Development Support Document
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Phenol

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Acronyms and Abbreviations

Acronyms and Abbreviations	Definitions
AEGL	Acute Exposure Guideline Level
AMCV	Air Monitoring Comparison Value
°C	degrees Celsius
CNS	central nervous system
d	day
DSD	development support document
ET	extrathoracic
ESL	Effects Screening Level
$^{acute}ESL$	acute health-based Effects Screening Level for chemicals meeting minimum database requirements
$^{acute}ESL_{generic}$	acute health-based Effects Screening Level for chemicals not meeting minimum database requirements
$^{acute}ESL_{odor}$	acute odor-based Effects Screening Level
$^{acute}ESL_{veg}$	acute vegetation-based Effects Screening Level
$^{chronic}ESL_{nonthreshold(c)}$	chronic health-based Effects Screening Level for nonthreshold dose response cancer effect
$^{chronic}ESL_{nonthreshold(nc)}$	chronic health-based Effects Screening Level for nonthreshold dose response noncancer effects
$^{chronic}ESL_{threshold(c)}$	chronic health-based Effects Screening Level for threshold dose response cancer effects
$^{chronic}ESL_{threshold(nc)}$	chronic health-based Effects Screening Level for threshold dose response noncancer effects
$^{chronic}ESL_{veg}$	chronic vegetation-based Effects Screening Level
GD	gestational day
h	hour(s)
H	humans
$H_{b/g}$	blood:gas partition coefficient

Acronyms and Abbreviations	Definitions
$(H_{b/g})_A$	blood:gas partition coefficient, animal
$(H_{b/g})_H$	blood:gas partition coefficient, human
Hg	mercury
HEC	human equivalent concentration
HQ	hazard quotient
kg	kilogram
LOAEL	lowest-observed-adverse-effect-level
MW	molecular weight
µg	microgram
$\mu g/m^3$	micrograms per cubic meter
mg	milligrams
mg/m^3	milligrams per cubic meter
min	minute
MOA	mode of action
n	number
N/A	Not applicable
NOAEL	no-observed-adverse-effect-level
POD	point of departure
POD_{ADJ}	point of departure adjusted for exposure duration
POD_{HEC}	point of departure adjusted for human equivalent concentration
ppb	parts per billion
ppm	parts per million
ReV	reference value
RGDR	regional gas dose ratio
SD	Sprague-Dawley
TCEQ	Texas Commission on Environmental Quality

Acronyms and Abbreviations	Definitions
TD	Toxicology Division
UF	uncertainty factor
UF_H	interindividual or intraspecies human uncertainty factor
UF_A	animal to human uncertainty factor
UF_{Sub}	subchronic to chronic exposure uncertainty factor
UF_L	LOAEL to NOAEL uncertainty factor
UF_D	incomplete database uncertainty factor
USEPA	United States Environmental Protection Agency
w	week

Chapter 1 Summary Tables

Table 1 for air monitoring and Table 2 for air permitting provide a summary of health- and welfare-based values resulting from an acute and chronic evaluation of phenol. Please refer to Section 1.6.2 of the TCEQ Toxicity Factor Guidelines (2012) for an explanation of values used for review of ambient air monitoring data and air permitting. Table 3 provides summary information on phenol's physical/chemical properties.

Table 1. Air Monitoring Comparison Values (AMCVs) for Ambient Air [a]

Short-Term Values	Concentration	Notes
Acute ReV	960 µg/m^3 (250 ppb) **Short-Term Health**	**Critical Effect(s):** Nasal and ocular irritation, CNS effects in rats
$^{acute}ESL_{odor}$	42 µg/m^3 (11 ppb) **Odor**	50% detection threshold
$^{acute}ESL_{veg}$	---	No data on vegetation effects found
Long-Term Values	**Concentration**	**Notes**
Chronic ReV	11 µg/m^3 (2.9 ppb) **Long-Term Health**	**Critical Effect(s):** Liver and kidney damage in monkeys, rats and mice
$^{chronic}ESL_{nonthreshold(c)}$ $^{chronic}ESL_{threshold(c)}$	--- ---	Data are inadequate for an assessment of human carcinogenic potential via the inhalation route
$^{chronic}ESL_{veg}$	---	No data on vegetation effects found

[a] Phenol is not monitored for by the TCEQ's ambient air monitoring program, so currently no ambient air data (i.e., peaks, annual averages, trends, etc.) are available to assess phenol's concentrations in Texas ambient air

Abbreviations for Tables 1 and 2: **ppb**, parts per billion; **µg/m^3**, micrograms per cubic meter; h, hour; **ESL**, Effects Screening Level; **AMCV**, Air Monitoring Comparison Value; **HQ**, hazard quotient; **ReV**, Reference Value; ^{acute}**ESL**, acute health-based ESL; ^{acute}**ESL$_{odor}$**, acute odor-based ESL; ^{acute}**ESL$_{veg}$**, acute vegetation-based ESL; ^{chronic}**ESL$_{nonthreshold(c)}$**, chronic health-based ESL for nonthreshold dose-response cancer effect; ^{chronic}**ESL$_{threshold(nc)}$**, chronic health-based ESL for threshold dose-response noncancer effects; and ^{chronic}**ESL$_{veg}$**, chronic vegetation-based ESL

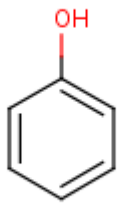
Table 2. Air Permitting Effects Screening Levels (ESLs)

Short-Term Values	Concentration	Notes
$^{acute}ESL$ [1 h] (HQ = 0.3)	290 µg/m^3 (75 ppb)[a]	**Critical Effect:** Nasal and ocular irritation, CNS effects in rats
$^{acute}ESL_{odor}$	42 µg/m^3 (11 ppb) **Short-Term ESL for Air Permit Reviews**	50% detection threshold
$^{acute}ESL_{veg}$	---	No data on vegetation effects found
Long-Term Values	**Concentration**	**Notes**
$^{chronic}ESL_{threshold(nc)}$ (HQ = 0.3)	3.3 µg/m^3 (0.87 ppb)[b] **Long-Term ESL for Air Permit Reviews**	**Critical Effect:** Liver and kidney damage in monkeys, rats, and mice
$^{chronic}ESL_{nonthreshold(c)}$ $^{chronic}ESL_{threshold(c)}$	--- ---	Data are inadequate for an assessment of human carcinogenic potential via the inhalation route
$^{chronic}ESL_{veg}$	---	No data on vegetation effects found

[a] Based on the acute ReV of 960 µg/m^3 (250 ppb) multiplied by 0.3 to account for cumulative and aggregate risk during the air permit review.

