Secretaries' Science Advisory Board

MEETING SUMMARY
Ground Floor Hearing Room of Archdale Building
January 29, 2018
10:00 AM – 12:30PM

The Department of Environmental Quality (DEQ) and the Department of Health and Human Services (DHHS) Secretaries' Science Advisory Board (SAB, or Board) met on Monday, January 29, 2018, in the Ground Floor Hearing Room of the Archdale Building in Raleigh. The SAB members in attendance were as follows: Dr. Jamie Bartram, Ph.D. (Chair), Dr. Tom Augspurger, Ph.D., Dr. Richard T. Di Giulio, Ph.D., Dr. David Dorman, DMV, Ph.D., DABVT, DABT, Dr. Elaina Kenyon, Ph.D., DABT, Dr. Thomas Starr, Ph.D., Dr. Woodhall Stopford, MD, MSPH, Dr. Michael Stoskopf, DVM, Ph.D., DACZM, Dr. John Vandenberg, Ph.D., Dr. Betsey Tilson, MD, MPH, Mr. Phillip Tarte, MPH (via telephone), Dr. Jaqueline MacDonald Gibson, Ph.D., Dr. Detlef Knappe, Ph.D., Dr. Gina Kimble, Ph.D., and Dr. Viney Aneja Ph.D. Also in attendance were DEQ Assistant Secretary Sheila Holman, DHHS Epidemiology Section Chief, Dr. Zack Moore, DEQ and DHHS support staff, and media.

I. Call to Order (Chairman Jamie Bartram)

Chairman Bartram began the meeting at 10:03 am. He stated that the expectations for this meeting are to ensure that the Board is being provided the information they need to move forward and begin making decisions at the following meeting. He thanked the representatives from the Netherlands for their leadership and for joining the meeting via videoconference. (note that the order of topics was changed during the meeting from the original agenda)

II. Approval of December 4, 2017 SAB Meeting Minutes

Dr. Knappe stated that he had suggested revisions to the meeting minutes prior to the meeting, and the minutes had been revised accordingly. The December 4, 2017 meeting minutes were approved unanimously.

III. Ethics Statement

Chairman Bartram read the ethics statement and reminded the members that if anyone had any potential conflict of interest to so indicate. No one identified conflicts.

IV. Presentation by Representatives from the Netherlands on their Established Health Goal followed by Question and Answer Session

Four representatives from the Netherlands joined the meeting via videoconference.
Ms Petra C.E. van Kesteren MSc
Mr J.J.A. (Andre) Muller BASc
Mr Martijn Beekman MSc
Mr Jan Wijmenga MSc.

Chairman Bartram asked that they walk us through how they arrived at their own water quality standard, and then they would have some discussion with the Board Members. Dr. Muller presented how they came to their water quality standard of 150 ng/L. He said that they used all available data and the same documents provided to the Board, except that they used one additional study that they did not see on the list for the Board, which was a 2017 study on GenX in mice but it is not likely to change the water limit. They derived a point of departure of 0.1 mg/kg body weight per day from the chronic study in rats, then compared GenX with PFOA, because PFOA is known to have a large difference in toxicokinetics between humans and test species, and since they were not sure if that was also applicable to GenX, they applied an additional factor of 66, which is the difference between the half-life of PFOA in humans compared to monkeys and applied the factor of 66 to GenX. They did not use an additional factor for sub-chronic to chronic because it was a chronic study, used the default value of 10 for variation between humans, and used 20% of the total allowed daily uptake for water, and assumed two liters of water for an adult of 70 kg.
Chairman Bartram asked the Board if they had any questions.
Dr. Starr asked if it was correct that the half-life they are using is for PFOA, the difference between monkeys and humans.
Dr. Muller said that is correct, they compared the half-life of PFOA in monkeys and humans and calculated a factor of 66, and applied that factor to GenX as an additional safety factor, since they were not sure that the same interspecies difference which was found for PFOA isn't also applicable to GenX.
Dr. Starr asked if there is any reason to believe that it would be the same factor, that the half-life of GenX in humans relative to monkeys would be 66.
Dr. Muller said there is no direct evidence that it would be the same, but there is a chemical structural similarity between both substances, there is a similarity in toxicological effects, and PFOA is not the only substance from this group of substances which shows clear differences in half-life between humans and animals, so from a precautionary point they applied the additional factor.
Dr. Starr asked if they have any way to characterize how much different from 66 the ratio could be for GenX.
Dr. Muller said they did not know, the factor of 66 was the only value they had that would indicate what the difference could be, but there is no GenX-specific information with regard to the half-life in humans.
Dr. Starr said this is a data gap that he is calling attention to that has been substituted with an assumption without any support in terms of compound-specific data, and it speaks to the point that he raised in the last meeting, which is that there's a lot of uncertainty in this process that is not reflected in a single number when you add it in to a calculation like this, and there needs to be some explicit way when they do this to speculate on the range that number could be within. He did not hear anything that would cause him to choose that number over any other.
Chairman Bartram said he understands that Dr. Starr is saying that if you only have one number, that number is your best, but it is very imprecise.
Dr. Starr said that is correct, and he is asking for consideration of how uncertain that number could be.
Dr. Dorman asked them to speak on the rationale for why they selected that point of departure, and clarified that they used a chronic study to derive the initial point of departure for the derivation of the water limit.

