NAC/AEGL Meeting 50: APRIL 13-15, 2010

Chemical: * APPROVE MINUTES **CAS Reg. No.:**

Action: Proposed_____ **Interim**_____ **Other**_____

Chemical Manager: **Staff Scientist:**

NAC Member	AEGL1	AEGL2	AEGL3	LOA	NAC Member	AEGL1	AEGL 2	AEGL3	LOA
Henry Anderson					John Hinz				
Marc Baril					Jim Holler	A			
Lynn Beasley					Clarion Johnson	A			
Alan Becker					Glenn Leach	A			
Robert Benson					Richard Niemeier				
Edward Bernas					Mattias Oberg				
Iris Camacho					Susan Ripple				
George Cushmac					George Rusch, Chair				
Richard Erickson					Daniel Sudakin				
Neeraja Erraguntla					Marcel vanRaaij	A			
David Freshwater					George Woodall				
Ralph Gingell					Alan Woolf				
					TALLY				
					PASS/ FAIL				

PPM, (mg/m^3)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	, ( )	, ( )	, ( )	, ( )	, ( )
AEGL 2	, ( )	, ( )	, ( )	, ( )	, ( )
AEGL 3	, ( )	, ( )	, ( )	, ( )	, ( )
LOA					
* = ≥10% LEL					
** = ≥ 50% LEL					
*** = ≥100% LEL					

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.
** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

* UNANIMOUSE TO APPROVE

NR= Not Recommended due to_____

AEGL 1 Motion by: John Hinz **Second by:** Woolf
AEGL 2 Motion by:_____ **Second by:**
AEGL 3 Motion by:_____ **Second by:**
LOA Motion by:_____ **Second by:**

GMR **Approved by Chair:** * _____ **DFO:** _____ **Date:** 4/13/10

* I CERTIFY THE MINUTES REPRESENT AN ACCURATE RECORD OF THIS MEETING.

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

September 9-11, 2009

Meeting-49 Highlights

EPA-RTP Auditorium (Room C111-A&B)
U.S. EPA
109 TW Alexander Drive
Research Triangle Park, NC 27711

INTRODUCTION

Chairman George Rusch opened the meeting by calling for an introduction of all committee members and guests. R. Julian Preston, Associate Director for Health, NHEERL, welcomed the group and provided a brief overview of the U.S. EPA Research Triangle Park facility.

The draft NAC/AEGL-48 meeting highlights were reviewed. A motion to accept the minutes as written was made by Bob Benson (second by David Freshwater) and passed unanimously (Appendix A). The Final NAC/AEGL-48 meeting highlights are included as Appendix B.

Ernie Falke announced that NAS/COT meeting 19 would be held in October, 2009, in Amsterdam, The Netherlands. Sixteen chemicals, including Jet Fuel, are on the agenda for this meeting. NAS AEGLs Volume 7 has been published and should have been distributed to NAC members, and a pre-publication version of NAS AEGLs Volume 8 is scheduled for release in September, 2009. The interim report from NAS/COT meeting 18 (May, 2008) has just been received by the AEGL Program.

Ernie Falke provided an update on the status of the Agent VX TSD in consideration of new data. A more thorough overview may be presented at the next NAC meeting to provide a balanced discussion between the NAC and Douglas Summerville, U.S. Army ECBC.

Ernie Falke announced that this meeting will be the last official NAC meeting for the Oak Ridge National Laboratory staff. A new contractor should be in place by NAC-50. Continuity issue concerns were expressed by several committee members.

Paul Tobin informed the NAC that the 12th Federal Notice containing 19 chemicals had been published. Any comments received will be discussed at NAC-50. Paul also introduced new NAC members: Neeraja Erraguntla (Texas), Mattias Oberg (Sweden), Richard Erickson (U.S. Navy), and Clarion Johnson (Exxon-Mobil).

The highlights of the NAC/AEGL-49 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-48 Agenda.

CHEMICAL REVISITS/STATUS UPDATES

Ricin (CAS No. 9009-86-3)

Staff Scientist: Robert Young, ORNL
Chemical Manager: Jim Holler, ATSDR

Bob Young informed the NAC that additional information regarding the new ricin data (Gomez et al., 2009) presented in a poster session at the Society of Toxicology meeting in March, 2009, had not yet been obtained. These new data, from acute inhalation toxicity studies in both rats and mice, suggest that the currently proposed ricin AEGL values (key study is Griffiths et al, 1995) may be too high. Further discussion of this chemical will be postponed until a published report if the Gomez data becomes available.

Lead (CAS No. 7439-92-1)

Staff Scientist: Jennifer Rayner, ORNL
Chemical Manager: George Woodall, U.S. EPA

Jennifer Rayner reviewed the sparse data set for lead (Attachment 3) and informed the NAC that data appear to be insufficient for derivation of AEGL values. George Woodall suggested that the NCEA staff conducting the ambient guideline reassessment may be a source of information. This chemical was put in holding status until appropriate data may be obtained.

Dichlorvos (CAS No. 62-73-7)

Staff Scientist: Jennifer Rayner, ORNL
Chemical Manager: John Hinz, U.S. Air Force

Jennifer Rayner provided a review of the available data and currently proposed AEGL values (balloted at NAC-47) (Attachment 4). Jennifer then presented data from a recently obtained study (MacDonald, 1982). After discussion (including vapor pressure, dose response, evaluation of whether to use as a key or supporting study) of the data from the MacDonald (1982) report, the committee chose not to use these data as a key or supporting study because of discrepancies in the data. The proposed AEGL values for dichlorvos were not revised and were considered to be protective of the population.

Hydrogen Selenide (CAS No. 7783-07-5)

Staff Scientist: Carol Wood, ORNL
Chemical Manager: Ernie Falke, U.S. EPA

Ernie Falke presented information (Zwart et al., 1989; 1992) concerning the derivation of the time scaling exponent 'n' for hydrogen selenide. Currently, an n of 2 is utilized; however, data may suggest that an n of 1 may be more appropriate. Extrapolation from the rat 1-hr LC_{01} of 66 ppm to 2 hours using an n of 2 to estimate the 2 hour LC_{01} yields a value of 47 ppm; this concentration is above the threshold for lethality at 2 hours (1/2 died at 40 ppm). This calls into question the derivation of n. Given the sparse of data used to derive n and the fact that the n of 2 does not predict what is expected at 2 hours, it may be reasonable to change the n to 1 (default). After discussion, the NAC decided maintain the value of n=2 because this n value was derived using methods consistent with the SOP. Furthermore, the resulting AEGL values are not meaningfully different. George Woodall, Marcel van Raaij, and Ernie Falke agreed to look at different ways to analyze the Zwart data as it applies to the C x t protocol.

REVIEW of PRIORITY CHEMICALS

Dimethyl Phosphite (CAS No. 868-85-9)

Staff Scientist: Cheryl Bast, ORNL
Chemical Manager: George Cushmac, U.S. DOT

Cheryl Bast presented a summary of the available data and an overview of the development of proposed AEGL values for dimethyl phosphite (DMP) (Attachment 5). AEGL-1 values were not proposed due to insufficient data. Proposed AEGL-2 values were based on clinical signs (labored breathing and ptosis) in mice exposed to 1575 ppm DMP for 6 hours (Hazleton, 1962). Inter- and intraspecies uncertainty factors of 3 each (total 10) were proposed because DMP is irritating, and much of the toxicity is likely caused by a direct chemical effect on the tissue; this type of portal-of-entry effect is not expected to vary greatly between species or among individuals. The interspecies uncertainty factor of 3 was also considered sufficient because no clinical signs were noted in rats or guinea pigs exposed to 1575 ppm for 6 hours. A modifying factor of 3 was also applied because of the sparse database and because the point-of-departure is a nominal concentration. Temporal scaling was performed using n=3 when extrapolating to shorter time points and n = 1 when extrapolating to longer time points using the $C^n \times t = k$ equation (NRC, 2001). The 30-minute AEGL-2 value was adopted as the 10-min value because of the added uncertainty of extrapolating from the 6-hr point-of-departure.

Two sets of AEGL-3 values were proposed. The first used the same point-of-departure, uncertainty factors and time scaling as used in the derivation of AEGL-2 values. However, no uncertainty factor was applied because the effects noted at the POD were below those defined by AEGL-3. The highest concentration causing no mortality in rats (843 ppm for 6 hr) was used as the point-of-departure for the second approach (Biodymanics, 1980a). Excessive lacrimation, partially closed

eyes, red nasal discharge, red-brown material around the nares, labored breathing, and unresponsiveness to sound stimuli were noted in rats exposed to 843 ppm DMP 6 hr/day for 5 days. Death was noted at the next concentration tested (934 ppm) essentially after one exposure because one rat was killed *in extremis* after day 1 of the study. Uncertainty factor application and time scaling are as described for AEGL-2. No MF was applied.

A motion was made by Susan Ripple, seconded by Jim Holler, to accept the AEGL-1 of NR, AEGL-2 values based on the Hazelton data, and AEGL-3 values based on the Biodynamics data for dimethyl phosphite. The motion passed. (Appendix C: 20 yes; 0 no; 0 abstain).

Summary of AEGL Values for Dimethyl Phosphite						
Classification	**10-minute**	**30-minute**	**1-hour**	**4-hour**	**8-hour**	**Endpoint (Reference)**
AEGL-1 (Nondisabling)	NR	NR	NR	NR	NR	Insufficient data
AEGL-2 (Disabling)	120 ppm (540 mg/m^3)	120 ppm (540 mg/m^3)	95 ppm (430 mg/m^3)	60 ppm (270 mg/m^3)	39 ppm (180 mg/m^3)	Labored breathing and ptosis in mice (Hazleton, 1962)
AEGL-3 (Lethal)	190 ppm (850 mg/m^3)	190 ppm (850 mg/m^3)	150 ppm (670 mg/m^3)	96 ppm (430 mg/m^3)	63 ppm (240 mg/m^3)	NOEL for mortality in rats (Biodynamics, 1980a)

NR: Not Recommended due to insufficient data. Absence of AEGL-1 values does not imply that concentrations below AEGL-2 are without effect.

