



Development Support Document
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Phenol

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TEXAS COMMISSION ON ENVIRONMENTAL QUALITY

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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
$\mu\text{g}/\text{m}^3$	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

1 **Chapter 1 Summary Tables**

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

7 **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
^{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
^{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

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

11 Abbreviations for Tables 1 and 2: **ppb**, parts per billion; **µg/m³**, micrograms per cubic meter; h,
12 hour; **ESL**, Effects Screening Level; **AMCV**, Air Monitoring Comparison Value; **HQ**, hazard
13 quotient; **ReV**, Reference Value; ^{acute}**ESL**, acute health-based ESL; ^{acute}**ESL_{odor}**, acute odor-
14 based ESL; ^{acute}**ESL_{veg}**, acute vegetation-based ESL; ^{chronic}**ESL_{nonthreshold(c)}**, chronic health-based
15 ESL for nonthreshold dose-response cancer effect; ^{chronic}**ESL_{threshold(nc)}**, chronic health-based
16 ESL for threshold dose-response noncancer effects; and ^{chronic}**ESL_{veg}**, chronic vegetation-based
17 ESL

18

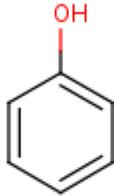
1 **Table 2. Air Permitting Effects Screening Levels (ESLs)**

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
^{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
^{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

2 ^a Based on the acute ReV of 960 µg/m³ (250 ppb) multiplied by 0.3 to account for cumulative
3 and aggregate risk during the air permit review.

4 ^b Based on the chronic ReV of 11 µg/m³ (2.9 ppb) multiplied by 0.3 to account for cumulative
5 and aggregate risk during the air permit review.

1 **Table 3. Chemical and Physical Data**

Parameter	Value	Reference
Molecular Formula	C ₆ H ₅ OH	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 (25°C)	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 µg/m ³ = 0.260 ppb 1 ppb = 3.85 µg/m ³ at 25°C	USEPA 2002

1 **Chapter 2 Major Sources and Uses**

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

7 **Chapter 3 Acute Evaluation**

8 The Development Support Document (DSD) is a summary of the key and supporting studies and
9 procedures used by the Toxicology Division (TD) to derive inhalation toxicity values. This
10 section is based on a review of current literature as well as background readings in ACGIH
11 (2001), NRC (2009), ATSDR (1998, 2008), OEHHA (2008), and USEPA (2002), which
12 describe in detail the acute toxicity of phenol.

13 **3.1 Health-Based Acute ReV and ^{acute}ESL**

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

17 **3.1.1 Physical/Chemical Properties**

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

25 **3.1.2 Key and Supporting Studies**

26 **3.1.2.1 Human Studies**

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

- 33 • In a study by Piotrowski (1971), eight human subjects were exposed for 8 h through a nose
34 and mouth inhalation mask to various concentrations of phenol from 5 to 20 mg/m³ (1.3-

1 5.1ppm) with 2 half-hour breaks (at 2.5 and 5.5 h after exposure began). This inhalation
2 system prevented any other exposure such as absorption through the skin. The main goal of
3 the inhalation portion of the study was to measure absorption by the lungs and the amount of
4 phenol excreted in the urine (i.e., to determine whether urinary excretion can serve as an
5 adequate biomarker of inhalation exposure) following an 8-h inhalation exposure.
6 Consequently, there was no mention of respiratory or adverse health effects described by the
7 author. Due to the purpose of this study, no health effects of any kind were tested for or
8 recorded and the study is not considered useful for identifying critical adverse effects or the
9 concentrations at which they may occur.