[b] Based on the chronic ReV of 11 µg/m^3 (2.9 ppb) multiplied by 0.3 to account for cumulative and aggregate risk during the air permit review.

Table 3. Chemical and Physical Data

Parameter	**Value**	**Reference**
Molecular Formula	C_6H_5OH	ATSDR 1998
Chemical Structure		ChemID Plus 2009
Molecular Weight	94.11	ATSDR 1998
Physical State at 25°C	Crystalline solid/liquid (8% water)	ATSDR 1998
Color	Colorless to light pink	ATSDR 1998
Odor	Aromatic, sweet and acrid	ATSDR 1998
CAS Registry Number	108-95-2	ATSDR 1998
Synonyms	Benzenol; hydroxybenzene; monophenol; oxybenzene; phenol alcohol; phenyl hydrate; phenylic acid; phenylic alcohol	ATSDR 1998
Solubility in water	87 g/L (25ºC)	ATSDR 1998
Log K_{ow}	1.46	ATSDR 1998
Vapor Pressure	0.3513 mm Hg at 25°C	ATSDR 1998
Relative Vapor Density (air = 1)	3.24	ATSDR 1998
Melting Point	43°C	ATSDR 1998
Boiling Point	181.8°C	ATSDR 1998
Conversion Factors	1 $\mu g/m^3$ = 0.260 ppb 1 ppb = 3.85 $\mu g/m^3$ at 25°C	USEPA 2002

Chapter 2 Major Sources and Uses

Phenol is both a naturally found and man-made chemical, and it's used in the production of a wide variety of manufacturing and consumer products. It ranks in the top 50 in production volume for chemicals produced in the United States, primarily for the production of phenolic resins (ATSDR 1998). Phenol is also present in medicinal products such as ointments, lotions, and analgesic rubs, and household items such as paint and soap (IPCS 1994).

Chapter 3 Acute Evaluation

The Development Support Document (DSD) is a summary of the key and supporting studies and procedures used by the Toxicology Division (TD) to derive inhalation toxicity values. This section is based on a review of current literature as well as background readings in ACGIH (2001), NRC (2009), ATSDR (1998, 2008), OEHHA (2008), and USEPA (2002), which describe in detail the acute toxicity of phenol.

3.1 Health-Based Acute ReV and ^{acute}ESL

Phenol has been classified by the ACGIH (2001) as an irritant to the eyes, mucous membranes, and skin. Additionally, short-term exposure to significantly elevated inhaled doses for a sufficient duration can lead to central nervous system (CNS) effects.

3.1.1 Physical/Chemical Properties

Phenol is a white crystalline solid that is very soluble in water, has a low K_{ow}, and slightly acidic. It is found naturally in the environment; however the largest sources of phenol are produced. The primary physical and chemical properties of phenol are summarized in Table 3. Phenol can be produced as a crystalline solid or a liquid, and its physical and chemical properties allow for the stable formation of both phases. Although typically emitted and reviewed for air permitting by the TCEQ as a vapor, it exists as a crystalline solid at room temperature so there may be some potential for aerosol/particulate emissions under certain conditions.

3.1.2 Key and Supporting Studies

3.1.2.1 Human Studies

Human inhalation data on the toxicity of phenol are limited and results are often confounded. Industrial exposures are often mixed with other common hazardous chemicals, such as formaldehyde, and it is difficult to tease out the adverse effects caused by each individual chemical. Subjects also have confounding life choices such as smoking. These confounders (i.e., co-exposures, smoking) make occupational studies less than informative (described further in section 4.1.3.1). A few limited quantitative studies have been conducted and are detailed here:

- In a study by Piotrowski (1971), eight human subjects were exposed for 8 h through a nose and mouth inhalation mask to various concentrations of phenol from 5 to 20 mg/m^3 (1.3-

5.1ppm) with 2 half-hour breaks (at 2.5 and 5.5 h after exposure began). This inhalation system prevented any other exposure such as absorption through the skin. The main goal of the inhalation portion of the study was to measure absorption by the lungs and the amount of phenol excreted in the urine (i.e., to determine whether urinary excretion can serve as an adequate biomarker of inhalation exposure) following an 8-h inhalation exposure. Consequently, there was no mention of respiratory or adverse health effects described by the author. Due to the purpose of this study, no health effects of any kind were tested for or recorded and the study is not considered useful for identifying critical adverse effects or the concentrations at which they may occur.

- NRC (2009) describes a study by Ogata et al. (1986) where urine from employees using phenol to treat fibers was analyzed for urinary metabolites. No information was given about the subjects, who were occupationally exposed during the workday to a range of vapor concentrations estimated to be between 1.22 and 4.95 ppm. No specific exposure duration was detailed. Additionally, the authors did not report any adverse health effects in the subjects they collected samples from; however, they did not specifically mention that there were none either. Thus, the study is not considered useful for identifying critical adverse effects for acute exposure or the concentrations at which they may occur.

A lack of well-conducted human studies has led to the use of an animal study to derive the acute ReV and ESL.

3.1.2.2 Animal Studies

3.1.2.2.1 Key Animal Study (Hoffman et al. 2001)

Regarding the Hoffman et al. (2001) key study used by the TCEQ, USEPA (2002) states that this study is the only one conducted using modern methodology and documentation (i.e., according to Good Laboratory Practice guidelines). In agreement with this statement and choice of study, NRC (2009) derived their AEGL1 value from this same inhalation study. The TCEQ did not identify any more appropriate and current studies for derivation of the acute ReV and ESL. A brief summary of the study is detailed below.

Hoffman et al. (2001) conducted a 2-w, 10-d inhalation study using 80 male and 80 female albino Fischer 344 rats divided into four treatment groups: 0, 0.5, 5.0, and 25 ppm phenol (analytical concentrations). Each group was exposed by nose-only inhalation for 6 h/d, 5 d/w for 2 w, for a total of 10 exposures. The phenol was diluted in distilled water and vaporized using a volatilization chamber. Half of the rats in each group were sacrificed the day after the 10th exposure, while the other half were allowed to recover from the exposure for 2 w before being sacrificed. The authors tested for an exhaustive number of endpoints, including hematology (e.g., red and white blood cell counts), clinical chemistry (e.g., blood urea nitrogen, creatinine), and a complete analysis on the weights and histology of all the major tissues and organs. The authors found no respiratory or neurological changes, either during exposure or following the recovery

period, which could be correlated to the concentration of phenol. This study gives a free-standing no-observed-adverse-effect-level (NOAEL) of 25 ppm for 2-w, 5 d/w, 6-h/d exposure.

