National Advisory Committee (NAC)
for Acute Exposure Guideline Levels (AEGLs) for Hazardous Substances

June 20-22, 2007

Meeting-43 Highlights

Swedish Seaman's Church
Rotterdam, Netherlands

INTRODUCTION

Marcel van Raaij welcomed the committee and members and guests introduced themselves.

The draft NAC/AEGL-42 meeting highlights were reviewed. A motion was made by Henry Anderson and seconded by Calvin Willhite to accept the minutes as proposed. The motion passed unanimously by a show of hands (Appendix A). The Final NAC/AEGL-42 meeting highlights are attached (Appendix B).

The highlights of the NAC/AEGL-43 meeting are summarized below along with the Meeting Agenda (Attachment 1) and the Attendee List (Attachment 2). The subject categories of the highlights do not necessarily follow the order listed in the NAC/AEGL-43 Agenda.

Ernest Falke distributed a CD to attendees. This CD contains the most recent versions of TSDs considered by the AEGL program to date. It includes Proposed, Interim,, and Final documents. Ernie Falke briefly discussed the NAS/COT schedules and process and noted the possibility of an alternate process for finalization. Although the NAS/COT process has been slow, there are currently 5 volumes published covering 31 priority chemicals.

Paul Tobin provided an overview of the AEGL program (Attachment 3) for guests and new participants. George Woodall commented on residual risk; some individuals are concerned that the AEGL values (especially AEGL-1) may not address situations where effects may last for longer than 1 day. He noted that some individuals take issue with the last paragraph in the preface of the AEGL TSDs relating to air concentrations below AEGL-1. George Rusch suggested that Paul Tobin investigate how the NAC/AEGL officially responds to issues regarding AEGL use and interpretation of the AEGL definitions. It was also suggested that the COT Subcommittee on AEGLs be tasked with this inasmuch as the definitions are part of the NAS-approved and published AEGL SOPs.

Dr. Sylvie Tissot (French National Coordinator for the OECD TGP INERIS) gave a brief overview of the AETL program (Attachment 4) noting that AETL 1, 2, and 3 were analogous to AEGL 1, 2, and 3 with the exception that the AETLs have an additional level-3 value for use in land planning (e.g., no use, limited use, etc.) in addition to values for emergency planning and response. Additionally, the AETLs do not consider sensitive populations.

Robin Fields (United Kingdom) stated that at the Ispra, Italy, meeting the ACUTEX program decided to include sensitive populations in its definitions.

REVISIT of CHEMICALS/ISSUES

Toluene (CAS No. 108-88-3) PBPK Issues

Staff Scientist: Sylvia Talmage, ORNL
Chemical Manager: George Woodall, U.S. EPA

George Woodall explained that at NAC-42 (March, 2007), AEGL-2 and AEGL-3 values for toluene were adopted. However, further discussion at NAC-42 led to consideration of another lethality study for AEGL-3 (Wada et al., 1989) (Attachment 5). The alternative study used Wistar rats which lacked modeling parameters. Therefore, a poll of the NAC affirmed support of the original approach and the toluene AEGL values originally considered.

Fluorosulfonic acid (CAS No. 7789-21-1) Update

Staff Scientist: Cheryl Bast, ORNL
Chemical Manager: Ernest Falke, U.S. EPA; George Rusch, Honeywell Corp.

There are no data currently available for development of AEGL values for fluorosulfonc acid.

Magnesium diamide (CAS No. 7803-54-5) Update

Staff Scientist: Cheryl Bast, ORNL
Chemical Manager: Ernest Falke, U.S. EPA; George Rusch, Honeywell

Cheryl Bast reported that this chemical is a no-data situation. Deliberations were tabled.

Silicon Tetrafluoride (CAS No. 7783-61-1) Revisit

Staff Scientist: Cheryl Bast, ORNL
Chemical Manager: Ernest Falke, U.S. EPA

Cheryl Bast provided a review/update for this chemical (Attachment 6). Data were insufficient for derivation of AEGL-1 values for silicon tetrafluoride. Therefore, AEGL-1 values were not proposed. In the absence of appropriate chemical-specific data, the proposed AEGL-3 values were divided by 3 to derive proposed AEGL-2 values for silicon tetrafluoride. This approach was justified by the relatively steep concentration-response curve.

