American Chemistry Council
n-Alkane VCCEP Consortium

Errata and Clarifications to n-Alkane Category: Decane, Undecane, Dodecane (CAS Nos. 124-18-5, 1120-21-4, 112-40-3) Voluntary Children's Chemical Evaluation Program (VCCEP) Tier 1 Pilot Submission Docket Number OPPTS – 00274D

September 9, 2004

The following are corrections or clarifications to the text of the June 17, 2004, Tier 1 VCCEP submission for decane, undecane, and dodecane.

Page 8: last sentence:

replace:

"Reproductive/developmental NOAELs of 5g/m3, 300 mg/kg/day and 1,000 mg/kg/day (equivalent to approximately 2 g/m3 and 7 g/m3, respectively) were identified. Since all of these values were larger than the subchronic NOAEL, no further risk assessment was conducted for reproductive or developmental effects."

with:

"The developmental NOAEL is 5000 mg/m3 and oral reproductive NOAELs are 1000 mg/kg/day for decane and 300 mg/kg/day for undecane; inhalation equivalents of about 7000 mg/m3 and 2000 mg/m3, respectively. Thus, the overall NOAEL for reproductive/developmental effects is in theinhalation equivalent range of 2000 - 7000 mg/m3. As these NOAELs are in the same range of the systemic NOAEL of 1000 mg/m3, reproductive/developmental effects were not found to be more sensitive than systemic toxicity."

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page 9: 1st paragraph; clarification

Replace

"Primary exposure of infants and children was in the home. In every domestic scenario relevant to infants, children and parents, including home renovation activities, Margins of Exposure (MOE) based on the subchronic NOAEL were comfortably in excess of 1,000 for both representative and upper bound

exposures. Worst case short term exposure based on modeling a home painting scenario was comfortably in excess of 100 for a short term (days), increasing rapidly to greater than 1,000 despite very conservative exposure assumptions. This suggests a low risk of harm to infants, children or parents."

with:

"Primary exposure of infants and children was in the home. In the chronic domestic scenario relevant to infants, children and parents, Margins of Exposure (MOE) based on the subchronic NOAEL were comfortably in excess of 1,000 for both representative and upper bound exposures. For short-term renovation activities (painting), MOEs based on the same subchronic NOAEL ranged from 2,000 for representative exposures to 275 for upper bound exposure. Considering such exposures would be of short duration, an MOE greater than 100 based on a subchronic NOAEL was considered protective. This is supported by the fact that the Margin of Safety (MOS) based on the chronic RfC was greater than 1.

Even worst case short term exposure concentrations based on EPA measurements in a home painting scenario with the infant in the room being painted, and with no ventilation other than 0.45 air changes per hour, was comfortably below the acute health criteria, and the subchronic based MOE exceeded 100 within 2 days, increasing rapidly to in excess of 1,000 despite the lack of additional ventilation. This suggests a low risk of harm to infants, children or parents."

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page 15, Section 3.2, 3rd paragraph;

replace: "C_{10}-C_{12} aliphatic fraction"

with: "C_9-C_{16} aliphatic fraction"

Clarification regarding Total Petroleum Hydrocarbon Criteria Working Group (TPHCWG) C_9-C_{16} aliphatic fraction RfC

The calculation of the RfC for C_9-C_{16} aliphatic fraction is provided in the TPHCWG 1997 document on pages 21- 24. In deriving the RfC, the TPHCWG considered three subchronic rat studies and two developmental studies on complex aliphatic hydrocarbon products in this range (summarized in Table 5 of the TPHCWG document on page 22). The subchronic data considered for the RfC included: 1) a 12-week inhalation study (6 hr/day, 5 days/wk) of a C_{10}-C_{11} isoparaffin product with a NOAEL of 5226 mg/m^3 (Mullin, 1990), 2) a 12-week inhalation study (6 hrs/day 5 days/wk) of a C_7-C_{11} aliphatic product (n-alkanes, isoparaffins, and cycloparaffins) with a NOAEL of 5485 mg/m^3 (Phillips and Egan, 1984), and, 3) a 90-day continuous inhalation study of JP-8 with a NOAEL of