3.1.2.2.2 Supporting Animal studies

Other animal studies evaluating the short-term effects of phenol inhalation are more limited (e.g., number of endpoints, methodology). However, the studies discussed below are informative as supporting studies in the derivation of the acute ReV and ESL.

- Flickinger (1976) describes communications with Koppers Company, Inc., that conducted a study using groups of six female Harlan-Wistar albino rats exposed for 8 h to a nominal concentration of 900 mg/m^3 (234 ppm) phenol aerosol. After 4 h of exposure, the animals experienced nasal and ocular irritation along with a loss in coordination, suggesting minor systemic effects to the CNS. After 8 h, 1 out of 6 of the rats showed more serious signs of CNS effects including tremors and prostration. All the animals appeared normal the next day suggesting that these were not permanent effects. The TCEQ considers 234 ppm to be the study lowest-observed-adverse-effect-level (LOAEL) for sensory irritation and neurological effects. A study NOAEL was not established.
- Dalin and Kristoffersson (1974) exposed male and female white rats (strain unknown) continuously to 100 mg/m^3 (25 ppm, nominal) phenol for 15 d. Environmental changes were controlled for by exposing the animals in their individual cages, and behavioral alterations such as changes in activity or coordination were recorded. After 3 days of continuous exposure, neurological effects such as twitching, balance issues, and disordered walking became apparent, and although the CNS symptoms subsided by day 5, the animals became slow and lethargic. Changes in serum components (e.g., lactate dehydrogenase) were noted although the significance was not determined. USEPA (2002) deemed 25 ppm to be the LOAEL for this lower-quality study (e.g., no histological exam). Similarly, the TCEQ considers 25 ppm to be the continuous exposure LOAEL for neurological effects with the continuous, multiple-day exposure duration potentially being the primary determinant of toxicity in this study versus Hoffman et al. (2001) which had a NOAEL of 25 ppm for a large number of endpoints (including neurological effects) for 6 h/d exposure.

3.1.2.3 Reproductive and Developmental Studies

No studies are available regarding the reproductive and/or developmental effects of phenol inhalation exposure in humans or animals. However a limited number of oral studies have been conducted and are outlined in the 2003 Reproductive Assessment Section of CalEPA's Office of Environmental Health Hazard Assessment (OEHHA 2003). A lack in significant alterations led ATSDR (2008), to conclude, and OEHHA and USEPA agreed, that "based on the limited available data, reproductive/developmental effects are unlikely to occur in humans following exposure to phenol at concentrations found in the environment or near hazardous waste sites."

Regarding human inhalation studies, some maternal occupational exposure assessments were available, although none of them were very detailed or gave significant results:

- Hernberg et al. (1983) examined maternal occupational exposure to disinfectants (including phenol) during early pregnancy and looked for a correlation to the occurrence of congenital defects, but no meaningful associations were found.
- Axelsson, et al. (1984) evaluated maternal occupational exposure to organic solvents during laboratory work during pregnancy, but there was no significant change in the number of miscarriages compared to nonexposed women. Five cases specifically reported phenol exposure, and all five of these pregnancies ended in normal deliveries.
- Several Polish studies looked at the placentas of women from areas that were prone to high levels of airborne toxic substances, the most hazardous being aromatic hydrocarbons, including phenol. Urinary levels of phenol were twice as high in the women from the highly polluted areas as they were from the not as polluted areas, and changes in the placental thickness, gestation length, and quality of the tissue suggested impairments of placental function associated with higher levels of airborne toxic substances. Nothing was mentioned, however, about the possibility of other chemicals that may have been present or influenced these observed phenotypes. Significant limitations including co-exposure to many chemicals make these types of studies of little value for dose-response assessment.

A few animal oral studies have also been conducted and are detailed in USEPA (2002):

- A set of studies done in 1983 by the Research Triangle Institute in 1983 treated timed-pregnant Sprague-Dawley (SD) rats with oral gavage doses of phenol at 0, 30, 60, and 120 mg/kg/d between gestational days (GD) 6-15. They looked at a variety of both maternal and fetal endpoints and found several significant treatment-related changes including a decrease in mean fetal weight per litter at 120 mg/kg/d. The USEPA considered the developmental NOAEL and LOAEL to be 60 and 120 mg/kg/d, respectively (2002).
- A second set of studies by the same group used timed-pregnant CD-1 mice and oral gavage doses of 0, 70, 140, and 280 mg/kg/d. Even higher doses were required to produce similar significant effects, including an increase in the number of dead pups per litter and a decrease in fetal body weight at the highest dose. This gave a developmental NOAEL of 140 mg/kg/d and a LOAEL of 280 mg/kg/d (USEPA 2002).
- Another rat study (Argus Research Laboratories 1997) showed a developmental NOAEL and LOAEL of 120 and 280 mg/kg/d, respectively, for decreased fetal body weight and delayed ossification (USEPA 2002).
- In a two-generation drinking water study in rats (Ryan et al. 2001), 30 SD rats/sex/group were exposed to 0, 200, 1000, or 5000 ppm phenol in drinking water. Parental (P1) rats were given phenol for 10 w prior to mating, during a 2-w mating period, throughout gestation, lactation, and until sacrifice. The males were sacrificed after successful mating. All of the P1 females were allowed natural parturition and were sacrificed at F1 weaning. The average daily intake during week 10 was 0, 14.7, 70.9, and 301.0 mg/kg/day for P1 males and 0, 20.0, 93.0, and 320.5 mg/kg/day for P1 females. For the F1 generation, intake during week 10 was 0, 13.5, 69.8, and 319.1 mg/kg/day for males and 0, 20.9, 93.8, and 379.5 mg/kg/day for females. The F1 generation (20 rats/sex/group) was treated following a protocol similar to

that used for the P1 generation, and F2 pups were sacrificed after weaning, on postnatal day 22. During treatment, rats were monitored for mortality, clinical signs, body weight, and food and water consumption. At sacrifice, the animals were necropsied, and reproductive organs from 20 animals per sex in the control and high-dose groups from the P1 and F1 generations were examined microscopically. In addition, the spleen, thymus, liver, and kidneys from 10 randomly selected P1 and F1 animals of each sex in the control and high-dose groups were examined. On the basis of the decreased parental and pup body weight (compared to the controls) and decreased pup survival, the lowest LOAEL is 301 mg/kg/d and the study NOAEL is 70.9 mg/kg/day (USEPA 2002).