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

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

20 **3.1.2.2 Animal Studies**

21 **3.1.2.2.1 Key Animal Study (Hoffman et al. 2001)**

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

28 Hoffman et al. (2001) conducted a 2-w, 10-d inhalation study using 80 male and 80 female
29 albino Fischer 344 rats divided into four treatment groups: 0, 0.5, 5.0, and 25 ppm phenol
30 (analytical concentrations). Each group was exposed by nose-only inhalation for 6 h/d, 5 d/w for
31 2 w, for a total of 10 exposures. The phenol was diluted in distilled water and vaporized using a
32 volatilization chamber. Half of the rats in each group were sacrificed the day after the 10th
33 exposure, while the other half were allowed to recover from the exposure for 2 w before being
34 sacrificed. The authors tested for an exhaustive number of endpoints, including hematology (e.g.,
35 red and white blood cell counts), clinical chemistry (e.g., blood urea nitrogen, creatinine), and a
36 complete analysis on the weights and histology of all the major tissues and organs. The authors
37 found no respiratory or neurological changes, either during exposure or following the recovery

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

3 **3.1.2.2 Supporting Animal studies**

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

- 7 • Flickinger (1976) describes communications with Koppers Company, Inc., that conducted a
8 study using groups of six female Harlan-Wistar albino rats exposed for 8 h to a nominal
9 concentration of 900 mg/m³ (234 ppm) phenol aerosol. After 4 h of exposure, the animals
10 experienced nasal and ocular irritation along with a loss in coordination, suggesting minor
11 systemic effects to the CNS. After 8 h, 1 out of 6 of the rats showed more serious signs of
12 CNS effects including tremors and prostration. All the animals appeared normal the next day
13 suggesting that these were not permanent effects. The TCEQ considers 234 ppm to be the
14 study lowest-observed-adverse-effect-level (LOAEL) for sensory irritation and neurological
15 effects. A study NOAEL was not established.
- 16 • Dalin and Kristoffersson (1974) exposed male and female white rats (strain unknown)
17 continuously to 100 mg/m³ (25 ppm, nominal) phenol for 15 d. Environmental changes were
18 controlled for by exposing the animals in their individual cages, and behavioral alterations
19 such as changes in activity or coordination were recorded. After 3 days of continuous
20 exposure, neurological effects such as twitching, balance issues, and disordered walking
21 became apparent, and although the CNS symptoms subsided by day 5, the animals became
22 slow and lethargic. Changes in serum components (e.g., lactate dehydrogenase) were noted
23 although the significance was not determined. USEPA (2002) deemed 25 ppm to be the
24 LOAEL for this lower-quality study (e.g., no histological exam). Similarly, the TCEQ
25 considers 25 ppm to be the continuous exposure LOAEL for neurological effects with the
26 continuous, multiple-day exposure duration potentially being the primary determinant of
27 toxicity in this study versus Hoffman et al. (2001) which had a NOAEL of 25 ppm for a large
28 number of endpoints (including neurological effects) for 6 h/d exposure.

29 **3.1.2.3 Reproductive and Developmental Studies**

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

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

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

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

- 18 • A set of studies done in 1983 by the Research Triangle Institute in 1983 treated timed-
19 pregnant Sprague-Dawley (SD) rats with oral gavage doses of phenol at 0, 30, 60, and 120
20 mg/kg/d between gestational days (GD) 6-15. They looked at a variety of both maternal and
21 fetal endpoints and found several significant treatment-related changes including a decrease
22 in mean fetal weight per litter at 120 mg/kg/d. The USEPA considered the developmental
23 NOAEL and LOAEL to be 60 and 120 mg/kg/d, respectively (2002).
- 24 • A second set of studies by the same group used timed-pregnant CD-1 mice and oral gavage
25 doses of 0, 70, 140, and 280 mg/kg/d. Even higher doses were required to produce similar
26 significant effects, including an increase in the number of dead pups per litter and a decrease
27 in fetal body weight at the highest dose. This gave a developmental NOAEL of 140 mg/kg/d
28 and a LOAEL of 280 mg/kg/d (USEPA 2002).
- 29 • Another rat study (Argus Research Laboratories 1997) showed a developmental NOAEL and
30 LOAEL of 120 and 280 mg/kg/d, respectively, for decreased fetal body weight and delayed
31 ossification (USEPA 2002).
- 32 • In a two-generation drinking water study in rats (Ryan et al. 2001), 30 SD rats/sex/group
33 were exposed to 0, 200, 1000, or 5000 ppm phenol in drinking water. Parental (P1) rats were
34 given phenol for 10 w prior to mating, during a 2-w mating period, throughout gestation,
35 lactation, and until sacrifice. The males were sacrificed after successful mating. All of the P1
36 females were allowed natural parturition and were sacrificed at F1 weaning. The average
37 daily intake during week 10 was 0, 14.7, 70.9, and 301.0 mg/kg/day for P1 males and 0, 20.0,
38 93.0, and 320.5 mg/kg/day for P1 females. For the F1 generation, intake during week 10 was
39 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
40 females. The F1 generation (20 rats/sex/group) was treated following a protocol similar to

