

## AGENDA ITEM 3

299a. Change AAL for 1,3-Butadiene

### **Reason for Action**

To revise the acceptable ambient level (AAL) for 1,3-butadiene per the recommendation of the Scientific Advisory Board (SAB).

### **Scope/Nature/Summary**

Currently, the acceptable ambient level for 1,3 butadiene is  $1.7 \times 10^{-4}$  milligrams per cubic meter (mg/m<sup>3</sup>). The Scientific Advisory Board recommends changing it to  $1.28 \times 10^{-3}$  mg/m<sup>3</sup>. Changing the AAL also requires changing the corresponding emission rate requiring a permit from 12 pounds per year to 32.5 pounds per year.

This change involves amending two rules: 15A NCAC 02D .1104, Toxic Air Pollutant Guidelines, and 02Q .0711, Emission Rates Requiring a Permit.

The amendment is being proposed at the suggestion of staff and recommendation of the Scientific Advisory Board.

### **Statutory Authority**

G.S.143-215.3(a)(1); 143-215.107(a)(3),(4),(5); 143.215.108; 143B-282.



North Carolina Department of Environment and Natural Resources  
Division of Air Quality

Michael F. Easley, Governor

William G. Ross, Jr., Secretary  
B. Keith Overcash, P.E.,  
Director

**MEMORANDUM**

To: Thomas Allen, Supervisor, Rules Development Branch  
Planning Section

From: Reginald C. Jordan, Ph.D., CIH, Liaison,  
Secretary's Science Advisory Board on Toxic Air Pollutants

Re: Completed NCSAB Recommendation for the Revision of the AAL for 1, 3-butadiene

Date: January 19, 2007

I have attached the summary for a completed review of 1, 3-butadiene by the Secretary's Science Advisory Board on Toxic Air Pollutants (NCSAB). The NCSAB has determined that the Acceptable Ambient Level for 1, 3-butadiene be revised from its existing concentration of  $1.7 \times 10^{-4} \text{ mg/m}^3$  to a concentration within an interval of concentrations, and has recommended an appropriate revised AAL concentration within that range. A leukemia health endpoint was chosen based on human epidemiological studies. These recommendations are summarized as follows:

<b>Compound</b>	<b>NCSAB Recommended Range</b>	<b>NCSAB Recommended Revised AAL</b>	<b>DENR Averaging Time</b>
1, 3-butadiene (CAS: 106-99-0)	$4.4 \times 10^{-4} - 1.68 \times 10^{-3}$ $\text{mg/m}^3$	$1.28 \times 10^{-3} \text{ mg/m}^3$	Annual average

**Summary of the Toxicity Assessment of 1, 3-Butadiene:  
A Report and with Recommendations to Revise the Acceptable Ambient Level  
Secretary's Science Advisory Board on Toxic Air Pollutants (NCSAB)**

## **Executive Summary**

The NCSAB has evaluated the toxicity of 1, 3-butadiene (BD) in response to a request made by the Division of Air Quality (DAQ). The current Acceptable Ambient Level (AAL) guideline for BD, established in 1991, is  $1.7 \times 10^{-4}$  mg/m<sup>3</sup>. Lifetime (70-year) continuous exposure to this concentration of BD was expected to pose no more than a  $10^{-5}$  (one in a hundred thousand) risk to human health based on a 1991 EPA human-adjusted Inhalation Unit Risk (IUR) value of  $5.8 \times 10^{-4}$  / (µg/m<sup>3</sup>). In 1991, BD was classified by EPA as a *probable* human carcinogen. In 1993, the NCSAB recommended revising the AAL to  $3.6 \times 10^{-4}$  mg/m<sup>3</sup> based on an updated EPA IUR of  $2.8 \times 10^{-4}$  / (µg/m<sup>3</sup>).

Upon review of the current toxicological and epidemiological literature, the NCSAB is recommending a revision of the AAL to  $12.8 \times 10^{-4}$  mg/m<sup>3</sup>. This revision is based primarily on a 2005[1] update to the 1995[2] epidemiological study by Delzell et. al. The data are from a large retrospective occupational cohort mortality study of about 16,000 male styrene-butadiene-rubber (SBR) workers in 8 North American plants. Although several toxicological endpoints were evaluated in this study, the NCSAB focused on worker mortality from leukemia, the most sensitive endpoint examined.

