report, the DAQ's methyl bromide AAL report, the ATSDR methyl bromide review, other states methyl bromide standards or action levels and the averaging period for the recommended AAL. There was a motion to change the averaging period from 24-hour to an annual period. That motion did not advance. There was then a motion to proceed to public hearing with the log fumigation rule and the addition of methyl bromide as a Toxic Air Pollutant (TAP) at the recommended value of 0.005 mg/m^3 and the 24-hour averaging time. There was an amended motion to provide a range of values within the rule, with the range being 0.005 to 0.078 mg/m^3. Following further discussions by the EMC and the EMC's legal counsel, the EMC's final recommendation was to include only the SAB's recommended AAL value (0.005 mg/m^3) in the 15A NCAC 2D .1104 rule to public comment, but requested the public notice include a request for public comment on a range of values from 0.005 to 0.078 mg/m^3 for a 24-hour period, including as the low-end of this range the upper-bound AAL range recommended by DAQ and

the SAB. The motion was passed by EMC unanimously. Currently the DAQ is preparing for public hearings anticipated to occur in late July. There will be a 30-day public notice for the public hearings and these notices are expected to be published within a couple of weeks. There will be a 60-day comment period that will begin with the release of the public notice. At the end of the 60-day period the DAQ gathers the public comments and provides those to the EMC hearing officer who will generate a report that includes rule information and the comments that were submitted during the public comments period. The EMC makes the final decision on what value will be set by rule as the AAL. Chairman Augspurger thanked Mr. Pjetraj for his summary. Dr. Vandenberg asked what was the basis of the EMC recommendation of the 0.078 mg/m^3 value which Mr. Pjetraj stated Dr. Mort would discuss this in her presentation. There were other questions by Board members.

Chairman Augspurger stated there have not been questions on the appropriateness of the 0.005 mg/m^3 value as the basis of the AAL throughout the SAB's review and public comment period, but there have been discussions of the interplay of the AAL value and the 24-hour averaging time. He asked if there had been similar discussions by the EMC. Mr. Pjetraj stated that most of the EMC discussion was related to other states' values. Chairman Augspurger asked if the EMC discussed or mentioned a desire for representation of the SAB at the EMC's meetings; Mr. Pjetraj said there was some discussion of members of the SAB and EMC being present at the others meeting and he would contact EMC and ask if that coordination needs to happen, and return an answer. A Board member asked for verification that if the 0.005 mg/m^3 AAL is as a 24-hour average, that means that no single day can exceed that limit, while if the AAL is set with an annual averaging time many days could exceed that limit as long as the average over 365 consecutive days was below the AAL value. Mr. Pjetraj confirmed this was the correct interpretation of the AAL and averaging time application.

Dr. Dorman provided Dr. Augspurger some feedback on MeBr, noting the RfC that IRIS developed is based on olfactory neuronal loss (ONL) and olfactory epithelial degeneration as seen in rodents. He indicated further that "... I have worked with agents that produce ONL (acetaldehyde, acrolein, hydrogen sulfide). Subchronic and chronic exposures result in lesions seen at lower concentrations versus single high dose acute studies. My sense is that ONL is more concentration dependent versus C X T (concentration x time) dependent so time averaging needs to consider peak concentrations more so than a C X T approach."

Chairman Augspurger then asked Dr. Mort for her presentation.

Dr. Mort discussed the timing of the distribution of the MBIP comments noting the package dated April 5 was addressed to Chairman Augspurger and DEQ administrative staff, neither of which had received the package; and noting that the package was sent to EMC by MBIP and the EMC forwarded the information to DEQ and Chairman Augspurger. Dr. Mort noted it came to DEQ after the 30-day public comment period had ended. As noted, the March 27 attachments to the April 5 comments were the subject of MBIP presentations and SAB discussion during the April 1 SAB meeting.

