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HUNDRED-AND-SEVENTY FOURTH MEETING OF THE SCIENCE ADVISORY BOARD (NCSAB) ON TOXIC AIR POLLUTANTS

Proceedings of the January 29, 2014 Teleconference

Dr. Starr called the meeting to order at 3:11 PM. NCSAB members Drs. Thomas Starr, Ivan Rusyn, Woodall Stopford, David Dorman, and Elaina Kenyon were in attendance. Therese Vick, Blue Ridge Environmental Defense League; Maria Hegstad, Inside EPA; and Nancy Jones and Dr. Candace Prusiewicz, DAQ were also in attendance.

Approval of December 2013 Minutes

Meeting minutes from the 173rd meeting held on December 4, 2013 were approved as amended by minor electronic comments by Dr. Kenyon.

Meeting minutes that have been approved by the NCSAB are posted on the Division of Air Quality website at http://daq.state.nc.us/toxics/risk/sab/sab_minutes.shtml.

Cadmium Discussion

Dr. Prusiewicz provided a brief recap of the 173rd NCSAB meeting where the discussion centered on the calculations used to derive a proposed candidate AAL for cadmium. Several calculations were done using the potency factor reported by Park et al., 2012; however the calculated values appeared questionable. Dr. Starr suggested that a life table analysis based on North Carolina lung cancer mortality rates be conducted using the potency factors reported by Park et al., 2012 to provide comparative values.

Dr. Prusiewicz briefly discussed how the life table analysis was conducted (using an identical life table constructed for the arsenic AAL analysis) and the underlying assumptions used. She also sought assistance from Dr. Kenyon in obtaining an electronic copy of Stayner et al., 1992, the paper preceeding Park et al, 2012. Dr. Kenyon was able to provide the paper for the NCSAB. Dr. Prusiewicz also contacted Dr. Robert L. Sielken, Jr., the biostatistician who developed the preliminary life table for the arsenic AAL document. She had questions about the units of measurement associated with reported potency (µg-yr/m^3) because they are based on cumulative exposure over the lifetime. In calculating a candidate AAL for cadmium using the Park et al., 2012 potency factor of 0.2145 (µg-yr/m^3)$^{-1}$, she had mistakenly divided by 45 or 78 years (estimated working lifetime or natural lifetime) which led to an erroneously low value. Both the Stayner publication and Sielken spreadsheet do not adjust for the difference between working and calendar years, as this difference is already accounted for in a cumulative exposure model.

Using the lung cancer mortality lifetable developed for arsenic, values were iteratively input into the EXCEL spreadsheet calculation until a one in one million risk estimate (1 x 10^{-6}) was obtained for a 78 year lifespan. The airborne concentration for a 78 year lifetime exposure calculated using this methodology compared favorably to the value obtained from direct calculation using the potency factor. The direct potency factor calculation is

Risk = Potency factor x Exposure

Dr. Sielken used a respiratory volume compensation factor (7.8 m^3 air breathed per work day/16 m^3 air breathed per day) to convert from occupational exposure to environmental exposures rather than a time-based conversion factor (8 hours worked /24 hours day). This translates to multiplying by roughly 0.5 rather than 0.33. He used a daily conversion factor 240 work days / 365 days per year, the traditional conversion to compensate for the number of occupational work days in a calendar year. The resulting exposure value was 1.53 x10^{-3} µg/m^3. This number is comparable to the lifetable analysis value. The values from the direct potency calculation and the lifetable analysis results are detailed in Table 8 on page 24 (see below) of the draft AAL document for cadmium.