Carcinogenicity bioassay studies using both rats and mice indicate that BD is a multi-site carcinogen, primarily in the lung, but with mammary tumors also occurring in both female rats and mice. Since the Delzell cohort is comprised primarily of white male workers, the potential risks of increased female breast cancer from BD exposures are not adequately characterized. In addition, EPA has recently published guidance indicating that childhood exposures to carcinogenic agents acting via a mutagenic mode of action may be more potent than equivalent adult exposures [3]. To reflect these and other residual uncertainties regarding potential human cancer risks from BD exposure, the NCSAB has made a prudent health policy decision to reduce the low end of the recommended AAL range for BD by a 2-fold factor..

The NCSAB also considered the EPA Integrated Risk Information System (IRIS)[4] data for the most sensitive non-cancer endpoint (ovarian atrophy, and has concluded that the recommended AAL of  $12.8 \times 10^{-4}$  mg/m<sup>3</sup> for leukemia mortality will also be protective against ovarian atrophy.

## **Background Information**

BD (CAS 106-99-0) is a colorless, highly flammable gas having a “mild gasoline-like” odor[5] at room temperature. It has a molecular weight of 54.09 g/mole and the molecular structure shown in Figure 1:

### Figure 1- Molecular Structure of BD

It is sparingly soluble in water, and soluble in alcohol, ether, benzene, and acetone.[6] The lower explosive limit (LEL) is 2.0% and upper explosive limit (UEL) is 11.5%. BD has a vapor density of 1.87 and vapor pressure: 1840 mmHg @ 21°C (245.3 kPa)[7]. 1 ppm = 2.21 mg/m<sup>3</sup> (25 °C); 1 mg/m<sup>3</sup> = 0.452 ppm (25 °C).

BD is produced by the petrochemical industry and it is used largely in the manufacture of styrene-butadiene rubber. It is also used in the manufacture of ABS (acrylonitrile-butadiene-styrene), nitrile, and chloroprene rubbers along with various latexes and resins.

Exposure to BD is normally through inhalation. The toxic effects in both humans and animals have been demonstrated in numerous studies via various routes of exposure. The Agency for Toxic Substances and Disease Registry (ATSDR) reports[5, pp. 15-17] that short term exposure to high concentrations of BD can result in eye, nose, and throat irritation in humans. Exposure to very high concentrations (which could occur during an accidental release) can lead to toxic effects on the central nervous system (neurotoxicity) like narcosis, unconsciousness, and even death.

Long-term studies in both animals and in humans have indicated that BD is carcinogenic. Animal studies have also demonstrated that certain metabolites of BD are genotoxic, and metabolism of BD in humans is expected to produce these same compounds. However, genotoxicity has not been observed even in heavily exposed humans[8, 9]. The National Toxicology Program (NTP) and EPA now classify BD as a known human carcinogen. IARC (International Agency for Research on Cancer) classifies BD as a probable human carcinogen. In addition, EPA has designated BD as a hazardous air pollutant under the National Emission Standards for Hazardous Air Pollutants (40 CFR 63).

According to the 1999 National-Scale Air Toxics Assessment (NATA) report[10] published in 2005, the mean and the median ambient air concentration of BD in North Carolina is 3 x 10<sup>-8</sup> milligrams per cubic meter (mg/m<sup>3</sup>) (1.6 x 10<sup>-5</sup> parts per billion (ppb)). The 95<sup>th</sup> percentile concentration is 5.4 x 10<sup>-8</sup> mg/m<sup>3</sup> (2.4 x 10<sup>-5</sup> ppb). Table 1 summarizes BD emissions by type and percent contribution<sup>1</sup>:

**Table 1 – Contributions to Ambient Air from Source Types in North Carolina**

Source Type	Approximate Contribution to
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<sup>1</sup> Point sources can be generally described as industrial facilities with defined points of emission (e.g., power plant, petrochemical plant, steel mill), area sources are generally smaller sources with less well characterized points of emission (e.g., a gasoline station, an auto body paint shop) and mobile sources include both on-road (like cars and trucks) and off-road (e.g., ships, airplanes, construction equipment, ski-mobiles) non-stationary sources. Mobile sources produce 1, 3-butadiene through the incomplete combustion of petroleum-based fuels.