Trimethyl Phosphite (CAS No. 121-45-9)

Staff Scientist: Cheryl Bast, ORNL
Chemical Manager: George Cushmac, U.S. DOT

Cheryl Bast presented a summary of the available data and an overview of the development of proposed AEGL values for trimethyl phosphite (TMP) (Attachment 6). The no-effect-level for clinical signs in rats (10 ppm) exposed to TMP 6 hr/day, 5 days/week for 4 weeks (Biodynamics, 1979) was used as the point-of-departure for AEGL-1 values. An intraspecies uncertainty factor of 3 was applied because the point-of-departure is from a repeated exposure study and the endpoint is not likely the result of a single exposure. An interspecies uncertainty factor of 1 was applied. Although an interspecies uncertainty factor (UF) of 3 might normally be applied, use of a total uncertainty factor of 10 yields AEGL-1 values that are not compatible with human occupational exposure data (AEGL-1 values derived with a total UF of 10 are 3.3, 2.3, 1.8, 1.1, and 0.60 ppm for 10-min, 30-min, 1-hr, 4-hr, and 8-hr, respectively). No effects were noted in workers repeatedly exposed up to 15 ppm (ACGIH, 1991). Temporal scaling was performed using n=3 when extrapolating to shorter time points and n = 1 when extrapolating to longer time points using the $C^n \times t = k$ equation (NRC, 2001). Extrapolation was used to derive the 10-minute value because the 6-hour point-of-departure is from a repeated exposure study.

The lens opacities in rats exposed to 101 ppm TMP 6 hours/day, 5 days/week for 4 weeks (Biodynamics, 1979) were used as the point-of-departure for AEGL-2 values. This endpoint was still present in some animals at 2-weeks post-exposure. An intraspecies uncertainty factor of 3 was applied because the point-of-departure is from a repeated exposure study and the endpoint is not

likely the result of a single exposure. The lens opacities observed in rats repeatedly exposed to 101 ppm TMP were noted after 2 weeks and continued to increase in frequency and severity after 4 weeks exposure, suggesting a cumulative effect. An interspecies uncertainty factor of 1 was applied. Although an interspecies UF of 3 might normally be applied, use of a total uncertainty factor of 10 yields AEGL-2 values that are not compatible with human occupational exposure data (AEGL-2 values derived with a total UF of 10 are 33, 23, 18, 12, and 6.0 ppm for 10-min, 30-min, 1-hr, 4-hr, and 8-hr, respectively). No effects were noted in workers repeatedly exposed up to 15 ppm (ACGIH, 1991). Time scaling is as described above for AEGL-1.

Up to 50% lethality was observed in mice exposed to 6450 ppm TMP for approximately 3 hours (Hazleton, 1962). In the absence of other appropriate data for deriving AEGL-3 values, this exposure concentration was divided by 3 to estimate a threshold for lethality (point-of-departure 2150 ppm). Inter- and intraspecies uncertainty factors of 3 each (total 10) were applied because TMP is highly irritating, and much of the toxicity resulting from an acute exposure is likely caused by a direct chemical effect on the tissue; this type of portal-of-entry effect is not expected to vary greatly between species or among individuals. Temporal scaling was performed using n=3 when extrapolating to shorter time points and n = 1 when extrapolating to longer time points using the $C^n \times t = k$ equation (NRC, 2001).

A motion was made by Bob Benson and seconded by Rick Niemeier to accept the AEGL-1, AEGL-2, and AEGL-3 values as proposed for trimethyl phosphite. The motion passed. (Appendix D: AEGL-1: 19 yes; 0 no; 1 abstain; AEGL-2 and AEGL-3: 20 yes; 0 no; 0 abstain).

Summary of AEGL Values for Trimethyl Phosphite						
Classification	**10-minute**	**30-minute**	**1-hour**	**4-hour**	**8-hour**	**Endpoint (Reference)**
AEGL-1 (Nondisabling)	11 ppm (56 mg/m^3)	7.6 ppm (39 mg/m^3)	6.1 ppm (31 mg/m^3)	3.8 ppm (19 mg/m^3)	2.5 ppm (13 mg/m^3)	NOEL for clinical signs in rats (Biodynamics, 1979)
AEGL-2 (Disabling)	110 ppm (560 mg/m^3)	77 ppm (390 mg/m^3)	61 ppm (310 mg/m^3)	38 ppm (190 mg/m^3)	25 ppm (128 mg/m^3)	Lens opacities in rats (Biodynamics, 1979)
AEGL-3 (Lethal)	560 ppm (2900 mg/m^3)	390 ppm (2000 mg/m^3)	310 ppm (1600 mg/m^3)	160 ppm (820 mg/m^3)	81 ppm (410 mg/m^3)	Estimated 3-hr lethality threshold in mice (Hazleton, 1962)

Methyl Iodide (CAS No. 74-88-4)

Staff Scientist: Sylvia Talmage, ORNL
Chemical Manager: Alan Becker, Florida A & M Univ.

Sylvia Talmage reviewed the history of the methyl iodide technical support document (Attachment 7). The document presented at NAC-44 in December 2007 was put on hold until data on the effect of excessive iodide/iodine intake in pregnant women could be clarified. The document presented at NAC-46 in December 2008 was put on hold until results of modeling studies with the adult rat and fetal rabbit were published. Although the modeling studies were not directly used to derive AEGL values for methyl iodide, the studies did identify effects and mode of action for the

various effects. Effects and mode of action for AEGL-relevant endpoints were: (1) lesions of the nasal passages in rats – glutathione depletion in nasal tissue and (2) neurotoxicity – effect of the circulating parent compound on nerve cells. Toxicity of iodide to the rabbit fetus was not used as a point of departure because iodide uptake is regulated in the human fetus whereas in the rabbit fetus it is not. Unregulated iodide uptake by the rabbit fetus leads to late fetal resorptions.

A weight-of evidence-approach was used to establish a point of departure for the AEGL-1. All data pertained to the rat. Both nasal lesions and neurotoxicity were addressed by the following relevant data: 27 ppm for 6 hours was a no-observed adverse effect level (NOAEL) for neurotoxicity (U.S. EPA 2006); 100 ppm for 1 hour was a NOAEL for nasal lesions (Reed et al., 1995); 100 ppm for 6 hours was a NOAEL for effect on breathing rate (DeLorme et al., 2009); 25 ppm was a 4-week NOAEL for nasal lesions and neurotoxicity (Monsanto et al., 1983); and 21 ppm was a subchronic NOAEL for nasal lesions and other effects (U.S. EPA, 2006). The actual point of departure, 27 ppm for 6 hours, was divided by uncertainty factors of 1 (uptake is greater in the rat than humans based on a higher blood:air partition coefficient for methyl iodide) and 3 (metabolism by glutathione is not expected to differ greatly among humans) for a total of 3 (27 ppm/3 = 9 ppm). The 6-hour 9 ppm value was time scaled ($C^n \times t = k$) with an n value of 2. The time-scaling factor was derived from several rat lethality data sets using the ten Berge log-probit model. In light of the no-effect value of 21 ppm in a subchronic study, the 8-hour AEGL-1 value was set equal to the 4-hour value.

The point of departure for the AEGL-2 was the 6-hour exposure to 100 ppm which resulted in reversible nasal lesions in the rat (Reed et al., 1995). Uncertainty factors and time scaling were the same as for the AEGL-1 above.

The lethality data sets of Eastman Kodak (1987), U.S. EPA (2006), and Reed et al. (1995) were entered into the ten Berge log probit model. The threshold for lethality was set at the lower limit of the 5% response (lower limit of the 95% confidence limit). The total uncertainty factor was 3. The program output automatically time-scaled the values (see table below). It was moved by Marcel van Raaij and seconded by George Woodall to accept the AEGL values. The motion passed (Appendix E: Yes: 19; No: 0; Abstain: 1).

Summary of AEGL Values for Methyl Iodide

Classification	10-min	30-min	1-h	4-h	8-h	Endpoint (Reference)
AEGL–1 (Nondisabling)	54 ppm	31 ppm	22 ppm	11 ppm	11 ppm	NOAEL for neurotoxicity- rat (U.S. EPA 2006)
AEGL–2 (Disabling)	200 ppm	120 ppm	82 ppm	41 ppm	29 ppm	Reversible lesions of the nasal passages – rat (Reed et al., 1995)
AEGL–3 (Lethal)	670 ppm	400 ppm	290 ppm	150 ppm	98 ppm	Four lethality data sets for the rat entered into ten Berge log-probit model (5% response)

The derived values for methyl iodide were compared with the interim values for methyl chloride and methyl bromide. The AEGL values were consistent with relative toxicity as determined by LC_{50} values in the rat.

Phosgene (CAS No. 75-44-5)

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

At NAC-48, the committee voted to revise phosgene AEGL values published as final in Volume 2 to incorporate new data. Cheryl Bast reviewed the new data and revised derivations (Attachment 8). The new data suggest that the dog may be more appropriate than the rat as an animal model for phosgene risk assessment. There is an instant, although transient, change in breathing reflex in the rat; therefore, exposures of less than 30 minutes may result in false negative responses. The recent data also suggest that with regard physiology of the respiratory tract and acinar structure of the lung, dogs are more similar to humans than rodents.