Table 1: Derivation comparison for candidate AALs for cadmium

	Central Estimate (mg/m^3)	Lower Bound Estimate (mg/m^3)	Upper Bound Estimate (mg/m^3)	Stringency Factor (compared with current AAL of 5.5×10^{-6} mg/m^3)
Direct Potency Calculation	1.53×10^{-6}	3.91×10^{-7}	1.24×10^{-5}	3-fold
Life Table Analysis	5.36×10^{-7}	1.35×10^{-7}	4.29×10^{-6}	10-fold

Source: Draft AAL document for cadmium and cadmium compounds (February 2014)

Of the two calculated candidate AALs, the value obtained using the lifetable analysis was the more conservative one. Hence, the recommended candidate AAL for cadmium is 5.4×10^{-7} mg/m^3 or 5.4×10^{-4} $\mu g/m^3$ (the central estimate value). This candidate AAL is an order of magnitude lower than the current cadmium AAL value of 5.5×10^{-6} mg/m^3 or 5.4×10^{-3} $\mu g/m^3$. This difference, as noted earlier by Dr. Stopford, is associated with using a more stringent risk criterion (one in one million compared with one in one hundred thousand) since cadmium is now considered to be a known human carcinogen.

Dr. Rusyn expressed concerns regarding the “messaging” of the draft AAL document. He noted that while he understands the methodology and rationale, he is more concerned with the messaging than the actual justification for the candidate AAL. Dr Rusyn emphasized the importance of clearly communicating to the stakeholders that the proposed AAL is based on newer data and is consistent with values established by other states. It is equally important to explicitly say if the new proposed value is more health protective or less health protective and why. He was concerned that the document was too technical and recommended clearly saying that the recommended candidate AAL reflects the fact that a risk level of one in one million is more protective than a risk level of one in one hundred thousand and this is the current state of the art. He thought the rest of the document was sufficient, but that simpler language should be used to help walk people through the document to explain what was done.

Dr. Kenyon agreed with Dr. Rusyn and questioned whether North Carolina had ever produced documentation for stakeholders written at a simpler level as ATSDR does. Dr. Prusiewicz responded that the supporting AAL summaries in the files vary widely in their technical levels. Dr. Rusyn suggested that the executive summary section of the document should end with some public health message putting the candidate AAL into context rather than just providing the number.

Dr. Dorman wondered if it wasn’t premature to put a public health message into the document because the board only serves as an advisory group recommending candidate AALs. The board has no way of knowing if the recommended AAL will be adopted. He noted that the SAB is not tasked with risk management or risk communication. He wondered if it shouldn’t be DENR’s responsibility to communicate with the public once a candidate AAL was adopted and formalized. Dr. Stopford recommended comparison of the candidate AAL to other exposure limits from other states (Table 3 on page 8 of the draft AAL document). He also suggested modifying Figure 1 to include the candidate AAL value. He thought this comparison with yearly monitored values would be informative. Dr. Kenyon agreed with Dr. Stopford’s suggestion. Dr. Rusyn also agreed, but suggested adding an interpretation of what a higher or lower candidate AAL means (ie. is it less or more stringent). This would be helpful not only for the public but also the legislature.

Dr. Dorman noted that the candidate AAL is below the analytical detection limit of the monitoring stations. The draft AAL document (page 5, last paragraph) reports a minimum detection limit (MDL) of $0.01\mu g/m^3$. Dr. Dorman thinks that this information is another public health message that should be conveyed to the public. Because so much of the cadmium monitoring data in the state was below the MDL, a Kaplan Meier non-parametric method was used to analyze the data set. Dr. Dorman agreed with the use of this truncated analysis of monitoring data but noted that if you compared the distribution to the candidate AAL, it would appear that a large portion of the North Carolina population was exposed to a concentration of cadmium in excess of the candidate AAL. Dr. Rusyn noted that even the current North Carolina AAL for cadmium is below the MDL.

Dr. Starr pointed out that the origin of 10^{-6} risk in this context was for the entire US population, and that a one in one million risk for 300 million people would amount to 300 extra deaths over a lifetime of 78 years or about four deaths a year over the entire US population attributable to cadmium exposure. In North Carolina, there would be fewer overall deaths compared with the national number of deaths. This was the argument that was made for using a 10^{-5} risk by the North Carolina Academy of Sciences and other states that have used 10^{-5} risk estimates for their individual states. Of course, if all states used a 10^{-5} risk estimate the national US risk estimate would be at 10^{-5}. He feels it would be useful to say something about this in the document and that using 10^{-5} is probably not the right thing to do. In conclusion, Dr. Starr summarized the board's evaluation of cadmium by saying that all the work they did on cadmium resulted in little change in the potency of cadmium. The major contributory factor in the proposed reduced AAL is the reduced level of risk that was used in the updated calculation.

