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SCREENING-LEVEL RISK ASSESSMENT FOR STYRENE-ACRYLONITRILE (SAN) TRIMER DETECTED IN SOIL AND GROUNDWATER

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A screening-level risk assessment was conducted for styrene-acrylonitrile (SAN) Trimer detected at the Reich Farm Superfund site in Toms River, NJ. Consistent with a screening-level approach, on-site and off-site exposure scenarios were evaluated using assumptions that are expected to overestimate actual exposures and hazards at the site. Environmental sampling data collected for soil and groundwater were used to estimate exposure point concentrations. Several exposure scenarios were evaluated to assess potential on-site and off-site exposures, using parameter values for exposures to soil (oral, inhalation of particulates, and dermal contact) and groundwater (oral, dermal contact) to reflect central tendency exposure (CTE) and reasonable maximum exposure (RME) conditions. Three reference dose (RfD) values were derived for SAN Trimer for short-term, subchronic, and chronic exposures, based upon its effects on the liver in exposed rats. Benchmark (BMD) methods were used to assess the relationship between exposure and response, and to characterize appropriate points of departure (POD) for each RfD. An uncertainty factor of 300 was applied to each POD to yield RfD values of 0.1, 0.04, and 0.03 mg/kg-d for short-term, subchronic, and chronic exposures, respectively. Because a chronic cancer bioassay for SAN Trimer in rats (NTP 2011a) does not provide evidence of carcinogenicity, a cancer risk assessment is not appropriate for this chemical. Potential health hazards to human health were assessed using a hazard index (HI) approach, which considers the ratio of exposure dose (i.e., average daily dose, mg/kg-d) to toxicity dose (RfD, mg/kg-d) for each scenario. All CTE and RME HI values are well below 1 (where the average daily dose is equivalent to the RfD), indicating that there is no concern for potential noncancer effects in exposed populations even under the conservative assumptions of this screening-level assessment.

In the early 1970s, a Union Carbide Corporation (UCC) manufacturing facility contracted with a company for the removal and disposal of drummed chemical waste. The removal company deposited some of these drums at the Reich Farm Site in Dover (renamed Toms River) Township, New Jersey, without the knowledge of UCC (Ghassemi 1976). Despite removal of drums by UCC, wastes leaked from them and migrated through the groundwater. In 1983, the U.S. Environmental Protection Agency (EPA) included the Reich Farm Site on its National Priority List (NPL) of Superfund Sites. Pursuant to a U.S. EPA-approved groundwater sampling program (part of the U.S. EPA approved remediation plan for the site), contaminants from Reich Farm were found to have migrated about 1 mile from the site to a well field that supplied drinking water to the neighboring community (ATSDR 2001).

In response to concerns of community members, the New Jersey Department of Health undertook a cancer incidence study for

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the years 1979 through 2000 for the Toms River section of Dover Township where the contaminated wells were located (Berry and Haltmeir 1997) and excess cancers such as leukemia or central nervous system cancer, were observed (Berry et al. 2003). A case-control study was then undertaken and many possible associations were examined, including sources of drinking water, to try to determine the cause(s) of the excess cancers. The study found few associations related to exposures. The authors did report a statistical association with exposure to one well, while acknowledging "that there is considerable uncertainty in the finding" (NJDHSS and ATSDR 2003). Extensive review of groundwater analyses was undertaken and the presence of a group of unregulated and unidentified organic compounds was observed at concentrations of 1 ppb or less.

The compound found at the highest levels was then identified as styrene-acrylonitrile trimer, SAN Trimer. SAN Trimer is a mixture of six isomers (four isomers of 4-cyano-1,2,3,4-tetrahydro-alpha-methyl-1-naphthaleneaceton itrile [THAN] and two isomers of 4-cyano-1,2,3,4-tetrahydro-1-naphthaleneproprionitrile [THNP]) (Gargas et al. 2008). SAN Trimer is a by-product of the production of acrylonitrile styrene plastics (Union Carbide Corporation 1998). Few, if any, manufacturers still use this process. At room temperature, SAN Trimer is a viscous, light brown liquid (NTP 2011a), with a Henry's law constant of 1.55×10^{-9} atm-m^3/mol (NTP 2011a), a density of 1.101 g/ml, a water solubility of 84.9 mg/L, and a log octanol/water partition coefficient of 3.1 (NTP 2011a).

