Secretaries' Science Advisory Board

MEETING SUMMARY
Archdale Building, Ground Floor Hearing Room, Raleigh, NC
Monday, October 7, 2019
10:00 AM-1:45 PM

The Department of Environmental Quality (DEQ) and the Department of Health and Human Services (DHHS) Secretaries' Science Advisory Board (SAB) met on Monday, October 7, 2019 at the Ground Floor Hearing Room of the Archdale Building in Raleigh, NC. SAB members in attendance were: Tom Augspurger, PhD (Chair); David Dorman, DVM, PhD, DABVT, DABT; Richard DiGiulio, PhD; Elaina Kenyon, PhD; Thomas Starr, PhD; Phillip Tarte, MPH; Betsey Tilson, M.D., MPH; and John Vandenberg, PhD. In attendance by telephone was: Detlef Knappe, PhD. Also in attendance were Sandy Mort, PhD, Sheila Holman, Brad Nelson and Randy Strait (DAQ), Virginia Guidry, Kennedy Holt and Kim Gaetz (DHHS), DEQ and DHHS support staff.

I. Call to Order (Chairman Tom Augspurger)

Chairman Augspurger called the meeting to order. He welcomed attendees and asked if any present, or on the telephone, wanted to comment on any agenda items; he had two reply they would like to speak. Chairman Augspurger thanked them for their interest, and indicated he would give them an opportunity to speak.

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 June 3, 2019

The draft meeting minutes were circulated to all members on July 1. Revised minutes were circulated August 5 and September 23. 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. The April minutes were approved and adopted unanimously by verbal vote.

IV. SSAB Member Update

Chairman Augspurger informed the Board that Jacqueline MacDonald Gibson has accepted the position of chair of the Department of Environmental and Occupational Health at

Indiana University. He thanked her for her dedication and service to the Board, and congratulated her on her new job.

Dr. David Dorman has received a Fulbright Scholarship, and has been granted a leave of absence from the SSAB from the conclusion of today's meeting to July 2020. This Fulbright Scholarship coincides with his sabbatical; he will continue to receive emails regarding SSAB business for awareness, but without the expectation of material review or participation in the meetings via telephone, as he will be overseas. This will allow him to focus on his sabbatical, and also reengage with his service to the SSAB when he returns. He wished Dr. Dorman a productive sabbatical, and the Board looks forward to his return.

One final note on staff: Dr. Sandy Mort is retiring from DEQ. The Board was notified of her retirement on August 26, and Chairman Augspurger thanked her for her service to the Board, saying the State of North Carolina will miss her coordination and her attendance, as well as her science contributions, both in writing and verbally. He said he personally appreciated her liaison capabilities between the Board and the agencies, said she had executed those duties very well, and thanked her again for her service. He then recognized Assistant Secretary Holman for her remarks.

Assistant Secretary Holman greeted the Board, and remarked that she knew Sandy wanted to quietly retire, but she felt she needed to publicly thank her for her service, not only to the Board, but also to the two agencies. Sandy served twelve years with Water Sciences in DEQ's Division of Water Quality, and seven and a half years with DHHS in Public Health. She returned to DEQ in 2015, working with the Division of Waste Management, until early 2018, when she took on the role of Environmental Toxicologist for DEQ. "Sandy has been my right arm" in relation to the SAB, said Mrs. Holman. Mrs. Holman went on to express her personal appreciation of Sandy's work, not only with the SAB, but also with DEQ and DHHS, as well as the Department's appreciation and wishes for a happy retirement.

Chairman Augspurger thanked Mrs. Holman for her remarks. He asked if there were any further changes to be expressed; there being none, he reminded the Board that the June meeting had been cancelled, and mentioned the updates that Sandy had provided to the Board on August 5 and 26 in preparation of this meeting.

Chairman Augspurger then turned the meeting over to Dr. Rebecca Sadosky for her Unregulated Contaminant Monitoring Rule study update.

V. Unregulated Contaminant Monitoring Rule (UCMR) study update

SAB UCMR4 Update 09-19.pdf

Dr. Sadosky greeted and thanked the Board and began her study update review. She said the data had just been downloaded just a few weeks ago, and this presentation is to explain what UCMR is, and where DEQ is in the process.