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

10 Although there are available oral data, the doses inducing adverse effects in these studies are
11 higher than those found in the inhalation studies described previously and used for the key and
12 supporting studies. Hoffman et al. (2001) estimates that their highest inhalation exposure level of
13 25 ppm is equivalent to an oral dose of 28 mg/kg/d, and a similar oral dose would correspond to
14 the LOAEL for the supporting study of Dalin and Kristoffersson (1974). In comparison, the RTI
15 group's lowest exposure found to cause any significant effect after GD 6-15 exposure was 60
16 mg/kg/d and 280-301 mg/kg/d are LOAELs from other developmental studies (i.e., Argus
17 Research Laboratories 1997, Ryan et al. 2001). This suggests that protecting against potential
18 nasal and ocular irritation and CNS effects will also protect against the potential
19 reproductive/developmental effects. Additionally, using the Hoffman inhalation study for a point
20 of departure eliminates the uncertainties that would arise from route-to-route extrapolation.

21 **3.1.3 Mode-of-Action (MOA) Analysis**

22 The precise MOA(s) for the adverse effects (e.g., eye and nose irritation, CNS) caused by
23 airborne phenol exposure is not known. Phenol acts as an irritant, and tissue damage,
24 inflammation, and irritation may occur at the site of absorption/contact. While the mechanism for
25 phenol-induced acute irritation of mucous membranes is not known, because phenol at higher
26 concentrations precipitates proteins from solution and dissolves in both water and organic
27 solvents, interference with normal protein, enzyme, and membrane function seems likely (NRC
28 2009). Animal studies have suggested that phenol also acts systemically by interfering with the
29 CNS, however the mechanism remains unclear (Flickinger, 1976; Dalin and Kristoffersson,
30 1974)

31 **3.1.4 Point of Departure (POD) for Key Animal Study and Critical Effects**

32 **3.1.4.1 Key Animal Study**

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

1 **3.1.4.2 Supporting Animal Study**

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

11 **3.1.5 Dosimetric Adjustments**

12 **3.1.5.1 Default Exposure Duration Adjustments**

13 The 6-h duration (C_1) for a single day exposure in the key study by Hoffman et al. (2001) was
14 adjusted to a POD_{ADJ} of 1-h exposure duration (C_2) using Haber's Rule as modified by ten Berge
15 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
16 in toxicity:

$$\begin{aligned} 17 \quad C_2 &= [(C_1)^3 \times (T_1 / T_2)]^{1/3} \\ 18 \quad &= [(25 \text{ ppm})^3 \times (6 \text{ h}/1 \text{ h})]^{1/3} \\ 19 \quad &= 45.428 \text{ ppm} = POD_{ADJ} \end{aligned}$$

20 **3.1.5.2 Default Dosimetry Adjustments from Animal-to-Human Exposure**

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

1 **3.1.6 Adjustments of the POD_{HEC}**

2 The POD_{HEC} based on a NOAEL from the Hoffman et al. (2001) study was used as the POD and
3 UFs were applied to derive the acute ReV (i.e., assume a threshold MOA for a noncarcinogenic
4 endpoint). The following uncertainty factors (UFs) were applied to the POD_{HEC} of 45.428 ppm:
5 10 for UF_H, 3 for UF_A, and 6 for UF_D, for a total UF of 180.