Proposed AEGL-3 values were based on an estimated 1-hour lethality threshold of 307 ppm (one-third the 1-hour LC_{50} of 922 ppm) (Scheel et al., 1968). This approach was justified by the relatively steep concentration-response with regard to lethality in another study (60% mortality in rats exposed to 100 ppm and 100% mortality at 150 ppm; exposures were 6 hr/day, up to 5 days) (IRI, 1988). Values were scaled across time using the $C^n \times t = k$ equation, where n = 3 when extrapolating to shorter time points and n = 1 when extrapolating to longer time points in order to derive values protective of human health (NRC, 2001). Uncertainty factors of 3 each were applied for inter- and intraspecies variability because contact irritation is not expected to vary greatly between or within species (total UF = 10). A modifying factor of 3 was also applied for the sparse data base; therefore, the total adjustment was 30. For the AEGL-1, Marcel van Raaij made a motion to derive AEGL-1 values based on irritation in rats repeatedly exposed to 0.3 ppm silicon tetrafluoride 6 hours/day, 5 days/week for 4 weeks (IRI, 1988). An intraspecies uncertainty factor of 3 was applied because contact irritation is not expected to vary greatly within species. An interspecies uncertainty factor of 1 was applied because only irritation was noted and did not increase in severity throughout a 4-week study. Furthermore, the irritation partially resolved between exposures. A modifying factor of 2 was applied for the sparse data base. Therefore, the total adjustment was 6. Values were held constant across time because minor irritation does not vary over time. Bob Benson seconded the motion which passed unanimously (Appendix C). For the AEGL-3, Bob Benson motioned (seconded by Calvin Willhite) to accept the AEGL-3 values as proposed (19 ppm, 13 ppm, 10 ppm, 2.6 ppm and 1.3 ppm for the 10-min, 30-min, 1-hr, 4-hr, and 8-hr durations, respectively, UFs of 3 and 3, MF of 3; and the AEGL-2 values as 1/3 of the level 3 values. The motion passed (YES: 17; NO: 0; ABSTAIN:0; Appendix C). Marcel van Raaij commented that the MF may be too high based upon considerations of the toxicity relative to HF.

Summary of AEGL Values for Silicon Tetrafluoride

Classification	10-min	30-min	1-h	4-h	8-h	Endpoint (Reference)
AEGL-1 (Nondisabling)	0.05 ppm (0.21 mg/m^3)	0.05 ppm (0.21 mg/m^3)	0.05 ppm (0.21 mg/m^3)	0.05 ppm (0.21 mg/m^3)	0.05 ppm (0.21 mg/m^3)	Irritation in rats (IRI, 1998)
AEGL-2 (Disabling)	6.3 ppm (27 mg/m^3)	4.3 ppm (18 mg/m^3)	3.3 ppm (14 mg/m^3)	0.87 ppm (3.7 mg/m^3)	0.43 ppm (1.8 mg/m^3)	One third the AEGL-3 values (NRC, 2001)
AEGL-3 (Lethal)	19 ppm (80 mg/m^3)	13 ppm (55 mg/m^3)	10 ppm (42 mg/m^3)	2.6 ppm (11 mg/m^3)	1.3 ppm (5.5 mg/m^3)	Estimated 1-hr lethality threshold in rats (Scheel et al., 1968)

Review of Developmental Toxicity

Marcel van Raaij, RIVM

Marcel van Raaij presented the work currently being conducted at RIVM regarding the relevance of developmental toxicity data in the development of acute exposure limits (Attachment 7). Overall, it was found that gross maternal toxicity observed in repeated dose developmental toxicity studies does not represent gross toxicity in single dose experiments; use of a NOAEL from a repeated dose developmental study will provide a conservative estimate of the NOAEL for a single dose of most developmental toxicants; and differences between single and repeated dose NOAELs is modest (for resorptions and malformations the difference is very limited).