MeBr slides_june 3
2019 SAB meeting.p

Dr. Mort explained that the 0.078 mg/m³ value presented for public comment by the EMC is a provisional intermediate exposure duration level published by ATSDR in their 2018 draft Methyl bromide review. As an intermediate MRL is derived to be protective for exposure durations of 15 days to not more than 365-days. It is based on a neurotoxic endpoint. Dr. Mort noted a discussion of this value was included in the AAL report, but DAQ did not recommend this draft value as appropriate to be health protective for the exposure durations of concern for residents living near log fumigation operations.

Dr. Mort identified three points that she would address in her response to the April 5th MBIP document including the application of the IRIS methyl bromide chronic reference concentration (RfC) for the AAL, the relevance of the referenced USEPA OPP methyl bromide risk assessment documents to the log fumigation AAL, and the human health risk evaluation methodology that served as the basis of the AAL recommendation. Dr. Mort noted the Board heard the April 1 MBIP assertions that DAQ was miss-applying the chronic RfC as the basis of the AAL, so that issue was considered by the Board prior to their vote on the methyl bromide AAL and the averaging period.

Dr. Mort noted that DAQ had reviewed the OPP documents prior to finalizing the methyl bromide report dated April 22, 2019 that went to the EMC, determining that there was no new

science that was relevant to the selection of the IRIS chronic RfC as the basis of the log fumigation AAL recommendations. The OPP documents include methyl bromide draft risk assessments for routes of exposure (ingestion/dietary and dermal). The inhalation studies in the OPP documents do not address receptor populations that are directly comparable to the "residential receptor" population of concern for the recommended AAL. The receptors addressed in the OPP evaluations, including those identified as "residential bystander" or "non-occupational spray-drift" and "bystander" exposures do not reflect exposure conditions that are of direct relevance for the chronic inhalation AAL. The OPP non-occupational bystander population considers a single acute exposure. Ambient bystander air exposures evaluated in the OPP reviews were assessed by collecting ambient air concentrations in agricultural application areas of California. The OPP noted there was uncertainty in the representativeness of this data.

The April 5th document also stated DAQ should consider the acute study data included in the OPP documents. Dr. Mort again noted that the exposure route for most of the acute study discussions were not for the inhalation route. Inhalation exposure studies mentioned in the OPP documents included a 1986 rat study that evaluated a mortality endpoint (LC50), another was a statistically weak study that evaluated neurological endpoints in dogs, and another evaluating neurotoxic endpoint in rabbits. Dr. Mort summarized the acute data as limited and inadequate and inappropriate for a chronic AAL.

Dr. Mort also discussed the MBIP's assertion that the additional 3-times uncertainty factor (UF) applied to the RfC to derive the lower-bound AAL recommendation to be protective of the human sub-population with the GSST1-related enhanced sensitivity to neurotoxic effects was inappropriate. Dr. Mort noted that the current toxicological science has identified that the default 10-time UF for human-population variability may not adequately cover the variability for all human population toxic responses. Dr. Mort noted that while the focus of the concern for this sub-population was the neurotoxic endpoint, mode-of-action (MOA) information suggests that pre-neurotoxicity would be anticipated prior to the known generalized cytotoxic effects associated with highly reactive metabolites of methyl bromide, known generation of reactive oxygen species (ROS), lipid and protein binding, and glutathione depletion in multiple tissues, including the liver and erythrocytes.

At the concluding of her presentation, Dr. Mort asked the Board members if they saw anything in the April 5 letter that calls into question the chronic AAL level provided by the Board to the EMC.

Dr. Vandenberg stated that the third document mentioned in Dr. Mort's slides (*Methyl Bromide. Draft Human Health Risk Assessment for Registration Review. 12/17/2018*) includes a description on page 47 of a bystander inhalation exposure assessment associated with containerized non-soil commodity fumigation uses, similar to the log fumigation process described by DAQ. The OPP assessment of those emissions using a model included looking at a range of weather conditions and treatment volume. Dr. Vandenberg read a statement from the text that the modeling indicated concentrations protective of residential bystanders were not achieved at the edge of the field. Dr. Mort noted the OPP review identified the same study as the critical study for chronic inhalation concerns as did the IRIS review, selecting the same critical effect, point of departure (POD), animal-to-human extrapolation method and uncertainty factors. Dr. Vandenberg stated he believes this information reinforces the 24-hour averaging period for the AAL for batch operations.