Dr. Rusyn referred to Table 3 of the draft AAL document (Select Air Regulatory/Advisory Levels for Cadmium - see below) and noted that California arrived at a similar value using a different inhalation unit risk factor (IUR). He indicated that he was comfortable with the draft cadmium AAL document and the analysis done since the board considered both cancer and non-cancer endpoints. He believes that proposed candidate AAL value based on a cancer endpoint is protective for non-cancer effects as well. He reiterated that he would like to go back and put the proposed candidate AAL value into context by explicitly describing what the proposed change in concentration value means.

Table 2: Select Air Regulatory/Advisory Levels for Cadmium[1,2]

Agency	Year	Exposure Concentration Recommendation Type	Cadmium Exposure Concentration ($\mu g/m^3$)	Health Endpoint	Reference
ATSDR	2012	Advisory	0.01	Non-cancer	Buchet et al., 1990 Jarup et al., 2000 Suwazono et al., 2006
ACGIH	1990	Advisory – Workplace	10 2 (resp. fraction)	Non-cancer	ACGIH TLVs and BEIs handbook (2013)
Cal/EPA	2000	Regulatory (1 x 10^{-6} risk/ Cal/EPA IUR)	0.00024	Cancer	Thun et al., 1985
New Jersey	2011	Regulatory (1 x 10^{-6} risk/ Cal/EPA IUR)	0.00024	Cancer	Thun et al., 1985
Michigan	Not listed	Regulatory (1 x 10^{-6} risk/ EPA IUR)	0.00056	Cancer	Thun et al., 1985
Minnesota	2009	Regulatory (1 x 10^{-5} risk/ EPA IUR)	0.0056	Cancer	Thun et al., 1985
Ontario, Canada	2007	Regulatory (Cumulative Exposure LOAEL Method)	0.005	Cancer/ Non-cancer	Thun et al., 1991
OSHA	1993	Regulatory-Workplace	5	Not reported	Not reported
Texas	2003	Regulatory (ESL)	0.01	Not reported	Not reported
WHO	2000	Advisory	0.005	Non-cancer	Thun et al., 1985 Thun et al., 1991

[1] Website URL addresses are listed in the Reference Section.
[2] Advisory air levels are air concentrations recommended by non-regulatory agencies. Such air concentrations are not enforceable.

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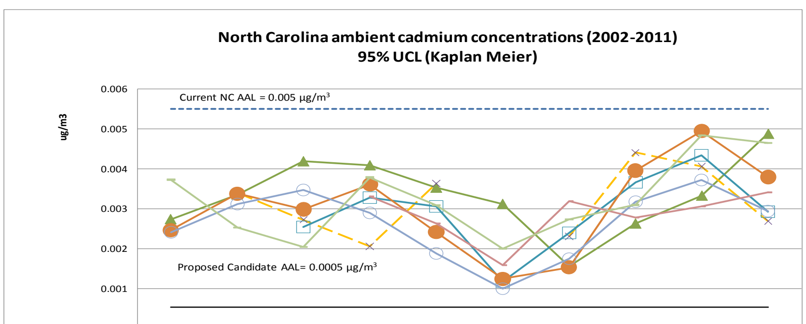
Dr. Starr noted that even at a 10^{-5} risk level, North Carolina is still below the MDL or maybe the level of quantitation which would actually be higher. He questioned how an economic entity would demonstrate compliance with the candidate AAL if it were adopted by the EMC. He indicated that all one could say is that airborne cadmium levels could not be measured at that level using the current analysis.

