Texas Commission on Environmental Quality Response to Public Comments Received on the April 29, 2011 Proposed Pentane, All isomers Development Support Document

The public comment period for the January 2011 Proposed Development Support Document (DSD) for pentane, all isomers ended in April 201. The American Chemistry Council's Hydrocarbon Solvents Panel ("ACC Panel") submitted comments on May 2, 2011. The Toxicology Division (TD) of the Texas Commission on Environmental Quality (TCEQ) appreciates the effort put forth by ACC to provide technical comments on the proposed DSD for pentane, all isomers. The goal of the TD and TCEQ is to protect human health and welfare based on the most scientifically-defensible approaches possible (as documented in the DSD), and evaluation of these comments furthered that goal. A summary of comments from ACC is provided below, followed by TCEQ responses. The full comments are provided in Appendix 1. Comments on issues that suggest changes in the DSD are addressed whereas comments agreeing with TCEQ's approach are not. TCEQ responses indicate what changes, if any, were made to the DSD in response to the comment.

Upon further review, the DSD has been revised. The acute ReV and ESL for n-BA have been revised by using the TNO (1999) Report (now is a part of Lammers et al. 2011) study as key study. The acute ReV and ESL have been revised from 44,000 ppb and 12, 000 ppb to 68,000 ppb and 20,000 ppb, respectively.

American Chemistry Council's Hydrocarbon Solvents Panel ("ACC Panel") (Appendix 1)

Comment No.1:

The ACC Panel commented that it is more appropriate that the McKee et al. (1998) and TNO (1999) studies be used as key studies for the pentane DSD instead of the Stadler et al. (2001), Glowa et al. (1991), and Swann et al. (1974) Studies.

TCEQ Response:

The TD agrees that it is more appropriate to use the 1998 McKee et al. study and the 1999 TNO report as key studies for acute evaluation. Accordingly, the proposed DSD has been revised and the TNO (1999) report which is now part of Lammers et al. (2011) was used as key study for developing acute ReV and ESL for pentane (see Section 3.2 Health-Based Acute ReV and ^{acute}ESL for details). The proposed acute ReV and ESL were subsequently revised. The revised ReV and ESL have been increased from 44,000 ppb and 12, 000 ppb to 68,000 ppb and 20,000 ppb, respectively.

Comment No.2 (on Page 7, Line 8-10):

The ACC Panel commented that the reason why iso- and neo-pentane could be less anesthetic and lethal than n-pentane is that they are less well absorbed.

TCEQ Response:

The TD agrees with ACC's comments. The DSD has been revised and referenced the Dahl et al. (1988) study.

Comment No.3 (on Page 7, Line 25):

The ACC Panel indicated that the Glowa et al. (1991) reference in missing in the DSD's reference section.

TCEQ Response:

The Glowa et al. (1991) reference has been added to the DSD's reference section.

Comment No.4 (on Page 8, Line 23-24):

The ACC Panel indicated that the point "the mechanism of n-pentane caused respiratory irritation." as stated in the DSD, is not clear. It recommended that TCEQ further clarify or remove this point.

TCEQ Response:

The TD agrees with ACC's comments and has removed that statement from the DSD.

Comment No.5 (on Page 9, Line 19-23):

The ACC Panel commented that there is a discrepancy between the mean analytically concentration reported in the high exposure group (7,132 ppm) and the NOAEL (6,800 ppm) in the McKee et al. (1998) study.

TCEQ Response:

The NOAEL of 6,800 ppm has been corrected to 7,132 ppm (see Section 3.2.2.1 McKee et al. (1998) Study)

Comment No. 6 (on Table 4 of DSD, Glowa (1991) Study):

The ACC Panel commented that the statement "the stimulation of the HPA axis at 5,000 ppm" by Glowa (1991) cannot be verified.

TCEQ Response:

The TD agrees with ACC's comments and has removed that statement from the Table 4 of DSD.

Comment No. 7 (on Table 4 of DSD, Swann et al. (1974) Study):

The ACC Panel commented that it cannot agree with the statement "at 32,000 ppm, periodic body movements were observed during the exposure, which indicates effects of irritation before the animals became lightly anesthetized during the recovery period" reported by Swann et al., (1974). ACC indicated that as n-pentane is rapidly eliminated, it seems surprising that the aesthesia was after rather than during the exposure period. It further commented that Swann et al. did not actually observe irritation but rather interpreted "sporadic body movements" as irritation.

TCEQ Response:

The TD agrees with ACC's comments and has revised the statement of "a NOAEL of 16,000 ppm for anesthesia and respiratory irritation was identified from this study" to "a NOAEL of 16,000 ppm for periodic body movements and a NOAEL of 32,000 ppm for anesthesia were identified from this study". Furthermore, since the exposure duration was only 5 min, the NOAELs were not used as a POD to develop the acute ReV and ^{acute}ESL.