	Ambient Air Concentration, %
Point	16
Area and Other	30
Mobile	54

### Acceptable Ambient Level (AAL) History

In 1987 the Air Toxics Panel of the North Carolina Academy of Sciences recommended an annual average AAL of  $3.5 \times 10^{-5}$  mg/m<sup>3</sup> for BD. In 1991, this AAL was revised to  $1.7 \times 10^{-4}$  mg/m<sup>3</sup>. In 1993, the NCSAB recommended that the AAL be revised again to  $4.6 \times 10^{-4}$  mg/m<sup>3</sup>. However, the current AAL for BD remains at  $1.7 \times 10^{-4}$  mg/m<sup>3</sup> (0.077 ppb) as an annual average.

### Human Studies

Since 1985, at least 15 independently conducted epidemiological studies of workers exposed to BD in monomer production and polymer production facilities have been reported in the open scientific literature (including follow-ups) [1, 11-24]. The 1995 study by Delzell *et. al* [2] has been reviewed extensively and used as the basis for two in-depth human health assessments of BD: the Health Canada report[25] and the EPA National Center for Environmental Assessment report[26]. Delzell retrospectively studied lymphohematopoietic mortality in an occupational cohort of about 16,000 male synthetic rubber workers who worked at least one year at any of seven U.S. or one Canadian polymer plants. Exposure estimates for workers performing defined job tasks were reported in Macaluso[22].

Recently, the 1995 Delzell study has been updated [1] to include seven more years of follow-up (through 1998) and 23 more deaths from leukemia (total of 81). As described in Macaluso [27], job group-specific exposure estimates were also updated and further refined after a detailed review of job practices, equipment used, and emissions from the equipment, re-confirmation of assumptions, and measurements in plants. Exposures to BD were determined to be approximately 5 times greater than those estimated previously. The results of this update were presented at the 2005 Health Effects Institute Annual Conference, and also to the NCSAB at its April 2005 meeting.

### Range of Risks Assessment

For its reassessment process, the NCSAB considered the weight of the evidence and decided to employ both the Delzell 1995 and its companion 2005 updated datasets. A  $10^{-6}$  excess risk level (one-in-a-million) was utilized because human study data for cancer mortality endpoints were available in the peer-reviewed literature. A proportional hazards model was used to relate relative risk to BD dose, where:

with:

RR = relative risk

Dose = cumulative exposure to BD, ppm-yr

$\beta$  = coefficient of cumulative exposure, (ppm·yr)<sup>-1</sup>

Cox regression estimates of  $\beta$  (central as well as upper and lower 95% confidence limit estimates) from both the 1995 Delzell study and its 2005 update were utilized in this assessment.

Lifetime risk was estimated actuarially using “Baseline survival to beginning of age category, US male, 2000” data [28], and “Leukemia mortality rate per 100,000, US white male 1998-2002” [29]. Age-specific cumulative exposure estimates associated with a constant BD concentration were adjusted iteratively to determine the BD concentration associated with a one-in-a-million (10<sup>-6</sup>) excess lifetime risk of death from leukemia. In the Delzell 1995 study,  $\beta$  was estimated to be 4.1 x 10<sup>-3</sup> (ppm-yr)<sup>-1</sup> (standard error (SE) = 1.9 x 10<sup>-3</sup>)[2, Table 67, p. 165]. For the Delzell 2005 update,  $\beta$  was selected as the average of lag-specific  $\beta$  estimates determined for lag times of 0, 5, 10, 15, and 20 years for trimmed data (dose < 1338 ppm-years), adjusted for plant and race: 1.43 x 10<sup>-3</sup> (ppm-yr)<sup>-1</sup> (SE = 4.03 x 10<sup>-4</sup>)[1, slide 27]. Results from trimmed data analyses were used to avoid the potential downward bias that could be introduced by the high dose relative risk estimates that appeared to plateau – i.e., at the very highest cumulative exposure levels in the cohort, increases in cumulative exposure produced little or no additional increase in relative risk.