Chairman Augspurger thanked Dr. Sadosky for her presentation and asked if there were any questions. He asked for those compounds that do not have a screening level, if that was only for NC, or if it is system-wide across states in the UCMR process; he was curious as to why they would be measured, if there is no indication of interpretation. In reply, Dr. Sadosky returned to slide 28 of her presentation, which indicated the applicability of UCMR4; that is how the program deals with those contaminants of which there is no health advisory level applied. She explained that EPA has health advisories for about 150 contaminants; there are thousands of chemicals out there, and the research has not been done on all of them. EPA is working on it, but testing is not complete; different states take different actions, according to the need, which may include setting their own health advisory levels for certain contaminants, setting drinking water standards, and so forth. That is not historically what has been done here in North Carolina. Chairman Augspurger thanked her for her explanation. Dr. Starr asked about method detection limits and data on the precision of the maximum and minimum reported concentrations (e.g., confidence intervals for the reported values); Dr. Sadosky replied she would look into his query and get back with him. Chairman Augspurger asked if there were any posted questions; there were none. He again thanked Dr. Sadosky for her timely and informative presentation.

VI. PFOA, PFOS Groundwater Quality Standard (15A NCAC 02L .202) Request for Comment

Chairman Augspurger said this was a late addition to the agenda, and there are copies of the slides and five (5) other attachments available. He called on Ms. Bridget Flaherty for her presentation and asked if Ms. Flaherty would let the Board know what is requested of it, and

what potential action is requested. Ms. Flaherty responded that this request was presented at last month's Environmental Management Commission (EMC) meeting, and she read out the request: *At the request of the Groundwater and Waste Management Committee of the Environmental Management Commission, the Division of Water Resources asks the Secretaries' Science Advisory Board to review and comment on DWR's recommendation to use the 2016 EPA Drinking Water Health Advisory values for PFOA and PFOS as a Groundwater Quality Standard (15A NCAC 021 .0202) for combined total PFOA and PFOS.*

Ms. Flaherty then continued with her presentation, attached here:

SSAB Oct 2019_Flaherty_PFOA

She requested that the SSAB submit its reply to the January 2020 meeting of the EMC. Chairman Augspurger replied that he believed that would work out. He then requested that Ms. Flaherty walk the Board through the attachments; she said they were the following:

- 15A NCAC 02L Groundwater Standards
- PFOS and PFOA Proposed Standard
- Groundwater SOP of September 2019
- EPA PFOS Health Advisory
- EPA PFOA Health Advisory

15A NCAC 02L Groundwater Stand

PFOS and PFOA proposed standard.

September 2019 GW_SOP unsigned.

EPA pfos_health_advisor

EPA pfoa_health_advisor

Chairman Augspurger then asked if anyone had any questions about the charge, the presentation, or any of the supplied documentation. Ms. Flaherty clarified that the Health Advisory is based on the EPA Drinking Water Health Advisory for PFOA and PFOS; Dr. Starr asked for the clarification. There were other questions about the specifics of the reference dose calculation; Ms. Flaherty said she would provide specifics as requested so the Board can make an accurate recommendation. There were no chat questions posted; all participating by phone were unmuted for them to participate, and none added any other questions. Chairman Augspurger thanked Ms.

Flaherty for her presentation and the detailed materials provided. He then asked if there were persons from the audience who wanted to address this specific issue; two people asked to speak.

Michael Watters asked to speak on behalf of the 800 well-owners whose wells are contaminated with PFOS and PFOA. He cited statistics to support his stance that the existing standards do not protect the populace, and he said the Notices of Violation issued to companies producing PFOS and PFOA did not enforce the existing standards. He recommended against adoption of 70 ng/L standards for PFOA and PFOS. He noted that under State rules for compounds that are not naturally occurring and when no numeric standard is adopted, the practical quantitation limit (PQL) drives regulation. He stated that the current PQL of 2 ng/L should be enforced. He is trying to get maps from the State of the wells surrounding the Chemours plant, going door-to-door informing residents of the dangers and levels of PFOS and PFOA in the wells. Chairman Augspurger thanked Mr. Watters for his comments, and his ongoing involvement in the issue. He said there was time for another comment, and any others must wait for the public comment time set aside at the end of the meeting. He then recognized Beth Markasino to speak.