- 6 • An intrahuman UF_H of 10 was used to account for intrahuman variability and potentially
7 sensitive subgroups;
- 8 • An animal-to-human UF_A of 3 was used to account for potential pharmacodynamic
9 differences between animals and humans (pharmacokinetic adjustment was already
10 performed); and
- 11 • A database deficiency UF_D of 6 was used to account for the lack of adequate human
12 inhalation studies, a more robust high-quality laboratory animal inhalation dataset,
13 information on potentially sensitive life stages (e.g., very young, elderly), etc. A full UF_D of
14 10 was not used since oral study information provided insight in addressing potential
15 reproductive/developmental concerns.

$$\begin{aligned} \text{acute ReV} &= \text{POD}_{\text{HEC}} / (\text{UF}_H \times \text{UF}_A \times \text{UF}_D) \\ &= 45.428 \text{ ppm} / (10 \times 3 \times 6) \\ &= 45.428 \text{ ppm} / 180 \\ &= 0.252378 \text{ ppm} \\ &= 252.378 \text{ ppb or } 250 \text{ ppb (rounded to two significant digits)} \end{aligned}$$

21 **3.1.7 Health-Based Acute ReV and ^{acute}ESL**

22 In deriving the acute ReV for phenol, no numbers were rounded between equations until the ReV
23 was calculated. Once the ReV was calculated, it was rounded to two significant figures. The
24 resulting 1-h acute ReV is 0.25 ppm (0.96 mg/m³) or 250 ppb (960 µg/m³) based on the Hoffman
25 et al. (2001) study. The rounded acute ReV was then used to calculate the ^{acute}ESL. At the target
26 hazard quotient (HQ) of 0.3, the ^{acute}ESL is 75 ppb (290 µg/m³) (Table 4).

27

1 **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
<i>Interspecies UF</i>	3
<i>Intraspecies UF</i>	10
<i>Incomplete Database UF</i> <i>Database Quality</i>	6
acute ReV [1 h] (HQ = 1)	960 µg/m³ (250 ppb)
^{acute}ESL [1 h] (HQ = 0.3)	290 µg/m³ (75 ppb)

2 **3.1.8 Phenol as Particulate Matter**

3 As mentioned in Section 3.1.1, phenol has certain chemical and physical properties that allow it
 4 to exist in both the vapor and particulate form. For air permitting by the TCEQ, phenol is
 5 typically in the vapor phase, and therefore only a vapor ^{acute}ESL was derived here. If the need for
 6 an ^{acute}ESL for phenol as an aerosol/particulate should arise, the vapor ^{acute}ESL value of 290
 7 µg/m³ can be used. However, because the ^{acute}ESL (290 µg/m³) is higher than the 24-h National
 8 Ambient Air Quality Standard (NAAQS) for PM₁₀, currently set at 150 µg/m³, any future air
 9 permit evaluations of phenol as particulate must also meet the NAAQS standard on a 24-h basis.

1 **3.2 Welfare-Based Acute ESLs**

2 **3.2.1 Odor Perception**

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

7 **Table 5. Accepted Odor Studies Conducted for Phenol**

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

8 Several scientific studies were identified as acceptable sources for odor threshold values as
9 described in TCEQ (2012): Punter (1980), Hoshika (1993), van Doorn et al. (2002), and Nagata
10 (2003) (some values found in USEPA 1992). According to guidelines for setting odor-based
11 effects screening levels (TCEQ 2012), odor detection values defined as the highest quality level
12 of odor thresholds (Level 1) will be considered first in setting the acuteESL_{odor} values. Since there
13 are multiple level 1 odor threshold values as defined by the TCEQ (2012), the geometric mean of
14 all of the level 1 values will be used. Accordingly, the acuteESL_{odor} for phenol was calculated to be
15 42 $\mu\text{g}/\text{m}^3$ (11 ppb). The odor value only applies to phenol in the vapor phase, and not as a
16 particulate.