Appropriate data were not available for deriving AEGL-1 values for phosgene. Odor cannot be used as a warning for potential exposure. The odor threshold is reported to be between 0.5 to 1.5 ppm, a value above or approaching AEGL-2 and AEGL-3 values, and tolerance to the pleasant odor of phosgene occurs rapidly. Furthermore, following odor detection and minor irritation, serious effects may occur after a clinical latency period of 24 hours. Therefore, AEGL-1 values are not recommended.

The NOAEL for increased PMNs in BAL fluid observed in dogs (2.3 ppm for 30 minutes) (Pauluhn, 2006c) was used as the basis for deriving AEGL-2 values. The dog was chosen over rodents because, with regard physiology of the respiratory tract and acinar structure of the lung, dogs are more similar to humans than rodents. This endpoint was chosen because BAL fluid changes are a sensitive marker of phosgene-induced noncardiogenic pulmonary high-permeability edema following acute inhalation exposure (Pauluhn et al., 2007). An uncertainty factor of 1 was applied for interspecies extrapolation. In rats, c x t products of between 48 ppm·min and 60 ppm·min induced increased protein in BAL fluid , and no increase was noted from 24-30 ppm·min. In mice and hamsters, a C x t product of 48 ppm·min induced an increase of protein in BAL fluid, and no increase was noted at 24 ppm·min. However, in dogs, a C x t product of 129 ppm·min was necessary to cause an increase in protein in BAL fluid, and no increase was observed at 63 ppm·min. Thus, the CT product required to induce an increase in protein in BAL fluid in dogs is approximately two-fold greater than in rodents, and the NOAEL for increased BAL protein in dogs (63 ppm·min) is higher than the lowest-observed adverse effect level (LOAEL) values in rodents (48-60 ppm·min). Additionally, with regard to physiology of the respiratory tract and acinar structure of the lung, dogs are more similar to humans than rodents (Pauluhn, 2006a, 2006b, 2006c; Pauluhn et al., 2007). Collectively, these data suggest that an interspecies uncertainty factor of no more than 1 is justified when extrapolating from laboratory animals to humans. An uncertainty factor of 3 was applied to account for sensitive human subpopulations. The intraspecies UF of 3 is considered sufficient due to

the steep concentration-response curve (death in 2/10 rats exposed to 52.3 ppm and 6/10 exposed to 61.9 ppm for 10 min; 4/10 exposed to 13.4 ppm and 10/10 exposed to 16.7 ppm for 30-min; 4/10 exposed to 7.4 ppm and 10/10 exposed to 11.8 ppm for 1-hr; Pauluhn, 2006a) which implies limited intra-individual variability. Also, the mechanism of phosgene toxicity (binding to macromolecules and irritation) is not expected to vary greatly between individuals. The concentration-time relationship for many irritant and systemically-acting vapors and gases may be described by $C^n \times t = k$, where the exponent, n, ranges from 0.8 to 3.5 (ten Berge et al., 1986). Haber's Law $C \times t = k$; n=1 has been shown to be valid for phosgene within certain limits and will be used for scaling of the AEGL values for phosgene.

The AEGL-3 values were based on an estimated 1-hour lethality threshold of 3.9 ppm ($BMCL_{05}$) in rats (Pauluhn, 2006a). The duration of exposure in this study is expected to minimize inaccuracy in the estimated lethality threshold due to bradypnea in the rats. Uncertainty factor application and time scaling are as described above for derivation of AEGL-2 values.

It was moved by Bob Benson and seconded by Marc Baril to accept the AEGL values. The motion passed (Appendix F: AEGL-1 and AEGL-2: Yes: 20; No: 0; Abstain: 0; AEGL-3: Yes: 19; No: 0; Abstain: 1). Values are listed in the table below.

Summary of Proposed AEGL Values for Phosgene

Classification	10-min	30-min	1-hr	4-hr	8-hr	Endpoint (Reference)
AEGL-1 (Nondisabling)	NR	NR	NR	NR	NR	Not Recommended
AEGL-2 (Disabling)	2.3 ppm (9.5 mg/m^3)	0.77 ppm (3.2 mg/m^3)	0.38 ppm (1.6 mg/m^3)	0.096 ppm (0.39 mg/m^3)	0.048 ppm (0.19 mg/m^3)	Increased PMNs in BAL fluid in dogs (Pauluhn, 2006c)
AEGL-3 (Lethal)	7.8 ppm (32 mg/m^3)	2.6 ppm (11 mg/m^3)	1.3 ppm (5.3 mg/m^3)	0.33 ppm (1.4 mg/m^3)	0.16 ppm (0.66 mg/m^3)	Estimated 1-hr lethality threshold ($BMCL_{05}$) in rats (Pauluhn, 2006a)

NR: Not Recommended. Absence of AEGL-1 values does not imply that exposure to concentrations below AEGL-2 are without effect.

Dicrotophos (CAS No. 141-66-2)

Staff Scientist: Robert Young, ORNL
Chemical Manager: Bob Benson, U.S. EPA

Dicrotophos was first discussed at NAC-47. At that meeting the NAC decided to defer action until the TSD for monocrotophos was available to allow the NAC to consider both chemicals together. Monocrotophos is the hydrolysis product of dichrotophos. Inhalation data in animals are limited to conflicting lethality data for rats, poorly characterized exposure-response data for nonlethal effects, and inadequate information on the exposure concentration-duration relationship. Sachsse et al. (1974) reported both 1-hour and 4-hour LC_{50} values of 90 mg/m^3 for male and female rats exposed to dicrotophos (technical; 87.8% purity). AEGL-1 values for dicrotophos were not recommended due to insufficient data. Data were also insufficient to derive AEGL-2 values. The limited exposure-response data for rats, however, indicate that the exposure-response relationship for

dicrotophos is steep; 480 mg/m^3 to 720 mg/^{3} for technical formulation and 810 mg/m^3 to 860 mg/m^3 for a 38% solution) for a 1-hour duration spanned a lethality rate from 0% up to 100%. Consistent with NRC (2001) guidelines, a 3-fold reduction of the AEGL-3 values would provide a justifiable estimate of the AEGL-2 values. The 1-hour LC_{50} value of 90 mg/m^3 reported by Sachsee et al. (1974) served as the initial point-of-departure (POD) for AEGL-3. This value was adjusted to 78.9 mg/m^3 to adjust for reported 87.7% purity of the test article. Due to the steep exposure-response relationship for dicrotophos, a lethality threshold of 26.3 mg/m^3 for rats was estimated by a 3-fold reduction of the 78.9 mg/m^3 LC_{50} value. Chemical-specific data with which to assess species variability in the toxicity of inhaled dicrotophos are unavailable (data are limited to rats). However, the variability in the toxicity of dicrotophos and other organophosphate cholinesterase inhibitors is, in part, dependent upon the interaction with other less critical targets such as plasma ChE, carboxylesterases, and red blood cell ChE. In this respect, these cholinesterases may function as an effective repository for organophosphate ChE inhibitors and serve as a buffer against cholinergic-mediated adverse effects. Plasma ChE levels are greater in humans than in rodents, and human plasma ChE activity represents a greater portion of blood ChE activity relative to animal species. Furthermore, baseline RBC ChE activity is higher in humans relative to animal species which provides an additional protective advantage. Therefore, the proposed interspecies uncertainty factor was limited to 3. The default intraspecies uncertainty factor of 10 was maintained for dicrotophos AEGL-3 values. The underlying mechanism of organophosphates is inhibition of cholinesterase by phosphorylation of the esteratic site of the enzyme. Cholinesterases in the blood and tissues are known to be instrumental in limiting the amount of organophosphate compounds reaching critical targets such as brain ChE and acetylChE at cholinergic synapses. Genetic polymorphism has been shown for A-esterases (paraoxonase/arylesterase) in blood and liver of humans. Individuals expressing forms with low hydrolyzing activity are considered to be more susceptible to organophosphate anticholinesterase poisoning. About 3% of individuals possess genetically determined low levels of plasma cholinesterase and these individuals may exhibit greater sensitivity to some anticholinesterase compounds. Evidence for gender and age-related variability in the toxic response to organophosphates has been reported for humans (summarized in NRC, 2003). In the absence of chemical-specific data showing that dicrotophos would act contrary to other organophosphate cholinesterase inhibitors, an intraspecies uncertainty factor of 10 was retained. In the absence of definitive data to derive n, temporal scaling default exponents of n = 3 were applied when extrapolating to shorter time points and n = 1 when extrapolating to longer time points (NRC 2001). John Hinz made the motion to accept the values as presented. Mark Baril seconded the motion. The motion passed (Appendix G: Y: 20; N: 0; Pass: 0).

AEGL Values for dicrotophos (mg/m^3)						
Classification	**10-min**	**30-min**	**1-h**	**4-h**	**8-h**	**Endpoint (Reference)**
AEGL-1 (Nondisabling)	NR	NR	NR	NR	NR	Not recommended; insufficient data
AEGL-2 (Disabling)	0.53	0.37	0.29	0.073	0.037	3-fold reduction of AEGL-3 values
AEGL-3 (Lethality)	1.6	1.1	0.88	0.22	0.11	Lethality threshold estimated as 3-fold reduction of 1-hr LC_{50} of 78.9 mg/m^3 (90 mg/m^3 reported adjusted for 87.7% purity of test article) ÷ 3 = 26.3 mg/m^3 in rats (Sachsse et al., 1974); UF=10x3

NR: Not Recommended. Absence of AEGL-1 values does not imply that concentrations below the AEGL-2 are without effect.