There is no current exposure to contaminants from Reich Farm (ATSDR, 2001), as UCC enhanced its groundwater treatment system to remove SAN Trimer from the groundwater. Groundwater treatment is ongoing at the well field, with the latest sampling data from 2010 and 2011 indicating not only that are standards for regulated compounds being met but that SAN Trimer concentrations are now below the interim cleanup criterion of 0.00015 mg/L. This interim level was established by the New Jersey Department of Environmental Protection (NJDEP) based upon limits of detection, since there was no known toxicological information on SAN Trimer at the time on which to establish a risk-based criterion. To fill this data gap, given the results from the exposure monitoring and the health studies, the ATSDR recommended that toxicity testing be undertaken for the SAN Trimer. An interagency workgroup established by the U.S. EPA nominated SAN Trimer for study by the National Toxicology Program (NTP). The NTP completed the toxicology studies designed by the SAN Trimer Interagency Working Group and the final technical report was issued (NTP 2011a; 2011b).

The aim of the study presented here was to conduct a screening-level risk assessment for SAN Trimer detected in soil and groundwater at the Reich Farm Superfund Site in Toms River, NJ, based on the available National Toxicology Program (NTP) toxicology studies including a recently completed cancer bioassay. This assessment is focused only on potential exposures to SAN Trimer. As a screening-level assessment, a number of assumptions and decisions are made that are conservative in nature, intended to be protective, and not predictive, of exposures and potential human health hazards. For these reasons, the hypothetical exposures and potential hazards described in this screening-level assessment are expected to overestimate actual exposures occurring at the site. For example, reference dose (RfD) values were derived for SAN Trimer based upon its effects on the liver in exposed rats, since that organ would be the most sensitive and therefore would yield more conservative results.

METHODS

Exposure Assessment

The identification of the exposure scenarios to be quantitatively evaluated for the Reich Farm site included a consideration of (1) points of contact, (2) complete exposure pathways, and (3) potential human receptors. Based on current and projected future use, an industrial land use scenario was considered most appropriate for evaluation of on-site environmental conditions, and a residential land use scenario was considered appropriate for off-site conditions. To determine whether a complete exposure pathway exists, it must be determined whether there is a point of contact between an affected medium and a likely receptor. Based on an estimated Henry's law constant of 1.55×10^{-9} atm-m^3/mol (NTP 2011a), SAN Trimer is not considered to be a volatile compound, and therefore inhalation exposure to SAN Trimer via volatilization from either soil or groundwater is an incomplete pathway. However, inhalation exposures to particulates released from soil were considered for on-site exposure scenarios. Additional exposure pathways are described in the following.

Reliable exposure point concentrations are required to estimate the magnitude of exposure to potential receptors. In this case, the concentration of SAN Trimer in soil was measured directly at different depths during 2003 and 2004; these data are used to quantify exposures via the ingestion, inhalation, and dermal contact routes. Soil samples were collected for SAN trimer analysis at 19 locations in three previously excavated areas (USACE 2005). Four intervals were sampled per location. Soil sample locations and intervals were determined based on a statistically based sampling approach (USACE 2005). Soil samples were analyzed for SAN Trimer using U.S. EPA Method 8270. The soil data for SAN Trimer from these sampling events were categorized as either surface soil (collected at depths less than 2.5 ft [0.76 m]) or total soil (collected at depths up to 29 ft [8.8 m]). This definition of surface soil differs from the U.S. EPA default assumption of less than 2 cm (U.S. EPA 2002a), to include U.S. EPA sample RF5 (0–2.5 ft [0.76 m]), which was assumed to reflect surface soil concentration. All other surface soil samples were collected from depths less than 2 ft (0.61 m).

For the soil investigations conducted in 2003 and 2004, soil sample locations and depth intervals were sampled between 1 and 3 times. In combining soil data across investigations, the following steps were taken to avoid inappropriate weighting of sample locations: (1) The maximum detected value for each depth interval was identified where multiple samples were obtained for a given location and depth; (2) for surface soils, the maximum detected value for the surface interval was used for each location; and (3) for total soils, the maximum values for each depth interval were averaged for each sample location, under an assumption that potential exposures to soils during excavation activities will occur across the entire soil column. Potential temporal variation between 2003 and 2004 (e.g., degradation) was ignored, and these data were assumed to be reflective of current and future conditions at the site. For on-site and off-site groundwater investigations conducted in 2010, sample locations were sampled between 1 and 16 times. In calculating exposure point concentrations for groundwater, the maximum detected concentration for each location was used. This screening-level approach is expected to overestimate actual exposures to SAN Trimer.