Dr. Muller confirmed that they used that study because it was the longest study available to understand the chronic impacts of human exposure, so they preferred to use the longest study available so they did not have to apply additional factors.
Dr. Dorman asked what outcome they focused on when deriving from that chronic study.
Dr. Muller said the effects in the chronic study were effects on the liver and the albumin and albumin/globulin ratio at the lowest effect level.
Dr. Knappe said he had a question regarding PPARα (peroxisome proliferator-activated receptor alpha) mediated effects of fluoro-chemicals, because some people would argue that there is no human health relevance when it comes to PPARα, but in their report a more nuanced approach was taken where they recognized that some PPARα effects may not be human health relevant, whereas others are. Dr. Knappe asked them to comment on how they analyzed the toxicological data and decided what is and what is not human health relevant.
Dr. Muller said if one looks at the opinion of the Risk Assessment Committee (RAC) of European Chemical Agency they looked at data from PFOA, and they got the impression that the direct effects of GenX are applicable to humans but some of the secondary effects which could include carcinogenicity may not be applicable because of PPARα, but it is difficult because there is not much data available for GenX itself, so they had to look at other substances.
Dr. Dorman asked if they had considered using the chronic NOAEL as their point of departure and then adjust from the NOAEL to derive a water limit knowing the questions regarding the uncertainty about the relevance of health effects seen at the LOAEL for humans. He said they could treat it as a negative study with a NOAEL for effects on liver, kidneys, etc. and then use that as a point of departure. He asked if they ever discussed that internally.
Dr. Muller said there was some discussion whether they use the 1 mg/kg as the NOAEL, but if they also look at the other studies with mice, for most of them the 0.1 mg/kg was derived as a NOAEL, so to be in line with these studies and the direct chronic data, using the NOAEL of 0.1 was the best way to derive the water limit.
Chairman Bartram asked for any more words of wisdom.
Dr. Muller said no general advice, and they wish the Board the very best as it is not an easy task.
Dr. Aneja said they have given some guidance to the Board on water quality standards and drinking water. He wonders if they have given any consideration on what the standards might be for air.
Dr. Muller said in their report they derived an air limit, and it was actually the first limit they had derived.
Dr. Aneja asked if they were examining a combination of air exposure and water exposure.
Mr. Beekman said the setting of limit values takes into account that exposure can occur from several sources, so for setting the drinking water limit value, for instance, the general rule is that only 20% of the total allowable daily intake (TDI) would come from exposure from drinking water. Taking that into account the drinking water limit value is set. If your drinking water has a concentration of GenX up to the allowable limit, only 20% of the allowable TDI would be through drinking water, just to be sure that additional exposure through air or through food may not lead to a hazardous situation.
Dr. Tilson said there was a discussion at the last meeting regarding using a relative source contribution other than 20% depending on the site-specific factors, such as geography.
Mr. Beekman said exposure at the factory in the Netherlands for people living within 2-5 miles of the facility is only for air and maybe also food because they have a different drinking water source that is not contaminated by GenX. The main exposure for people living beyond 5 miles is through

drinking water, as the water source is downstream of the factory, but exposure through air would be non-existent.
Dr. Aneja asked if 2-5 miles was arbitrary or set using modeling.
Mr. Beekman said a dispersion model was run to estimate exposure to people via air, and that for exposure outside the perimeter of the factory, the limit was not exceeded, so it is not a driving force for them. They are also doing an analysis of crops grown, within a one mile radius. There have been samples taken from vegetable gardens, and they received the initial results last week but have not checked or verified the results yet, but it might be a relevant source of exposure for people living close to the factory.
Dr. Knappe said in the ES&T (Sun et al. authors) paper there were other compounds in the water besides GenX. He is curious if they are pursuing additional standards or health goals for those compounds, or whether the existence of those other compounds affect how they view their GenX health goal.
Mr. Beekman said this is an interesting question because there is the issue of additional substances that might work on the same endpoint. They know historically PFOA has been used at the factory Dordrecht and has been emitted so that is a concern. For the time being they have not found any other byproducts, but he knows that in NC the Nafion® production could give byproducts which could also lead to exposure, but they do not have that kind of production. In the Netherlands, it is purely a production of Teflon® and other polymers, and GenX is not produced there, it is only used. Nafion® byproducts have not been detected.
Dr. Knappe asked if there had been any follow up on field data or fish testing for bioaccumulation in fish or other aquatic animals.
Mr. Beekman said they do not have any additional testing results, but the facility is required to do fish testing as part of their permit applications requirements, and they will have the results of this testing in May, and they will hopefully be able to revise the water quality standard for the factory.
Dr. Knappe asked if they varied the relative source derivation of 20% based on the expected exposure variations between air, water, and food.
Dr. Muller said they used 20% as the default for drinking water.
Dr. Knappe asked what type of crop they are referring to when they mention food, and if they were referring to corn.
Mr. Beekman said the university did a study on leaves and grass for PFOA and GenX. Since this is not easily transferable to edible crops, they decided to test vegetable gardens for PFOA and GenX at 10 sites at various distances from the factory. They tested carrots, beet roots, lettuce, several other vegetables, about 60% of samples had no detected PFOA or GenX. Gardens very close to the factory did show GenX and PFOA at measurable levels. An estimation was made of a person's possible exposure from the garden, considering how much they might ingest from the garden. They also considered the effect of washing the vegetables, and the sample size was limited as it only included vegetables available during the month of testing.
Dr. MacDonald Gibson asked if their relative source contribution considered additional potential exposure from consumer products such as non-stick pans. She asked if they also attempted to do any kind of formal uncertainty analysis where they represented all of the random variables in their calculations.
Mr. Beekman said a statistical analyst did conduct such an analysis for random variables. Consumer products would not be considered a relevant source as they would not contain any GenX or PFOA, certainly not after the first few uses as it should not be part of the finished product, but they are unsure about products that contain Teflon® in spray form. The EU has decided to limit