Monocrotophos (CAS No. 6923-22-4)

Staff Scientist: Robert Young, ORNL
Chemical Manager: Bob Benson, U.S. EPA

Bob Young provided a review of the available data and draft AEGL values for monocrotophos (Attachment 9). Data are limited to LC_{50} studies for 1 and 4 hours duration of exposure. The 1 hour LC_{50} was 94 mg/m^{3}and the 4 hour LC_{50} was 80 mg/m^3. AEGL-1 values for monocrotophos were not recommended due to insufficient data. Data were also insufficient regarding effects consistent with AEGL-2 tier severity. No exposure-response data were available that identified effects consistent with AEGL-2 tier severity or that enabled an assessment of an exposure-response relationship. The available studies provided lethality benchmarks but no individual or exposure-specific response data. Although one study reported that typical cholinergic responses were observed in all exposure groups, the severity of the responses was not specified and it was unknown as to which, if any, of the exposures were without lethal responses. In the absence of data consistent with the AEGL-2 tier, the AEGL-2 values were estimated as a 3-fold reduction of the AEGL-3 values under the assumption that the exposure-response curve for monocrotophos was very steep like that of other organophosphates. The 1-hour LC_{50} of 94 mg/m^3 and 4-hour LC_{50} of 80 mg/m^3 (adjusted to 66.1 and 56.2 mg/m^3, respectively, to account for the 70.3% purity of the test article) for rats reported by Sachsse et al. (1974) were used as initial points-of-departure (POD) for derivation of AEGL-3 values. Lethality thresholds for these exposure durations were estimated as a 3-fold reduction of the adjusted 1-hr and 4-hr LC_{50} values; 22.0 mg/m^3 for 1-hour duration and 18.7 mg/m^3 for a 4-hour duration. Although data for monocrotophos are limited, this approach was justified by the fact that other organophosphates exhibit a steep exposure-response relationship, and it is assumed that monocrotophos having the same mode of action would likely exhibit a similar exposure-response relationship. The use of two duration-specific values within the AEGL duration span reflects the available data more than a default time scaling across the 10-minute to 8-hour time span. Uncertainty factor application is as described above for dicrotophos. The default procedure for time scaling was used (n = 3 or 1) as no data are available to derive a value of n. John Hinz made the motion to accept the values. Mark Baril seconded the motion. The motion passed (Appendix H: Yes: 20; No: 0; Abstain: 0).

AEGL Values for Monocrotophos (mg/m^3)						
Classification	**10-min**	**30-min**	**1-h**	**4-h**	**8-h**	**Endpoint (Reference)**
AEGL-1 (Nondisabling)	NR	NR	NR	NR	NR	Not recommended; insufficient data
AEGL-2 (Disabling)	0.43	0.31	0.24	0.21	0.10	AEGL-2 values estimated by a one-third reduction of AEGL-3 values
AEGL-3 (Lethality)	1.3	0.92	0.73	0.62	0.31	lethality threshold estimated as a 3-fold reduction of 1-hour and 4-hour rat LC_{50} values of 66.1mg/m^3 and 56.2 mg/m^3 (adjusted for 70.3% purity from 94 and 80 mg/m^3) to 22.0 and 18.8 mg/m^3 respectively) (Sachsse et al., 1974); UF=3x10; $C^n x\ t = k$, where n=1 or 3

NR: Not Recommended. Absence of AEGL-1 values does not imply that concentrations below the AEGL-2 are without effect.

Methamidophos (CAS No. 10265-92-6)

Staff Scientist: Sylvia Talmage, ORNL
Chemical Manager: Henry Anderson, Wisconsin Department of Health

Data on the organophosphate pesticide, methamidophos, were presented by Sylvia Talmage (Attachment 10). All acute inhalation studies used the rat as the test species; methamidophos was administered as a liquid aerosol. Lethality data from two different laboratories, Sanga 1983; 1984 and Pauluhn 1986, did not agree. In both laboratories, nominal concentrations were several-fold higher than analytical concentrations, indicating that the aerosol atmosphere was difficult to maintain. The data of Pauluhn was chosen to derive values because it followed a better concentration-response curve, analytical concentrations correlated with nominal concentrations, and cholinesterase activity was measured. The committee rejected a 4-hour NOAEL for clinical signs of 11.4 mg/m^3 for the higher value of 24.3 mg/m^3, also a 4-hour NOAEL for clinical signs (Pauluhn 1986). Clinical signs were observed at the next higher concentration of 45.0 mg/m^3. At 24.3 mg/m^3, plasma cholinesterase activity was 36% of the control value and erythrocyte cholinesterase activity was 92% of the control value. Because of the disparity in the data between the two laboratories, the 24.3 mg/m^3 value was divided by a data base modifying factor of 2. Oral dosing studies showed rapid metabolism in both rats and humans. Therefore, an interspecies uncertainty factor of 3 was applied. Infants are believed to be the sensitive population regarding organophosphate toxicity. But, oral dosing studies of adult and juvenile rats failed to show that juveniles were more sensitive than adults. Therefore an intraspecies uncertainty factor of 3 was applied. The total modifying/ uncertainty factor was 20 (2x10). In the absence of time-scaling data, the 4-hour value of 1.2 mg/m^3 was time-scaled to shorter and longer exposure durations using the default values of 1 and 3, respectively. Because the key study was 4 hours, the 10-minute AEGL-1 was set equal to the 30-minute value.

The 4-hour exposure of rats to 45.0 mg/m^3 in the study by Pauluhn (1986) was chosen as the point of departure for the AEGL-2. Clinical signs consisted of tremor, staggering, and reduced motility. Plasma and erythrocyte cholinesterase activity were 13 and 70% of control, respectively. Mortality of 30% occurred at the next higher exposure of 195.5 mg/m^3. The same modifying and uncertainty factors and time scaling were applied as for the AEGL-1 above.

The 4-hour exposures of rats to methamidophos delivered as a liquid aerosol at concentrations of 11.4 to 350.3 mg/m^3 in the study of Pauluhn (1986) were used to develop AEGL-3 values. The threshold for lethality was calculated using U.S. EPA's Benchmark Concentration (BMC) program (V2.8). The $BMCL_{05}$ was 56.27 mg/m^3, and the BMC_{01} was 101.54 mg/m^3. Although the lower value, in this case the $BMCL_{05}$ of 56.27 mg/m^3, is generally chosen as the threshold for mortality in developing AEGL-3 values, this value was considered an artifact of the large gap between tested concentrations of 45.0 and 195.5 mg/m^3. The 56.27 mg/m^3 value is also close to the 45.0 mg/m^3 value that resulted in effects considered consistent with the definition of AEGL-2. The 4-hour BMC_{01} of 101.54 mg/m^3 for methamidophos delivered as a liquid aerosol was considered the threshold for mortality in rats. The same modifying and uncertainty factors and time scaling were applied as for the AEGL-1 and AEGL-2 above. It was moved by Henry Anderson and seconded by Rick Niemeier to accept the values as proposed. The motion passed (Appendix J Yes: 16; No 0: Abstain: 3).

Summary of AEGL Values for Methamidophos

Classification	10-min	30-min	1-h	4-h	8-h	Endpoint (Reference)
AEGL-1 (Nondisabling)	2.4 mg/m^3	2.4 mg/m^3	1.9 mg/m^3	1.2 mg/m^3	0.61 mg/m^3	No clinical signs – rat (Pauluhn 1986)
AEGL-2 (Disabling)	4.5 mg/m^3	4.5 mg/m^3	3.6 mg/m^3	2.3 mg/m^3	1.1 mg/m^3	Clinical signs of tremor, reduced motility – rat (Pauluhn 1986)
AEGL-3 (Lethal)	10 mg/m^3	10 mg/m^3	8.1 mg/m^3	5.1 mg/m^3	2.5 mg/m^3	4-hour $BMCL_{01}$ for lethality – rat (Pauluhn 1986)

Mevinphos (CAS No. 7786-34-7)

Staff Scientist: Jennifer Rayner, ORNL
Chemical Manager: Daniel Sudakin, Oregon State University

Jennifer Rayner provided a review of the extremely sparse data set and draft AEGL values for mevinphos (Attachment 11). Only one study is available and data cannot be validated. After discussion, a motion was made by George Woodall and seconded by John Hinz to place mevinphos in holding status due to lack of data. If new data become available, mevinphos will be reevaluated. The motion passed. *(*Appendix J: 16 yes; 0 no; 4 abstain).

Phosphamidon (CAS No. 13171-21-6)

Staff Scientist: Sylvia Talmage, ORNL
Chemical Manager: Ed Bernas, AFLCIO

Data on the organophosphate pesticide, phosphamidon, were presented by Sylvia Talmage

(Attachment 12). All acute data originated in a single laboratory, and all acute data addressed lethality. In the absence of data that meets the definition of an AEGL-1, an AEGL-1 was not recommended. Data that addressed the definition of an AEGL-2 were also sparse. Based on the fact that dividing an LC_{50} value by 3 generally results in a non-lethal value (NRC 2001), the AEGL-2 values were calculated by dividing the AEGL-3 values by 3.

The 4-hour nose-only exposure of rats to phosphamidon at a concentration of 102 mg/m^3 (Sachsse et al., 1980) was selected as the point of departure for the AEGL-3. This value is the most conservative of the three 4-hour LC_{50} values provided for the rat. Only the 4-hour LC_{50} value of 102 mg/m^3 was provided; tested concentrations were not reported. Because of the sparse data base and conflicting values reported for 1- and 4-hour exposures, the 4-hour LC_{50} value of 102 mg/m^3 was divided by a data base modifying factor of 2. In the absence of empirical data on a non-lethal concentration, a non-lethal concentration may be calculated by dividing the LC_{50} by 3 (Rusch et al., 2009). A larger divisor in conjunction with modifying and inter- and intraspecies uncertainty factors would reduce the 4-hour AEGL-3 value to less than the 0.5 mg/m^3 concentration tolerated by rats for 42 days (Battelle Institute 1965). An interspecies uncertainty factor of 3 was applied. Rats were more sensitive to the toxicity of phosphamidon than guinea pigs, but not as sensitive as mice. An intraspecies uncertainty factor of 10 was applied because there is little information regarding metabolism differences among humans. The total modifying/uncertainty factor is 60 (2x3x10). The resulting 4-hour value of 0.57 mg/m^3 was time-scaled ($C^n \times t = k$) from the 4-hour data point using n values of 3 and 1 for extrapolation to shorter and longer exposure duration, respectively. Because the key study was 4 hours, the 10-minute value was set equal to the 30-minute value. It was moved by Bob Benson and seconded by Susan Ripple to accept the values (listed in the table below). The motion passed (Appendix K: Yes: 16; No 1: Abstain: 3).