For characterizing potential on-site and off-site exposures, the arithmetic mean and its upper confidence limit (UCL) were used to reflect central tendency exposure (CTE) and reasonable maximum exposure (RME) conditions, respectively. In calculating mean and UCL values, nondetect samples were evaluated using the detection limit divided by the square root of 2. UCL values were determined using U.S. EPA ProUCL software (version 4.1.00) to account for geospatial variation. The detection frequency, arithmetic mean, UCL, and maximum detected concentrations of SAN Trimer in each exposure category for soil and groundwater are provided in Table 1.

The following exposure scenarios are evaluated for site soils and groundwater for current and potential future conditions.

ON-SITE EXPOSURE SCENARIOS

Short-Term Exposure

Short-term exposure (defined here as approximately 2 wk) scenarios at the site include excavation workers and visitors, as defined in the following. This definition is

TABLE 1. Concentrations of SAN Trimer in Soil and Groundwater[a]

	Detection frequency		Concentration (by location; mg/kg soil or mg/L groundwater)		
Media	By sample	By location	Mean	UCL[b]	Maximum
Surface soil (0–2.5 ft)	18/22	9/10	1.2	4.4	7.0
Total soil (0–29 ft)	72/123	19/19	1.6	3.3	7.3
On-site groundwater[c]	5/15	4/9	0.0038	NC[e]	0.034
Off-site groundwater[d]	14/109	7/20	0.000056	0.00015	0.00033

[a]Concentrations calculated from data from soil and groundwater sampling (URS 2005).

[b]UCLs were calculated using U.S. EPA ProUCL software (version 4.1.00).

[c]Samples collected in 2010 from on-site monitoring wells: MP-6, MP-9, MW-2S, MW-4S, MW-6S, MW-8S, MW-12S, MW-14S, MW-21D (URS 2011).

[d]Samples collected in 2010 from off-site monitoring wells: CHMW-4, MP-1R, MP-2R, MP-3, MP-4, MP-7, MP-8, MP-10, MP-12, MP-13, MW-16D,
MW-Dugan, MW-Swain, OW-1, OW-2, UWTR-20, UWTR-44, Well 26, Well 26B, Well 28 (URS 2011).

[e]Not calculated. Data for on-site groundwater were not adequately described by a parametric distribution, therefore the maximum detected concentration was used in place of the UCL to assess RME exposures.

consistent with U.S. EPA Office of Water's definition of short-term exposure in deriving 10-d health advisories, with the ATSDR definition of short-term in deriving acute minimal risk levels (MRL), and with the recommended definition of short-term of 1–30 d (U.S. EPA 2002b).

- *Excavation worker scenario*—Potential excavation activities were assumed to involve intrusive activities involving direct contact with total soil on a daily basis for a short period of time. Although total soils include samples collected at depths of up to 29 ft (8.8 m), excavations at the site are generally expected considerably shallower than that, particularly for smaller renovation and construction projects (e.g., erecting fences, etc.). The exposure pathways assumed for this scenario were the ingestion of, dermal contact with and inhalation of particulates from total soil during excavation activities. Exposures to on-site groundwater are not expected to occur for this scenario because (1) depth to groundwater exceeds 20 ft (6.1 m) below grade and (2) potable use of groundwater within the historic plume is prohibited by municipal ordinance and a state administrative control (due to general groundwater contamination).
- *Pica child visitor scenario*—These visitors were assumed to be engaged in outdoor activities that may bring them in contact with surface soil on a daily basis for a short period of time. The pica child visitor is considered to reflect a "worst-case" on-site visitor scenario with respect to exposures to on-site soil, and likely overestimates more likely exposures at the site (e.g., a youth trespasser scenario). Although the site is industrial, child exposure scenarios were specifically included in this assessment, due to potential concerns with increased rates of childhood cancers (Berry and Haltmeir 1997; Berry et al. 2003). Visitors were not assumed to be involved in intrusive activities such as excavation or construction. The exposure pathways assumed for this scenario were the ingestion of, dermal contact with, and inhalation of particulates from surface soil. Exposures to on-site groundwater are not expected to occur for this scenario because: (1) depth to groundwater exceeds 20 ft (6.1 m) below grade, and (2) potable use of on-site groundwater within the historic plume is prohibited.

Subchronic Exposure

Subchronic exposure (defined here as greater than 30 d, but less than 10% of expected lifetime) scenarios at the site include a child visitor, as defined in the following. This is consistent with the U.S. EPA definition for subchronic exposure (U.S. EPA 2002b).