the allowable level of PFOA in virtually all applications starting in 2020, so the levels are expected to drop off dramatically. They have no data on whether GenX can be found in products or not.
Dr. Knappe asked if they have also considered looking at eggs and dairy products.
Mr. Beekman said they discussed this with the products authority last week. No data is available from Europe or the Western Hemisphere. There is data on eggs from China but the exposure level there is not the same as it is in the Netherlands so is not comparable.
Dr. Knappe said there is a Swedish study done on eggs showing that the PFOS levels can be quite high. He asked if they have done sampling of air emissions.
Mr. Beekman said they had not done measurements for air, emissions samples have not been taken except by Chemours.
Dr. Knappe said they have derived a TDI for total exposure and asked if they have actually been applying risk assessment measures to see what the total potential exposure is to individuals from drinking water, bathing, showering, from food, from air exposures, from consumer products, and are they actually moving toward that. He asked if they have done anything like that for individual source of exposures or total.
Dr. Muller said they had not done that yet and the questions are still ongoing and are relevant.
Mr. Beekman said they also found an additional source of GenX which is a company that dries Teflon® for Chemours. He said samples taken in nearby water bodies found very high levels of GenX in the mg/L range. They also found GenX in a pond used for recreational activities like swimming, and assessed whether swimming could be a relevant exposure source for humans, but it was not considered dangerous at the levels found.
Dr. Knappe asked if they anticipated doing a risk assessment for certain types of exposures or in total.
Mr. Beekman said since the second source was found over Christmas the factory's nearby municipality has come to them with multiple questions, and they are working with them on it, but at the moment they do not have an answer for that question.
Chairman Bartram thanked the Netherlands colleagues for their time and support and wished them success in their own endeavors before ending the videoconference, and then asked the Board if they would like to have any further discussion on the topics discussed.
Dr. Starr commented that he was confused by the answer they provided to Dr. Dorman on the LOAEL vs NOAEL choice, and the comment they made that the point of using mg/kg/day seemed to arise from other studies, other than the rat chronic study.
Chairman Bartram asked if the Board wanted to follow up with a message to the Netherlands colleagues.
Dr. Dorman said ultimately what the Board will need to do is defend their own point of departure.
Dr. MacDonald Gibson suggested that in the calculation of the reference dose they are dividing the point of departure by 3 different uncertainty factors, an intake rate, a body weight, and then multiplying it by a relative source contribution, and each of those has either uncertainty or variability in it by orders of magnitude, and the choice of any of those things is a policy matter, and is not based on science. She said she does think it might be worth exploring representing what those uncertainties might be and putting it all together just to see what is the range of uncertainty as best we can quantify it right now. That applies to the point of departure also as there are multiple possible choices. It is uncertain which is the best study. There is experimental error in the studies and it would not be too difficult to do this, and she thinks rather than just picking numbers almost out of thin air with these uncertainty factors and relative source contributions they have to look carefully at what the real range is of those potential simulations and it would not be that difficult.

Chairman Bartram asked Asst. Secretary Holman about the mention at the end of the call about a source of exposure from a drying facility that they were subcontracting in the Netherlands, and asked if she knew whether Chemours has similar subcontracted facilities or drying facilities here in NC.
Asst. Secretary Holman said DEQ does not believe that is happening in NC but they are working with the company to verify that. She said DEQ asked early on where products are going, but DEQ is verifying where any of the products such as sludge are going, and verifying any possible places in the environment in NC the chemical may be going.
Chairman Bartram suggested that DEQ find out if Chemours does their drying on site, and if not, ask them where drying is done.
Dr. Knappe said they are making fluoropolymer onsite, just not Teflon®.
Dr. Stopford noticed that they are using a different study for developing their risk assessment than NC is and he concurs that if you have a chronic study and it's at a NOAEL of 0.1 mg/kg/day, that is the that should be used, not a 28-day study.
Chairman Bartram pointed out that other Board members agreed. He mentioned the letter that the Board members had received which raises the issue of human relevance of outcomes of some of the selected studies.
Dr. Aneja said he remains ambivalent based on the discussion from the Netherlands saying they have made no attempt at determining the source strength and yet they have done the dispersion modeling, and he is wondering how that can be done. He said you need to know the source strength to be able to do it, or maybe they did it for another species altogether, so he is a bit concerned.
Chairman Bartram said he was also concerned and when he read the report his impression was that they had gotten that data, so he wants to review that report again because he did understand how a dispersion model can be done with no data input.
Dr. Dorman said he had the impression that they did have data but it was obtained from the company, they did not do testing themselves.
Dr. Knappe said likely the data is from process models, not actual data, and that DEQ is also doing models.
Asst. Secretary Holman confirmed that DEQ is running process models, but will have stack testing data soon.
Dr. Augspurger said it will be prudent to find out the results of fish testing for bioaccumulation.
Asst. Secretary Holman said they will have results by May 22, 2018.
Dr. Tilson said she is still having difficulty reconciling sub-chronic vs point of departure of 0.1 mg/kg and is not sure why they used it.