Summary of AEGL Values for Phosphamidon

Classification	10-min	30-min	1-h	4-h	8-h	Endpoint (Reference)
AEGL-1 (Nondisabling)	Not recommended	Not recommended	Not recommended	Not recommended	Not recommended	Insufficient data
AEGL-2 (Disabling)	0.37 mg/m^3	0.37 mg/m^3	0.30 mg/m^3	0.19 mg/m^3	0.093 mg/m^3	One-third of the AEGL-3 values
AEGL-3 (Lethal)	1.1 mg/m^3	1.1 mg/m^3	0.90 mg/m^3	0.57 mg/m^3	0.28 mg/m^3	4-hour LC_{50} for lethality divided by 3 – rat (Sachsse et al., 1980)

Not recommended: absence of AEGL-1 values does not imply that exposure below AEGL-2 levels is without effect.

Fenamiphos (CAS No. 22224-92-1)

Staff Scientist: Jennifer Rayner, ORNL
Chemical Manager: George Woodall, U.S. EPA

Data on fenamiphos were presented by Jennifer Rayner (Attachment 13). No AEGL-1 values were proposed because the derived AEGL-1 values were too close to or exceeded AEGL-2 values. The

AEGL-2 was derived by dividing the AEGL-3 by three due to lack of experimental data and the steep exposure-response relationship observed. Male rats experienced 5% mortality after exposure to 75 mg/m^3 for 1 hour, 30% mortality at 87 mg/m^3, and 60% mortality at103 mg/m^3. All 20 rats died after exposure to 187 mg/m^3 (Kimmerle 1972). In a study by Thyssen (1979a), 20% of the male rats died after exposure to 119 mg/m^3 for 1 hour, 60% died after exposure to 145 mg/m^3, and 90% died after exposure to 148 mg/m^3. Female rats had 70% mortality at 145 mg/m^3 and 90% mortality after exposure to 148 mg/m^3 for 1 hour. In a 4-hour study by Thyssen (1979a), male rats experienced 60% mortality at 100 mg/m^3 and 100% mortality at 155 mg/m^3, and female rats experienced 50% mortality at 100 mg/m^3 90% mortality at 155 mg/m^3, and 100% mortality at 191 mg/m^3. The lack of experimental data and the steep exposure-response relationship justify estimating AEGL-2 values by a 3-fold reduction of AEGL-3 values (NRC 2001). The AEGL-3 was derived using the $BMCL_{05}$ of 46.6337 mg/m^3 for lethality in female rats exposed for 4 hours to fenamiphos (Thyssen 1979a). Lethality data were sufficient for empirical derivation of a time-scaling factor (*n*) for use in the equation $C^n \times t = k$. The value of n was 4.8 and was used to time scale AEGL values. The mechanism of action of organophosphate anticholinesterases is well understood and their activity on cholinergic systems is the same across species. Variability in response is primarily a function of varying cholinesterase activities and types of cholinesterase. Humans have greater levels of plasma cholinesterase than do other species which allows for greater binding of anticholinesterase compounds such as fenamiphos, thereby decreasing the availability of the compound to brain cholinesterase. Therefore, the interspecies uncertainty factor is limited to 3. The documented variability in sensitivity among different age groups and genders, and the known genetic polymorphisms in A-esterases justify retention of the intraspecies uncertainty factor of 10. The uncertainty factor application and rationale are the same as those applied in the derivation of AEGLs for other organophosphate anticholinesterases (NRC 2003).

A motion was made by John Hinz and seconded by Rick Niemeier to accept the values as presented. The motion passed (Appendix L: 19 yes; 0 no; 0 abstain).

Summary of AEGL Values for Fenamiphos

Classification	10-minute	30-minute	1-hour	4-hour	8-hour	Endpoint (Reference)
AEGL-1 (Nondisabling)	NR	NR	NR	NR	NR	Not recommended due to exceeding AEGL-2 values
AEGL-2 (Disabling)	1.0 mg/m^3	0.80 mg/m^3	0.70 mg/m^3	0.53 mg/m^3	0.43 mg/m^3	Derived by 3-fold reduction of the AEGL-3 values (NRC 2001; Thyssen 1979a)
AEGL-3 (Lethal)	3.0 mg/m^3	2.4 mg/m^3	2.1 mg/m^3	1.6 mg/m^3	1.3 mg/m^3	Derived based upon a 4-hr $BMCL_{05}$ of 46.6337 mg/m^3 in rats (Thyssen 1979a)

NR: Not Recommended. Absence of AEGL-1 values does not imply that concentrations below the AEGL-2 are without effect.

Automotive Gasoline (CAS No. 86290-81-5; 8006-61-9)

Staff Scientist: Sylvia Talmage, ORNL
Chemical Manager: John Hinz, U.S. Air Force

John Hinz provided background information and the approach for derivation of AEGL values for automotive gasoline vapor. Where data were available, values were based on wholly vaporized gasoline. Sylvia Talmage addressed calculation of the values (Attachment 14). The data base for gasoline vapor is rich. Clinical studies addressed irritation and central nervous system depression. Rodent studies addressed general toxicity, neurotoxicity, reproductive and developmental toxicity, genetic toxicity, and chronic toxicity/carcinogenicity. The AEGL-1 was based on the sensory irritation study of Davis et al. (1960) in which volunteers were exposed to three different blends of gasoline vapor. Each blend was tested at approximately 880, 2200, and 4400 mg/m^3 for 30 minutes. Because of increased ocular tearing, the suggested point of departure for the AEGL-1 of 4400 mg/m^3 was rejected in favor of the 2200 mg/m^3 value. The 30-minute exposure to all three blends of gasoline vapor at 2200 mg/m^3 produced subjective eye irritation at a higher incidence (15/30 subjects) than under control conditions (1/20 subjects). The incidence of objective eye irritation, observed photographically, although scored as slight (+1 on a scale of 1 to 4), was higher in the 2200 mg/m^3 group (15/30) than in the control group (2/20). Incidences of ocular tearing were similar in this group (3/30) and the control group (2/20). Incidences of subjective and objective eye irritation were greater at the higher concentration of 4400 mg/m^3. Because the eye irritation when measured objectively was slight (less than marked), an intraspecies uncertainty factor of 3 was applied to protect sensitive subjects. There is adaptation to the slight irritation that defines the AEGL-1. Therefore, the same value of 730 mg/m^3 (2200 mg/m^3/3) was used across all exposure durations.

Tested concentrations in rodent studies of acute duration were not high enough to induce narcotic effects. The acute studies were conducted for 4 hours at the limit concentration of 5000 mg/m^3. The AEGL-2 values were based on the subchronic study of Schreiner et al. (2000) in which male and female Sprague-Dawley rats inhaled 22,500 mg/m^3 gasoline vapor (whole-body) for 6 hours/day, 5 days/week for 13 weeks. The rats failed to show clinical signs indicative of neurotoxicity during exposure. The point of departure, the 6-hour exposure to 22,500 mg/m^3, was divided by interspecies and intraspecies uncertainty factors of 1 and 3, respectively for a total uncertainty factor of 3. An interspecies uncertainty factor of 1 is sufficient because solvent uptake is generally greater in rodents than in humans based on higher blood:air partition coefficients for several hydrocarbons. Although humans differ in the rate at which they metabolize chemicals, the susceptibility of the general population to central nervous system depressants varies by no more than 2- to 3-fold as indicated by the minimum alveolar concentration, the concentration of an anesthetic that produces immobility in 50% of patients. Therefore, an intraspecies uncertainty factor of 3 is sufficient. Higher uncertainty factors would result in values inconsistent with the clinical study of Davis et al. (1960). Time scaling may not be relevant for hydrocarbons that act as anesthetics as blood concentrations of the major light components of gasoline rapidly approach steady-state. Therefore, the 6-hour value of 7500 mg/m^3 (22,500 mg/m^3/3) was used across all exposure durations. The 7500 mg/m^3 value is supported by the study of Kuna and Ulrich (1984) in which no toxic signs were observed in squirrel monkeys exposed to 6350 mg/m^3 for six hours/day for 13 weeks.

None of the concentrations tested in acute or subchronic studies with rodents resulted in mortality. It is not apparent that concentrations high enough to cause death from inhalation of gasoline vapor can be attained. Based on the likelihood that lethal concentrations of gasoline vapor cannot be attained/sustained under ambient conditions, an AEGL-3 was not determined.

A motion was made by Henry Anderson and seconded by Bob Benson to accept the values. The motion passed (Appendix M: 20 yes; 0 no; 0 abstain).

Summary of AEGL Values for Automotive Gasoline Vapor						
Classification	**10-min**	**30-min**	**1-h**	**4-h**	**8-h**	**Endpoint (Reference)**
AEGL-1 (Nondisabling)	730 mg/m^3	730 mg/m^3	730 mg/m^3	730 mg/m^3	730 mg/m^3	Slight eye irritation in humans (Davis et al., 1960)
AEGL-2 (Disabling)	7500 mg/m^3 *	7500 mg/m^3 *	7500 mg/m^3 *	7500 mg/m^3 *	7500 mg/m^3 *	No clinical signs at highest tested concentration of 22,500 mg/m^3 – rat (Schreiner et al., 2000)
AEGL-3 (Lethal)	Not determined	Not determined	Not determined	Not determined	Not determined	No data**

*The AEGL-2 value is higher than 1/10 of the lower explosive limit (LEL) of gasoline in air (LEL = 14,000 ppm). Therefore, safety considerations against hazard of explosion must be taken into account.
**A lethal concentration was not attained in the available acute, subchronic, and chronic toxicity studies.