REVIEW of PRIORITY CHEMICALS

16 Selected Chlorosilanes

Allyl trichlorosilane (CAS Reg. No. 107-37-9)
Amyl trichlorosilane (CAS Reg. No. 107-72-2)
Butyl trichlorosilane (CAS Reg. No. 7521-80-4)
Chloromethyl trichlorosilane (CAS Reg. No. 1558-25-4)
Dichlorosilane (CAS Reg. No. 4109-96-5)
Diphenyl dichlorosilane (CAS Reg. No. 80-10-4)
Dodecyl trichlorosilane (CAS Reg. No. 4484-72-4)
Hexyl trichlorosilane (CAS Reg. No. 928-65-4)
Nonyl trichlorosilane (CAS Reg. No. 5283-67-0)
Octadecyl trichlorosilane (CAS Reg. No. 112-04-9)
Octyl trichlorosilane (CAS Reg. No. 5283-66-9)
Propyl trichlorosilane (CAS Reg. No. 141-57-1)
Trichloro(dichlorophenyl)silane (CAS Reg. No. 27137-85-5)
Trichlorophenylsilane (CAS Reg. No. 98-13-5)
Trichlorosilane (CAS Reg. No. 10025-78-2)
Vinyl trichlorosilane (CAS Reg. No. 75-94-5)

Staff Scientist: Cheryl Bast, ORNL
Chemical Manager: Ernest Falke, U.S. EPA

Cheryl Bast summarized the data in the TSD (Attachment 8). The chlorosilanes are corrosive, and inhalation exposure may cause nasal, throat, or lung irritation, coughing, wheezing, and /or shortness of breath. Chlorosilanes react rapidly with water, steam, or moisture and decompose to form hydrogen chloride gas and silanols, which condense spontaneously to form highly cross-linked polymeric gels. Although chemical-specific data are not available for many of the title chlorosilanes, acute inhalation data from rat studies are available for structurally-similar chlorosilanes (n-propyltrichlorosilane, methyltrichlorosilane, vinyltrichlorosilane, ethyltrichlorosilane, methylvinyldichlorosilane, methyldichlorosilane, dimethyldichlorosilane, dimethylchlorosilane, and trimethylchlorosilane). These data suggest that the acute toxicity of monochlorosilanes, dichlorosilanes, and trichlorosilanes is due to the hydrogen chloride hydrolysis product; acute toxicity of these chlorosilanes is both qualitatively (based on clinical signs) and quantitatively (based on molar equivalents of hydrogen chloride) similar to that of HCl (Jean et al., 2006). Complete hydrolysis of one mole of a monochlorosilane would yield a maximum of one mole of hydrogen chloride. Complete hydrolysis of a dichlorosilane would yield a maximum of two moles of hydrogen chloride, and complete hydrolysis of a trichlorosilane would yield a maximum of three moles of hydrogen chloride. Therefore, proposed AEGL values for dichlorosilanes were derived by dividing the hydrogen chloride AEGL values by a molar adjustment factor of two, and similarly, proposed AEGL values for the title trichlorosilanes were derived by dividing the hydrogen chloride AEGL values by a molar adjustment factor of three. A motion was made by Ernest Falke and seconded by Dieter Heinz to adopt AEGL-1, AEGL-2, and AEGL-3 values for all 16 chlorosilanes as proposed. The motion passed (YES: 17; NO: 0; ABSTAIN: 0; Appendix D for dichlorosilanes and Appendix E for trichlorosilanes). Suggestions for document revision included: adding a statement to the executive summary and introduction saying that only HCl is released into the air; adding a paragraph to the introduction on reported chlorosilane releases (amount, reason, etc), and adding footnotes to tables showing the formula to convert ppm to mg/m^3. This should be done so that separate tables will not be needed for each of the 21 chlorosilanes at several places in the document.