- *Child visitor scenario*—Visitors were assumed to be engaged in outdoor activities that may bring them in contact with site media on an intermittent basis (50–100 d/yr) for 6 yr. The child visitor was not assumed to be involved in intrusive activities such as excavation or construction, and this is expected to overestimate more likely visitor exposures at the site (e.g., a youth trespasser scenario). Although the site is industrial, child exposure scenarios were specifically included in this assessment, due to potential concerns with increased rates of childhood cancers (Berry and Haltmeir 1997; Berry et al. 2003). The exposure pathways assumed for this scenario were the ingestion of and dermal contact with surface soil, and inhalation of particulates. Exposures to on-site groundwater are not expected to occur (for the reasons cited earlier).

Chronic Exposure

Chronic exposure (defined here as greater than 10% of expected lifetime) scenarios at the site include a general worker, as defined in the following. This is consistent with the U.S. EPA definition for chronic exposure (U.S. EPA 2002b).

- *General worker scenario*—Workers include maintenance workers and others performing outdoor activities that may bring them in contact with site soil on a daily basis (250 d/yr). The outdoor worker was not assumed to be involved in intrusive activities such as excavation or construction. The exposure pathways assumed for this scenario were the ingestion of and dermal contact with surface soil, inhalation of particulates, and ingestion of on-site groundwater, despite the fact that potable use of groundwater by individuals and private entities within the area of the historic plume is restricted by municipal ordinance and a state administrative control.

Off-Site Exposure Scenarios

Subchronic and chronic scenarios for exposures near the site are described in the following.

Subchronic Exposure Subchronic exposure scenarios near the site include a child resident:

- *Child resident*—Off-site soils are not expected to have been impacted by the site, and therefore exposure to site-related contaminants in off-site soils is considered an incomplete pathway. However, for purposes of this risk assessment, off-site residents who are down gradient from the site are assumed to come in contact with SAN Trimer via dermal contact with and ingestion of groundwater. This is a conservative assumption since potable use of groundwater by individuals and private entities within the area of the historic plume is restricted by municipal ordinance and a state administrative control.

Chronic Exposure Chronic exposure scenarios near the site include a child/adult resident:

- *Child/adult resident*—Off-site soils are not expected to have been impacted by the site, and therefore exposure to site-related contaminants in off-site soils is considered an incomplete pathway. However, off-site residents who are down gradient from the site are assumed to come in contact with SAN Trimer via dermal contact with and ingestion of groundwater. This is a conservative assumption, since potable use of groundwater by individuals and private entities within the area of the historic plume is restricted by municipal ordinance and a state administrative control.

Exposure Parameters

Consistent with a screening-level assessment, the exposure scenarios described earlier and the parameter values used to quantify these exposures are considered to be conservative in nature, and likely overestimate any actual exposures to SAN Trimer at the site. For the purpose of characterizing the potential noncancer hazards associated with exposures to SAN Trimer in soil, estimates of average daily doses (ADD) are determined using the mean and UCL concentrations in soil and groundwater. The ADD represents the average daily dose received only for the length of the exposure (i.e., not average over a lifetime). The equations used for quantifying exposure to the SAN Trimer in site soil and the rationale for each value to be used are discussed below. Exposure parameters are presented for the potential exposure routes (i.e., ingestion and dermal contact) and points of contact (i.e., soil). Exposure parameter values were selected to provide both a characterization of CTE conditions, consisting primarily of central tendency values, and of RME conditions, consisting of a mixture of upper bound and central tendency values. In general, exposure values were taken from established U.S. EPA and New Jersey guidance documents (including NJDEP 2009; U.S. EPA 2009; 2004). These documents provide guidance for the selection of exposure parameters for the equations defined next.