Comment No. 8 (on Table 4 of DSD, Stadler et al. (2001) Study):

The ACC Panel commented that the increases in calcium and phosphorus reported by Stadler et al. (2001) at 3,000 ppm were not observed by McKee et al. (1998) in a study at higher levels, for longer duration.

TCEQ Response:

The TD agrees with ACC's comments that the ascribed effects by Stadler et al. (2001) as treatment-related as a fairly conservative position. Furthermore, in a 90 day inhalation toxicity study by McKee et al. (1998), no effects on serum chemistry, and no resulting adverse effects in any of the test animals exposed with concentrations up to 20,000 mg/m^3 (6,800 ppm). The toxicological significance of the serum chemistry data reported by Stadler et al. (2001) was not used as the POD to develop acute ReV and ^{acute}ESL. The DSD has been revised accordingly.

Comment No. 9 (McKee et al. (1998) Study):

The ACC Panel commented that the reference for the McKee et al. (1998) study was not valid.

TCEQ Response:

The reference for the McKee et al. (1998) study has been corrected accordingly in the reference section.

Comment No. 10 (Page 13):

The ACC Panel commented that according to Dahl et al. (1988), inhaled n-pentane is actually not well absorbed.

TCEQ Response:

The TD appreciates this clarification. The DSD has been revised and added the Dahl et al. (1988) study to the reference accordingly.

Comment No. 11 (Section 3.2 of the DSD):

The ACC Panel commented that the effects observed in the Swann et al. (1974) and the Glowa (1991) studies are questionable. Thus, it is more appropriate to use the free-standing NOAEL identified from the Lammers et al. (2011) study as POD to develop the acute ReV and ^{acute}ESL. It further commented that it is more defensible to use a NOAEL of 10,000 ppm rather than 1,000 ppm should the Stadler et al. (2001) be used as acute key study. ACC recommended that TCEQ revise Section 3.2 based on the Lammers et al. (2011) study.

TCEQ Response:

The TD agrees with ACC's comments. The TNO (1999) report which is now part of Lammers et al. (2011) was selected as key study for developing acute ReV and ESL for pentane. The Swann

et al. (1974), the Glowa (1991), and the Stadler et al. (2001) studies have been moved to the Supporting Animal Studies Section (Section 3.2.2). The proposed DSD has been revised accordingly (see Response to Comment No. 1).

Comment No. 12 (Section 3.5.3 of the DSD, Uncertainty Factor):

The ACC Panel commented that the use of a total uncertainty factor (UF) of 30 for the adjustment of the POD_{HEC} does not appear to be supported by the data. It further commented that, as shown by Lammers et al. (2007), the responses of rats and humans to substances that produce acute CNS effects are reasonably similar. It indicated that, as reported by Patty and Yant (1929), there were no effects in human following exposure for 10 min to 5, 000 ppm pentanes. The ACC Panel recommended that TCEQ use a UF_A of 1 instead of 3 for interspecies variability.

TCEQ Response:

The TD appreciates with ACC's comments. The DSD was not revised based on the comments. A total UF of 30 was originally used for the POD_{HEC} of 1,333 ppm which was the lowest POD_{HEC} among those three selected key studies (Swann et al. 1974, Glowa 1991, and Stadler et al. 2001). However, since these studies were not used as acute key studies in the revised DSD, a revised total UF of 100 has been used to adjust a POD_{HEC} of 6,756 ppm based on the Lammers et al. (2011) key study. The total UF of 100 consists of a UF_H of 10, a UF_A of 3, and a UF_D of 3 (see Section 3.5.3 for details). The derived acute ReV is 68 ppm which is consistent with that derived by ACC (83 ppm) based on the NOAEL of 5,000 ppm reported by Patty and Yant (1929). As indicated in Section 3.2, the Patty and Yant (1929) study, however, was considered insufficient for the development of an acute ReV and ESL because the physiological response reported by the tested subjects during the odor intensity tests was subjective and the number of tested subjects was small.

Comment No. 13 (Page 17):

The ACC Panel commented that the statement "the major noncarcinogenic potential from repeated inhalation exposure to n-pentane is neurological and renal effects", as stated in Section 4.2, is misleading. It indicated that there is no evidence that repeated inhalation exposure produces neurological effects. ACC further commented that pentane has not been found to cause renal effects that are relevant to human health.

TCEQ Response:

The TD agrees with ACC's comments. The aforementioned statement has been deleted from the Section 4.2 of the proposed DSD.

APPENDIX 1

American Chemistry Council's Hydrocarbon Solvent Panel ("ACC")

Comments Regarding the TCEQ Development Support Document for Pentane, All Isomers