Dr. Rusyn noted that although they have not tried it, there are new mass spectrometry techniques at UNC that can probably detect cadmium at the proposed concentration. Dr. Starr asked Dr. Prusiewicz if she had additional information about the analytical method currently used for quantitation of monitored ambient air cadmium levels; specifically its age and if there are any improvements coming. She said she did not, but she shared that Inductively Coupled Plasma (ICP) is a more sensitive method for metals analysis although she did not know what the MDL of that method. However, North Carolina and the rest of the nation use the X-ray method that EPA directs. North Carolina cannot independently change to a different analytical method even if a more sensitive method exists. Dr. Starr requested that the analytical method be documented as an EPA-approved method. Dr. Rusyn noted that an Agilent GCMS application described their equipment as having a 0.01 ng/g the limit of detection and a 0.8 µg/g quantification limit. Dr. Starr noted that would be in a solid substrate, not air, but Dr. Rusyn thought this could be converted to a lower than the current MDL in air by pulling the cadmium through a filter to get it onto a solid substrate.

Dr. Prusiewicz mentioned that Dr. Stopford had suggested earlier that a line be added in Figure 1 depicting the current or proposed AAL or both. She emphasized that it is important to remember that an AAL is used in the permitting process and that comparison of an AAL with an ambient exposure level is not recommended. This is because the ambient concentration of a pollutant is the summation of the contribution of all sources including mobile, stationary, natural and area or nonpoint sources. The AAL is applied only to stationary source emissions and is used for modeling purposes. NCDENR does not measure the concentration of cadmium in the air to determine compliance, they model it. The draft cadmium AAL document (page 5) estimates that point sources contribute only about 12 percent of the cadmium in the ambient air for North Carolina. AALs established for stationary source emissions should not be directly compared with measured ambient concentrations since ambient concentrations are comprised of contributions from many different sources.

Figure 1



	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Current NC AAL	0.0055	0.0055	0.0055	0.0055	0.0055	0.0055	0.0055	0.0055	0.0055	0.0055
Candidate NC AAL	0.00054	0.00054	0.00054	0.00054	0.00054	0.00054	0.00054	0.00054	0.00054	0.00054
Asheville	0.0027	0.0034	0.0042	0.0041	0.0035	0.0031	0.0016	0.0026	0.0033	0.0049
Hickory		0.0034	0.0027	0.0021	0.0036		0.0023	0.0044	0.0041	0.0027
Lexington			0.0026	0.0033	0.0031	0.0012	0.0024	0.0037	0.0043	0.0029
Charlotte	0.0025	0.0034	0.0030	0.0036	0.0024	0.0013	0.0015	0.0040	0.0050	0.0038
Raleigh	0.0024	0.0031	0.0035	0.0029	0.0019	0.0010	0.0018	0.0032	0.0037	0.0029
Rockwell				0.0033	0.0026	0.0016	0.0032	0.0028	0.0031	0.0034
Winston-Salem	0.0037	0.0025	0.0021	0.0038	0.0031	0.0020	0.0027	0.0031	0.0048	0.0047

Dr. Stopford agreed with Dr. Prusiewicz but noted that the AAL (as calculated) is actually a measurement of the acceptable exposure level, without modeling, so it can be compared to the ambient exposure level from all sources. The AAL value being proposed is below the median measured ambient concentrations (down in the brush) and he believes it would be useful to see the visual comparisons in Figure 1. Dr. Kenyon is inclined to think it may generate more confusion and suggested some boiler plate language at the beginning of the executive summary that explains how an AAL is actually used to allow people to interpret these values in context. Dr. Starr agreed with both Dr. Stopford and Dr. Kenyon.

Dr. Starr pointed out another issue with Figure 1. Since the 95th percent upper confidence limits for the concentrations are plotted, this signifies that there were not enough measurements to characterize the distribution. He thought it would be useful to say that there is only a 5 percent chance that you would get a measurement that is higher than the one presented. He noted that it is most likely that the median would be undetectable and he doesn't know how many of the observations would be above the median. Dr. Starr asked what percent of the measurements were above the detection limit? Dr. Dorman noted that the document specifies greater than 50 percent of the measurements were non-detected. Dr. Prusiewicz said that the majority of the data were either zero or below the detection limit although for each year there were a few values that were extremely high, high enough to be questioned, for each of the locations. Dr. Dorman recollected previous discussions where the board questioned the accuracy of the very high values reported and the confidence in those values.