Summary of AEGL Values Selected Chlorosilanes							
Compound	**Classification**	**10-min**	**30-min**	**1-h**	**4-h**	**8-h**	**Endpoint (Reference)**
DICHLOROSILANES Dichlorosilane	AEGL-1	0.90 ppm	0.90 ppm	0.90 ppm	0.90 ppm	0.90 ppm	Hydrogen chloride AEGL-1 values divided by a molar adjustment factor of 2 adopted as AEGL-1 values for Dichlorosilane (NRC, 2004)
Diphenyl dichlorosilane	AEGL-2	50 ppm	22 ppm	11 ppm	5.5 pm	5.5 ppm	Hydrogen chloride AEGL-2 values divided by a molar adjustment factor of 2 adopted as AEGL-2 values for Dichlorosilane (NRC, 2004)
	AEGL-3	310 ppm	110 ppm	50 ppm	13 ppm	13 ppm	Hydrogen chloride AEGL-3 values divided by a molar adjustment factor of 2 adopted as AEGL-3 values for Dichlorosilane (NRC, 2004)
TRICHLOROSILANES Allyl trichlorosilane Amyl trichlorosilane Butyl trichlorosilane Chloromethyl trichlorosilane	AEGL-1	0.60 ppm	0.60 ppm	0.60 ppm	0.60 ppm	0.60 ppm	Hydrogen chloride AEGL-1 values divided by a molar adjustment factor of 3 adopted as AEGL-1 values for Trichlorosilanes (NRC, 2004)
Dodecyl trichlorosilane Hexyltrichlorosilane Nonyl trichlorosilane Octadecyl trichlorosilane Octyl trichlorosilane	AEGL-2	33 ppm	14 ppm	7.3 ppm	3.7 pm	3.7 ppm	Hydrogen chloride AEGL-2 values divided by a molar adjustment factor of 3 adopted as AEGL-2 values for Trichlorosilanes (NRC, 2004)
Propyl trichlorosilane Trichloro(dichlorophenyl)silane Trichlorophenylsilane Trichlorosilane Vinyl trichlorosilane	AEGL-3	210 ppm	70 ppm	33 ppm	8.7 ppm	8.7 ppm	Hydrogen chloride AEGL-3 values divided by a molar adjustment factor of 3 adopted as AEGL-3 values for Trichlorosilanes (NRC, 2004)

Silicon Tetrachloride (CAS No. 10026-04-7)

Staff Scientist: Cheryl Bast, ORNL
Chemical Manager: Ernest Falke, U.S. EPA

Cheryl Bast summarized the data in the TSD (Attachment 9). Chemical-specific data are limited for silicon tetrachloride; however, acute inhalation data from rat studies are available for structurally-similar chlorosilanes. These data suggest that the acute toxicity of chlorosilanes is due to the hydrogen chloride hydrolysis product; acute toxicity of these chlorosilanes is both qualitatively (based on clinical signs) and quantitatively (based on molar equivalents of hydrogen chloride) similar to that of HCl. Complete hydrolysis of one mole of silicon tetrachloride would yield a maximum of four moles of hydrogen chloride. Therefore, proposed AEGL values for silicon tetrachloride were derived by dividing the hydrogen chloride AEGL values by a molar adjustment factor of four. A suggestion was made to provide production volume, release incidences and rate of hydrolysis and to include silicon tetrachloride in the "Selected Chlorosilanes" TSD (see above). Bob Benson motioned (second by George Woodall) to adopt the AEGL values as proposed but to revisit the values if it is found that compete hydrolysis does not occur. The motion passed unanimously (YES: 17; NO: 0; ABSTAIN: 0; Appendix F)

Summary of AEGL Values for Silicon Tetrachloride

Classification	10-mim	30-min	1-h	4-h	8-h	Endpoint (Reference)
AEGL-1	0.45 ppm (0.68 mg/m^3)	0.45 ppm (0.68 mg/m^3)	0.45 ppm (0.68 mg/m^3)	0.45 ppm (0.68 mg/m^3)	0.45 ppm (0.68 mg/m^3)	Hydrogen chloride AEGL-1 values divided by a molar adjustment factor of 4 adopted as AEGL-1 values for silicon tetrachloride (NRC, 2004)
AEGL-2	25 ppm (39 mg/m^3)	11 ppm (16 mg/m^3)	5.5 ppm (8.3 mg/m^3)	2.8 ppm (4.3 mg/m^3)	2.8 ppm (4.3 mg/m^3)	Hydrogen chloride AEGL-2 values divided by a molar adjustment factor of 4 adopted as AEGL-2 values for silicon tetrachloride (NRC, 2004)
AEGL-3	160 ppm (230 mg/m^3)	53 ppm (78 mg/m^3)	25 ppm (39 mg/m^3)	6.5 ppm (9.8 mg/m^3)	6.5 ppm (9.8 mg/m^3)	Hydrogen chloride AEGL-3 values divided by a molar adjustment factor of 4 adopted as AEGL-3 values for silicon tetrachloride (NRC, 2004)

Agent BZ (quinuclidinyl benzilate) (CAS No. 6581-06-2)