Beth Markasino spoke on behalf of NC Stop GenX, a non-profit organization. She said that DEQ has been aware of PFOA and PFOS for quite a while, having informed DuPont to stop emissions of PFOA and PFOS in 2012; it has continued even to today, with the Chemours plant. They were self-regulating, and have not complied with DEQ's request. Emissions have been documented as still happening, around the Chemours plant, in the wells, in the groundwater and air. She cited New Jersey's, New York's, Vermont's and California's standards, which are lower than what is currently enforced in North Carolina.

Chairman Augspurger thanked Ms. Markasino for her comments, and responded that the Board would take her and Mr. Watters' comments under advisement.

VII. Methyl Bromide AAL Update

Chairman Augspurger then recognized Mr. Mike Abraczinskas for his presentation on methyl bromide (attached here).

2019-10-07_Abraczi
nskas_NCDAQ_MeBr

Mr. Abraczinskas thanked the Board for the opportunity to update them on the Ambient Air Level (AAL) work his Division has done for methyl bromide (MeBr), and what the SSAB recommended in April 2019. In May 2019 the Environmental Management Commission (EMC) approved the following for public comment/hearing (June 17-August 30):

- 0.005 mg/m^3 (24-hr. average time) – based on upper bound value recommended by SSAB
- 0.078 mg/m^3 (24-hr. average time) – minimal risk level (intermediate) from the April 2018 Draft for Public Comment Toxicological Profile for Bromomethane prepared by the Agency for Toxic Substances and Disease Registry (ATSDR)

There were two (2) public hearings held in Raleigh and Wilmington; there were 1,468 comments received with general agreement/support for the rule and use of 0.005 mg/m^3 RfC. However, the matter of concern in the comments was the 24-hour averaging time, primarily from the regulated community and those associated with them. This was the subject of many discussions, and has been the source of uncertainty in those discussions. He reviewed the averaging time rationale from the SSAB recommendations (slide #4 in his presentation), and the most pertinent feedback from the public comments regarding averaging time (slide #5).

Mr. Abraczinskas said, in light of these suggestions and observations from the comments, "do we have it right, in regard to the averaging time?", and asked the Board for their review and input.

Chairman Augspurger thanked Mr. Abraczinskas for his presentation, and asked that he return to the slide concerning the SSAB rationale, and opened the floor for discussion. Mr. Tarte asked that Mr. Abraczinskas review the reasoning behind the exposure scenarios in terms of facility operations; of the five (5) active permits, three are operational and they operate in batches, in short-term exposure, making it rare there is a continued exposure. However, there are busy periods where there are more intense operations, but the most frequent scenario is short batches of emissions over the course of days or weeks, and with some seasonality. There were two (2) major source permit applications that would have expanded the number of operations

considerably, but they were subsequently withdrawn; however, this did open the possibility of higher/more prolonged emissions. There was considerable discussion.

Chairman Augspurger provided commentary on slide #4 noting that the there were additional aspects to the SSAB's rationale on averaging time. He noted that with no specific exposure scenarios provided, there was concern and need to consider all of potential scenarios, and that without an acute RfC to compliment the chronic RfC, these was concern that unbounded periodic high concentrations (and associated effects) could be averaged in with long-term low concentrations and still be in compliance with a long-term average. Also, a previous comment from a SSAB member was reiterated that methyl bromide toxicity may be more concentration dependent versus concentration x time dependent so time averaging needs to consider peak concentrations.

Dr. Vandenberg commented that he had followed up with what ATSDR has analyzed in regard to MeBr, and their 0.005 mg/m^3 RfC was not intended to be applied to short-term situations. He said it can be applied that way and would be very protective, even perhaps over-protective. He referenced the ATSDR 0.078 mg/m^3 intermediate value that went to public comment as an option to consider for short-term exposures along with the potential for an ATSDR no-effect level which may be available in a few months (they are incorporating one more study now). He then asked if the Board can revisit the levels; Mr. Abraczinskas said the public comment period has ended, and the findings have been handed off to the Hearing Officer, a member of the EMC, who will present his determination potentially as early as November. Dr. Vandenberg said he was making the point that ATSDR seemed to be leaning toward the 0.078 mg/m^3 value as protective over an up to 14-d period and there may be merit to considering that as a 24-hour exposure level. Chairman Augspurger noted DAQ originally brought just the chronic RfC to the SSAB for review noting they indicated lack of comfort with data to derive an acute RfC. The SSAB feedback noted that a chronic RfC will have independent utility and we remain available to review studies or approaches on an acute RfC, more focused exposure scenarios, or other new data or perspectives.