Clarification from Beth Dittman (DHHS) – note that this was not covered during the meeting, but is being provided to add clarity on this issue:

As clarification, RIVM used a NOAEL of 0.1 mg/kg/day from the 2-year rat study as a point of departure for their GenX drinking water limit derivation. They determined this NOAEL based on increased albumin/globulin ratio in male rats exposed to 1 mg/kg/day GenX. It is important to note that the registrant deemed this endpoint as non-adverse, which is why the registrant reported a NOAEL of 1.0 mg/kg/day for the 2-year rat study. For explanation on RIVM's perspective on the relevance of this endpoint, see pg. 81 of Beekman et al 2016. For the registrant's perspective on the relevance of this endpoint, see section 4.2.6.4 of the study report titled "Combined Chronic Toxicity/Oncogenicity Study 2-Year Oral Gavage Study in Rats".

N.C. DHHS used a NOAEL of 0.1 mg/kg/day from two sub-chronic studies in mice as a point of departure after consultation with risk assessors from the U.S. EPA. Per email communication with the EPA: "Consistent with the point of departure (POD) used in EPA's 2008 Standard Review Risk Assessment and based on similar effects observed in longer term studies, EPA intends to use a NOAEL of 0.1 mg/kg/day in its re-assessment of GenX. This NOAEL (0.1 mg/kg/day) was determined in two separate mouse studies: repeated dose 28-day oral toxicity study in mice and oral reproduction/developmental toxicity screening study in mice. While the lowest NOAEL determined in the oral chronic toxicity/oncogenicity study in rats (1 mg/kg/day) is from a study which employed a longer dosing duration, this NOAEL is higher than the NOAEL of 0.1 mg/kg/day from studies in mice."

Dr. Dorman suggested the Board follow up on the question with a formal letter.
Chairman Bartram said the Board is looking forward to the May results.

V. Follow-up from December 4, 2017 Meeting on GenX Health Studies, Dr. Zack Moore, DHHS

Dr. Vandenberg asked if the presentations given during the meeting would be available as they are helpful to have access to, and the Board members stated that they are posted on the SAB meeting website and available to the public.

a. Presentation on Point of Departure in response to questions raised during or after the December 4 SAB meeting

   Dr. Moore said that a question had been raised regarding the selection of 0.1 mg/kg/day point of departure, and stated that this was a no adverse effect level (NOAEL) that has been seen in two mouse studies, one being the 28-day oral toxicity study in mice, another being a reproductive and developmental toxicity screening in mice. Dr. Moore provided a summary table of these studies and the NOAELs that were determined from the studies. To address Dr. Tilson's question from the prior discussion, the NOAEL from the two-year chronic rat study that was determined by the registrant was 1 mg/kg/day for cancer, but for other effects it was 0.1 mg/kg/day, which was the interpretation of the Netherlands. 0.1 mg/kg/day is the level at which there were changes to the albumin to globulin (A/G) ratio. The level DHHS selected of 0.1 mg/kg/day is the lowest available, it is supported by other studies and referenced by other groups, and by the EPA in the 2008 standard review risk assessment and they have indicated that they are planning to use this same NOAEL going forward since it is consistent with effects observed in longer term studies.

   There was a question about the choice to use a non-cancer endpoint and whether there was sufficient data available to calculate a cancer slope factor and use cancer as an endpoint for these calculations. The two-year chronic rat study did show an increase in certain tumor types, however some of those tumor types did not exhibit a strong dose-response relationship, others were seen only at the highest dose, so we do not have all of the information needed or staff to calculate a cancer slope factor, or choose the correct model needed, so like the Netherlands DHHS opted to select the non-cancer endpoint for our derivation. Dr. Moore provided a table entitled *Repeated Oral Dose Studies ≥ 28 Days*

Submitted by Registrant to show the multiple studies which used the 0.1 mg/kg/day NOAEL level associated with similar with similar endpoints of liver outcomes, and similar order of magnitude of order. Dr. Dorman commented that the information provided should also show the source of the studies, and that the table is confusing as it appears to show that the adverse effects occur at the given NOAEL levels, which is not the case. Chairman Bartram asked that the table be clarified prior to posting on the SAB webpage, and Dr. Moore replied that it would be clarified. Dr. Stopford asked if the Board can assume that the information provided by Chemours is from previous studies done by DuPont, and Dr. Moore confirmed that the information provided was a part of the supporting studies for the registration, except that he did not believe DHHS received the business information on the last study listed in the documents provided to the Board for this meeting, which was the prenatal and developmental study in rats. Dr. Vandenberg mentioned that some documents provided were labeled as confidential, and asked if they should be treated as confidential. Asst. Secretary Holman clarified that the company has agreed to allow the documents to be posted on the public SAB website. Dr. Kenyon gave a follow-up comment to what Dr. Dorman mentioned, stating that one of the questions she will be looking to determine in a study where multiple dose levels were used is whether it is amenable to benchmark dose modeling because it lets you use all the dose response information and is not constrained by the specific dose levels that were selected for the study. Dr. Moore responded that the information that has now been provided by Chemours may allow for benchmark dose modeling, although the summary information provided at the time was not sufficient, and that DHHS would be interested in the Board's opinion.