Although there are available oral data, the doses inducing adverse effects in these studies are higher than those found in the inhalation studies described previously and used for the key and supporting studies. Hoffman et al. (2001) estimates that their highest inhalation exposure level of 25 ppm is equivalent to an oral dose of 28 mg/kg/d, and a similar oral dose would correspond to the LOAEL for the supporting study of Dalin and Kristoffersson (1974). In comparison, the RTI group's lowest exposure found to cause any significant effect after GD 6-15 exposure was 60 mg/kg/d and 280-301 mg/kg/d are LOAELs from other developmental studies (i.e., Argus Research Laboratories 1997, Ryan et al. 2001). This suggests that protecting against potential nasal and ocular irritation and CNS effects will also protect against the potential reproductive/developmental effects. Additionally, using the Hoffman inhalation study for a point of departure eliminates the uncertainties that would arise from route-to-route extrapolation.

3.1.3 Mode-of-Action (MOA) Analysis

The precise MOA(s) for the adverse effects (e.g., eye and nose irritation, CNS) caused by airborne phenol exposure is not known. Phenol acts as an irritant, and tissue damage, inflammation, and irritation may occur at the site of absorption/contact. While the mechanism for phenol-induced acute irritation of mucous membranes is not known, because phenol at higher concentrations precipitates proteins from solution and dissolves in both water and organic solvents, interference with normal protein, enzyme, and membrane function seems likely (NRC 2009). Animal studies have suggested that phenol also acts systemically by interfering with the CNS, however the mechanism remains unclear (Flickinger, 1976; Dalin and Kristoffersson, 1974)

3.1.4 Point of Departure (POD) for Key Animal Study and Critical Effects

3.1.4.1 Key Animal Study

Hoffman et al. (2001) found no pathological changes in rats after a 6h/d, 5d/w, 2-w phenol vapor inhalation study. This study provides a free-standing NOAEL of 25 ppm which will be conservatively used as the POD based on a single day's 6-h exposure from the 2-w exposure study.

3.1.4.2 Supporting Animal Study

The animal study of Flickinger (1976) provides a supporting LOAEL closer in duration (4 h) to the duration of interest (i.e., 1 h) than the continuous exposure Dalin and Kristoffersson (1974) study which found neurological effects after day 3 of 15 days of exposure. The study by Flickinger (1976) found that rats treated for 4 h at 234 ppm phenol experienced nasal and ocular irritation and neurological effects. These are considered as the critical adverse effects. Because this was the only dose used, 234 ppm is a free-standing LOAEL. If a LOAEL-to-NOAEL uncertainty factor (UF_L) of 10 was applied to this LOAEL to account for the study not having a NOAEL, the resulting estimated NOAEL value (23.4 ppm) would be very similar to the Hoffman et al. study NOAEL-based POD (25 ppm).

3.1.5 Dosimetric Adjustments

3.1.5.1 Default Exposure Duration Adjustments

The 6-h duration (C_1) for a single day exposure in the key study by Hoffman et al. (2001) was adjusted to a POD_{ADJ} of 1-h exposure duration (C_2) using Haber's Rule as modified by ten Berge et al. (1986) ($C_1^n \times T_1 = C_2^n \times T_2$) with n = 3, where both concentration and duration play a role in toxicity:

$$C_2 = [(C_1)^3 \times (T_1 / T_2)]^{1/3}$$
$$= [(25\ \text{ppm})^3 \times (6\ \text{h}/1\ \text{h})]^{1/3}$$
$$= 45.428\ \text{ppm} = POD_{ADJ}$$

3.1.5.2 Default Dosimetry Adjustments from Animal-to-Human Exposure

Phenol is very water soluble and causes sensory irritation to the ocular and nasal region. However, while phenol acts as a point-of-entry (POE) irritant (Category 1 gas), it also acts systemically (i.e., as a Category 3 gas) on the CNS to cause neurological effects (e.g., loss in coordination and balance). The USEPA considers phenol a Category 2 gas due to its intermediate chemical and physical properties (USEPA 2002). As a critical effect, eye irritation would suggest using a pharmacokinetic dosimetric animal-to-human adjustment factor (DAF) of 1. The same can be said for nasal irritation given that USEPA (2012) suggests an RGDR of 1 for the extrathoracic (ET) region (i.e., external nares to the beginning of the trachea), which includes the nose. Likewise, in regard to the CNS effects, the default pharmacokinetic animal-to-human dosimetric adjustment for a Category 3 gas is a blood:gas partition coefficient animal/human ratio of 1 (TCEQ 2012). Thus, all these considerations support using a dosimetric animal-to-human adjustment of 1 for the POD_{ADJ} (i.e., use a DAF_r of 1). Thus, the POD_{HEC} is equal to the POD_{ADJ} of 45.428 ppm.

3.1.6 Adjustments of the POD_{HEC}

The POD_{HEC} based on a NOAEL from the Hoffman et al. (2001) study was used as the POD and UFs were applied to derive the acute ReV (i.e., assume a threshold MOA for a noncarcinogenic endpoint). The following uncertainty factors (UFs) were applied to the POD_{HEC} of 45.428 ppm: 10 for UF_H, 3 for UF_A, and 6 for UF_D, for a total UF of 180.

- An intrahuman UF_H of 10 was used to account for intrahuman variability and potentially sensitive subgroups;
- An animal-to-human UF_A of 3 was used to account for potential phamacodynamic differences between animals and humans (pharmacokinetic adjustment was already performed); and
- A database deficiency UF_D of 6 was used to account for the lack of adequate human inhalation studies, a more robust high-quality laboratory animal inhalation dataset, information on potentially sensitive life stages (e.g., very young, elderly), etc. A full UF_D of 10 was not used since oral study information provided insight in addressing potential reproductive/developmental concerns.

$$\begin{aligned} \text{acute ReV} &= POD_{HEC} / (UF_H \times UF_A \times UF_D) \\ &= 45.428 \text{ ppm} / (10 \times 3 \times 6) \\ &= 45.428 \text{ ppm} / 180 \\ &= 0.252378 \text{ ppm} \\ &= 252.378 \text{ ppb or } 250 \text{ ppb (rounded to two significant digits)} \end{aligned}$$

3.1.7 Health-Based Acute ReV and ^{acute}ESL

In deriving the acute ReV for phenol, no numbers were rounded between equations until the ReV was calculated. Once the ReV was calculated, it was rounded to two significant figures. The resulting 1-h acute ReV is 0.25 ppm (0.96 mg/m^3) or 250 ppb (960 µg/m^3) based on the Hoffman et al. (2001) study. The rounded acute ReV was then used to calculate the ^{acute}ESL. At the target hazard quotient (HQ) of 0.3, the ^{acute}ESL is 75 ppb (290 µg/m^3) (Table 4).