17 **3.2.2 Vegetation Effects**

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

19 **3.3 Short-Term ESL and Values for Air Monitoring Evaluation**

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

- 21
- 22 • acuteESL_{odor} = 42 $\mu\text{g}/\text{m}^3$ (11 ppb)
 - 23 • acute ReV = 960 $\mu\text{g}/\text{m}^3$ (250 ppb)
 - acuteESL = 290 $\mu\text{g}/\text{m}^3$ (75 ppb)

1 For air permit reviews, the TCEQ considers chemicals with VP > 0.01 mm Hg as vapors (TCEQ
2 2012), which is the case for phenol (Table 3). Consequently, the short-term ESL for air permit
3 evaluations is the acute^{ESL_{odor}} of 42 µg/m³ (11 ppb) as it is lower than the health-based acute^{ESL}
4 (Table 2). In the event phenol is emitted as aerosol/particulate, the 1-h ESL for air permit
5 evaluations vapor acute^{ESL} of 290 µg/m³ will be used, although the 24-h NAAQS value of 150
6 µg/m³ must also be met on a 24-h basis. Although we do not currently monitor for phenol, the
7 acute^{ESL_{odor}} of 42 µg/m³ (11 ppb) is lower than the acute ReV of 960 µg/m³ (250 ppb). Both
8 values may be used for the evaluation of ambient air monitoring data in the future (Table 1). The
9 acute^{ESL} (HQ = 0.3) would not be used to evaluate ambient air monitoring data.

10 **3.4 Acute Inhalation Observed Adverse Effect Level**

11 Risk assessors, and the general public, often ask to have information on the levels in air where
12 health effects would be expected to occur. So, when possible, the TCEQ provides chemical-
13 specific observed adverse effects levels in DSDs (TCEQ 2012). As the basis for development of
14 inhalation observed adverse effect levels is limited to available data, future studies could
15 possibly identify a lower POD for this purpose. Regarding critical effects due to acute phenol
16 exposure, the animal study by Flickinger (1976) provides a LOAEL closer in duration (4 h) to
17 the acute duration of interest (i.e., 1 h) than the Dalin and Kristoffersson (1974) study. The study
18 by Flickinger (1976) found a 4-h rat LOAEL of 234 ppm for nasal and ocular irritation and
19 neurological effects. This animal LOAEL was used as the animal acute inhalation observed
20 adverse effect level for extrapolation to humans. No duration adjustment was made (TCEQ
21 2012). As discussed in Section 3.1.5.2, for these effects the animal-to-human dosimetric
22 adjustment results in a LOAEL_{HEC} equal to the animal exposure concentration (e.g., a DAF of 1
23 is used). Thus, the 4-h LOAEL_{HEC} based on this animal study is estimated to be 234 ppm.

24 The LOAEL_{HEC} determined from an animal study represents a concentration at which it is
25 possible that similar effects could occur in some individuals exposed to this level over the same
26 duration as used in the study (4 h) or longer. Importantly, effects are not a certainty due to
27 potential interspecies and intraspecies differences in sensitivity. As the basis for development of
28 inhalation observed adverse effect levels is limited to available data, future studies could
29 possibly identify a lower POD for this purpose. The acute inhalation observed adverse effect
30 level of 234 ppm (900 µg/m³) is provided for informational purposes only (TCEQ 2012).

31 The margin of exposure between the estimated acute inhalation observed adverse effect level of
32 234 ppm (234,000 ppb) and the acute ReV of 250 ppb is a factor of 936.