The NCSAB analyses have used both 70-year and 78-year lifespans in the range of risks analysis because:

- 70-years has been the default lifespan over which lifetime risks have been estimated, and
- The current average lifespan in the United States over all races and sexes is approximately 78 years [30].

Since an 85-year lifespan was utilized in the IRIS BD risk assessment summary[4], the NCSAB also included a calculation using this value to facilitate direct comparisons.

To determine the BD concentration at which the additional lifetime risk of death from leukemia was estimated to be no greater than one in a million, the following calculations were performed:

$$\beta(LCL, UCL) = \beta \pm 1.645 \times SE$$

$$exposure\ concentration \left( \frac{mg}{m^3} \right) = \frac{dose\ (ppm \cdot yr)}{lifespan\ (yr)} \times \frac{7.8m^3}{15.6m^3} \times \frac{240\ days}{365\ days} \times \frac{54.1}{24.45} \left( \frac{mg}{ppm} \right)$$

where:

$\beta(LCL)$  = 95% lower confidence limit of the Cox regression coefficient for cumulative BD exposure, (ppm-yr)<sup>-1</sup>

$\beta(UCL)$  = 95% upper confidence limit of the Cox regression coefficient for cumulative BD exposure, (ppm-yr)<sup>-1</sup>

SE = standard error of  $\beta$ , (ppm-yr)<sup>-1</sup>

The AAL is expressed as a continuous 24-hour human equivalent concentration in milligrams per cubic meter (mg/m<sup>3</sup>) of inhaled air, and it applies at the property lines of facilities emitting BD. Candidate AALs specific to each lifespan are shown in Tables 2 and 3 below:

**Table 2 – Candidate AALs based on Delzell 1995 data**

<b>Lifespan, yr</b>	<b>70<sup>2</sup></b>	<b>78</b>	<b>85<sup>3</sup></b>
<b>AAL (mg/m<sup>3</sup> x 10<sup>-4</sup>) using <math>\beta_{LCL}</math></b>	<b>13.9</b>	<b>6.5</b>	<b>4.0</b>
<b>AAL (mg/m<sup>3</sup> x 10<sup>-4</sup>) using <math>\beta</math></b>	<b>9.7</b>	<b>4.5</b>	<b>2.8</b>
<b>AAL (mg/m<sup>3</sup> x 10<sup>-4</sup>) using <math>\beta_{UCL}</math></b>	<b>5.5</b>	<b>2.5</b>	<b>1.6</b>

**Table 3 – Candidate AALs based on Delzell 2005 data**

<b>Lifespan, yr</b>	<b>70<sup>2</sup></b>	<b>78</b>	<b>85<sup>3</sup></b>
<b>AAL (mg/m<sup>3</sup> x 10<sup>-4</sup>) using <math>\beta_{LCL}</math></b>	<b>36.3</b>	<b>16.8</b>	<b>10.6</b>
<b>AAL (mg/m<sup>3</sup> x 10<sup>-4</sup>) using <math>\beta</math></b>	<b>27.6</b>	<b>12.8</b>	<b>8.1</b>
<b>AAL (mg/m<sup>3</sup> x 10<sup>-4</sup>) using <math>\beta_{UCL}</math></b>	<b>18.9</b>	<b>8.8</b>	<b>5.6</b>

### Sources of Uncertainty

There are several sources of residual uncertainty in the NCSAB derivation of candidate AALs for BD:

- (1) Uncertainties regarding exposure reconstruction and relative risk estimates

The NCSAB used the Delzell 1995 and the Delzell 2005 update in its reassessment of cancer risk associated with exposure to BD. Both EPA [26] and Health Canada [25] have commented on potential exposure misclassification in Delzell 1995. This is a limitation of most epidemiological studies. The Delzell 2005 update utilizes a more in-depth job, task, and exposure classification for the cohort. Exposure estimates were developed using historical exposure data, plant equipment analysis, and exposure modeling. However, as noted by Macaluso[27], the leukemia decedents were known at the time of the exposure reassessment. This has the potential to bias the exposure estimates, but since workers held different jobs at various times during their employment, the ultimate effect(s) of this potential bias are difficult to determine. Other limitations in the exposure assessment

<sup>2</sup> To provide continuity with NCSAB past practice  
<sup>3</sup> for reference purposes only

include a lack of industrial hygiene data to validate many of the exposure estimates and possible inaccuracies in the linkage of exposure estimates to poorly specified job groups.