Cadmium (CAS No. 7740-43-9)

Staff Scientist: Jennifer Rayner, ORNL
Chemical Manager: Susan Ripple, Dow Chemical

Jennifer Rayner reviewed the data set and draft AEGL values for cadmium (Attachment 15). The AEGL-1 values are based on the experimental concentration, 0.55 mg Cd/m^3, that caused slight respiratory irritation in rats (Takenaka et al., 2004). After a 6 hour exposure, increased neutrophils and multifocal alveolar inflammation were observed. At the next higher experimental exposure, pneumonitis was observed (Grose et al., 1987). Although the exposure was a whole-body exposure, the size of the ultrafine particles (51 nM MMAD, 1.7 GSD) would mimic a gaseous state and the majority of the aerosol would be inhaled and not deposited on the fur. An intraspecies uncertainty factor of 3 was applied because at acute exposures, cadmium is a direct-acting respiratory irritant. Rabbits and rats exposed to cadmium from 1-6 hours exhibited pneumonitis, increased lung weight, and pulmonary inflammatory cell influx. This mode of action is not expected to differ among species. Human data suggested that cadmium is a direct-acting irritant following acute exposures. After a five hour exposure to cadmium, workers experienced cough, throat irritation, dyspnea, and pulmonary edema (Beton et al., 1966). Therefore, an intraspecies UF of 3 was applied. This mode of action is not expected to differ among individuals. In the absence of an empirically derived chemical-specific scaling exponent, temporal scaling was performed using n=3 when extrapolating

to shorter time points and n = 1 when extrapolating to longer time points using the $C^n \times t = k$ equation. The 30-minute AEGL-1 value was adopted as the 10-minute value due to the added uncertainty of extrapolating from a 6-hour time point to 10 minutes (NRC 2001). The AEGL-2 values are based on the experimental concentration, 5.3 mg Cd/m^3, that caused overt respiratory irritation and pathology in rats (Buckley and Bassett 1987). The 3 hour exposure resulted in reduced weight gain and increased lung weight, protein content, DNA content, number of cuboidal alveolar cells, number of inflammatory cells, and focal areas of interstitial thickening. Uncertainty factor application and time scaling are as described for AEGL-1. The AEGL-3 values are based on the 2 hour LC_{50} for cadmium fume in rats, 112 mg/m^3 (Rusch et al., 1986). The LC_{50} was divided by 3 to estimate a threshold of lethality. Uncertainty factor application and time scaling are as described for AEGL-1.

Motions were made to accept AEGL-1 (motion: Bob Benson; second: John Hinz), AEGL-2 (motion: Marcel van Raaij; second: Bob Benson), and AEGL-3 (motion: Marc Baril; second: Bob Benson) values as proposed. The motions passed (Appendix N: 17 yes; 0 no; 0 abstain).

Summary of AEGL Values Cadmium						
Classification	**10-min**	**30-min**	**1-hr**	**4-hr**	**8-hr**	**Endpoint (Reference)**
AEGL-1 (Nondisabling)	0.13 mg/m^3	0.13 mg/m^3	0.10 mg/m^3	0.063 mg/m^3	0.041 mg/m^3	Respiratory irritation, 0.55 mg Cd/m^3 for 6 hr (Takenaka et al., 2004)
AEGL-2 (Disabling)	1.4 mg/m^3	0.96 mg/m^3	0.76 mg/m^3	0.40 mg/m^3	0.20 mg/m^3	Overt respiratory tract irritation and pathology, 5.3 mg/m^3 CdO for 3 hr (Buckley and Bassett, 1987)
AEGL-3 (Lethal)	8.5 mg/m^3	5.9 mg/m^3	4.7 mg/m^3	1.9 mg/m^3	0.93 mg/m^3	Threshold of lethality based on the 2-hr rat LC_{50} for Cd fumes, 112 mg/m^3 (Rusch et al., 1986)

Red Phosphorus (CAS No. 7723-14-0)

Staff Scientist: Robert Young, ORNL
Chemical Manager: Glenn Leach, U.S. Army

Bob Young reviewed the data set and draft AEGL values for red phosphorus (Attachment 16). Data were unavailable with which to directly derive AEGL-1 values for red phosphorus. A 3-fold reduction of the AEGL-2 values was considered a justified approach for deriving the AEGL-1 values because the progression of effects from AEGL-1 severity to AEGL-2 severity represents a continuum of the same mode of action (contact irritation) and effect. Comparison of the AEGL-1 values to the limited human exposure data indicates that notable effects (greater than those characterizing the AEGL-1 tier) would be unlikely following exposure to AEGL-1 concentrations. Information regarding the response of humans to red phosphorus or red phosphorus/butyl rubber

smoke lacked definitive exposure terms and was not considered sufficient for development of AEGL-2 values. The AEGL-2 severity effects in animals (necrosis, hemorrhage, and edema in the respiratory tract) were consistently associated with exposures that also caused deaths. Necropsies of animals surviving through the post-exposure observation period generally revealed only minor signs of toxicity that were not consistent with AEGL-2 severity but clearly showed the respiratory tract as a target of toxicity. Results from the multispecies study by Ballantyne (1998), showed no lethality and only pulmonary congestion in mice exposed one hour to smoke of unformulated red phosphorus (111 mg/m^3). The data reported by Ballantyne (1998) were also considered the most relevant for deriving AEGL values for red phosphorus because pure unformulated red phosphorus was used rather than the butyl rubber formulations. Mice appeared to be more sensitive than rabbits, dogs, or rats. The 1-hour exposure of mice to 111 mg red phosphorus/m^3 that resulted in pulmonary congestion was considered an appropriate point-of-departure (POD) for AEGL-2 derivation with a total uncertainty factor application of 10 (3 for intraspecies variability and 3 for interspecies variability). Red phosphorus is a direct-contact irritant which is primarily due to the formation of ortho-phosphoric acid. The toxicodynamic aspect of exposure to red phosphorus is a greater determinant of the toxic response than is toxicokinetics which justifies an intraspecies uncertainty factor of 3. Because the mouse appeared to be a sensitive species and the critical effect associated with the POD are of minimal severity for the AEGL-2 tier, the interspecies uncertainty factor of 3 is considered adequate. Further reduction of the AEGL-2 values by additional uncertainty adjustment would result in AEGL-2 values inconsistent with the limited information available for humans. In the absence of an empirically derived exponent (n), temporal scaling from the experimental durations of the respective PODs to AEGL-specific durations was performed using $n = 3$ when extrapolating to shorter time points and $n = 1$ when extrapolating to longer time points using the $C^n x\ t = k$ equation (NRC, 2001). For AEGL-3 development, human data lacked definitive exposure terms but served as supporting data. As for AEGL-2, the Ballantyne (1998) study was considered more relevant for deriving AEGL values for red phosphorus due to its use of pure unformulated red phosphorus rather than the butyl rubber formulations. The 1-hour $BMLC_{05}$ of 469 mg/m^3 for rats exposed to red phosphorus smoke was used as the POD for AEGL-3 derivation. Although results of the Ballantyne (1998) study indicated the mouse is a more sensitive species, the BMC analyses of the mouse data showed the BMC model to be a poor fit (p=0.09 for the mouse data vs. p=0.66 for the rat data). Furthermore, overall data in rats are more robust. The lethality benchmark values from the Ballantyne data are lower than those from other studies. Animal lethality data exhibited considerable variability that would normally warrant an interspecies uncertainty factor of 10. However, this would result in AEGL-3 values inconsistent with human occupational data. The interspecies variability is primarily the result of the extreme sensitivity of guinea pigs which the investigators and the NRC (1997a) considered uniquely susceptible and inappropriate for human health risk assessment. Therefore, the interspecies uncertainty factor was limited to 3. Red phosphorus is a direct-contact irritant which is a function of the formation of ortho-phosphoric acid. The toxicodynamic aspect of exposure to red phosphorus was considered a greater determinant of the toxic response than toxicokinetics, thereby justifying an intraspecies uncertainty factor of 3. As previously noted, greater uncertainty application would result in AEGL-3 values inconsistent with the human experience data. Time scaling was performed as described for AEGL-2. A motion was made by Bob Benson and seconded by John Hinz to accept the values. The motion passed (Appendix O: AEGL-1: 14 yes; 1 no; 4 abstain; AEGL-2: 16 yes; 1 no; 2 abstain; AEGL-3: 16 yes; 0 no; 3 abstain).

AEGL Values For Red Phosphorus (mg/m^3)						
Classification	**10-min**	**30-min**	**1-hr**	**4-hr**	**8-hr**	**Endpoint (Reference)**
AEGL-1 (Nondisabling)	6.7	4.7	3.7	0.93	0.47	3-fold reduction of the AEGL-2 values as a protective estimate of AEGL-1 severity
AEGL-2 (Disabling)	20	14	11	2.8	1.4	Mild pulmonary congestion in mice; 1-hr exposure to 111 mg/m^3 (Ballantyne, 1998); UF= 3 x 3; n=1 or 3
AEGL-3 (Lethality)	85	59	47	12	5.9	Rat 1-hr $BMCL_{05}$ of 469 mg/m^3 (Ballantyne, 1998); UF= 3 x 3; n=1 or 3

SPECIAL PRESENTATIONS

Organophosphate (OP) Pesticide Uncertainty Factors

A general discussion of OP uncertainty factors was led by Jennifer Rayner and Ernie Falke (Attachment 17). The NAC is preparing several TSDs for OP pesticides and there is a need to better justify uncertainty factors. Bob Young is preparing a white paper to address OP uncertainty factor issues to determine if chemical class generalizations may be valid for the OP pesticides. However, it is possible that data may not be sufficient to support OP chemical-class uncertainty factors; thus, chemical-specific uncertainty factors and justifications could be necessary. Ernie Falke, George Woodall, and Bob Benson volunteered to serve on an OP working group.