Dr. Moore also discussed the PPARα issue that was raised in a letter to the Board members, stating that the concern that the liver toxicity endpoint used by DHHS did not have relevance to human health because it may have been dependent on a PPARα mechanism of action. Dr. Moore reported that many of the toxicity studies for PFOA have been conducted in PPARα-null or humanized rodents and adverse effects on the liver were still present. So while PPARα mediated effects do appear to be an important mechanism of action, they do not appear to be the only mechanism of action for liver toxicity. Supporting documentation from EPA's PFOA and PFOS lifetime health advisory indicated that hepatic necrosis, fibrosis, inflammation, or steatosis, should be considered relevant to human health, as opposed to hepatocellular hypertrophy (increased liver-to-body ratio) which would be considered non-adverse as there was evidence for PPARα activation in that endpoint. In the studies that were used for DHHS's point of departure, hepatocellular necrosis was among the endpoints of liver effects and therefore considered relevant to human health. A Board member asked if the NOAELs for those other effects would be any different than the one that was used as a basis for the provisional health goal. Dr. Moore replied that they would not be any different to his knowledge, with the exception that he cannot speak to the chronic rat study, but the same finding would be true for the NOAELs for the other studies. Dr. Stopford asked if an article last month in the Archives of Toxicology on a review of the relevance of PPARα had been factored into DHHS's calculations. Dr. Moore replied that it had not been factored in, and Dr. Stopford asked that it be included in a discussion for the next meeting.

b. Review of Uncertainty Factors

- Intraspecies Uncertainty Factor – this factor is used to account for the variation in sensitivity to toxic effects among members of the human population. Differences in sensitivity can be due to a variety of factors and the value that was used in this instance was 10, which is the default value and there is not enough evidence to deviate from the default value, similar to the colleagues from the Netherlands.
- Interspecies Uncertainty Factor – aware that some PFAS show vast differences in interspecies kinetics and have much longer half-lives in humans as compared to some of the experimental animals, however there is not enough information to determine interspecies variability for GenX, there is no specific human data for GenX on pharmacokinetics or half-life. There has been some evidence that GenX has a shorter half-life compared to PFOA in rodents and primates. DHHS made the decision that there was not sufficient evidence to deviate from the default value of 10, which is different than the decision that was made by the Netherlands colleagues who used 66 based on the experience with PFOA.
- Sub-Chronic to Chronic Uncertainty Factor – this factor is used to account for uncertainties in extrapolating from any less-than-chronic NOAELs to chronic NOAELs since it is generally assumed that longer exposure times could result in adverse effects at lower concentrations. The study that DHHS chose as their key study, which was the same study that was used by EPA in their decision-making, is a sub-chronic study so DHHS did use a value of 10. Since the same NOAEL was used by the Netherlands but from a chronic study, they did not include this uncertainty factor in their calculations.
- LOAEL to NOAEL Uncertainty Factor – this uncertainty factor was not relevant here since we had an available NOAEL, so DHHS did not include this uncertainty factor.
- Modifying Factor – this is an uncertainty factor that can range between 0 and 10, and depends on the professional assessment of scientific uncertainties of the data base not explicitly treated by any of the other uncertainty factors. Not used in calculation of the Provisional Health Goal for GenX in drinking water due to NOAELs from several studies identical or within same order of magnitude with identical or similar health endpoints (i.e. liver toxicity); and uncertainty factors adequately address uncertainties of the database. (default of 1)
- Reference Dose Calculation - showed how those factors were used in deriving the reference dose of 0.0001 mg/kg/day

c. Discussion of Relative Source Contribution

The Relative Source Contribution is used to account for potential other sources of the contaminant, for GenX little to no information currently available about other exposure routes. When there is an absence of information about other potential sources of exposure in the environment, the default for a drinking water calculation would be 20% of the relative source contribution, so this is what was used, and which is intended to err on the protective side of populations that have multiple potential exposure sources. This is what is also used for the EPA lifetime health advisory for PFOA and PFOS and is what is used in the North Carolina 15A NCAC 2L groundwater calculations for organics. Dr. Moore provided a slide summarizing how the reference dose, relative source contribution, and points of departure and uncertainty factors were used to calculate the provisional health goal for GenX. The body weights and intake rates used in the calculation were for infants,

as they are the most vulnerable population, and were based on the volume of water per body weight that they consume, which led to the provisional health goal of 140 parts per trillion.