Chairman Augspurger summarized the points made by the various members of the Board, and that the recommendation was addressing chronic exposure. Dr. Dorman asked for clarification of what definition is used for chronic RfC in the context of NC rules or legislative

language. Mr. Abraczinskas said there is no language in rule or statute addressing the definition. Dr. Dorman indicated he thought the State desired an estimate protective over a lifetime of exposure and stated further he saw no compelling reason to believe the earlier SSAB recommendation was the wrong one -- perhaps it is conservative, but it is justifiable. Dr. Starr expressed concerns regarding uncertainty factors, the chronic exposure, the use of a 24-hour averaging time and we may need to consider an acute RfC as well. Dr. Vandenberg mentioned the nature of the exposures as short-term batches and therefore the need for an acute RfC to match to those type of releases. Mr. Abraczinskas said that all past practice for all AALs has been to apply a 24-hour averaging time; he reiterated that the question to the Board is if it is appropriate to use a 24-hour averaging time to the chronic RfC for MeBr. Dr. Kenyon spoke to the averaging time issue as well noting the connection to the adverse effect the RfC is trying to protect against -- if there are concerns with short-term effects, then that speaks to need for a short averaging time, and if there are concerns for a toxicological effect from long term exposures, then that calls for a long averaging time.

The Board has considered the chronic vs. acute exposure, and the seeming mismatch of the application of the RfC for both, and advised the agencies that without an acute RfC, the use of a 24-hour averaging time was scientifically supportable. The time to derive and apply an acute RfC instead of just a chronic RfC to reduce this uncertainty is a management issue. Chairman Augspurger noted the SSAB asked early-on for a characterization of the exposures and lacking that, have to address all potential exposure scenarios. Chairman Augspurger summarized the three points of the discussion (comfortable with the chronic RfC, we have to cover all potential exposure scenarios (acute and chronic), and we heard the State was not comfortable with the science to support an acute RfC to address those short term exposures), then asked if there were further comments. Dr. Starr indicated that the compilation of the 5-year data to show the worst 24-hour levels of exposure would be considered the acute level, and the average would be the chronic level. He indicated data could be provided on how different the 24-hour worst case is from the average 24-hour case from a 5-year average.

Chairman Augspurger summarized that there has been no new information on acute studies that might support the derivation of an acute RfC or new information on industry-specific exposure scenarios to prompt the Board to change their findings. Dr. Vandenberg commented

that the 0.005 mg/m^3 is a very protective RfC for MeBr and perhaps with additional work, a higher value may also be evaluated and determined as protective. There were other comments by the Board, agreeing that it is a management decision on whether to wait for an acute RfC or proceed with only the chronic RfC as well as to what is chronic vs. acute from a state regulatory perspective and how to apply the RfC. Chairman Augspurger noted that new science on short-term toxicity values or realistic exposure scenarios would be new information the Board could consider and we're ready to look into those if asked. Mr. Abraczinsaks thanked the Board for their comments and discussion. Chairman Augspurger then called for a short break, to reconvene at noon.