Chairman Augspurger asked if any of the studies or the April 5 letter would change or influence the Board's recommendation. He also asked for comments from the Board. Dr. Starr said the use of the word "irrelevant" is perhaps too strong when considering the relevance of drinking water studies to effects associated to inhalation exposures; he suggested the use of "less relevant." Dr. Kenyon said methyl bromide is a reactive gas, and any route-to-route extrapolation is highly questionable due to dosimetry issues and deriving a value in this manner is inappropriate. She then said she is comfortable that the Board has done what could be done with the information we have; an acute study for an acute AAL is a legitimate concern for the batch operation and seasonal nature of the fumigation operations. Dr. Knappe said that he was concerned that the 0.078 mg/m^3 value was included in the discussion, rather than the 0.002 to 0.005 mg/m^3 range and is concerned that a person living next to a fumigation operation may be exposed for a duration longer than 365 days, even with an intermittent operation. Chairman Augspurger asked whether the new information either in the MBIP document or the OPP documents, would change or influence the Board's recommendation: Drs. DiGiulio, Vandenberg, Kenyon, Starr, MacDonald-Gibson, and Knappe all replied that it would not change the recommendation. Chairman Augspurger then asked if there is no disagreement over the

level, is there a better way to convey our recommendation? Is there a communication that can be provided concerning the perceived mismatch of an AAL based on a value protective of a chronic exposure and applying it as a 24-hour averaging time, is there an addendum needed to better convey this so that it is understandable beyond the SAB? Dr. Starr stated we could relate that the controlled chronic rat study considered controlled, consistent exposure concentrations that did not have large excursions beyond those consistent exposures and is equivalent to a consistent 24-hour average exposure and does not provide information about large, such as 10-time peak excursions, above the average exposure concentrations.

Chairman Augspurger noted that when considering lifetime exposures a few pulses of elevated acute exposures may lead to effects and that exposure is a function of duration, magnitude and frequency, and the Board considered the exposures to be a lifetime of short-term exposures, which is consistent with a definition of chronic. Dr. Vandenberg said the Board has considered the evidence, and his opinion of the Board's recommendation has not changed in light of what he has seen since then. Dr. Mort reported that Dr. Stoskopf said he saw no reason to alter the recommendation based on the April 5 documents. Chairman Augspurger also noted that Dr. Dorman provided input in writing emphasizing that nasal lesions can be produced in a variety of ways, noting that the type of exposure, the concentration and time are important as it relates to observed effects for different compounds

Chairman Augspurger asked what DAQ needs from the Board; Mr. Abraczinskas, Director of DAQ, said he appreciated the Board's thoughtful discussion and dialogue of the April 5 documents and their consideration. Chairman Augspurger then asked the Board how they thought the SAB should move forward regarding the EMC's discussions; Dr. Vandenberg asked if there should be a Board presence at the EMC meetings, perhaps a liaison relationship formed between the Boards. Chairman Augspurger said that is something that the Board would consider moving forward, and he agreed to follow-up.

Chairman Augspurger then opened the floor for the public forum.

VI. Public Forum

Chairman Augspurger asked if there were any members of the public present who wished to speak; there being none, he reminded the Board of the next meeting scheduled August 5, 2019 at 10:00 AM. He thanked the Board members, DEQ and DHHS support staff and members of

the public for their attendance. Dr. Starr moved to adjourn and Dr. Vandenberg seconded; the Chairman adjourned the meeting at 12:32 PM.

Respectfully submitted,

Louise G. Hughes
Assistant to DEQ Assistant Secretary Sheila Holman