Table 4. Derivation of the Acute ReV and ^{acute}ESL

Parameter	**Values and Descriptions**
Study	Hoffman et al. 2001
Study Population	80 male and 80 female Fischer rats
Study Quality	High
Exposure Concentrations	Nose-only inhalation of phenol vapor at 0, 0.5, 5, and 25 ppm
Exposure Duration	6h/d,5d/w, 2 w (60h total)
POD	25 ppm (free-standing NOAEL)
Critical Effects	Nasal and ocular irritation, CNS effects
Extrapolation from 6 h to 1 h	Haber's rule with n=3
POD_{HEC} (1 h)	45.428 ppm
Total UF	180
Interspecies UF	3
Intraspecies UF	10
Incomplete Database UF *Database Quality*	6 Low to medium
acute ReV [1 h] (HQ = 1)	**960 µg/m^3 (250 ppb)**
^{acute}ESL [1 h] (HQ = 0.3)	**290 µg/m^3 (75 ppb)**

3.1.8 Phenol as Particulate Matter

As mentioned in Section 3.1.1, phenol has certain chemical and physical properties that allow it to exist in both the vapor and particulate form. For air permitting by the TCEQ, phenol is typically in the vapor phase, and therefore only a vapor ^{acute}ESL was derived here. If the need for an ^{acute}ESL for phenol as an aerosol/particulate should arise, the vapor ^{acute}ESL value of 290 µg/m^3 can be used. However, because the ^{acute}ESL (290 µg/m^3) is higher than the 24-h National Ambient Air Quality Standard (NAAQS) for PM_{10}, currently set at 150 µg/m^3, any future air permit evaluations of phenol as particulate must also meet the NAAQS standard on a 24-h basis.

3.2 Welfare-Based Acute ESLs

3.2.1 Odor Perception

Phenol has a very distinct aromatic and acrid odor, smelling sickeningly sweet and tarry (ATSDR 1993). Published odor detection threshold values that met the criteria accepted by AIHA, USEPA, and TCEQ (AIHA 1989; USEPA 1992 and TCEQ 2012) are summarized in Table 5.

Table 5. Accepted Odor Studies Conducted for Phenol

Investigator	Odor Detection Threshold Value	Quality Level
Nagata (2003)	22 µg/m^3 (5.6 ppb)	1
van Doorn (2002)	67 µg/m^3 (16 ppb)	1
van Doorn (2002)	70 µg/m^3 (18 ppb)	1
Hoshika (1993)	46 µg/m^3 (12 ppb)	1
Hoshika (1993)	38 µg/m^3 (10 ppb)	1
Punter (1980)	230 µg/m^3 (60 ppb)	3
$^{acute}ESL_{odor}$	**42 µg/m^3 (11 ppb)**	

Several scientific studies were identified as acceptable sources for odor threshold values as described in TCEQ (2012): Punter (1980), Hoshika (1993), van Doorn et al. (2002), and Nagata (2003) (some values found in USEPA 1992). According to guidelines for setting odor-based effects screening levels (TCEQ 2012), odor detection values defined as the highest quality level of odor thresholds (Level 1) will be considered first in setting the $^{acute}ESL_{odor}$ values. Since there are multiple level 1 odor threshold values as defined by the TCEQ (2012), the geometric mean of all of the level 1 values will be used. Accordingly, the $^{acute}ESL_{odor}$ for phenol was calculated to be 42 µg/m^3 (11 ppb). The odor value only applies to phenol in the vapor phase, and not as a particulate.

3.2.2 Vegetation Effects

After a literature review, there was no data found on any adverse effects of phenol on vegetation.

3.3 Short-Term ESL and Values for Air Monitoring Evaluation

The acute evaluation resulted in the derivation of the following values:

- $^{acute}ESL_{odor}$ = 42 µg/m^3 (11 ppb)
- acute ReV = 960 µg/m^3 (250 ppb)
- $^{acute}ESL$ = 290 µg/m^3 (75 ppb)

For air permit reviews, the TCEQ considers chemicals with VP > 0.01 mm Hg as vapors (TCEQ 2012), which is the case for phenol (Table 3). Consequently, the short-term ESL for air permit evaluations is the $^{acute}ESL_{odor}$ of 42 µg/m^3 (11 ppb) as it is lower than the health-based $^{acute}ESL$ (Table 2). In the event phenol is emitted as aerosol/particulate, the 1-h ESL for air permit evaluations vapor $^{acute}ESL$ of 290 µg/m^3 will be used, although the 24-h NAAQS value of 150 µg/m^3 must also be met on a 24-h basis. Although we do not currently monitor for phenol, the $^{acute}ESL_{odor}$ of 42 µg/m^3 (11 ppb) is lower than the acute ReV of 960 µg/m^3 (250 ppb). Both values may be used for the evaluation of ambient air monitoring data in the future (Table 1). The $^{acute}ESL$ (HQ = 0.3) would not be used to evaluate ambient air monitoring data.

3.4 Acute Inhalation Observed Adverse Effect Level

Risk assessors, and the general public, often ask to have information on the levels in air where health effects would be expected to occur. So, when possible, the TCEQ provides chemical-specific observed adverse effects levels in DSDs (TCEQ 2012). As the basis for development of inhalation observed adverse effect levels is limited to available data, future studies could possibly identify a lower POD for this purpose. Regarding critical effects due to acute phenol exposure, the animal study by Flickinger (1976) provides a LOAEL closer in duration (4 h) to the acute duration of interest (i.e., 1 h) than the Dalin and Kristoffersson (1974) study. The study by Flickinger (1976) found a 4-h rat LOAEL of 234 ppm for nasal and ocular irritation and neurological effects. This animal LOAEL was used as the animal acute inhalation observed adverse effect level for extrapolation to humans. No duration adjustment was made (TCEQ 2012). As discussed in Section 3.1.5.2, for these effects the animal-to-human dosimetric adjustment results in a $LOAEL_{HEC}$ equal to the animal exposure concentration (e.g., a DAF of 1 is used). Thus, the 4-h $LOAEL_{HEC}$ based on this animal study is estimated to be 234 ppm.

The $LOAEL_{HEC}$ determined from an animal study represents a concentration at which it is possible that similar effects could occur in some individuals exposed to this level over the same duration as used in the study (4 h) or longer. Importantly, effects are not a certainty due to potential interspecies and intraspecies differences in sensitivity. As the basis for development of inhalation observed adverse effect levels is limited to available data, future studies could possibly identify a lower POD for this purpose. The acute inhalation observed adverse effect level of 234 ppm (900 µg/m^3) is provided for informational purposes only (TCEQ 2012).