In addition, there were questions concerning possible confounding in the Delzell 1995 study results by exposures of SBR workers to other potentially carcinogenic compounds such as dimethyldithiocarbamate (DMDTC) and styrene [31, as cited in [21]]. However, the 2005 updated results do not demonstrate a statistically significant difference between  $\beta$ 's estimated by controlling only for plant and race and those estimated by controlling for plant, race, and DMDTC[1, slides 27-28].

The Cox regression coefficients ( $\beta$ 's) for cumulative BD exposure used in this assessment were drawn from the proportional hazards models of the Delzell 1995 and 2005 data. Both central estimate and 95% confidence limit estimates were utilized in the NCSAB AAL determinations. Upper and lower confidence limits were employed to reflect residual uncertainty in the relative risk estimates obtained by Delzell et al.

## (2) Uncertainties regarding the dose-response relationship

There are several dose-response models that EPA has stated "...fit the data equally well." [26, p. 10-14]. Uncertainty remains regarding the functional form of the true dose-response relationship between leukemia mortality and cumulative BD exposure. A conservative (health protective) assumption is that the relationship is linear at low doses, implying that all nonzero BD exposures carry some cancer risk.

A simple linear model of relative risk has this property, but the influences of other covariates such as age, birth cohort, lifestyle factors, plant, and exposures to other toxic materials, can lead to negative relative risk estimates. The Cox proportional hazards model assumes that the logarithm of the relative risk is linearly related to the covariates, and thus it cannot generate negative relative risk estimates. At sufficiently low doses, this model also produces a relative risk estimate that is linearly related to exposure. Use of the Cox proportional hazards model has become a common practice in modern epidemiologic analyses of occupational cohort mortality.

The Delzell 1995 and 2005 analyses both employed cumulative BD exposure, i.e., ppm-years, as the dose metric. However, a very recent report by Sielken et al. [32] indicates that the cumulative number of peak BD exposures (number of occasions that job-specific BD concentrations were estimated to be at least 100 ppm) may better explain the increased leukemia mortality observed in the BD worker cohort. Sielken et al. (2006) have shown that if cumulative BD exposure and cumulative number of BD peak episodes are both included as explanatory covariates in a linear relative risk model for leukemia mortality (estimated via Poisson regression), then BD peaks is the only statistically significant exposure covariate.

If peak BD exposures are the primary cause of the increased leukemia mortality observed in the SBR worker cohort, then the potential cancer risks posed by far lower environmental BD concentrations may well be negligible. However, considerable uncertainty remains regarding the true role of peak BD exposures. For example, the 100-ppm exposure cut

point used to define peak episodes is somewhat arbitrary, and the duration of peak episodes may also be a critical and complicating factor. The consensus of the NCSAB is that additional research is required to further clarify the role of peak BD exposures before this approach can be confidently adopted.

(3) Uncertainties regarding the representativeness of estimated risks

The risk estimates utilized herein have been developed by combining data regarding the recent leukemia mortality experience of predominantly white male workers in the styrene-butadiene rubber industry and US national white male rates of mortality from leukemia and other causes. There is thus uncertainty about whether these estimates are representative of the mortality risks that might be associated with environmental BD exposures in North Carolina.

The greatest uncertainty regarding representativeness relates to the extrapolation of risks from occupational to environmental exposure conditions, because there are simply no reliable data linking environmental BD exposures to increased mortality from any cause. US national white male rates for leukemia mortality during the period 1998-2002 were nearly 2-fold greater than those for white females and nonwhite males and females. Thus, risks estimated with these rates may substantially overstate the risks that BD exposure poses to these other population groups.