VIII. Hexavalent Chromium (Cr+6)

Chairman Augspurger recalled the meeting, saying the next topic is regarding hexavalent chromium (Cr+6), followed by the public comment period. There was a small group of Board members that drafted a response to the charge and the information regarding Cr+6. This group wrote a summary of the work of the Board and the science behind the recommendation of the Board. This document was circulated for Board review, and he asked for any comments. Dr. Vandenberg asked Dr. Kenyon about the pharmacokinetics of the different valence states. Dr. Kenyon replied that the difference between Cr+3 and Cr+6, which is the toxic version, is that Cr+3 moves more slowly through the tissues, and the biggest uncertainty is not being able to measure the valence state as the site of action. PBPK models can help with this uncertainty in accounting for external dose and dose at a target site. Dr. Starr asked if there are any PBPK models developed well enough to be used for regulatory purposes; Dr. Kenyon replied EPA uses them for several different chemicals, but there is not one for Cr6+ at EPA that is developed and through peer review at this time. Dr. Dorman commented that it seems a non-linear approach is implied by the document, and the PBPK model can be used as a theoretical construct rather than in extrapolation as a point of departure. Drs. Starr and Tilson participated in more discussion of this. Dr. Dorman asked about the mutagenicity data; he said there seemed to be mixed data and that any positive mutagenicity data could indicate default to a linear approach (he asked whether recommending a threshold model would require a 100% null for mutagenicity). Since it seems like there is mixed mutagenicity data, we don't have a null. Dr. Starr discussed some of the mutagenicity data which showed effects only at the highest doses; Dr. Dorman indicated his query was more procedural on whether there were process documents to follow. Dr. Dorman

asked if any of the rules or guidelines, applied by other agencies (e.g., IARC and EPA), would apply to the deliberations of the SSAB. Dr. Starr indicated, from an SSAB history perspective, that there are not Board-specific rules. Chairman Augspurger noted that the draft synthesis document is set-up to follow EPA's guidance on cancer risk assessment. Dr. Mort stated that DEQ would follow the EPA's 2005 guidance on cancer risk assessment. Chairman Augspurger reviewed the charge, stating the Board is to provide recommendations as to what science is to be used to develop regulatory standards:

> ***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.***

There was more discussion of guidelines on what data to use, how it is synthesized, and how genotoxicity is addressed in the EPA 2005 guidelines. Chairman Augspurger noted that there were practical applications to Dr. Dorman's question in that guidance could dictate decision analysis process versus how we have the draft document set-up to weigh the evidence. Drs. Tilson, Vandenberg, Augspurger, Starr, and Dorman discussed the interaction between data and data synthesis guidance we cited in the draft and some of the findings summarized in the section on a mutagenic MOA.

Chairman Augspurger asked if there were any other questions or comments on the draft document; there were none, so he presented an initial draft observation for consideration in working toward consensus recommendations and identifying where the Board lacks consensus, noting that anyone on the SSAB can propose a synthesis statement and see how it resonates with the other members (either working toward consensus or identifying important areas of disagreement):

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> **"The SSAB recommends that State base any health protective drinking water goal on the full body of hexavalent chromium toxicity data, examining the modes of**

action in various in vivo and in vitro studies and applying the low dose-response modeling most appropriate for individual studies and endpoints, then apply a weight of evidence approach to the compiled toxicity data."

Dr. Vandenberg commented he found it a reasonable statement, including the weight of evidence. Dr. Dorman reiterated that the 2005 EPA guidelines state that "a non-linear approach should be selected when there are sufficient data to ascertain mode of action, and conclude that it is not linear at low doses and the agent does not demonstrate mutagenic or other activity consistent with linearity at low doses." He emphasized it is "and", not "or". Chairman Augspurger asked that that concept be held for a moment, since we could craft a summary statement on what decision guidelines the SSAB would use (noting that the State just indicated they would follow EPA's guidelines), but what is up for discussion is his proposed statement on what data to use as one potential summary recommendation moving forward. He indicated the idea of this statement was whether there would be a subset of data to preferentially focus on rather than all of it. Dr. Vandenberg indicated the statement reflected that there is not any data we would ignore. Dr. Dorman stated he could live with the statement as a draft; he asked if a review of the whole body of data would be too large a task rather than focusing on only certain routes of exposure (asking the Board if inhalation and IP data are relevant). Dr. Dorman indicated more emphasis on the low dose data may be appropriate. Dr. Kenyon wanted the Board to give higher priority to the data generated from oral studies of lesions in rodents with data to both inform mode of action and model dose response to derive a health protective value -- NTP bioassays in this case. She would place more emphasis on mutagenicity studies in rodents including mechanistic data. Chairman Augspurger restated the first potential consensus statement, including Dr. Kenyon's suggestions to use the highest quality lifetime studies (probably NTP bioassays) and place the greatest emphasis on studies that inform the mode of action by which adverse effects developed. Also emphasize any mechanistic studies carried out in similar human tissues along with associated pharmacokinetics information. There was no disagreement with the statement in general of placing more emphasis on the lifetime exposure bioassays with mechanistic data to inform mode of action.