Discussion of Benchmark Software

Presenters: Allen Davis and Jeffrey Gift, U.S. EPA

Allen Davis and Jeff Gift presented information on the most recent version of the benchmark software (BMDS 2.1) (Attachment 18). The presentation focused on use of the program, c x t modeling, and selection of appropriate models.

ADMINISTRATIVE MATTERS

Future Meetings:
April 13-15, 2010: San Francisco, CA

All items in the agenda were discussed as thoroughly as the time permitted. The meeting highlights were prepared by Cheryl Bast, Sylvia Talmage, 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 49 agenda
Attachment 2. Meeting 49 attendee list
Attachment 3. Lead presentation
Attachment 4. Dichlorvos presentation
Attachment 5. Dimethyl phosphite presentation
Attachment 6. Trimethyl phosphite presentation
Attachment 7. Methyl iodide presentation
Attachment 8. Phosgene presentation
Attachment 9. Monocrotophos presentation
Attachment 10. Methamidophos presentation
Attachment 11. Mevinphos presentation
Attachment 12. Phosphamidon presentation
Attachment 13. Fenamiphos presentation
Attachment 14. Gasoline presentation
Attachment 15. Cadmium presentation
Attachment 16. Red phosphorus presentation
Attachment 17. OP Uncertainty factor presentation
Attachment 18. BMDS presentation
Attachment 19. NAC- 49 meeting certification

LIST OF APPENDICES

Appendix A. Ballot for approval of NAC-48 meeting highlights
Appendix B. Final NAC-48 Meeting Highlights
Appendix C. Ballot for dimethyl phosphite
Appendix D. Ballot for trimethyl phosphite
Appendix E. Ballot for methyl iodide
Appendix F. Ballot for phosgene
Appendix G. Ballot for dicrotophos
Appendix H. Ballot for monocrotophos
Appendix I. Ballot for methamidophos
Appendix J. Ballot for mevinphos
Appendix K. Ballot for phosphamidon
Appendix L. Ballot for fenamiphos
Appendix M. Ballot for gasoline
Appendix N. Ballot for cadmium
Appendix O. Ballot for red phosphorus

NAC/AEGL Meeting 50: April 13-15, 2010

Chemical: Hydrogen bromide **CAS Reg. No.: 10035-10-6**

Action: Proposed x **Interim** _____ **Other: NAS Comments**

Chemical Manager: Ripple **Staff Scientist: Talmage**

NAC Member	AEGL1	AEGL2	AEGL3	LOA	NAC Member	AEGL1	AEGL 2	AEGL3	LOA
Henry Anderson		Y			John Hinz		Y		
Marc Baril		Y			Jim Holler		A		
Lynn Beasley		Y			Clarion Johnson		A		
Alan Becker		Y			Glenn Leach		A		
Robert Benson		Y			Richard Niemeier		Y		
Edward Bernas		Y			Mattias Oberg		Y		
Iris Camacho		Y			Susan Ripple		Y		
George Cushmac		Y			George Rusch, Chair		Y		
Richard Erickson		Y			Daniel Sudakin		Y		
Neeraja Erraguntla		Y			Marcel vanRaaij		A		
David Freshwater		Y			George Woodall		A		
Ralph Gingell		Y			Alan Woolf		Y		
					TALLY		19/19		
					PASS/ FAIL		P		

PPM, (mg/m^3)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	, ( )	, ( )	, ( )	, ( )	, ( )
AEGL 2	, (150)	, (50)	, (25)	, (13)	, (13)
AEGL 3	, ( )	, ( )	, ( )	, ( )	, ( )
LOA					
* = ∃10% LEL					
** = ∃ 50% LEL					
*** = ∃100% LEL					

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.
** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

NR= Not Recommended due to _____

AEGL 1 Motion by: _____ **Second by:** _____
AEGL 2 Motion by: HINZ **Second by:** NIEMEIER
AEGL 3 Motion by: _____ **Second by:** _____
LOA Motion by: _____ **Second by:** _____

Approved by Chair: _____ **DFO:** _____ **Date:** 4/14/10

NAC/AEGL Meeting 50: April 13-15, 2010

Chemical: Hydrogen iodide **CAS Reg. No.: 10034-85-2**

Action: Proposed X **Interim** _____ **Other: NAS Comments**

Chemical Manager: Falke **Staff Scientist: Talmage**

NAC Member	AEGL1	AEGL2	AEGL3	LOA	NAC Member	AEGL1	AEGL 2	AEGL3	LOA
Henry Anderson		Y			John Hinz		Y		
Marc Baril		Y			Jim Holler		A		
Lynn Beasley		Y			Clarion Johnson		A		
Alan Becker		Y			Glenn Leach		A		
Robert Benson		Y			Richard Niemeier		Y		
Edward Bernas		Y			Mattias Oberg		Y		
Iris Camacho		Y			Susan Ripple		Y		
George Cushmac		Y			George Rusch, Chair		Y		
Richard Erickson		Y			Daniel Sudakin		X		
Neeraja Erraguntla		Y			Marcel vanRaaij		A		
David Freshwater		Y			George Woodall		A		
Ralph Gingell		Y			Alan Woolf		Y		
					TALLY		19/19		
					PASS/ FAIL		P		

~~PPM, (mg/m³)~~	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	,( )	,( )	,( )	,( )	,( )
AEGL 2	,(150)	,(50)	,(25)	,(13)	,(13)
AEGL 3	,( )	,( )	,( )	,( )	,( )
LOA					
* = ∃10% LEL					
** = ∃ 50% LEL					
*** = ∃100% LEL					

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.
** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

NR= Not Recommended due to _____

AEGL 1 Motion by: _____ **Second by:** _____
AEGL 2 Motion by: HINZ **Second by:** NIEMEIER
AEGL 3 Motion by: _____ **Second by:** _____
LOA Motion by: _____ **Second by:** _____

Approved by Chair: _____ **DFO:** _____ **Date:** 4/14/10

NAC/AEGL Meeting 50: April 13-15, 2010

Chemical: Chlorine pentafluoride **CAS Reg. No.: 13637-63-3**

Action: Proposed_____ Interim____x____ Other_NAS Comments

Chemical Manager: Falke **Staff Scientist: Talmage**

NAC Member	AEGL1	AEGL2	AEGL3	LOA	NAC Member	AEGL1	AEGL 2	AEGL3	LOA
Henry Anderson	Y	Y	Y		John Hinz	Y	Y	Y	
Marc Baril	Y	Y	Y		Jim Holler	A	A	A	
Lynn Beasley	Y	Y	Y		Clarion Johnson	A	A	A	
Alan Becker	Y	Y	Y		Glenn Leach	A	A	A	
Robert Benson	Y	Y	Y		Richard Niemeier	Y	Y	Y	
Edward Bernas	Y	Y	Y		Mattias Oberg	Y	Y	Y	
Iris Camacho	Y	Y	Y		Susan Ripple	Y	Y	Y	
George Cushmac	Y	Y	Y		George Rusch, Chair	Y	Y	Y	
Richard Erickson	A	A	A		Daniel Sudakin	Y	Y	Y	
Neeraja Erraguntla	Y	Y	Y		Marcel vanRaaij	A	A	A	
David Freshwater	Y	Y	Y		George Woodall	A	A	A	
Ralph Gingell	Y	Y	Y		Alan Woolf	Y	Y	Y	
					TALLY	18/18	18/18	18/18	
					PASS/ FAIL	P	P	P	

PPM, (mg/m^3)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	,(0.30)	,(0.30)	,(0.30)	,(NR)	,(NR)
AEGL 2	,(3.0)	,(2.0)	,(1.0)	,(0.48)	,(0.33)
AEGL 3	,(21)	,(12)	,(8.0)	,(3.9)	,(2.9)
LOA					
* = ∃10% LEL					
** = ∃ 50% LEL					
*** = ∃100% LEL					

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.
** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

NR= Not Recommended due to INADEQUATE DATA AND TENDENCY FOR AEGL-1 + AEGL-2 TO CONVERGE AT 4/8 HR

AEGL 1 Motion by: BERNSAD **Second by:** ANDERSON
AEGL 2 Motion by:_____ **Second by:**_____
AEGL 3 Motion by:_____ **Second by:**_____
LOA Motion by:_____ **Second by:**_____

Approved by Chair: [signature] **DFO:** [signature] **Date:** 4/14/10

NAC/AEGL Meeting 50: April 13-15, 2010

Chemical: Bromine pentafluoride **CAS Reg. No.: 7789-30-2**

Action: Proposed_____ Interim____x____ Other_NAS Comments

Chemical Manager: Falke **Staff Scientist: Bos**

NAC Member	AEGL1	AEGL2	AEGL3	LOA	NAC Member	AEGL1	AEGL 2	AEGL3	LOA
Henry Anderson		Y			John Hinz		Y		
Marc Baril		Y			Jim Holler		A		
Lynn Beasley		Y			Clarion Johnson		A		
Alan Becker		Y			Glenn Leach		A		
Robert Benson		Y			Richard Niemeier		Y		
Edward Bernas		Y			Mattias Oberg		Y		
Iris Camacho		Y			Susan Ripple		Y		
George Cushmac		Y			George Rusch, Chair		Y		
Richard Erickson		Y			Daniel Sudakin		Y		
Neeraja Erraguntla		Y			Marcel vanRaaij		A		
David Freshwater		Y			George Woodall		A		
Ralph Gingell		Y			Alan Woolf		Y		
					TALLY		19/19		
					PASS/ FAIL		P		