Staff Scientist: Robert Young, ORNL
Chemical Manager: Glenn Leach, USACHPPM

Robert Young presented a summary of the available data and an overview of the development of proposed AEGL values for Agent BZ (Attachment 10). Data from military studies with informed human volunteers provided the best basis for assessing critical effects (cognitive dysfunction incapacitation regarding military type tasks) for AEGL-2 development. Data did not allow for assessing effects that would be consistent with the AEGL-1 tier and, therefore no AEGL-1 values were recommended. Lethality data (short-term exposure only; generally less than 40 minutes) were available for several laboratory species. The AEGL -3 values were based upon lethality data in monkeys with a 10-fold reduction in an LCt_{50} serving as the POD. The available data did not allow for benchmark analysis. Following discussion regarding the difficulty in assessing critical effect for AEGL-specific tiers and that most of the exposure data are for very short durations, it was the consensus of the NAC to set AEGL values only for 10 minutes, 30 minutes and 1 hour durations. There was also discussion regarding the absence of developmental/reproductive toxicity data for Agent BZ. Following discussion regarding the relevance of such effects for a muscarinic receptor blocker, it was the consensus of the NAC to apply an MF of 3 to the proposed values to account for the absence of such data. The NAC voted unanimously (YES: 14; NO: 0; ABSTAIN: 0; Appendix G) to accept a 3-fold reduction (for absence of developmental/reproductive toxicity data) of the proposed values for the 10-minute, 30-minute, and 1-hour durations only (motion by Calvin Willhite, second by Dieter Heinz). It was proposed to have Dr. James Ketchum (an expert and principal investigator on the BZ studies) review the AEGL TSD and proposed AEGL values.

Summary of AEGL Values for Agent BZ (mg/m^3)

Classification	10-minute	30-minute	1-hour	4-hour	8-hour	Endpoint (Reference)
AEGL–1	NR	NR	NR	NR	NR	Not recommended; insufficient data
AEGL–2	0.20	0.067	0.030	NR	NR	Incapacitation threshold in human volunteer subjects (Ketchum, 1967); intersp. UF= 1; intrasp. UF=3; MF=3, n=1
AEGL–3	3.7	1.2	0.62	NR	NR	Estimated lethality threshold in monkeys (DoA, 1974); intersp. UF= 10; intrasp. UF=3; MF=3; n=1)

Chlorosulfonic Acid (CAS No. 7790-94-5)

Staff Scientist: Sylvia Milanez, ORNL
Chemical Manager: Ernest Falke, U.S. EPA; Susan Ripple, Dow Chemical Co.

An overview of the available data and the derivation of draft AEGL values were provided by Sylvia Milanez (Attachment 11). Chlorosulfonic acid hydrolyzes to sulfuric acid and hydrogen chloride. There was extensive discussion of the data and numerous approaches and potential AEGL values suggested, especially for the AEGL-3 tier, as well as discussion regarding use of the time scaling exponent from the sulfuric acid AEGLs. Ultimately, a POD of 735 mg/m^3 (highest non-lethal concentration in rats exposed for 1-hr; drooling, unkempt fur and wheezing were noted; Katz, 1987) was selected with a total uncertainty factor adjustment of 30 (intraspecies of 3 justified because of steep concentration-response, and Interspecies of 10 because data were not available to determine species variability). A time scaling *n* value of 3.7, derived from sulfuric acid data, was utilized. A motion to accept the values (45, 31, 25, 6.1, and 6.1 mg/m^3 for the 10-min., 30-min., 1-hr, 4-hr, and 8-hr durations, respectively) was made by Calvin Willhite and seconded by Dieter Heinz. The motion passed (YES: 13; NO: 1; ABSTAIN: 3; Appendix H). For AEGL-2, there was discussion regarding the use of a key study involving chlorosulfonic acid or developing values based on the H_2SO_4 AEGL-2 values. The use of the H_2SO_4 AEGL-2 values (8.7 mg/m^3 for all time points) was considered more appropriate because the values resulting from the Katz study were inconsistent with the H_2SO_4 analysis. A motion by Marcel van Raaij (seconded by Dieter Heinz) to accept values of 4.4 mg/m^3 for all AEGL-2 durations (H_2SO_4 AEGL-2 values divided by a MF of 2 to account for the greater toxicity of chlorosulfonic acid relative to H_2SO_4) passed (YES: 17; NO: 0; ABSTAIN: 0; Appendix H). Similarly, the AEGL-1 values were based upon a 2-fold reduction of the AEGL-1 values for H_2SO_4 (0.20 mg/m^3 for all durations). The motion made by Bob Benson (second by Ernest Falke) to accept the values passed (YES: 17; NO: 0; ABSTAIN: 0; Appendix H).