Dr. Vandenberg mentioned that benchmark dose modeling could be used to determine the point of departure instead of NOAEL, but that is based upon doing modeling of the doses available. A quick look at the data that was provided showed that there were several dose groups that were used, and asked if DHHS has had a chance to look and see if that data would be suitable for benchmark dose modeling to replace the NOAEL as the point of departure benchmark. Dr. Moore asked Beth Dittman, M.S., Environmental Toxicologist with DHHS to provide an answer to the question. Ms. Dittman stated that most of the studies for registration which were provided usually had 3 doses plus the control sometime and that EPA Risk Assessment Division staff indicated that the data would be sufficient for benchmark dose modeling and the input of the Board would be welcome. Dr. Vandenberg stated that it uses more information when you use the modeling and it can give you a more precise point of departure and can provide a stronger scientific case. He asked if DHHS will do the modeling, and Ms. Dittman said she does not know that they have the resources right now to do the modeling and have not had the experience doing so. Although she is aware that EPA has made the model suite available online and she is familiar with the concept of benchmark dose modeling, she has not done it personally, and mentioned that the Board has quite a bit of expertise as well. Chairman Bartram asked when the results of modeling would be available to the Board, if the modeling was possible, and said that it seems the answer to that question is that it is not known, so he asked how we can move this forward. Dr. Moore said input from the Board would be welcome on the subject, but the modeling is not something that is planned to be forthcoming from DHHS. Chairman Bartram stated that the Board would likely prefer to use the data that are available to do benchmark dosing instead of the NOAEL as the point of departure if it is suitable. Dr. MacDonald Gibson stated that running the modeling itself is really not that difficult since you can download the software and there are instructions from EPA, and she could have students do it pretty easily, or someone from DHHS staff could follow the instructions. The only difficult part is that you do have to make a number of judgement calls about which type of model you want to use. Dr. Aneja asked about the intake used in the calculation and if it only refers to the intake of water, or if it includes intake from other sources. Dr. Moore replied that it is only referring to water intake. Dr. Aneja mentioned that maybe food and air intake also need to be considered, and asked how DHHS accounts for this discrepancy. Dr. Moore said it is accounted for with the relative source contribution default estimate that 20% comes from water, which is intended to be conservative or protective. Although it is possible that it could be below 20% from drinking water, but he did not anticipate that this would be the case with GenX, based on other PFAS compounds. Chairman Bartram said that there is a perverse outcome by applying very low attributed fractions in this approach where, as an exposure route becomes less important, it is regulated more stringently, so the 20% is more than simply something that is protective. Unless there is very strong evidence to force down the apportionment lower, it can have a perverse regulatory outcome, so it is not as simple as erring on the low side to be on the safe side, but can create very strange outcomes in some circumstances. This decision to go

below 20% attribution may appear conservative but can mis-orient regulatory effort by over-emphasizing exposures of low significance.

Dr. Dorman wished to revisit the discussion of benchmark dose modeling, and while inputting data into the spreadsheet can be easy, the challenge can be in deciding which endpoint you are actually modeling because you will have many histopathology, clinical chemistry, etc. so it's not clear to him from a Board perspective what endpoints they would be modeling. He said it would be helpful to have a robust evidence table stating for example that the evidence of toxicity in these studies was based on clin-path change and this is the magnitude of the change, versus histologic evaluation because you are going to end up having apples and oranges; although on face value the studies may sound very similar, the actual endpoints you may be trying to model may be quite different. Dr. Moore said that there is such a table prepared by EPA with distinct endpoints that can be provided to the Board. Dr. Dorman asked if it include the CBI data that they were given the day before, and Dr. Moore confirmed that it does, and Dr. Dorman said the evidence table needs to get updated with the CBI. Dr. Vandenberg said they really need to see the evidence tables to support the summary judgements, and that it is not hard to model, but it can be the documentation that is very challenging. Dr. Dorman said the transparency of how they are choosing specific endpoints within the body of evidence is also important. Dr. Vandenberg said he was not sure he understood the point made of not having time to do modeling, and Chairman Bartram said he wanted to be clear whether there was a reasonable expectation that they might have the outcome of modeling available for review so that decisions could be made the next time the Board meets, and does not know the answer but he knows that is a lot more involved in this than simply plugging data into a spreadsheet, but he does not know what the reasonable expectation looks like. Dr. Dorman said he feels that once they have the robust evidence table is put together, they will be able to identify the endpoints they want and the model they want to apply and run it through the EPA models, so the biggest trick is making sure they have the evidence table. If the state can provide the evidence table as a draft for review, they can know how complete it is. Dr. Moore said they will make every effort to get the evidence table to the Board. Chairman Bartram asked if we need the table in advance of the next meeting. Dr. Dorman asked if they could have it a few weeks ahead of the meeting to review it and send it back with any questions or revisions. Dr. Vandenberg said they have the modelers at the EPA and can carve out the time for training state staff. Once the state has completed tables they can get the model set up which is a substantial effort, but he has not had a chance to review the data yet. Dr. Moore said they have colleagues at EPA they can turn to and will make every effort., and make sure they are plugging in all the correct information that is needed. Dr. Vandenberg said the timeline is feasible for the next meeting but it would require the state to do the preparation work. Dr. Dorman said they would need to have incidence data for each of the dose groups, and can have further discussions on the specifics and what evidence to use. Dr. MacDonald Gibson said that is where the expert toxicological judgement comes in that takes the time. Dr. Starr asked if the table will include the 28-day studies and the chronic studies for non-cancer endpoints. Dr. Moore said both studies will be included.