1000 mg/m^3 (Mattie, 1991). The developmental data were not used in deriving the RfC, but the NOAELs are 5226 mg/m^3 for the C_{10}-C_{11} isoparaffin product (Mullin, 1990) and 5485 mg/m^3 for the C_7-C_{11} aliphatic product (unpublished). The TPHCWG derived RfCs for each of these studies separately by converting to a continuous exposure, except for the Mattie 1991 study which was a continuous exposure study, and then dividing the adjusted NOAELs by a total uncertainty factor of 1000. This total uncertainty factor was based on a subchronic to chronic uncertainty factor of 10, an uncertainty factor of 10 for interspecies extrapolation (animal to human), and an human intraspecies uncertainty factor of 10. For each study considered, the resulting RfC was approximately 1 mg/m^3, forming the basis for the TPHCWG's recommended RfC of 1.0 mg/m^3.

The TPHCWG RfC was used in the Risk Assessment (Section 8) derivations of chronic and short-term Margins of Safety (MOS), providing secondary support for the calculation of Margins of Exposure based the health benchmarks developed by the Consortium for C_{10}-C_{12} n-alkanes.

The data from the Phillips and Egan 1984 subchronic study and the unpublished developmental toxicity study of the C_7-C_{11} aliphatic product were considered in the VCCEP submission (Section 7). The data from the Mullin 1990 studies were not considered as they are specific to isoparaffins (no n-alkane content) and data from the Mattie study as not considered as no toxicology data on fuels were considered due to their wider range and aromatic content.

The published studies cited in the TPHCWG document were:
Phillips RD, Egan GF Subchronic inhalation exposure of dearomatized white spirit and C10-C11 isoparaffinic hydrocarbon in Sprague-Dawley rats. Fundam Appl Toxicol. 1984 Oct;4(5):808-18.

Mullin LS, Ader AW, Daughtrey WC, Frost DZ, Greenwood MR. Toxicology update isoparaffinic hydrocarbons: a summary of physical properties, toxicity studies and human exposure data. J Appl Toxicol. 1990 Apr;10(2):135-42.

Mattie DR, Alden CL, Newell TK, Gaworski CL, Flemming CD. A 90-day continuous vapor inhalation toxicity study of JP-8 jet fuel followed by 20 or 21 months of recovery in Fischer 344 rats and C57BL/6 mice. Toxicol Pathol. 1991;19(2):77-87.

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page 34: last paragraph,

"These compare with a subchronic NOAEL of 1,000 mg/kg/day (see 7.3. Repeat Dose Toxicity: Health Benchmark) indicating Margin of Exposure in excess of 150,000."

Replace with:

"These compare with a reproductive/developmental NOAEL of 300 mg/kg/day (see section 7.4) indicating Margin of Exposure in excess of 45,000"

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page 35

Table 6.3 "1. Representative Intake":
Replace the line

"MOE*	Margin of Exposure	213,000"

with:

"MOE*	Margin of Exposure	64,000"

Table 6.3 "Upper Bound Intake":

Replace the line

"MOE*	Margin of Exposure	150,000"

with:

"MOE*	Margin of Exposure	45,000"

Replace the line:

"*MOE based on subchronic NOAEL of 1,000 mg/kg/d (section 7.10.2)"

with:

"*MOE based on reproductive/developmental NOAEL of 300 mg/kg/d (section 7.4)"

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page 41

Replace the paragraph:

"Assuming even an unrealistic 25% n-dodecane content in the fuel, the dose per accidental exposure amounts to only 8.2×10^{-3} mg/kg and a chronic exposure of 1.1×10^{-3} mg/kg/day assuming 50 days per year of such incidents. These are essentially negligible doses compared with repeat dose subchronic oral NOAELs

of 1,000 mg/kg/day and only 1% of the chronic RfD of 0.1 mg/kg/day. Margins of Exposure were in excess of 88,000 on a chronic basis for a fuel containing up to 25% of decane, undecane, and dodecane."

with:

"Assuming even an unrealistic 25% n-dodecane content in the fuel, the dose per accidental exposure amounts to only 8.2×10^{-3} mg/kg and a chronic exposure of 1.1×10^{-3} mg/kg/day assuming 50 days per year of such incidents. These are essentially negligible doses compared with repeat dose reproductive/developmental oral NOAELs of 300 mg/kg/day and only 1% of the chronic RfD of 0.1 mg/kg/day. Margins of Exposure were in excess of 270,000 on a chronic basis for a fuel containing up to 25% of decane, undecane, and dodecane."