Summary of AEGL Values for Chlorosulfonic Acid (mg/m^3)						
Classification	**10-minute**	**30-minute**	**1-hour**	**4-hour**	**8-hour**	**Endpoint (Reference)**
AEGL–1	0.10	0.10	0.10	0.10	0.10	2-fold reduction of H_2SO_4 AEGL-1 values
AEGL–2	4.4	4.4	4.4	4.4	4.4	2-fold reduction of H_2SO_4 AEGL-2 values
AEGL–3	45	31	25	6.1	6.1	Lethality threshold, severe clinical signs in rats (Katz, 1987)

Methanesulfonyl Chloride (CAS No. 124-63-0)

Staff Scientist: Cheryl Bast, ORNL
Chemical Manager: Roberta Grant, TCEQ

Cheryl Bast noted that there are only limited data for this chemical and that a time scaling value (n) may be possible with new data (Attachment 12). Dr. Sylvie Tissot offered to help obtain the new studies for discussion at a future meeting. George Woodall initiated and Calvin Willhite seconded a motion to table deliberations on methanesulfonyl chloride pending acquisition of the report (new data) in question. The motion passed (YES: 15; NO: 2; ABSTAIN: 0; Appendix I).

Osmium Tetroxide (CAS No. 20816-12-0)

Staff Scientist: Robert Young, ORNL
Chemical Manager: Dieter Heinz, NFPA

Robert Young presented an overview of relevant data and development of the draft AEGL values (Attachment 13). Toxicity data for osmium tetroxide were limited to reports indicating ocular and respiratory tract irritation following occupational exposure and lethality data in animals. Data were insufficient for AEGL-1 derivation (approved by NAC poll; YES: 16; NO: 0; ABSTAIN 1; Appendix J). AEGL-2 values were based upon occupational exposure to 0.02 ppm for 2-6 hours (McLaughlin et al. 1946). The proposed AEGL values were based upon the 6-hour exposure duration but following a brief discussion it was decided to calculate the AEGL-2 values based on the lower (2-hour) limit of the exposures reported by McLaughlin et al.; this exposure resulted in reversible ocular irritation, headache, visual disturbances Uncertainty factors include 3 for intraspecies variability for a direct-contact irritant and 1 for interspecies (human occupational exposure). Time scaling used the default values of 1 and 3 for the $C^n \times t = k$ relationship. The resulting AEGL-2 values (0.015, 0.011, 0.0084, 0.0033, 0.0017 ppm for 10-min, 30-min, 1-hr, 4hr, and 8 hr) were approved (motion by Bob Benson, second by Dieter Heinz. YES: 16; NO: 1; ABSTAIN 0; Appendix J). The AEGL-3 values (5.0, 5.0, 4.0, 2.5, 2.0 ppm for 10-min, 30-min., 1-hr, 4-hr, and 8-hr motion by Bob Benson, second by Dieter Heinz) were approved (YES: 16; NO: 0; ABSTAIN 1; Appendix J). These values were based upon a NOAEL of 20 ppm for 8 hrs (10-day observation period) for lethality in rats (Shell Development Co. report provided courtesy of Ralph Gingell and Shell Health Services), uncertainty factors of 3 and 3 and default time scaling.

Summary of AEGL Values for Osmium Tetroxide (ppm)						
Classification	**10-minute**	**30-minute**	**1-hour**	**4-hour**	**8-hour**	**Endpoint (Reference)**
AEGL–1	NR	NR	NR	NR	NR	Not recommended; insufficient data

AEGL–2	0.015	0.011	0.0084	0.0033	0.0017	NOAEL for AEGL-2 effects; 0.02 pm, 2 hrs (McLaughlin et al., 19446), UF=3; n=1or3
AEGL-3	5.0	5.0	4.0	2.5	2.0	NOAEL for lethality in rats (20 ppm, 8 hrs) (Shell Development Co., 1955); UF=3x3; n=1 or 3.