The margin of exposure between the estimated acute inhalation observed adverse effect level of 234 ppm (234,000 ppb) and the acute ReV of 250 ppb is a factor of 936.

Chapter 4 Chronic Evaluation

4.1 Noncarcinogenic Potential

The inhalation data on phenol are very limited, and the information available is often poorly collected with concurrent exposure to other chemicals and factors such as formaldehyde and

smoking. The toxicological profiles of phenol from the USEPA (2002) and the ATSDR (2008) were reviewed for this section along with conducting a literature review for any more current studies. However, because of the insufficient nature of the human data, the relevant animal study with the appropriate UFs will ultimately be used to derive the chronic ReV.

4.1.2 Physical/Chemical Properties

The primary physical and chemical properties of phenol are discussed in Chapter 3 and summarized in Table 3.

4.1.3 Key and Supporting Studies

4.1.3.1 Human Studies

Several occupational studies have looked at workers exposed to phenol vapor, but unfortunately these data are not useable due to either co-exposures to other hazardous chemicals, such as formaldehyde, insufficient data collected on exposure, and/or lack of a dose-response relationship. A few of these studies can be found in the USEPA (2002) and ATSDR (1998, 2008) toxicological profiles for phenol:

- Dosemeci et al. (1991) assessed workers from five manufacturing plants to determine if there was a correlation between phenol exposure and increased mortality rates. He examined a wide array of causes of death, including various cancers, heart and organ diseases, and accidental deaths. None of the variables examined showed a significant increase in relation to phenol exposure, however some small reductions in mortality rates were found.
- Kauppinen et al. (1986) found an increase in respiratory cancer in workers exposed to phenol, but they found no dose-response relationship for phenol. The workers had been exposed to other hazardous chemicals (pesticides), and the significance was lost once the study was adjusted for incidence of smoking (as cited in EPA 2002; ATSDR 2008).
- In Baj et al. (1994), workers at a factory producing a common liquid wood preservative were exposed to a mixture of formaldehyde, phenol, and chlorohydrocarbons. All of the workers in the study complained of respiratory symptoms after 6 months of exposure, but the authors were unable to correlate it to a specific chemical or dose (ATSDR 1998).
- Shamy et al. (1994) examined workers from an oil refining plant exposed to phenol alone or to a combination of organic solvents including phenol, benzene, and toluene. It was estimated that the time-weighted, average air concentration for the phenol-only exposed group was 5.4 ppm. Several biochemical markers were found to be altered, including increases in serum aspartic aminotransferase (AST) and alanine aminotransferase (ALT) and decreases in creatinine levels. Small but statistically significant increases were also observed in serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT). However, while the authors found some statistically significant differences, these biochemical endpoints lack sufficient information on the level of change which should be considered adverse for chemical risk assessment. Small, statistically significant

hematopoietic effects (e.g., increases in hemoglobin) were also found but were not adverse (USEPA 2002). Finally, as it appears that the phenol-exposed workers may have also been exposed to other organic compounds, the observed effects cannot be clearly attributed to phenol exposure (USEPA 2002).

Due to the lack of sufficient human data, an animal study was used to develop the chronic ReV.

4.1.3.2 Animal Study

Since relevant human toxicity data are limited as well as chronic animal data, the TCEQ will utilize a subchronic animal study. A subchronic study meets the minimum database for development of a chronic ReV under Table 5-2 of the TCEQ Guidelines (TCEQ 2012), although with low database confidence. The Sandage (1961) 90-d, subchronic study will be used as the key study and source for a POD. Although this study has some shortcomings as noted by USEPA (2002) (e.g., exposure methods, limited records), in the absence of more well-conducted studies this study can be used for developing the chronic ReV and ESL.

The following summary of Sandage (1961) is based on (some verbatim) information presented in USEPA (2002), ATSDR (1998), and IPCS (1994). In an unpublished 90-d study, groups of 10 male rhesus monkeys, 50 male Sprague-Dawley rats, and 100 male albino mice were exposed to average phenol concentrations of 0 or 4.72 ppm (18.2 mg/m^3) continuously for 90 d. Exposure was interrupted for 14 h on day 39 and for 36 h on days 68-69. The phenol concentration was reported to remain in the desired ranges of 4.5-5.5 ppm after the first three days. During the exposure, no deaths were observed in the test animals. Body weight gain in mice was comparable to that in controls but was slightly higher in exposed rats and monkeys. A complete hematological examination showed no significant changes in the three test species following phenol exposure. Blood biochemistry (alkaline phosphatase, cholinesterase, amylase, lipase, and glutamic oxaloacetic transaminase) was evaluated in monkeys only. Urinalysis was apparently conducted in all species, but kidney function tests (urine volume and specific gravity) were conducted only in monkeys and rats. The study authors reported that there were no effects on any of the endpoints (although supporting data were not provided).

At the end of the exposure period, approximately half of the animals underwent a stress test in which the animals swam a smooth-walled tank until exhausted. These animals were sacrificed immediately after the test, and the other animals were held for a 2-w recovery period prior to sacrifice. Histopathological evaluations were conducted in 5-8 organs, including the liver, kidney, and lung (Table 6). It appears that all of the monkeys and about half of the rats and mice were evaluated (although it is not clear whether some of the rodents were evaluated after the recovery period).

Table 6. Summary of the pathology report from Sandage (1961)

Percent of animals showing pathology	**Monkey Control Group**	**Monkey Phenol Group**	**Rat Control Group**	**Rat phenol Group**	**Mouse Control Group**	**Mouse Phenol Group**
Phenol Concentration	--	4.72 ppm	--	4.72 ppm	--	4.72 ppm
Liver	0	30%	0	20%*	Not reported	Not reported
Kidney	0	20%	0	20%*	Not reported	Not reported
Lung	30%	Not reported	35%	Not reported	6%	20%*

* denotes statistical significance by a Fisher's exact test conducted by the authors.

Although the authors characterized the histology findings as "essentially negative" without providing detailed information (e.g., descriptions of the observed lesions), it is notable that liver and kidney pathology was observed in 30% and 20% of the monkeys (compared with 0% of the controls), respectively, and in 20% of the rats for these organs (compared with 0% of the controls) (Table 6). It is unclear why the authors did not consider these changes to be histologically significant (e.g., pathology in 6/7 monkeys was considered minimal or doubtful) and statistical significance was not reported in the study. Liver and kidney pathology was reported in 20% of the phenol-exposed rats (compared with 0% of the controls) and lung pathology was reported in 20% of the phenol-exposed mice (compared with 6% of the controls). The incidences of liver and kidney pathology in the rat and lung pathology in the mouse were statistically significant in a Fisher's exact test done for this assessment. *The TCEQ therefore considers the free-standing LOAEL for this study based on rat liver/kidney pathology and mouse lung pathology to be 4.72 ppm (18.2 mg/m^3).* Although the incidence of lung pathology was not reported in exposed monkeys and rats, a relatively high incidence of lung pathology in the control animals (30% and 35%, respectively) decreased the sensitivity of the evaluation in these species. No other significant pathological changes were reported in the test animals.