Chairman Augspurger said he would work on the statement and send it back to the Board, revisiting the point that Dr. Dorman made on guidelines (EPA, IARC, CDC, NIEHS, other

states, etc.) the Board would follow for crafting recommendations. There was discussion of which guidelines should be used; the general consensus was to use the EPA cancer risk assessment guidelines.

Dr. Starr thought we might need to revisit the first statement which was too broad regarding the most relevant data. He noted that we started with synoptic reviews and presentations rather than all data. We may not need that initial statement of looking at all the data. Dr. Dorman commented that from the first statement crafted, it seems cancer is the driver for creating a recommendation for Cr+6, not looking back at all the toxicity studies, rather looking at the relevant cancer data and relevant cancer mode of action which narrows the data and studies considered.

Dr. Dorman also suggested that the Board recommend the State look at authoritative reviews as starting points, without having to revisit the literature, whether ATSDR, IRIS EPA or other authoritative review documents. Chairman Augspurger asked whether peer reviewed publications would be considered authoritative reviews. They would not be according to NAS per Dr. Dorman. Dr. Kenyon clarified "authoritative review" as independent, peer-reviewed documents. Dr. Tilson said she thought that's what the Board is doing for the State, reviewing the literature in order to craft a recommendation. Chairman Augspurger agreed, stating the Board is helping to guide the State as to where to direct their energies in regard to Cr+6. Chairman Augspurger asked for other potential consensus statements, and hearing none then referred to the following as another potential consensus statement for the group to consider:

> **The SSAB recommends that State risk assessment staff participate in or closely monitor the IRIS update of hexavalent chromium toxicity. The EPA's data synthesis and review is going on now; a contemporary review of that magnitude is extremely valuable for further refinement of mode of action recommendations. According to the most recent IRIS timeline, the target date for the hexavalent chromium Public Comment Draft is late 2020.**

There was discussion of this with Dr. Vandenberg noting that it undr EPA development and then under EPA review so no real role for others to participate at this time. Chairman Augspurger

suggested that using the review the EPA is generating or following its development could be helpful. He then recognized Dr. Mort for her comments.

Dr. Mort said, after consulting with Assistant Secretary Holman, what DEQ wants from the SSAB is to tell the Department if the Board believes there is adequate support for the mutagenic mode of action for the cancer endpoint. There is an IRIS non-cancer RfD that DEQ used; there is an EPA cancer slope factor that was used for some programs, as part of the Superfund screening level program. The question is whether or not a mutagenic mode of action is supported by the literature and studies already done; if it is not, in her personal, professional opinion, the oral cancer slope factor is the most protective, and the Department should continue to use that. The problem with using the cancer slope factor is that it is not an IRIS number; however, the IRIS non-cancer RfD is based on studies done in the 1950s, and there is more up-to-date data available. Despite the problems with those numbers, the amount of time it would take for the Departments' (DEQ and DHHS) toxicologists to make a review of the literature, in light of the fact IRIS is in the process of completing an update, it is not the best use of the staffs' time. The salient point is the question of whether the mutagenic mode of action is supported, and whether the Departments should continue to use the cancer slope factor available currently. Chairman Augspurger replied that the Board is working toward those recommendations at this meeting, just taking it in steps. Dr. Tilson indicated we should be commenting on data sufficiency for a nonlinear approach as an alternative to the more conservative linear approach and to err on the side of being health protective in the face of the associated uncertainty. Dr. Vandenberg stated his perspective that there is enough evidence for a potential mutagenic mode of action. There is uncertainty of cytotoxicity versus genotoxicity which is a sequencing issue. His judgment is that it is reasonable to conclude that drinking water exposure to hexavalent chromium has a potential mutagenic mode of action that leads to a linear approach. Dr. Kenyon said it depends on how relevant you think the NPT bioassays are to humans considering the differences in stomach structure and pH between species. She wanted to hear Dr. Starr's perspective on the data he summarized for supporting a non-mutagenic mode of action. Dr. Starr acknowledges you cannot exclude a mutagenic mode of action, but that there is plenty of evidence for a diffuse epithelial hyperplasia mode of action. While we cannot prove the negative of a genotoxic mode of action, we at least need to acknowledge the other mode of action as plausible and even credible. His judgment is the nonlinear mode is more credible since it pulls

together more types of data. Dr. Dorman noted the Heath Canada review ultimately went with a nonlinear threshold response. Dr. Kenyon noted it speaks to the point she was making about which mode of action studies are most relevant to the putative endpoint being used as a critical effect.