Replace the paragraph:

"Applying an even more conservative scenario by assuming 1 hour exposure per day to both hands on a daily basis (250 days per year), chronic margins of exposure still exceeded 4,000 as shown in Table 6.4 below."

with

"Applying an even more conservative scenario by assuming 1 hour exposure per day to both hands on a daily basis (250 days per year), chronic margins of exposure still exceeded 13,000 as shown in Table 6.4 below."

In Table 6.4:

1. Exposure Duration 15 minutes/day; 50 days/year

replace the lines:

"Sub-chronic NOAEL	100			mg/kg/d
MOE Per Event	3040	60800	12160	
MOE Chronic	22192	443839	88768"	

with:

"Sub-chronic NOAEL	300			mg/kg/d
MOE Per Event	9120	182399	36480	
MOE Chronic	66576	1331516	266303"	

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page 42

In Table 6.4:
2. Exposure Duration 60 minutes/day; 250 days/year

replace the lines:

"Sub-chronic NOAEL	100			mg/kg/d
MOE Per Event	760	15200	3040	
MOE Chronic	1110	22192	4438"	

with:

"Sub-chronic NOAEL	300			mg/kg/d
MOE Per Event	2280	45600	9120	
MOE Chronic	3329	66576	13315"	

Replace the third paragraph:

"The daily dose of such a contaminated water supply would result in dose of 6.8×10^{-3} mg/kg/day of n-decane and 4.8×10^{-4} mg/kg/day n-dodecane. Such intakes, unrealistic as they are, provide Margin of Exposure of about 150,000 based on the subchronic NOAEL of 1,000 mg/kg/day."

with:

"The daily dose of such a contaminated water supply would result in dose of 6.8×10^{-3} mg/kg/day of n-decane, 5.7×10^{-4} mg/k g/day n-undecane, and 4.8×10^{4} mg/kg/day for n-dodecane. Such intakes, unrealistic as they are, provide Margin of Exposure of over 40,000 based on the reproductive/developmental NOAEL of 300 mg/kg/day."

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page 48

replace: “MacFarland and Holdsworth 1987”

with: “Snyder, 1987”

Note: this is not a change in reference. MacFarland and Holdworth were contributing authors to Ethel Browning’s Toxicology and Metabolism of Industrial Solvents, Second Edition but the citation in the reference section is to Snyder, the editor.

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page 49

under Dermal:

Second sentence:

replace: “EMBSI 1983a,b”

with: “EMBSI 1983d,e”

Third sentence:

replace: “EMBSI 1983a”

with: “EMBSI 1983d”

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page 55

replace: “Carpenter, 1975”

with: “Carpenter, 1978”

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page 58

under Mutagenicity:

add: “c” after EMBSI, 1991

under Cytogenicity:

add “d” after EMBSI 1991

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page 60

replace: “Lammers et al, 2000”

with: “TNO, 2000”

Note: this is not a change in reference, Lammers was one of the authors of the TNO study but the citation in the reference section is to TNO.

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page 75, 2nd full paragraph

remove: "(See Appendix I)"

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page 88-96, Reference Section

The following references should be added to the reference section:

Barnes DG, Dourson M. Reference dose (RfD): description and use in health risk assessments. Regul Toxicol Pharmacol. 1988 Dec;8(4):471-86.

Bingham E, Falk HL. Environmental carcinogens. The modifying effect of cocarcinogens on the threshold response.Arch Environ Health. 1969 Dec;19(6):779-83.

Collins JF, Salmon AG,Budroe JD, Marty MA and Alexeeff. Available toxicity data on alternative dry cleaning chemicals. Abstract #1789 presented at the 2004 SOT meeting.

*ExxonMobil Biomedical Sciences, Inc. 1978. A Segment II Teratology Study in Rats Following Inhalation Exposure. Study No. 77-1567. (Unpublished report – robust summary provided in Appendix B.)