For the purposes of this assessment, in the absence of more detailed information on significance and region(s) of the lung affected, lung pathology in the mouse will not be used as an endpoint since dosimetric extrapolation to humans (i.e., calculating a $RGDR_r$ and POD_{HEC}) cannot be determined. That is, the $LOAEL_{HEC}$ for lung lesions in this study cannot be determined in the absence of information on the nature of the lung lesions (in agreement with USEPA 2002). There is also a greater increase in the incidence of liver and kidney pathology compared to the incidence of lung pathology, further supporting the use of these endpoints over the lung.

Consequently, based on statistically significant increases in liver and kidney pathology in the rat, 4.72 ppm (18.2 mg/m^3) will be used as a free-standing LOAEL for derivation of the chronic ReV and ESL.

4.1.3.3 Reproductive and Developmental Studies

No studies are available regarding the reproductive and/or developmental effects of phenol inhalation exposure in humans and animals. Although there is a lack of animal data in regards to the inhalation route of exposure, a limited number of oral studies have been conducted as discussed previously in Section 3.1.2.3. A lack in significant alterations led to the conclusion that reproductive/developmental effects are unlikely to occur in humans following exposure to phenol at concentrations found in the environment of near hazardous waste sites.

In regard to human studies, some maternal occupational exposure assessments were available, although none of them were very detailed or gave significant results:

- Hernberg et al. (1983) examined maternal occupational exposure to disinfectants (including phenol) during early pregnancy and looked for a correlation to the occurrence of congenital defects, but no meaningful associations were found.
- Axelsson, et al. (1984) evaluated maternal occupational exposure to organic solvents during laboratory work during pregnancy, but there was no significant change in the number of miscarriages compared to nonexposed women. Five cases specifically reported phenol exposure, and all five of these pregnancies ended in normal deliveries.
- Several Polish studies looked at the placentas of women from areas that were prone to high levels of airborne toxic substances, the most hazardous being aromatic hydrocarbons, including phenol. Urinary levels of phenol were twice as high in the women from the highly polluted areas as they were from the not as polluted areas, and changes in the placental thickness, gestation length, and quality of the tissue suggested impairments of placental function associated with higher levels of airborne toxic substances. Nothing was mentioned, however, about the possibility of other chemicals that may have been present or influenced these observed phenotypes. Significant limitations including co-exposure to many chemicals make these types of studies of little value for dose-response assessment.

A few animal oral studies have also been conducted and are detailed in USEPA (2002):

- The Research Triangle Institute in 1983 treated timed-pregnant Sprague-Dawley (SD) rats with oral gavage doses of phenol at 0, 30, 60, and 120 mg/kg/d between GD 6-15. They looked at a variety of both maternal and fetal endpoints and found several significant treatment-related changes including a decrease in mean fetal weight per litter at 120 mg/kg/d. The USEPA considered the developmental NOAEL and LOAEL to be 60 and 120 mg/kg/d, respectively (USEPA 2002).
- A second set of studies by the same group used timed-pregnant CD-1 mice and oral gavage doses of 0, 70, 140, and 280 mg/kg/d. Even higher doses were required to produce similar

significant effects, including an increase in the number of dead pups per litter and a decrease in fetal body weight at the highest dose. This gave a developmental NOAEL of 140 mg/kg/d and a LOAEL of 280 mg/kg/d (USEPA 2002).

- Another rat study (Argus Research Laboratories 1997) showed a developmental NOAEL and LOAEL of 120 and 280 mg/kg/d, respectively, for decreased fetal body weight and delayed ossification (USEPA 2002).
- As discussed in more detail in Section 3.1.2.3, the lowest LOAEL in a two-generation rat drinking water study (Ryan et al. 2001) was 301 mg/kg/d for decreased parental and pup body weight (compared to the controls) and the study NOAEL was 70.9 mg/kg/day (USEPA 2002).

All of the oral doses producing these effects would be significantly higher than an estimated oral dose corresponding to the inhalation rat LOAEL of 4.72 ppm from the key animal study (e.g., perhaps ≈ 10 mg/kg/d). This suggests that protecting against potential liver and kidney pathology will also protect against the potential reproductive/ developmental effects.

4.1.4 Mode of Action

Phenol is readily absorbed through the lungs, skin, and stomach, and once in the body it passes easily into the blood stream. Although the short-term studies discussed in Section 3.1.2 show that sufficiently high acute inhalation exposure to phenol can result in POE (e.g., nasal, ocular) and CNS effects, longer-term exposure studies in laboratory animals indicate that systemic effects on organs such as the liver and kidney are also possible. The mechanism(s) by which phenol may act on these organ systems, however, remains unclear.

4.1.5 PODs for Key Study, Critical Effects and Dosimetric Adjustments

Based on the key study presented above (Sandage 1961), the TCEQ identifies 4.72 ppm (18.2 mg/m^3) as the free-standing LOAEL and subchronic POD based on rat liver/kidney pathology.

4.1.5.1 Default Exposure Duration Adjustments

The 90-d exposure duration used in the key study was a subchronic, continuous exposure protocol. Therefore, no duration adjustment to continuous exposure is needed.

4.1.5.2 Default Dosimetry Adjustments from Animal-to-Human Exposure

The critical effects of kidney and liver pathology are systemic in nature. Therefore, phenol is acting as a Category 3 gas. For Category 3 gases, when available, animal and human blood:gas partition coefficients are used to dosimetrically adjust for species differences in toxicokinetics (TCEQ 2012).

$$POD_{HEC} = POD_{ADJ} \times ((H_{b/g})_A / (H_{b/g})_H)$$

where: $H_{b/g}$ = ratio of the blood:gas partition coefficient

A = animal

H = human

However, where these data are lacking as in the case here, a default value of 1 is used (TCEQ 2012).

$$POD_{HEC} = POD_{ADJ} \times ((H_{b/g})_A / (H_{b/g})_H) = 4.72 \text{ ppm} \times 1 = 4.72 \text{ ppm}$$

4.1.6 Adjustments of the POD_{HEC}

For the noncarcinogenic effects of phenol, UFs are applied to a POD to derive a ReV (i.e., assume a nonlinear MOA for a noncarcinogenic endpoint). The following UFs were considered appropriate for application to the POD_{HEC} of 4.72 ppm: 10 for UF_H, 3 for UF_A, 3 for UF_{Sub}, 6 for UF_L, and 6 for UF_D, for a total potential UF of 3,240.