Exposure via incidental soil ingestion:

$$ADD = \frac{C \times IS \times CF \times EF \times ED}{BW \times AT}$$

Exposure via dermal contact with soil:

$$ADD = \frac{C \times AF \times ABS \times SA \times Fso \times CF \times EF \times ED}{BW \times AT}$$

Exposure via inhalation of particulates:

$$ADD = \frac{C \times \left(\frac{1}{PEF}\right) \times IR \times \left(\frac{ETs}{24}\right) \times EF \times ED}{BW \times AT}$$

Exposure via ingestion of groundwater:

$$ADD = \frac{C \times IW \times EF \times ED}{BW \times AT}$$

Exposure via dermal contact with groundwater (calculated under the assumption that exposure times are less than the time to reach steady state):

$$ADD = \frac{ED \times EF \times SA \times 2 \times FA \times Kp \times Cw \times \sqrt{6 \times Tl \times \frac{ET}{\pi}}}{BW \times AT}$$

Age-adjusted intake rates (AAIR) were calculated for the off-site child/adult resident scenario to account for differences in exposure rates (water ingestion, skin surface area) for time spent as a child (i.e., the first 6 yr) and adult (i.e., remaining 6 or 27 yr for CTE and RME evaluations, respectively) using the following equation:

$$AAIR = \frac{IR(child) \times ED(child)}{BW(child)} + \frac{IR(adult) \times ED(adult)}{BW(adult)}$$

Because the AAIR values already include values for exposure duration and body weight embedded within them, these exposure parameters are set to a value of 1 in the exposure equations already given when AAIR are used.

Exposure parameter values are defined next and summarized in Table 2 for all scenarios evaluated.

- *ABS (dermal absorption fraction, unitless)*—A default value of 10% absorbed from skin was assumed for the dermal absorption of SAN Trimer from soil (U.S. EPA 2004).
- *ADD (average daily dose, mg/kg-d)*.
- *AF (soil adherence factor, mg/cm^2)*—Values in Table 2 for the soil adherence factor were defined for the general worker (based on groundskeeper), excavation worker (based on construction worker), and child visitor scenarios (based on child playing in dry soil) (U.S. EPA 2004).
- *AAIR (age-adjusted intake rate, mg-yr/kg-d for ingestion, cm^2-yr/kg-d for dermal)* = age-adjusted intake rate, calculated.
- *AT (averaging time, d)*—Averaging times for noncancer endpoints were calculated as Exposure Duration (years) multiplied by 365 d/year.

TABLE 2. Summary of Exposure Parameter Values (See Text for Rationale)

		On-site exposure scenario (CTE, RME)				Off-site exposure scenario (CTE, RME)		
Parameter (units)	Description	General worker	Excavation worker	Child VISITOR	Pica child visitor	Child resident	Adult resident	Age-adjusted
ABS (unitless)	Dermal absorption factor	0.1, 0.1	0.1, 0.1	0.1, 0.1	0.1, 0.1		NA	
ADD (mg/kg-d)	Average daily dose		Calculated				Calculated	
AF (mg/cm^2)	Soil adherence factor	0.02, 0.1	0.1, 0.3	0.04, 0.4	0.04, 0.4		NA	
AT (d)	Averaging time				Calculated: ED*365			
BW (kg)	Body weight	70, 70	70, 70	15, 15	15, 15	15, 15	70, 70	1, 1*
Cs (mg/kg)	Concentration of SAN Trimer in soil	1.2, 4.4	1.6, 3.3	1.2, 4.4	1.2, 4.4		NA	
Cw (mg/L)	Concentration of SAN Trimer in groundwater	0.0038, 0.034	NA	NA	NA		0.000056, 0.00015	
CFs (kg/mg)	Conversion factor, soil	0.000001	0.000001	0.000001	0.000001		NA	
CFw (L/cm^3)	Conversion factor, water	0.001	NA	NA	NA		0.001	
ED (yr)	Exposure duration	6.7, 25	0.038, 0.038	6, 6	1, 1	6, 6	6, 27	1, 1*
EF (d/yr)	Exposure frequency	250, 250	250, 250	50, 100	14, 14		350, 350	
ETs	Exposure time (inhalation of soil particulates)	8, 8	8, 8	1, 2	1, 2		NA	
ETw (h/d)	Exposure time (contact with groundwater)	NA	NA	NA	NA	0.33, 1	0.25, 0.58	0.25, 0.58
FA (unitless)	Fraction absorbed	1	1	1	1		1	
Fso (unitless)	Fraction total skin exposed to soil	0.1, 0.2	0.2, 0.4	0.2, 0.4	0.2, 0.4		NA	
IR (m^3/d)	Inhalation rate	15, 20	15, 20	9.5, 15.9	9.5, 15.9		NA	
IS (mg/d)	Ingestion rate for soil	50, 100	50, 100	25, 118	1000, 1000		NA	
IW (L/d)	Ingestion rate for water	0.7, 1.15	NA	NA	NA	0.74, 1.3	1.4, 2.3	0.42, 1.4*
Kp (mg/cm)	Permeability coefficient	NA	NA	NA	NA		0.012, 0.012	
PEF (m^3/kg)	Particulate emission factor	1.4E+09	1.4E+09	1.4E+09	1.4E+09		NA	
SA (cm^2)	Skin surface area	18000, 18000	18000, 18000	6600, 6600	6600, 6600	6600, 6600	18000, 18000	4183, 9583*
Tl (h)	Lag Time	NA	NA	NA	NA	0.41	0.41	0.41