(4) Uncertainty regarding potentially sensitive subpopulations

The NCSAB risk assessment is based on leukemia mortality among white male workers employed at North American plants that manufactured SBR. This assessment was limited to mortality from leukemia because the SBR study lacked information on relationships between leukemia incidence and BD exposure. The EPA risk assessment was extrapolated to leukemia incidence using an assumption that the exposure-response relationship for leukemia incidence is the same as that for leukemia mortality, apart from the approximately two-fold differences between baseline incidence and mortality rates. There are no specific data to support this assumption.

EPA also applied an approximately 2-fold modifying factor for the potentially increased sensitivity of children to mutagenic carcinogens. Genetic variability (e.g., polymorphisms in genes that regulate the metabolism of BD to mutagenic intermediates and in genes that regulate the detoxification of those metabolites) and lifestyle differences may also impact susceptibility to BD. It is not known if the variability in these factors among North Carolina residents is reflected adequately in the SBR workers' mortality experience included in the Delzell exposure-response analyses.

(5) Uncertainty regarding female mammary tumors and other tumor sites

EPA employed an additional adjustment factor of 2 [26, p. 10-21] to account both mammary tumors observed in both female mice and rats as well as tumors occurring at other sites in both males and females. The rationale proposed by EPA for use of this additional factor was that the Delzell cohort was comprised primarily of white males, so the

potential for BD to cause increases in female breast cancer could not be adequately evaluated.

(6) Overall Uncertainty

To be protective of public health in the face of these residual uncertainties, the NCSAB has reduced the lower end of its recommended AAL range by a 2-fold “uncertainty” factor. It is important to recognize that this is a conservative health policy decision, and that the magnitude of the chosen reduction (2-fold) has no specific data-derived basis.

**Supporting Animal Studies: Cancer**

In a lifetime chronic inhalation and carcinogenicity study of B6C3F<sub>1</sub> mice conducted under the auspices of the National Toxicology Program (NTP)[33], groups of 70 male and 70 female mice were exposed to BD via inhalation over 6 hr/day, 5 days/wk for periods up to 103 weeks. Exposure concentrations were 0, 6.25, 20, 62.5, 200, and 625 ppm. Groups of 90 males and females were exposed at 625 ppm. Exposure was found to produce tumors at multiple sites (e.g., lymphohematopoietic system, heart, lungs, forestomach, ovary, Harderian gland, mammary gland, liver). Tumors occurred in female mice at lower concentrations than males.

In chronic studies using Sprague-Dawley rats[34-36], in which groups of males and females were exposed via inhalation to 0, 1000, or 8000 ppm for 6 hr/day, 5 days/wk over 24 months (105 weeks for females, 111 weeks for males), tumors were found in mammary glands, pancreas, testicles, thyroid glands, and Zymbal glands. Tumors occurred in female rats at lower concentrations than males.

EPA derived the site-specific human risk estimates shown in Table 4 from NTP study data[33] as summarized in Tables 10-9 through 10-11 of the EPA health assessment document[26, pp. 10-31 - 10-33], where:

$$Exp.Conc.@10^{-6} risk, \frac{mg}{m^3} = EC_{10} \times \frac{10^{-6}}{10^{-1}} \times \frac{54.1 \frac{g}{mol}}{24.45 \frac{mol}{L}} = \frac{10^{-6}}{(0.1/LEC_{10})} \times \frac{54.1 \frac{g}{mol}}{24.45 \frac{mol}{L}}$$

**Table 4 – Summary of EPA’s Human Equivalent 70-year Lifespan Risk Estimates Based on Site-Specific Data for B6C3F1 Mice**