Dr. Dorman said the Board should provide comment on what the general approach the state has used to date, and that the approach is the common or classical approach and is consistent with how EPA has done it, and that he would not have done it any other way. He wants the public to have some trust in the state's approach so far. Dr. MacDonald Gibson agreed that the approach is exactly the same approach used by the EPA to set maximum contaminant levels under the safe drinking water act for decades, so the state is completely consistent with national policy setting approaches, so her comment is only that she thinks there are problems with the way the nation has been doing it, and that there are better techniques available these days, but everything the state did is in line with national policy. Dr. Vandenberg agreed that outside of these beginning discussions about using benchmark dosing, everything done so far is the straightforward approach and what the Netherlands had done is a little unusual. Dr. Knappe said a topic to discuss is that the discharge from Chemours had other compounds at higher concentrations than GenX, so they should keep in mind that GenX is a by-product in a mixture of other by-products, whereas the Netherlands plant releases Gen-X predominantly. Dr. Moore said that is also a concern the state has, and that there currently is not information available to do these type of calculations, and then there is the question of cumulative or additive toxicity which they have been discussing with other colleagues dealing with this same issue, and that there is not currently a basis for assuming a cumulative approach.

VI. Discussion of SAB Deliverable Expectations by DEQ and DHHS

Chairman Bartram requested that DEQ and DHHS provide some clarification on what type of deliverables the Board is being asked to or will be expected to produce. Asst. Secretary Holman referred to the discussion at the December 4 meeting regarding the SAB Priority Table, and requested that the Board members provide DEQ insight and assistance with setting a reference dose which would then be used to establish water quality standards for GenX. She referred to the fact that the previously established Science Advisory Board was charged with guiding DEQ in establishing air quality standards, so previous SAB documentation could be provided to use as examples. Dr. Zack Moore requested that the Board members review and provide recommendations on the derivation and calculation of the health goal for GenX, including the point of departure, factors, calculations, the option to use the benchmark dose in lieu of a NOAEL, and feedback on any future modifications. Dr. Augspurger asked if these two charges should be completed concurrently, or if one charge had priority over the other. Dr. Moore replied that the charge to review the health goal should have priority to establish processes, and because the health goal and processes can be shared with DEQ to advise the regulatory perspective. Dr. Augspurger suggested that the Board should first recommend any modifications to the health goal calculation. He also asked why Assistant Secretary Holman had mentioned the reference dose, and she responded that DEQ needed the reference dose to begin work on setting (risk-based) water quality standards. Chairman Bartram asked if these charges/priorities should be housed in the SAB Principles and Practices document which could be a living document.

Dr. MacDonald Gibson asked in what format the Board's review should be provided, and if the Board should be actively seeking assistance and comments from other states by generating a report or documents to send out for comment. Asst. Secretary Holman stated that DEQ has been corresponding with other states and will continue to correspond with other states who are working

on similar issues. DEQ recently met with staff from Michigan DEQ who shared their recent experience working with an advisory board to handle PFOA and PFOS contamination. She suggested that DEQ can assist the Board by drafting reports or other documents containing the Board's recommendations, and providing the drafts to the Board for the review, revision, and approval prior to distribution of final reports. Dr. Vandenberg expressed concern that in his experience, boards normally work independently of the agency. Chairman Bartram clarified that the two agencies would only assist the Board with drafting documents, but the Board would have final approval of any reports issued by the Board. Dr. Vandenberg asked if this would be a conflict of interest. Chairman Bartram clarified that it would not be a conflict if the task of this Board is to review the work product of DEQ and DHHS and provide comment and advice. Dr. Dorman asked what the Board's role is, especially regarding assisting with regulatory decisions vs. policy decisions. Asst. Secretary Holman, with the assistance of DEQ staff Connie Brower, explained that the Clean Water Act requires that water quality standards be established, and in North Carolina they are established in state regulations which are adopted under the authority of the Environmental Management Commission (EMC). Asst. Secretary Holman then stated that the health goals established by DHHS are set by policy, and are not set by regulation. Chairman Bartram clarified that this Board's role is to review and provide advice/comment to DEQ in setting the water quality standards prior to presenting the standards to the EMC for adoption. For example, if science suggested that a policy or proposed regulation or standard is contradictory or inappropriate, this Board should point out the contradiction, etc. and provide comment. Dr. MacDonald Gibson pointed out that many aspects of health goal calculations are policy decisions, generally set by the US FDA long ago without basis in science, which later advised the US EPA calculations. Dr. Augspurger said that it is appropriate for this Board now to recommend tools or calculations or factors that are more specific and directly applicable to the current situation and to the specific compounds in question.

VII. Discussion of Precautionary Principle

Chairman Bartram asked Asst. Secretary Holman to speak on the idea of the precautionary principle in response to multiple comments the Board has received related to the idea. Asst. Secretary Holman said that DEQ had developed a brief background document to summarize the precautionary principle concept. The four approaches to the precautionary principle are as follows:

a. Non-preclusion: scientific uncertainty should not automatically preclude regulation of activities that pose a potential risk of significant harm.
b. Margin of Safety: regulatory controls should incorporate a margin of safety. Activities should be limited below the level at which no adverse effect has been observed or predicted.
c. Best Available Technology: activities that present an uncertain potential for significant harm should be subject to the best available technology requirements to minimize the risk of harm unless the proponent of the activity shows that it presents no appreciable risk of harm.
d. Prohibitory: activities that present an uncertain potential for significant harm should be prohibited unless the proponent of the activity can show that it presents no appreciable risk of harm.