Note. Asterisk indicates because parameters BW and ED are embedded in the age-adjusted intake rates, their values are set to 1 for use in the exposure equations. Units for the age-adjusted intake rates are L-yr/kg-d and cm^2-yr/kg-day for water intake and skin surface area, respectively.

- *BW (body weight, kg)*—Values in Table 2 for all scenarios reflect default central tendency values for body weight for adults and children (U.S. EPA 2009).
- *Cs (concentration in soil, mg/kg)*—Arithmetic mean and upper 95% confidence limit (UCL) concentration values were calculated from site soil monitoring data (Table 1).
- *Cw (concentration in water, mg/L)*—Arithmetic mean and UCL concentration values were calculated from and off-site groundwater monitoring data (Table 1).
- *CFs (Conversion factor for soil, 0.000001 kg/mg).*
- *CFw (Conversion factor for water, 0.001 L/cm^3).*
- *ED (exposure duration, years)*—Exposure duration values for child and excavation worker scenarios in Table 2 are assumed values, which reflect the subchronic and short-term exposures evaluated. Exposure duration values for the general worker and adult resident reflect the mean and upper bound values for occupational and residential tenure, respectively (U.S. EPA 2009).
- *EF (exposure frequency, d/year)*—Exposure frequency values for the excavation worker and visitor scenarios in Table 2 are assumed. Exposure frequency values for the general worker and residential scenarios reflect default values assuming that 2 wk out of the year is spent away from work/home.
- *ETs (exposure time at site, h/d*—For the inhalation of particulates, the exposure time values in Table 2 reflect assumptions for time spent on-site.
- *ETw (exposure time for water contact, h/d)*—For dermal contact with groundwater, exposure time values in Table 2 reflect typical mean and upper bound values for showering/bathing in children and adults (U.S. EPA 2004).
- *FA (fraction absorbed from water, unitless)*—A default value of 1 was assumed for the fraction of SAN Trimer absorbed from water.
- *Fso (fraction of total skin surface area in contact with soil, unitless)*—Values for the fraction of skin exposed to soil in Table 2 are assumed, with high values adopted for the excavation worker and visitor scenarios (20–40% of total skin surface area) than for the general worker (10–20%).
- *IR (inhalation rate, m^3/d)*—Inhalation rate values in Table 2 reflect central tendency and upper bound values for adults and children (U.S. EPA 2009).
- *IS (ingestion of soil, mg/d)*—For adult scenarios, 50 mg/d reflects the central tendency value for soil ingestion (U.S. EPA 2009), while the upper bound value of 100 mg/d is assumed. For the child visitor scenario, values of 25 and 118 mg/d reflect the mean and upper bound values as determined by a meta-analysis of child soil ingestion studies (Stanek et al. 2012).
- *IW (ingestion of water, L/d)*—Drinking-water ingestion rates in Table 2 for residential scenarios reflect the average and upper bound values for adults and children (U.S. EPA 2009). Ingestion rates equivalent to one-half of the adult residential rates were assumed for the general worker scenario.
- *Kp (dermal permeability coefficient, mg/cm)*—A permeability coefficient value for SAN Trimer was estimated using the equation (U.S. EPA 2004): $Kp = -2.8 + 0.66 \times \log Kow - 0.0056 \times MW$, where, $\log Kow = 3.1$ and $MW = 210$.
- *SA (skin surface area, cm^2)*—Total skin surface area values in Table 2 reflect central tendency values for male and female adults and children (U.S. EPA 2004).
- *Tl (lag time, h)*—A lag time of 0.41 h for styrene (U.S. EPA 2004) was adopted as a surrogate value for SAN Trimer.

Toxicity Assessment

Reference doses (RfD) were derived for SAN Trimer using the following equation:

$$RfD = POD/UFtotal$$

where RfD is the reference dose (mg/kg-d), POD the point of departure, determined using benchmark dose methods (mg/kg-d), and UFtotal the total uncertainty factor, accounting for interspecies variation (UFa), intraspecies variation (UFh), LOAEL-to-NOAEL extrapolation (UFl), subchronic to chronic extrapolation (UFs), and database uncertainties (UFd). RfD values for SAN Trimer were derived for short-term, subchronic, and chronic exposures, as described later.