Dr. Dorman inquired about the life table analysis performed with respect to the North Carolina population. He did not see a citation specifying where the lifetable lung mortality rates were obtained. This needs to be included so that the analysis is transparent and replicable. Dr. Prusiewicz noted that this information was referenced in the arsenic AAL document. She will add this reference as a standalone reference rather than cross reference the arsenic analysis. Dr. Starr pointed out that all of the data was referenced but had not made its way into the document. He also suggested that an appropriately QC'd spreadsheet of the lifetable analysis should be posted on the web so that people could perform their own analyses. She had considered adding an attachment that contained a snapshot of the spreadsheet, but Dr. Starr said that would not help. People need to be able to see the equations in the spreadsheet and work with them.

Dr. Starr proceeded to explain and summarize the methodology used in a lifetable analysis. Epidemiological worker studies report results using inverse units of cumulative exposure (ie.units are expressed as risk per ppm-working year with a working year defined as 8 hours/day, 240 days/year). For environmental exposures, the exposure period could be spread out over any period of the 78 year lifetime. The risk would be the same for an individual having many years of exposure to a low concentration as it would be for a worker having two years exposure to a very high concentration. The model is insensitive to exposure pattern differences except for the baseline mortality rate (which is age specific). Hence, age specificity is factored into the lifetable analysis. Every year a person is exposed, a multiplying factor (equal to potency x cumulative exposure) is applied. This is a multiplier on the baseline rate of mortality for that age category. These age-specific contributions to risk are summed over time from age zero to age 78 to give the probability of having died of lung cancer at any point during the 78 year interval. The probability is adjusted for competing risks of mortality from other causes because the person who dies of lung cancer at age 45 has not died earlier from lung cancer or anything else. So the age-specific competing risks of death from other causes are taken into explicitly account and that is the great advantage of a lifetable analysis.

The only adjustment required is the working year/calendar year exposure adjustment. The exposure is adjusted for the amount of air a person breathes in an 8-hour working day during 240 working days a year, relative to a continuous exposure of 24-hours a day and 365 days per year. Those adjustments reduce the AAL by a factor of 2 for hours per day and 2/3rds for 240/365 days per year. This is a commonly accepted method used to convert workday risks to risks from continuous environmental exposure (even though it is complex and difficult to follow). It is the best way because it takes into account competing risks and gives you a realistic estimate of what the risks may be from a continuous lifetime exposure. Exposures are assumed to continue outside the age range that workers typically are exposed: ages 18-65 (although there is no data for occupational exposures outside this working lifetime). Dr. Starr feels that putting a spreadsheet for people to work with up on the web and providing references for the mortality data on survivorship that is in the lifetable is important so that interested parties can update the data or go back to the original sources and do their own calculations.

Dr. Starr asked if anyone had reservations about going to the 10^{-6} risk level and no one responded. He asked that Dr. Prusiewicz make it clear in the document that the factor driving the change in the AAL from the current value to the candidate value is the change in the criterion risk level from 10^{-5} to 10^{-6}. Also, there is a slight contribution to increasing the risk from increasing the lifespan from 70 years to 78 years, since the age-specific rate of death from lung cancer increases with age. He believes the board has done good work in their evaluation of cadmium in that they used more data and improved methodology. He is troubled by the fact that the AAL value the board will be proposing is so far below the limit of detection in ambient air monitoring. He wondered how an economic entity would be able to demonstrate compliance.

Dr. Kenyon explained that the AAL concentration used in permitting stationary sources is compared with a modeled concentration at the fenceline; it is not compared with actual monitored values. Therefore, the value makes sense to her. Dr. Starr suggested that they do as Dr. Rusyn had suggested and put in the boilerplate information about how this number is used and perhaps adding that ambient measurements may not be consistent with these numbers. Dr. Kenyon noted that this is a problem that they run into frequently and is not unique to cadmium. Dr. Starr noted that the same case occurred with arsenic and the SAB was not being asked to address it. Dr. Starr requested another addition to Figure 1. There is no discussion of what the Kaplan-Meyer method is and how many observations are represented by each data point plotted on the graph. He felt it would be useful to add a discussion of these, that each data point had "x" number of observations associated with it and the number of observations that were above the MDL. Dr. Prusiewicz agreed to put that data in a table below the figure, but noted that there are values in the database that are reported that are below the MDL.