The European Union has incorporated the precautionary principle into environmental legislation. She discussed a document developed by the European Parliamentary Research Service, which may warrant further review. There is less effort to embrace the concept in the US. As with other states,

North Carolina's primary regulatory mechanism is through risk management. However, one example of this principle in practice in the US is the City of San Francisco, which conducts a full evaluation of the risk to the environment for all the city's purchases from cleaning supplies to computers. Dr. Vandenberg asked why the San Francisco example is relevant if current law in North Carolina focuses on risk management. Asst. Secretary Holman responded that the example shows the concept of the precautionary principle in relation to risk management. Chairman Bartram clarified that he felt it was important to discuss the principle to respond to comments from the public during SAB meetings. Dr. Knappe said the example lacks a connection to this situation since purchasing is different from the release of emerging contaminants. They would be interested to see a document that is more relevant to the current situation, especially due to the fact that a risk assessment may be able to be done for GenX, but not necessarily for other compounds. Dr. Augspurger said the principle would fit under the Board's charge of providing recommendations for a range of values and scientific guidance to inform staff making policy or risk management decisions. Dr. Dorman said that DEQ and DHHS staff can help the Board by showing or explaining why certain assumptions were made or policies chosen to allow for discussion. Dr. Tilson said they should keep the precautionary principle in mind going forward for emerging contaminants when a direct assessment cannot be made or known health information is not available. Chairman Bartram emphasized that the Board's charge in the future will include compounds or substances where much less science is available, and are data poor, and the precautionary principle may be relevant, so the idea is worth developing, and reflecting on how the information can assist the Board with emerging contaminants.

VIII. SAB Principles and Practices

Chairman Bartram stated that the Board was currently operating under the Principles and Practices document of the previously established Science Advisory Board for Air Quality Standards, and proposed that they continue operating under this document and consider it a living document to be updated regularly as needed, unless any board members opposed. No board members opposed.

IX. Public Comment Forum

Beth Markesino, Wilmington South GenX Water Group (over 11,000 members) – pointed out that it has been over nine months of water contamination, and that 24 other non-regulated chemicals are present in their water in addition to GenX. She stated that she has over 6,000 documents that she had from the EPA, but that DEQ is not publishing all available forms and information on their website, for example the fact that Chemours has been cited for dumping in the last two weeks. She believes that the SAB Board members should be provided this information, and there is a lack of communication between the SAB and DEQ. She believes the SAB should be divided into multiple panels to address the multiple issues at hand, as there are brilliant minds on the panel, and they should divide and conquer to get things accomplished. The public is looking to the SAB minds to help them. She brought with her a container of water contaminated by Chemours and mentioned that they are still restricted to using bottled water. She pointed out that there is no clear border for the contamination, and that in some locations the GenX levels are 400 parts per trillion, while in other locations the levels are 4,000 parts per billion. She stated that she has already lost a child to this, and that everyone needs to join together to solve this issue, instead of DEQ reporting that no progress has been made and there is nothing new to report at each

meeting. They want to see progress and get answers at the next meeting. They want to see research being done and see DEQ and the SAB put their minds together and share information with the people from the Netherlands and from Michigan who are also working on this issue to find a solution. She thanked the Board for their time.

Chairman Bartram thanked her for sharing that, and that the Board understands the passion and intensity of the intervention, and that there is no lack of goodwill among the Board to do whatever it can to deal with health issues in the state. He asked if anyone else wished to speak. No one else requested to speak.

X. Next Meetings

Chairman Bartram stated that the March 19, 2018 meeting would again be in the Ground Floor Hearing Room of the Archdale Building, and would focus on making decisions on GenX instead of data gathering.

Chairman Bartram also stated that the April 30, 2018 meeting would be located in the western part of the state, and the discussion would focus on Hexavalent Chromium.

Chairman Bartram proposed a preliminary date of June 18, 2018 for the following meeting, and also proposed to schedule the subsequent meeting during the week of July 23, 2018.

Dr. Di Giulio commented that discussion should also address the mixtures of compounds and the effect of their interaction, not just identifying the compounds. Dr. Dorman requested more information on standards for drinking water, groundwater, and surface water. DEQ Asst. Secretary Holman offered to have DEQ give an overview presentation on federal drinking water standards and North Carolina groundwater and surface water quality standards at the March meeting to further the discussion on GenX and future/emerging contaminant water quality standards. Dr. Knappe asked if DEQ was considering a drinking water standard for GenX, which would shift responsibility for compliance to the water providers, and would in turn require dischargers to comply with the Clean Water Act requirement that they shall not discharge any contaminant which would require the water provider to change or add new processes to treat or remove that contaminant. Assistant Secretary Holman stated that DEQ had not made a decision on the matter but are discussing the options.

The SAB meeting adjourned at 12:36 pm, January 29, 2018.