All dose-response modeling was performed using U.S. EPA benchmark dose software (BMDS, version 2.1.2), in a manner consistent with U.S. EPA guidelines (U.S. EPA 2000). Default values for the benchmark response rates were selected based upon the type of data assessed: (1) For quantal datasets (e.g., incidence) the dose corresponding to a 10% increase in extra risk (BMD10) and its 95% lower confidence limit (BMDL10) were used; and (2) for continuous data sets (e.g., organ weight changes) the dose corresponding to a change equivalent to one standard deviation in the response for unexposed animals (BMDSD) and its 95% lower confidence limit (BMDLSD) were used. Short-term, subchronic, and chronic reference doses (RfD) for SAN Trimer, which correspond to the exposure durations defined for exposure scenarios already described, are derived next.

Risk Characterization

The ADD values estimated for each exposure scenario are compared to RfD values corresponding to the appropriate exposure duration, usually the following equation:

$$HI = ADD/RfD$$

where HI is the hazard index (unitless), ADD the average daily dose, summed across routes of exposure (mg/kg-d), and RfD the reference dose (mg/kg-d).

If the HI value is smaller than 1, then a noncancer hazard is not expected to present an unacceptable risk under the conditions defined in the exposure scenarios. HI values above 1 do not necessarily imply a potential hazard exists, since the RfD includes an uncertainty factor (in this case, a factor of 300) that may maintain an adequate margin of safety even for exposures equivalent to or numerically higher than the RfD. An HI above 1 serves to indicate that additional action or investigation may be required. An HI above a value of the total uncertainty factor value would indicate that the exposures are greater than the POD (i.e., doses where effects are observed in rats).

RESULTS

Exposure Assessment

Total ADD values were calculated for each exposure scenario by summing the route-specific ADD values for ingestion, inhalation, and dermal contact ADD (Table 3). For the on-site excavation worker, pica child, and child visitor scenarios, ingestion of soil was identified as the most important pathway. For the on-site general worker scenario, ingestion of groundwater was the largest contributor to total exposure. For the off-site resident scenarios, dermal contact with groundwater was the largest contributor to total exposure.

Toxicity Assessment

Short-Term Oral RfD Union Carbide Corporation sponsored a 14-d study using male and female rats (Huntingdon 1999). In this study, male and female Sprague-Dawley rats were dosed with 0, 30, 75, 150, or 300 mg/kg-d of SAN Trimer in via oil gavage. Clear signs of toxicity (clinical signs and histopathological changes) were noted at the highest dose. Some evidence of toxicity (clinical signs, organ weight changes, organ discoloration) was observed in animals exposed to 150 mg/kg-s. No effects were observed in animals exposed to 75 mg/kg-d or less. This study identifies a no-observed-effect level (NOEL) of 75 mg/kg-d. For risk assessment purposes, the effects of SAN Trimer exposure on liver weight were conservatively assumed to serve as a precursor endpoint for the histopathological effects observed in the chronic study (see discussion of liver foci below). Based upon the dose-response data for liver weight changes in male and female rats (Table 4), BMDSD and BMDLSD values of 63 and 41 mg/kg-d were predicted by the best fitting model (exponential model, Akaike information criterion [AIC] =

TABLE 3. Average Daily Dose (ADD) Values for Four Exposure Scenarios

				ADD (CTE – RME, mg/kg-d)			
Location	Duration	Scenario	Media	Oral	Inhalation	Dermal contact	Total
On-site	Short-term	Excavation worker	Total SOIL	7.8E-07–3.2E-06	5.6E-11–1.5E-10	5.6E-07–7.0E-06	1.3E-06–1.0E-05
		Pica child	Surface soil	8.0E-05–2.9E-04	2.3E-11–2.8E-10	4.2E-07–3.1E-05	8.0E-05–3.2E-04
	Subchronic	Child visitor	Surface soil	2.7E-07–9.5E-06	3.1E-12–7.6E-11	5.8E-08–8.5E-06	3.3E-07–1.8E-05
	Chronic	General worker	Surface soil	5.9E-07–4.3E-06	4.2E-11–2.1E-10	4.2E-08–1.5E-06	2.7E-05–3.9E-04
			On-site groundwater	2.6E-05–3.8E-04	—	—	2.7E-05–3.9E-04
Off-site	Subchronic	Child resident	Off-site groundwater	2.6E-06–1.2E-05	—	2.8E-04–1.3E-03	2.8E-04–1.3E-03
	Chronic	Child/adult resident	Off-site groundwater	1.9E-06–6.1E-06	—	1.9E-04–6.6E-04	2.0E-04–6.7E-04