<b>Tumor Site</b>	<b>Human Equivalent EC<sub>10</sub>, ppm</b>	<b>Exposure Concentration @10<sup>-6</sup> risk, (mg/m<sup>3</sup> x 10<sup>-4</sup>)</b>	<b>Human Equivalent 0.1/LEC<sub>10</sub>, (ppm<sup>-1</sup>)</b>	<b>Exposure Concentration @10<sup>-6</sup> risk, (mg/m<sup>3</sup> x 10<sup>-4</sup>)</b>
<b>Female Mouse</b>				
Histiocytic sarcoma	30.8	6.82	0.124	0.18
Heart hemangiosarcoma	11.6	2.57	0.011	2.05
Forestomach	9.22	2.04	0.021	1.06
Lymphocytic lymphoma	8.08	1.79	0.023	0.96
Mammary gland	5.09	1.13	0.031	0.71
Ovary	4.74	1.05	0.035	0.64
Harderian gland	4.00	0.89	0.043	0.52
Liver	2.82	0.62	0.061	0.36
Lung	1.06	2.35	0.136	0.16
<b>Male Mouse</b>				
Lymphocytic lymphoma	46.6	103	0.006	1.68
Forestomach	19.2	42.5	0.008	2.94
Heart hemangiosarcoma	12.0	26.6	0.013	3.56
Histiocytic sarcoma	7.42	16.4	0.021	0.31
Liver	3.80	8.41	0.043	0.52
Harderian gland	1.92	4.25	0.072	1.06
Lung	1.48	3.27	0.099	0.22

## Supporting Animal Studies: Non-Cancer Effects

The toxicology of BD has been extensively studied in animal systems, particularly in rats and mice. Reviews of these studies have been compiled in several references[25, 26, 37]. Although the database is not extensive, BD appears to have low acute toxicity in animal systems. Subchronic dominant lethal studies[38, 39] of mice (65 ppm, 6 hr/day, 5 day/wk, 4 weeks) have shown that fetal death is the most sensitive reproductive endpoint.

In a lifetime chronic inhalation and carcinogenicity study of B6C3F<sub>1</sub> mice conducted under the auspices of the National Toxicology Program (NTP)[33], the most sensitive reproductive endpoints were ovarian atrophy (at 6.25 ppm) in female mice and testicular atrophy (at 625 ppm) in male mice.

EPA's IRIS[4] Inhalation Reference Concentration (RfC) of 0.9 ppb ( $20 \times 10^{-4} \text{ mg/m}^3$ ) for chronic inhalation exposure to BD is based on ovarian atrophy and was determined using data from a two-year inhalation bioassay[33]. Because of high early mortality in mice exposed to 625 ppm, this group was excluded from analysis. Over a lifetime of exposure, female mice in all BD-exposed groups experienced statistically significant increases in ovarian atrophy. Human equivalent exposures were determined by adjusting the 6-hour/day, 5-day/week animal exposure to 24 hours/day, 7 days/week. Ovarian atrophy was modeled only to age 50 in humans because "...1,3-butadiene-induced ovarian atrophy is believed to result from follicular failure, and after menopause, follicles would no longer be viable."

## NCSAB Acceptable Ambient Level Recommendation

As discussed previously, candidate AALs were generated from Delzell 1995 and Delzell 2005 epidemiological data for leukemia mortality, using 70- and 78-year lifespans and central as well as upper and lower 95% confidence limit estimates of  $\beta$ . Only the 1995 Delzell data were utilized in the EPA and Health Canada health assessment documents. However, the NCSAB has chosen to rely on the more recent Delzell 2005 data in establishing its recommended AAL range for a 78-year lifespan, which is summarized in Table 5.

**Table 5 – AAL Candidates ( $\text{mg/m}^3$ )  $\times 10^{-4}$  at  $10^{-6}$  risk, 78-year lifespan**

Delzell 2005, $\beta_{\text{LCL}}$	16.8
Delzell 2005, $\beta$	12.8
Delzell 2005, $\beta_{\text{UCL}}$	8.8

The NCSAB recommends that the Acceptable Ambient Level for BD be revised from  $1.7 \times 10^{-4} \text{ mg/m}^3$  to  $12.8 \times 10^{-4} \text{ mg/m}^3$ , the preferred central estimate within the recommended AAL range of risks of  $(4.4, 16.8) \times 10^{-4} \text{ mg/m}^3$ . Note that the low end of the recommended AAL range was determined by dividing the candidate AAL obtained with the upper 95% confidence limit estimate of the Cox regression coefficient ( $\beta_{\text{UCL}}$ ) by a factor of 2 to account for residual uncertainties.

Adoption of an AAL in this range will also be protective against ovarian atrophy, the most sensitive non-cancer endpoint observed in BD-exposed laboratory animals.