PPM, (mg/m^3)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	,( )	,( )	,( )	,( )	,( )
AEGL 2	,( )	,( )	,( )	,(0.48)	,(0.33)
AEGL 3	,( )	,( )	,( )	,( )	,( )
LOA					
* = ∃10% LEL					
** = ∃ 50% LEL					
*** = ∃100% LEL					

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.
** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

NR= Not Recommended due to_____

AEGL 1 Motion by:_____ **Second by:**_____
AEGL 2 Motion by: HINZ **Second by:** WOOLF
AEGL 3 Motion by:_____ **Second by:**_____
LOA Motion by:_____ **Second by:**_____

Approved by Chair: [signature] **DFO:** [signature] **Date:** 4/14/10

Chemical: Chloroacetone **CAS Reg. No.: ~~13637-63-3~~ 78-95-5** V7

Action: Proposed_____ Interim___x___ Other_NAS Comments

Chemical Manager: Ripple **Staff Scientist: Bast**

NAC Member	AEGL1	AEGL2	AEGL3	LOA	NAC Member	AEGL1	AEGL 2	AEGL3	LOA
Henry Anderson			Y		John Hinz			Y	
Marc Baril			Y		Jim Holler			A	
Lynn Beasley			Y		Clarion Johnson			A	
Alan Becker			Y		Glenn Leach			A	
Robert Benson			Y		Richard Niemeier			Y	
Edward Bernas			Y		Mattias Oberg			Y	
Iris Camacho			Y		Susan Ripple			Y	
George Cushmac			Y		George Rusch, Chair			Y	
Richard Erickson			Y		Daniel Sudakin			Y	
Neeraja Erraguntla			Y		Marcel vanRaaij			A	
David Freshwater			Y		George Woodall			A	
Ralph Gingell			Y		Alan Woolf			Y	
					TALLY			19/19	
					PASS/ FAIL			P	

PPM, (mg/m^3)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	,( )	,( )	,( )	,( )	,( )
AEGL 2	[redacted]( )	[redacted],( )	,( )	,( )	0.53,( )
AEGL 3	,( )	,( )	,( )	,( )	1.6,(6.1)
LOA					
* = ∃10% LEL					
** = ∃ 50% LEL					
*** = ∃100% LEL					

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.
** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

NR= Not Recommended due to _____

AEGL 1 Motion by: _____ **Second by:** _____
AEGL 2 Motion by: Benson **Second by:** Hinz
AEGL 3 Motion by: Benson **Second by:** Hinz
LOA Motion by: _____ **Second by:** _____

Approved by Chair: [signature] **DFO:** [signature] **Date:** 4/14/10

NAC/AEGL Meeting 50: April 13-15, 2010

Chemical: Methyl isothiocyanate **CAS Reg. No.: 556-61-6**

Action: Proposed x **Interim** _____ **Other:** * Raise from proposed to Interim

Chemical Manager: Ripple **Staff Scientist: Young**

NAC Member	AEGL1	AEGL2	AEGL3	LOA	NAC Member	AEGL1	AEGL 2	AEGL3	LOA
	*								
Henry Anderson	Y				John Hinz	Y			
Marc Baril	Y				Jim Holler	A			
Lynn Beasley	Y				Clarion Johnson	A			
Alan Becker	Y				Glenn Leach	A			
Robert Benson	Y				Richard Niemeier	Y			
Edward Bernas	Y				Mattias Oberg	Y			
Iris Camacho	Y				Susan Ripple	Y			
George Cushmac	Y				George Rusch, Chair	Y			
Richard Erickson	Y				Daniel Sudakin	Y			
Neeraja Erraguntla	A				Marcel vanRaaij	A			
David Freshwater	Y				George Woodall	Y			
Ralph Gingell	Y				Alan Woolf	Y			
					TALLY	19/19			
					PASS/ FAIL	P			

PPM, (mg/m^3)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	, ( )	, ( )	, ( )	, ( )	, ( )
AEGL 2	, ( )	, ( )	, ( )	, ( )	, ( )
AEGL 3	, ( )	, ( )	, ( )	, ( )	, ( )
LOA					
* = ∃10% LEL					
** = ∃ 50% LEL					
*** = ∃100% LEL					

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.
** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

NR= Not Recommended due to _____

AEGL 1 Motion by: Benson **Second by:** Freshwater
AEGL 2 Motion by: _____ **Second by:** _____
AEGL 3 Motion by: _____ **Second by:** _____
LOA Motion by: _____ **Second by:** _____

Approved by Chair: _____ **DFO:** _____ **Date:** 4/14/10

NAC/AEGL Meeting 50: APRIL 13-15, 2010

Chemical: ~~HYDROGEN~~ SELENIDE **CAS Reg. No.:** 7783-79-1

Action: Proposed_____ **Interim**_____ **Other** Response to COT Comments

Chemical Manager: **Staff Scientist:**

NAC Member	AEGL1	AEGL2	AEGL3	LOA	NAC Member	AEGL1	AEGL 2	AEGL3	LOA
Henry Anderson	~~Y~~	Y	Y		John Hinz		P	P	
Marc Baril		P	P		Jim Holler		A	A	
Lynn Beasley		Y	Y		Clarion Johnson		A	A	
Alan Becker		Y	Y		Glenn Leach		A	A	
Robert Benson		Y	Y		Richard Niemeier		Y	Y	
Edward Bernas		P	P		Mattias Oberg		Y	Y	
Iris Camacho		Y	Y		Susan Ripple		Y	Y	
George Cushmac		Y	Y		George Rusch, Chair		Y	Y	
Richard Erickson		Y	Y		Daniel Sudakin		Y	Y	
Neeraja Erraguntla		A	A		Marcel vanRaaij		A	A	
David Freshwater		Y	Y		George Woodall		Y	Y	
Ralph Gingell		P	P		Alan Woolf		Y	Y	
					TALLY		15/15	15/15	
					PASS/ FAIL		P	P	

PPM, (~~mg/m~~^{3})	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	,(NR)	,(NR)	,(NR)	,(NR)	,(NR)
AEGL 2	,(0.66)	,(0.44)	,(0.33)	,(0.20)	,(0.15)
AEGL 3	,(2.2)	,(1.4)	,(1.1)	,(0.65)	,(0.49)
LOA					
* = ≥10% LEL					
** = ≥ 50% LEL					
*** = ≥100% LEL					

AEGL-1 NOT UP FOR DISCUSSION

BALLOT

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.
** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

NR= Not Recommended due to_____

AEGL 1 Motion by:_____ **Second by:**
AEGL 2 Motion by:_____ **Second by:**
AEGL 3 Motion by: WOODALL **Second by:** BENSON
LOA Motion by:_____ **Second by:**

Approved by Chair: [signature] **DFO:** [signature] **Date:** 4/14/10

NAC/AEGL Meeting 50: April 13-15, 2010

Chemical: Carbon Dioxide (ETHICAL REVIEW OF HUMAN STUDIES) **CAS Reg. No.: 124-38-9**

Action: Proposed x **Interim** _____ **Other:**

PRESENTED BY IRIS CAMACHO

Chemical Manager: Marcel van Raaij **Staff Scientist: Bast**

NAC Member	~~AEGL 1~~ NO VALIDATED STUDIES	~~AEGL 2~~	~~AEGL 3~~ NO GLP	LOA
Henry Anderson	Y		Y	
Marc Baril	Y		Y	
Lynn Beasley	Y		Y	
Alan Becker	Y		N	
Robert Benson	Y		Y	
Edward Bernas	Y		Y	
Iris Camacho	Y		Y	
George Cushmac	Y		Y	
Richard Erickson	Y		Y	
Neeraja Erraguntla	Y		Y	
David Freshwater	Y		Y	
Ralph Gingell	Y		Y	

NAC Member	~~AEGL 1~~	~~AEGL 2~~	~~AEGL 3~~	LOA
John Hinz	Y		Y	
Jim Holler	A		A	
Clarion Johnson	A		A	
Glenn Leach	A		A	
Richard Niemeier	Y		Y	
Mattias Oberg	Abstain		Abstain	
Susan Ripple	Y		Y	
George Rusch, Chair	Y		Y	
Daniel Sudakin	Y		Y	
Marcel vanRaaij	A		A	
George Woodall	Y		Y	
Alan Woolf	Y		Y	
TALLY	19/20		19/20	
PASS/ FAIL	P		P	

PPM, (mg/m^3)	10 Min	30 Min	1 Hr	4 Hr	8 Hr
AEGL 1	, ( )	, ( )	, ( )	, ( )	, ( )
AEGL 2	, ( )	, ( )	, ( )	, ( )	, ( )
AEGL 3	, ( )	, ( )	, ( )	, ( )	, ( )
LOA					
* = ∃10% LEL					
** = ∃ 50% LEL					
*** = ∃100% LEL					

*Safety considerations against the hazard(s) of explosion(s) must be taken into account.
** and ***Extreme safety considerations against the hazard(s) of explosion(s) must be taken into account.

NR= Not Recommended due to _____

AEGL 1 Motion by: HINZ **Second by:** NIEMEIER
AEGL 2 Motion by: HINZ **Second by:** BARIL
AEGL 3 Motion by: _____ **Second by:** _____
LOA Motion by: _____ **Second by:** _____

Approved by Chair: _____ **DFO:** Paul S. Tobin **Date:** 4/13/10