Pentaborane (CAS No. 19624-22-7)

Staff Scientist: Sylvia Milanez, ORNL
Chemical Manager: George Woodall, U.S. EPA

Sylvia Milanez presented the data summary and development of the draft AEGL values for pentaborane (Attachment 14). Bob Benson requested that the Benchmark Dose Analysis be provided in the appendix of the TSD and queried the acceptability of the data. George Woodall noted that the data were good; $BMCL_{05}$ and BMC_{01} were very close. A discussion ensued regarding the value of n to be used for extrapolating across time. A value of 1.3, based on rat lethality data ranging from 5-60 min. (Weir et al., 1961;1964), was chosen instead of the originally proposed n = 1 based on dog data ranging from 2-15 minutes. The rat data were considered more robust and covered a larger span of time. Bob Benson then motioned (second by Marcel van Raaij) to accept the AEGL-3 values based on a threshold for lethality in rats. The motion passed unanimously (YES: 17; NO: 0; ABSTAIN: 0; Appendix K). Discussion on the AEGL-2 focused on the POD. Bob Benson noted that the1-hour exposure at 3 ppm was not an acceptable POD because the dogs were not subjected to the conditioned avoidance response (CAR) test, which was the most sensitive test of neurotoxicity. Thus, a 60-min exposure to 1.4 ppm was considered a NOAEL for CNS toxicity in dogs and was used as the POD for AEGL-2. Use of the exponent, n, of 1.3 from rat data was considered appropriate because rats and dogs were similarly sensitive and the critical effect in both species was neurotoxicity. Applying UF values of 3 and 3 and n of 1.3 for C^n x t = k, the AEGL-2 values of 0.56, 0.24, 0.14, 0.048, 0.028 ppm for 10-min., 30-min, 1-hr, 4-hr, and 8-hr were unanimously accepted (YES: 17; NO: 0; ABSTAIN: 0; Appendix K; motion by Bob Benson, second by George Woodall). AEGL-1 values were not recommended due to insufficient data (included as part of the preceding motion) (YES: 17; NO: 0; ABSTAIN: 0; Appendix K).

Summary of AEGL Values for Pentaborane (ppm)

Classification	10-minute	30-minute	1-hour	4-hour	8-hour	Endpoint (Reference)
AEGL–1	NR	NR	NR	N R	NR	Not recommended

AEGL–2	0.56	0.24	0.14	0.048	0.028	1.4 ppm NOAEL for CNS effects; UF=3x3; n=1.3
AEGL-3	2.8	1.2	0.70	0.24	0.14	Rat $BMCL_{05}$; UF=3x3, n=1.3

GENERAL ISSUES

ADMINISTRATIVE MATTERS

The site and time of future meetings was discussed briefly but not determined.

All items in the agenda were discussed as thoroughly as the time permitted. The meeting highlights were prepared by Cheryl Bast and Robert Young, Oak Ridge National Laboratory.

LIST OF ATTACHMENTS

The attachments were distributed during the meeting and will be filed in the EPA Docket Office.

Attachment 1. Meeting 43 agenda
Attachment 2. Meeting 43 attendee list
Attachment 3. AEGL Program Overview
Attachment 4. AETL Program Overview
Attachment 5. Toluene background information
Attachment 6. Review/update for silicon tetrafluoride
Attachment 7. RIVM Developmental toxicity presentation
Attachment 8. Selected chlorosilanes presentation
Attachment 9. Silicon tetrachloride presentation
Attachment 10. Agent BZ presentation
Attachment 11. Chlorosulfonic acid presentation
Attachment 12. Methanesulfonyl chloride presentation
Attachment 13. Osmium tetroxide presentation
Attachment 14: Pentaborane presentation

LIST OF APPENDICES

Appendix A. Ballot for NAC-42 meeting summary
Appendix B. Final NAC-42 Meeting Highlights
Appendix C. Ballot for silicon tetrafluoride
Appendix D. Ballot for dichlorosilanae, diphenyl dichlorosilane
Appendix E. Ballot for trichlorosilanes
Appendix F. Ballot for silicon tetrachloride
Appendix G. Ballot for agent BZ
Appendix H. Ballot for chlorosulfonic acid
Appendix I. Ballot for methanesulfonyl chloride
Appendix J. Ballot for osmium tetroxide
Appendix K. Ballot for pentaborane