ExxonMobil Biomedical Sciences, Inc. 1983a. Acute Oral Toxicity Study in the Rat. Study No. 320501. (Unpublished report – robust summary provided in Appendix B.)

ExxonMobil Biomedical Sciences, Inc. 1983b. Acute Oral Toxicity Study in the Rat. Study No. 320701. (Unpublished report – robust summary provided in Appendix B.)

ExxonMobil Biomedical Sciences, Inc. 1983c. Acute Oral Toxicity Study in the Rat. Study No. 320601A. (Unpublished report – robust summary provided in Appendix B.)

ExxonMobil Biomedical Sciences, Inc. 1983d. Acute Dermal Toxicity Study in the Rabbit. Study No. 320506. (Unpublished report – robust summary provided in Appendix B.)

ExxonMobil Biomedical Sciences. 1983e. Acute Dermal Toxicity Study in the Rabbit. Study No. 320706. (Unpublished report – robust summary provided in Appendix B.)

ExxonMobil Biomedical Sciences, Inc. 1991c. Microbial Mutagenesis in Salmonella Mammalian Microsome Incorporation Assay, Study No. 187425. (Unpublished report – robust summary provided in Appendix B.)

ExxonMobil Biomedical Sciences, Inc. 1991d. In vivo Mammalian Bone Marrow Micronucleus Assay. Study No. 187430. (Unpublished report – robust summary provided in Appendix B.)

ExxonMobil Biomedical Sciences, Inc. 1994. Acute Dermal Toxicity Study in the Rabbit. Study No. 140506C. (Unpublished report – robust summary provided in Appendix B.)

Krause, C Chutsch, M, et al, 1991; Umwelt-Survey band IIIc:Wohn-Innerraum: Raumluft (Living spaces:indoor air). WaBoLu-Hefte 4/1991. Institute for Water, Soil and Air Hygiene of the Federal Health Offic, Berlin.

LeBret, E Van de Wiel, HJ et al, 1986. Volatile organic compounds in Dutch homes. Environ. Int. 12:2323-332

Petroquimia Espanola S.A. (PETRESA). 1984. Acute Oral Toxicity to Rats of PETREPAR® n-C14. (Unpublished report – robust summary provided in Appendix B.)

Sasol Italy. 1994. Study of the Capacity of the Test Article LINPAR® 10 to Induce Chromosome Aberrations in V79 Chinese Hamster Lung cells.

USEPA, 1986; Exposure Factors Handbook: Volume I - General Factors - EPA/600/P-95/002Ba, Volume II - Food Ingestion Factors - EPA/600-P-95/002Bb, Volume III - Activity Factors - EPA/600/P-95-002Bc

USEPA, 2002; Child-specific Exposure Factors Handbook EPA-600-P-00-002B Interim Report

Wallace, LA, Pellizzari, ED, Hartwell, TD, Sparacino, C, Whitmore, R, Sheldon, L, Zelo, H, Perritt, R (1987). The TEAM study: Personal exposures to toxic substances in air, drinking water and breath of 400 residents of New Jersey, North Carolina, and North Dakota. Environmental Research 43:290-307.

W.H.O., 1989: Indoor Air Quality: Organic Pollutants, Copenhagen, WHO Regional Office for Europe. (EURO Reports and Studies III)

Yoshimura et al., 1996. Ministry of Health and Welfare, Japan, 1996. Single Dose Oral Toxicity Test of Undecane in Rats. Toxicity City Testing Reports of Environmental Chemicals, Vol. 4, 578-614. (Robust summary provided in Appendix B.)

Page 90, Reference Section

Insert “a” after 1991 in first ExxonMobil Biomedical Sciences, Inc. reference.

Insert “b” after 1991 in second ExxonMobil Biomedical Sciences, Inc. reference.

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page F-5

Table F-1

1. Representative Intake:

replace the line :

"MOE* Margin of Exposure 213,000"

with:

"MOE* Margin of Exposure 64,000"

2. Upper Bound Intake:

replace the line :

"MOE* Margin of Exposure 150,000"

with:

"MOE* Margin of Exposure 45,000"

replace the line:

"*MOE based on subchronic NOAEL of 1,000 mg/kg/d"

with:

"*MOE based on reproductive/Developmental NOAEL of 300 mg/kg/d"