Chairman Augspurger then moved to slide 4 to ascertain how it resonated as a potential consensus statement:

> **Data from drinking water studies with rats and mice have been the subject of robust mechanistic toxicity assessments between 2011 and 2019. Mutagenicity data are negative; there were not dose-related increases in K-Ras mutant frequency, micronuclei formation, or change in mitotic or apoptotic indices. Toxicant localization and histological examinations have helped elucidate the mode of action in the rodent drinking water papers. If considering the mouse and rat drinking water exposure papers only, there is strong support for a non-mutagenic mode of action involving chronic wounding of intestinal villi and crypt cell hyperplasia.**

Dr. Kenyon stated the concern she would have is that inhalation exposure to Cr6+ does result in cancer in humans, so pay attention to what that body of data tells us about studies of Cr6+ in gastrointestinal tissues. Look at mechanistic studies that elucidate mode of action. Dr. Dorman indicated that Canadian synthesis dismissed mutagenic effects seen with Cr6+ in tissues other than GI tract because there needed to be close concordance with mutagenic responses and tumors. But, if you look at the total evidence across multiple organs, it shows mutagenic ability, so you need to ask whether site concordance is a major driver for the mode of action data. That speaks to his earlier comment on guidelines we'd follow since there are data which show Cr6+ is mutagenic.

Chairman Augspurger asked the Board to comment on the draft statement before them focused on the oral route studies and 2011 and 2019 literature on mode of action. Dr. Dorman indicted those are a narrow slice of the literature and there are oral genotox studies with mutagenic effects in other tissues. Dr. Starr said the draft statement could be modified to reference just the oral cavity and stomach. Dr. Dorman said if the basic question is whether Cr6+ is mutagenic, then site concordance is not a major driver. Dr. Starr said we are also looking for

coherence in multiple endpoints in the same tissues. Dr. Dorman stated that you have modes of action for mutagenicity that are not assessed in NTP studies. Are those modes of action that have identified in other tissues being thoroughly evaluated in the gut? He stated the robustness of those assessment for mutagenicity in the gut are much more limited than the wider spectrum of mutagenic responses that have been examined in other tissues.

Chairman Augspurger then moved to slide 5:

The mixed positive and negative results from laboratory studies via non-inhalation exposures, coupled with clear evidence in humans that Cr+6 via inhalation is mutagenic and carcinogenic, provide sufficient evidence to conclude a mutagenic mode of action is potentially operative for Cr+6 exposures via drinking water.

Dr. Vandenberg indicated this statement was OK. Dr. Starr suggested it be reworded accordingly:

The mixed positive and negative results from laboratory studies via non-inhalation exposures, coupled with clear evidence in humans that Cr+6 via inhalation is mutagenic and carcinogenic, provide evidence that a mutagenic mode of action is potentially operative for Cr+6 exposures via drinking water.

There was discussion of this. Dr. Kenyon replied it is these mixed results that give pause to relying on only the earlier statement of the interpretation of the NTP bioassays and regenerative hyperplasia. Dr. Augspurger noted that Dr. Knappe is listening and sent his perspective which he would read:

"I concur that the evidence for a non-linear approach is more compelling than for a linear approach. However, I am not certain that we have sufficiently conclusive evidence to rule out the linear approach. Therefore, I suggest a precautionary approach in the meantime, meaning I favor the more conservative linear approach. Thinking ahead, in terms of a drinking water standard, additional considerations can be included to assure a standard that is both health-protective and technically feasible. But that will be a separate discussion."