33 **Chapter 4 Chronic Evaluation**

34 **4.1 Noncarcinogenic Potential**

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

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

5 **4.1.2 Physical/Chemical Properties**

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

8 **4.1.3 Key and Supporting Studies**

9 **4.1.3.1 Human Studies**

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

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

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

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

6 ***4.1.3.2 Animal Study***

7 Since relevant human toxicity data are limited as well as chronic animal data, the TCEQ will
8 utilize a subchronic animal study. A subchronic study meets the minimum database for
9 development of a chronic ReV under Table 5-2 of the TCEQ Guidelines (TCEQ 2012), although
10 with low database confidence. The Sandage (1961) 90-d, subchronic study will be used as the
11 key study and source for a POD. Although this study has some shortcomings as noted by USEPA
12 (2002) (e.g., exposure methods, limited records), in the absence of more well-conducted studies
13 this study can be used for developing the chronic ReV and ESL.

14 The following summary of Sandage (1961) is based on (some verbatim) information presented in
15 USEPA (2002), ATSDR (1998), and IPCS (1994). In an unpublished 90-d study, groups of 10
16 male rhesus monkeys, 50 male Sprague-Dawley rats, and 100 male albino mice were exposed to
17 average phenol concentrations of 0 or 4.72 ppm (18.2 mg/m³) continuously for 90 d. Exposure
18 was interrupted for 14 h on day 39 and for 36 h on days 68-69. The phenol concentration was
19 reported to remain in the desired ranges of 4.5-5.5 ppm after the first three days. During the
20 exposure, no deaths were observed in the test animals. Body weight gain in mice was
21 comparable to that in controls but was slightly higher in exposed rats and monkeys. A complete
22 hematological examination showed no significant changes in the three test species following
23 phenol exposure. Blood biochemistry (alkaline phosphatase, cholinesterase, amylase, lipase, and
24 glutamic oxaloacetic transaminase) was evaluated in monkeys only. Urinalysis was apparently
25 conducted in all species, but kidney function tests (urine volume and specific gravity) were
26 conducted only in monkeys and rats. The study authors reported that there were no effects on any
27 of the endpoints (although supporting data were not provided).

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

1 **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%*

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

3 Although the authors characterized the histology findings as “essentially negative” without
 4 providing detailed information (e.g., descriptions of the observed lesions), it is notable that liver
 5 and kidney pathology was observed in 30% and 20% of the monkeys (compared with 0% of the
 6 controls), respectively, and in 20% of the rats for these organs (compared with 0% of the
 7 controls) (Table 6). It is unclear why the authors did not consider these changes to be
 8 histologically significant (e.g., pathology in 6/7 monkeys was considered minimal or doubtful)
 9 and statistical significance was not reported in the study. Liver and kidney pathology was
 10 reported in 20% of the phenol-exposed rats (compared with 0% of the controls) and lung
 11 pathology was reported in 20% of the phenol-exposed mice (compared with 6% of the controls).
 12 The incidences of liver and kidney pathology in the rat and lung pathology in the mouse were
 13 statistically significant in a Fisher's exact test done for this assessment. *The TCEQ therefore*
 14 *considers the free-standing LOAEL for this study based on rat liver/kidney pathology and mouse*
 15 *lung pathology to be 4.72 ppm (18.2 mg/m³).* Although the incidence of lung pathology was not
 16 reported in exposed monkeys and rats, a relatively high incidence of lung pathology in the
 17 control animals (30% and 35%, respectively) decreased the sensitivity of the evaluation in these
 18 species. No other significant pathological changes were reported in the test animals.

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

1 Consequently, based on statistically significant increases in liver and kidney pathology in the rat,
2 4.72 ppm (18.2 mg/m³) will be used as a free-standing LOAEL for derivation of the chronic ReV
3 and ESL.