Dr. Dorman asked for clarification regarding finalizing the cadmium AAL (ie. would the board defer a vote until the next meeting or vote electronically before the next meeting?). Dr. Starr asked if members would like to do that or continue on to a decision on the specific candidate AAL? Dr. Rusyn sent an email to board members during the meeting summarizing the changes to be made to the document in bullet form. Dr. Kenyon said she felt that the email covered everything that they had discussed with the exception of adding some language about how the AAL is actually used. For transparency's sake, Dr. Prusiewicz paraphrased Dr. Rusyn's bullet points about what pending modifications to the document.

- Clarification that the candidate AAL was based on a newer analysis by Park et al., 2012. Park et al. used Poisson regression to estimate a potency factor (for cumulative exposure). Workers were stratified into groups based on cumulative exposure.
- The proposed cadmium candidate AAL is based on a 10^{-6} risk criterion compared with the current AAL that was based on a 10^{-5} risk criterion.
- The cadmium candidate AAL is based on a cancer mortality endpoint and is presumed to be protective for noncancer endpoints.
- The candidate AAL is in line with values established by other states that use a 10^{-6} risk criterion.
- The candidate AAL is more stringent by approximately 10-fold (which corresponds to the change in the risk criterion).
- Both the candidate and current AAL values for cadmium are below the MDL of the analytical method used in ambient air monitoring.
- Boilerplate language will be added describing how North Carolina uses the AAL in the permitting process.

Dr. Starr suggested that it would be useful to include the limit of quantitation in the document in additional to the MDL. Dr. Rusyn sent an electronic excerpt from an ATSDR document that has references to detection limits in the air that could be referred to in the summary. In reference to noncancer endpoints, it was suggested both cancer and noncancer candidate AAL values be included in a table in the document. This would show that the proposed cancer AAL is protective for noncancer effects. It was agreed that the range of candidate AALs be reported for each noncancer endpoint.

Public Forum
There were no comments from the public.

Other Business
There was no other business.

Planning for April 9, 2014 Meeting

The next meeting will be April 9, 2014 at 3 pm at 217 West Jones Street, Raleigh, North Carolina. Dr. Rusyn said he will be in Europe and asked that the telephone line be opened so that he could join in, even though it would be an in person meeting. Dr. Stopford will also attend by teleconference. Dr. Prusiewicz hopes she can get the revised draft cadmium document out to the board within a week, and receive their comments within another week. Board members would then vote electronically to approve. She will post it for a 30-day public comment period and have those comments available for the board to review at the next meeting. In response to a question from the public, she noted that she would both email the version of the document for public comments to known stakeholders and post it to the website.

The next scheduled meeting will be held at **3:00 PM on WEDNESDAY, April 9, 2014** at the Green Square Building in Raleigh. The call-in number is **(919) 733-2441.**

The meeting was adjourned at 4:11 PM.

Respectfully submitted,

Candace Prusiewicz, Ph.D.
Liaison, Science Advisory Board

These minutes were accepted at the 175th SAB meeting on May 28, 2014.

REFERENCE:

North Carolina Department of Environment and Natural Resources, Division of Air Quality (2013). Risk assessment for arsenic and inorganic compounds.

Park RM, Stayner LT, Petersen MR, Finley-Couch M, Hornung R, Rice C. (2012) Cadmium and lung cancer mortality accounting for simultaneous arsenic exposure. Occup Environ Med 69:303-309.

Stayner L., Smith R, Thun M, Schnorr T, Lemen R (1992) A dose-response analysis and quantitative assessment of lung cancer risk and occupational cadmium exposure. Ann Epidemiol (2) 3: 177-194.