- An UF_H of 10 was considered appropriate to account for potential intrahuman variability since information on potentially sensitive subpopulations is lacking;
- An UF_A of 3 was considered appropriate to account for potential interspecies toxicodynamic differences since dosimetric adjustment for toxicokinetic differences was conducted;
- An UF_{Sub} of 3 was considered appropriate to account for the use of a subchronic study due to some of the specific properties of phenol, such as a relatively rapid elimination half-life of < 4 h (ATSDR 2008) and a log K_{ow} well below 4 (Table 3), leading to reduced concern about bioaccumulation and chronic effects differing significantly from subchronic effects;
- A somewhat reduced UF_L of 6 was considered appropriate considering that while statistically significant increases occurred in the incidence of liver and kidney pathology, the study authors considered the histology findings “essentially negative,” implying a reduced level of concern; and
- A database UF_D of 3 was considered applicable because although there is a deficiency in the scientific research on the effects of chronic inhalation exposure to phenol (e.g., lack of additional useful inhalation studies in humans or animals or chronic studies of high quality): (1) toxicokinetic considerations reduce concern about chronic effects differing significantly from subchronic effects; (2) oral study information provides insight in addressing potential reproductive/developmental concerns; and (3) there is a lack of independence between the UF_D and the UF_{Sub} of 3 already being utilized.

$$\begin{aligned} \text{chronic ReV} &= POD_{HEC} / (UF_H \times UF_A \times UF_{Sub} \times UF_L \times UF_D) \\ &= 4.72 \text{ ppm} / (10 \times 3 \times 3 \times 6 \times 3) \\ &= 4.72 \text{ ppm} / 1{,}620 \\ &= 0.0029135 \text{ ppm} \\ &= 2.9135 \text{ ppb or } 2.9 \text{ ppb (rounded to two significant digits)} \end{aligned}$$

4.1.7 Health-Based Chronic ReV and $^{chronic}ESL_{threshold(nc)}$

In deriving the vapor chronic ReV, no numbers were rounded between equations until the ReV was calculated. The chronic ReV was rounded to two significant figures, resulting in a value of 2.9 ppb (11 µg/m^3), and then used to calculate the $^{chronic}ESL_{threshold(nc)}$. At the target hazard quotient of 0.3, the $^{chronic}ESL_{threshold(nc)}$ is 0.87 ppb (3.3 µg/m^3) (Table 7).

Table 7. Derivation of the Chronic ReV and $^{chronic}ESL$

Parameter	**Values and Descriptions**
Study	Sandage (1961)
Study Population	10 male Rhesus monkeys, 50 male Sprague-Dawley rats, and 100 male albino mice
Study Quality	Low
Exposure Concentrations	0 and 4.72 ppm (continuous)
Critical Effects	Liver and kidney pathology in rats
POD	4.72 ppm (free-standing LOAEL)
Exposure Duration	90 d (subchronic)
Extrapolation to continuous exposure (POD_{ADJ})	Not needed as the study exposure regimen was continuous
POD_{HEC}	4.72 ppm
Total UF	1,620
Interspecies UF	10
Intraspecies UF	3
LOAEL UF	6
Subchronic to chronic UF	3
Incomplete Database UF *Database Quality*	3 Low-medium
Chronic ReV (HQ = 1)	**11 µg/m^3 (2.9 ppb)**
$^{chronic}ESL_{nonlinear(nc)}$ (HQ = 0.3)	**3.3 µg/m^3 (0.87 ppb)**

4.1.8 Phenol as Particulate Matter

As mentioned in Section 3.1.1, phenol has certain chemical and physical properties that allow it to exist in both the vapor and particulate form. For air permitting by the TCEQ, phenol is typically in the vapor phase, and therefore only a vapor ${}^{chronic}ESL_{nonlinear(nc)}$ was derived here. If the need for a ${}^{chronic}ESL_{nonlinear(nc)}$ for phenol as an aerosol/particulate should arise, the ${}^{chronic}ESL_{nonlinear(nc)}$ of 3.3 µg/m^3 can be used.

4.2 Carcinogenic Potential

In 1999, the International Agency for Research on Cancer (IARC 1999) conducted a thorough literature review in order to examine the possible carcinogenicity of phenol. The IARC labeled phenol as *not classifiable as to its carcinogenicity to humans* (Group 3) since the data were considered inadequate for an assessment of human carcinogenic potential (NRC 2009). More recently, and in agreement with IARC, the USEPA (2002) indicated that data are *inadequate for assessment of human carcinogenic potential*.

To date, there are no human or animal inhalation studies indicating that phenol is carcinogenic. More specifically, there is not a well-conducted chronic inhalation carcinogenicity study that could be used to conduct dose-response modeling. Consequently, a chronic carcinogenic inhalation value cannot be and was not developed.

4.3 Welfare-Based Chronic ESL

No data were found regarding long-term vegetation effects.

4.4 Long-Term ESL and Values for Air Monitoring Evaluation

The chronic evaluation resulted in the derivation of the following values:

- Chronic ReV = 11 µg/m^3 (2.9 ppb)
- ${}^{chronic}ESL_{threshold(nc)}$ = 3.3 µg/m^3 (0.87 ppb)

The long-term ESL for air permit reviews is the ${}^{chronic}ESL_{threshold(nc)}$ of 3.3 µg/m^3 (0.87 ppb) (Table 2). Although we do not currently monitor for phenol, the chronic ReV of 11 µg/m^3 (2.9 ppb) could be used for the evaluation of ambient air monitoring data in the future (Table 1). The ${}^{chronic}ESL_{threshold(nc)}$ (HQ = 0.3) would not be used to evaluate ambient air monitoring data.

4.5 Chronic Inhalation Observed Adverse Effect Level

Observed inhalation adverse effect levels are described in more detail in Section 3.4 and in TCEQ 2012. For phenol, the chronic POD is based on findings that the study authors deemed “essentially negative.” While the TCEQ conservatively evaluated the findings with an abundance of caution to establish a free-standing LOAEL, the study authors’ comments on the overall findings as well as on the findings in monkeys make this study difficult to use to estimate a

human adverse effect level with an acceptable level of uncertainty. Therefore, a chronic inhalation observed effect level was not derived.

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