4 ***4.1.3.3 Reproductive and Developmental Studies***

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

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

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

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

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

- 1 significant effects, including an increase in the number of dead pups per litter and a decrease
2 in fetal body weight at the highest dose. This gave a developmental NOAEL of 140 mg/kg/d
3 and a LOAEL of 280 mg/kg/d (USEPA 2002).
- 4 • Another rat study (Argus Research Laboratories 1997) showed a developmental NOAEL and
5 LOAEL of 120 and 280 mg/kg/d, respectively, for decreased fetal body weight and delayed
6 ossification (USEPA 2002).
 - 7 • As discussed in more detail in Section 3.1.2.3, the lowest LOAEL in a two-generation rat
8 drinking water study (Ryan et al. 2001) was 301 mg/kg/d for decreased parental and pup
9 body weight (compared to the controls) and the study NOAEL was 70.9 mg/kg/day (USEPA
10 2002).

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

15 **4.1.4 Mode of Action**

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

22 **4.1.5 PODs for Key Study, Critical Effects and Dosimetric Adjustments**

23 Based on the key study presented above (Sandage 1961), the TCEQ identifies 4.72 ppm (18.2
24 mg/m³) as the free-standing LOAEL and subchronic POD based on rat liver/kidney pathology.

25 ***4.1.5.1 Default Exposure Duration Adjustments***

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

28 ***4.1.5.2 Default Dosimetry Adjustments from Animal-to-Human Exposure***

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

$$33 \quad \text{POD}_{\text{HEC}} = \text{POD}_{\text{ADJ}} \times ((\text{H}_{\text{b/g}})_{\text{A}} / (\text{H}_{\text{b/g}})_{\text{H}})$$

34 where: $\text{H}_{\text{b/g}}$ = ratio of the blood:gas partition coefficient

35 A = animal

1 H = human

2 However, where these data are lacking as in the case here, a default value of 1 is used (TCEQ
3 2012).

$$4 \quad \text{POD}_{\text{HEC}} = \text{POD}_{\text{ADJ}} \times ((\text{H}_{\text{b/g}})_{\text{A}} / (\text{H}_{\text{b/g}})_{\text{H}}) = 4.72 \text{ ppm} \times 1 = 4.72 \text{ ppm}$$

5 **4.1.6 Adjustments of the POD_{HEC}**

6 For the noncarcinogenic effects of phenol, UFs are applied to a POD to derive a ReV (i.e.,
7 assume a nonlinear MOA for a noncarcinogenic endpoint). The following UFs were considered
8 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
9 UF_{L} , and 6 for UF_{D} , for a total potential UF of 3,240.

- 10 • An UF_{H} of 10 was considered appropriate to account for potential intrahuman variability
11 since information on potentially sensitive subpopulations is lacking;
- 12 • An UF_{A} of 3 was considered appropriate to account for potential interspecies toxicodynamic
13 differences since dosimetric adjustment for toxicokinetic differences was conducted;
- 14 • An UF_{Sub} of 3 was considered appropriate to account for the use of a subchronic study due to
15 some of the specific properties of phenol, such as a relatively rapid elimination half-life of <
16 4 h (ATSDR 2008) and a log K_{ow} well below 4 (Table 3), leading to reduced concern about
17 bioaccumulation and chronic effects differing significantly from subchronic effects;
- 18 • A somewhat reduced UF_{L} of 6 was considered appropriate considering that while statistically
19 significant increases occurred in the incidence of liver and kidney pathology, the study
20 authors considered the histology findings “essentially negative,” implying a reduced level of
21 concern; and
- 22 • A database UF_{D} of 3 was considered applicable because although there is a deficiency in the
23 scientific research on the effects of chronic inhalation exposure to phenol (e.g., lack of
24 additional useful inhalation studies in humans or animals or chronic studies of high quality):
25 (1) toxicokinetic considerations reduce concern about chronic effects differing significantly
26 from subchronic effects; (2) oral study information provides insight in addressing potential
27 reproductive/developmental concerns; and (3) there is a lack of independence between the
28 UF_{D} and the UF_{Sub} of 3 already being utilized.