### **Averaging Time**

Based on the carcinogenicity of BD, the NC Division of Air Quality has determined that the AAL should be expressed as an annual average.

## **Comparison with the EPA Cancer Risk Assessment**

The EPA health assessment of BD as reported in IRIS[26] is for leukemia incidence based on the Delzell *et. al.* 1995 analysis, use of a linearized multi-stage dose-response model, and an assumed 85-year lifespan. The resulting 95% upper confidence limit estimate of the inhalation unit risk (IUR) is 0.04/ppm. EPA also employed an adjustment factor of 2 to allow for possible increases in mammary tumors in females as well as tumors at other sites in both males and females, producing a final IUR estimate of 0.08/ppm. The AAL that would correspond to this adjusted IUR is  $0.28 \times 10^{-4} \text{ mg/m}^3$ .

Respectfully Submitted,

### **Secretary's Science Advisory Board on Toxic Air Pollutants**

Thomas B. Starr, Ph.D. and Chairman  
Woodhall Stopford, MD, MSPH  
Elaina Kenyon, Ph.D., DABT  
J. Wayne Spoo, DVM, DABT, DAVBT  
Man-Sung Yim, Sc.D.

Liaison to the Secretary's Science Advisory Board  
Reginald C. Jordan, Ph.D., CIH

Unanimously adopted: January 18, 2007

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## **AGENDA ITEM 4**

458. Remove Voided Parts of Prevention of Significant Deterioration (PSD) Rule

### **Reason for Action**

To remove parts of the Prevention of Significant Deterioration Rule voided by court action on the federal PSD regulations.

### **Scope/Nature/Summary**

In June 2005 the D. C. Circuit Court vacated portions of the federal PSD regulation dealing with the “clean unit test” and “pollution control projects”. EPA petitioned for re-hearing of the case that prompted the vacature, but the request was denied. This change involves amending Rule 15A NCAC 02D .0530, Prevention of Significant Deterioration, the state PSD rule, by removing the definition of “pollution control project” in Paragraph (b)(2) to be consistent with the federal regulation. Also, paragraphs (j) and (k) on the “clean unit test” are to be removed for consistency with the federal requirements.

The amendment is being proposed at the suggestion of staff.

### **Statutory Authority**

G. S. 143-215.3(a)(1); 143-215.107(a)(3); 143-215.107(a)(5); 143-215.107(a)(7); 143-215.108(b); 150B-21.6.

## **AGENDA ITEM 5**

### 459. Update Bulk Gasoline Plant Rule

#### **Reason for Action**

To remove obsolete language and exclude gasoline bulk plants from the general 15 lb VOC/day exemption in 15A NCAC 02D .0902, Applicability.

#### **Scope/Nature/Summary**

The Bulk Gasoline Plants rule, 15A NCAC 02D .0926, is proposed to be amended to update the rule, provide consistency in terminology throughout, and clarify existing language based on field inspector experience. The language in 15A NCAC 02D .0902, Applicability, is also proposed to be revised to exclude bulk plants from the general 15 lb VOC /day exemption.

The amendments are being proposed at the suggestion of staff.

#### **Statutory Authority**

G. S. 143-215.3(a)(1); 143-215.107(a)(5).

## **AGENDA ITEM 6**

### 460. Revise Permit Exemption for Landfills

#### **Reason For Action**

To clarify the permit exemption for landfills in 15A NCAC 02Q .0102, Activities Exempted from Permit Requirements.

#### **Scope/Nature/Summary**

The permit exemption rule is proposed to be amended to clarify its applicability to landfills. 15A NCAC 02Q .0102, Activities Exempted from Permit Requirements, is proposed to be revised to remove the reference to “flares” from the description of exempt landfills. The term creates confusion regarding whether a flare is a control device or an emission source and is unnecessary. No monitoring is required. The proposed amendment will eliminate confusion and result in landfills being treated like other sources: sources exempted from permitting are not required to be permitted simply because of the addition of a control device. Any landfill required to have a permit under the Title V program will remain subject to those permitting requirements.

The amendment is being proposed at the suggestion of staff.

#### **Statutory Authority**

G. S. 143-215.3(a)(1); 143-215.107(a)(4); 143-215.108.