Dr. Tilson asked if we could add a clarifying statement that there is evidence for both modes of action and sufficient uncertainty in the literature to choose one or the other. Dr. Starr said it could be stated another way as the remaining uncertainties were large enough that we could not choose among the modes of action, and therefore err on the side of safety. Dr. Dorman indicated some of these uncertainties are 1) data for the non-mutagenic effects in the drinking water studies are fairly limited suite of endpoints, and 2) whether or not you need site concordance in mode of action and tumor site. Chairman Augspurger supplied the following altered statement:

> **The SSAB has considered the strengths, limitations and extent of the available studies. Multiple MOAs may be occurring simultaneously and the sequence of events leading to cancer formation is uncertain. Significant data gaps and uncertainties remain for non-mutagenic effects (e.g. mode of action studies in the rodent drinking water studies address a limited suite of endpoints, and there is a lack of site concordance between mode of action data and tumor responses). We conclude that Cr+6 via drinking water exposure may cause mutational changes, supporting a linear no-threshold dose-response relationship.**

He then asked the Board to read and respond to the altered statement. There was discussion of this. Dr. Vandenberg asked that "for non-mutagenic effects" be removed. Chairman Augspurger stated the altered statement, minus "non-mutagenic", and summarized the other statements' content. Dr. Dorman objected to "lack of site concordance", saying there is a different way to state it: "(e.g., mode of action studies in the rodent drinking water studies address a limited suite of endpoints, and there is evidence of mutagenic responses in animals other than where tumors occur)." Another alteration suggested was replace "animals" with "tissue." Chairman Augspurger said this draft is further along to a recommendation than the Board was several months ago, and he thanked the Board for their participation and suggestions. He said he would circulate the altered draft for review. He then opened the public comment period, asking who had signed in to speak. He recognized Xavier Boatwright [the only one to sign in from Clean Water for NC was Hope Taylor].

IX. Public Comment

Mr. Boatwright with Clean Water for North Carolina, who can see the smokestacks from his backyard in Asheville. We have been asking for information from DEQ regarding Cr+6,

wood preservation, other industrial practices which pollute our wells. This is a very serious issue, especially to the impacted communities. We really do want the Board to help DEQ and developing a standard that is protective of children, the elderly, and other fragile populations, which has not been discussed here. California's standard is seen as protective of those populations, and he encouraged the Board to examine other states' work. He thanked the Board for their time and the opportunity to speak.

Chairman Augspurger thanked Mr. Boatwright for his comments and his attendance, and his commitment to clean water for NC. He then asked if there were others who wished to speak; he recognized Deborah Graham.

Ms. Graham lives in Salisbury, NC and stands against Duke Energy and coal ash; she and her family still use bottled water for the past 1,633 days. She is thankful for the SSAB; she appreciates DEQ for holding Duke Energy accountable for the leaking coal ash pits; her home is within 1,000 feet of three of those pits, and is a cancer survivor as of May 3, 2019. She said the citizens of NC need a health-based drinking water standard that is enforced; she and the other citizens of NC need to be able to trust state leadership again. The standard was stated to be 0.07 mg/m3 for Cr+6; over 942 households received letters that the water was over the standard, hers being one of them (DHHS monitors well water; DEQ monitors city water). These households received a letter from DHHS that the water was over the standard for Cr+6 and unsafe for drinking. She received another letter, 11 months later, from DEQ, saying the water was safe, due to new data studied. She said the "new data" was from a rat study, conducted in 1972. She is not satisfied that is "new data;" she urges that the Board uphold, through recommendation, the site-based drinking water standard it has proposed to DEQ. She asks for a water standard that is protective of the elderly and children, as well as all citizens of NC.

Chairman Augspurger thanked Ms. Graham for her comments and asked if there were any others who wished to comment.

There being none, he asked for a motion to adjourn, and reminded the Board in the December meeting there would be PFAS research from Rebecca Frye and Jamie DeWitt, there would be internal discussion with DHHS regarding the Cr+6 research. He thanked everyone for

their participation in the meeting and moving the discussion forward to recommendation on Cr+6. The meeting adjourned by unanimous verbal vote.

Respectfully submitted,

Louise G. Hughes

Assistant to Sheila Holman, Assistant Secretary for the Environment, DEQ