$$\begin{aligned} 29 \text{ chronic ReV} &= \text{POD}_{\text{HEC}} / (\text{UF}_{\text{H}} \times \text{UF}_{\text{A}} \times \text{UF}_{\text{Sub}} \times \text{UF}_{\text{L}} \times \text{UF}_{\text{D}}) \\ 30 &= 4.72 \text{ ppm} / (10 \times 3 \times 3 \times 6 \times 3) \\ 31 &= 4.72 \text{ ppm} / 1,620 \\ 32 &= 0.0029135 \text{ ppm} \\ 33 &= 2.9135 \text{ ppb or } 2.9 \text{ ppb (rounded to two significant digits)} \end{aligned}$$

1 **4.1.7 Health-Based Chronic ReV and ^{chronic}ESL_{threshold(nc)}**

2 In deriving the vapor chronic ReV, no numbers were rounded between equations until the ReV
3 was calculated. The chronic ReV was rounded to two significant figures, resulting in a value of
4 2.9 ppb ($11 \mu\text{g}/\text{m}^3$), and then used to calculate the ^{chronic}ESL_{threshold(nc)}. At the target hazard
5 quotient of 0.3, the ^{chronic}ESL_{threshold(nc)} is 0.87 ppb ($3.3 \mu\text{g}/\text{m}^3$) (Table 7).

6

1 **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
<i>Interspecies UF</i>	10
<i>Intraspecies UF</i>	3
<i>LOAEL UF</i>	6
<i>Subchronic to chronic UF</i>	3
<i>Incomplete Database UF</i> <i>Database Quality</i>	3 Low-medium
Chronic ReV (HQ = 1)	11 µg/m³ (2.9 ppb)
^{chronic}ESL_{nonlinear(nc)} (HQ = 0.3)	3.3 µg/m³ (0.87 ppb)

2 **4.1.8 Phenol as Particulate Matter**

3 As mentioned in Section 3.1.1, phenol has certain chemical and physical properties that allow it
 4 to exist in both the vapor and particulate form. For air permitting by the TCEQ, phenol is
 5 typically in the vapor phase, and therefore only a vapor ^{chronic}ESL_{nonlinear(nc)} was derived here. If
 6 the need for a ^{chronic}ESL_{nonlinear(nc)} for phenol as an aerosol/particulate should arise, the
 7 ^{chronic}ESL_{nonlinear(nc)} of 3.3 µg/m³ can be used.

1 **4.2 Carcinogenic Potential**

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

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

12 **4.3 Welfare-Based Chronic ESL**

13 No data were found regarding long-term vegetation effects.

14 **4.4 Long-Term ESL and Values for Air Monitoring Evaluation**

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

- 16 • Chronic ReV = $11 \mu\text{g}/\text{m}^3$ (2.9 ppb)
- 17 • $^{\text{chronic}}\text{ESL}_{\text{threshold(nc)}} = 3.3 \mu\text{g}/\text{m}^3$ (0.87 ppb)

18 The long-term ESL for air permit reviews is the $^{\text{chronic}}\text{ESL}_{\text{threshold(nc)}}$ of $3.3 \mu\text{g}/\text{m}^3$ (0.87 ppb)
19 (Table 2). Although we do not currently monitor for phenol, the chronic ReV of $11 \mu\text{g}/\text{m}^3$ (2.9
20 ppb) could be used for the evaluation of ambient air monitoring data in the future (Table 1). The
21 $^{\text{chronic}}\text{ESL}_{\text{threshold(nc)}}$ (HQ = 0.3) would not be used to evaluate ambient air monitoring data.

22 **4.5 Chronic Inhalation Observed Adverse Effect Level**

23 Observed inhalation adverse effect levels are described in more detail in Section 3.4 and in
24 TCEQ 2012. For phenol, the chronic POD is based on findings that the study authors deemed
25 “essentially negative.” While the TCEQ conservatively evaluated the findings with an abundance
26 of caution to establish a free-standing LOAEL, the study authors’ comments on the overall
27 findings as well as on the findings in monkeys make this study difficult to use to estimate a
28 human adverse effect level with an acceptable level of uncertainty. Therefore, a chronic
29 inhalation observed effect level was not derived.

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