TABLE 4. Relative Liver Weight Changes in Male and Female Rats Following Short-Term and Subchronic Exposure to SAN Trimer

Exposure duration (reference)	Dose (mg/kg-d)	*n*	Mean (% of body weight)	SD (% of body weight)
2 wk (Huntingdon 1999)	0	12	3.25	0.25
	30	12	3.39	0.22
	75	12	3.62	0.33
	150	11	4.26	0.41
	300[a]	1[a]	5.51[a]	—[a]
18 wk (NTP 2011a)	0	20	3.28	0.12
	10	20	3.39	0.095
	20	20	3.47	0.159
	40	20	3.58	0.163
	80	20	3.72	0.149
	150	20	3.93	0.122

[a]Due to frank toxicity observed at this dose level, an insufficient number of animals survived for this dose group to be included in the BMD modeling.

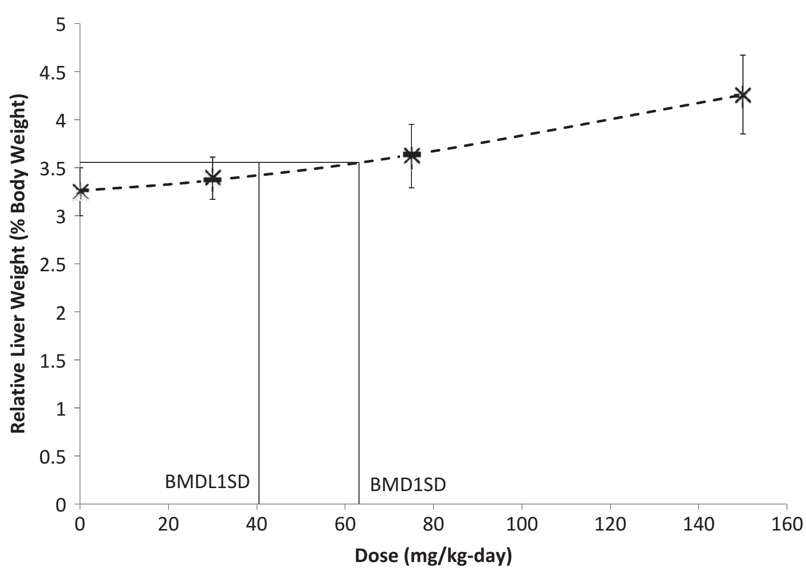

FIGURE 1. Benchmark dose modeling results based on relative liver weight changes in male and female rats exposed to SAN Trimer for 2 weeks (Huntingdon 1999). X = arithmetic mean; error bars = standard deviation; dashed line = exponential model; solid lines = BMD and BMDL.

–60.7, Figure 1). AIC values for all other models were greater than –60 (poorer fits), and generally these models returned BMDSD values that were nearly identical to the exponential model. In deriving a short-term RfD, a total uncertainty factor was defined as follows:

- *UFa*—A default factor of 10 was adopted for interspecies variation.
- *UFh*—A default factor of 10 was adopted for intraspecies (intraindividual) variation.
- *UFs*—A value of 1 was adopted for UF since the duration of the toxicity study corresponds directly to the duration of interest.
- *UFl*—A value of 1 was adopted for UFl since BMD methods were adopted, and the endpoints were considered to be relatively mild.
- *UFd (database deficiencies)*—A factor of 3 was used to account for deficiencies in the toxicological database for SAN Trimer, namely, that toxicity testing has only been conducted in a single species. Because the available rat studies were designed specifically to examine the endpoints of interest and window of susceptibility (early life), a higher value (10) is not required.

Application of a total uncertainty factor of 300 (10 × 10 × 1 × 1 × 3) to the POD value yields a short-term RfD value of 0.1 mg/kg-d (41 mg/kg-d/300 rounded to one significant figure) for SAN Trimer.

Subchronic Oral RfD NTP conducted an 18-wk perinatal study using male and female rats (NTP 2011a). In this study, male and female F344 rats were dosed with 0, 100, 200, 400, 800, or 1600 ppm of SAN Trimer in feed (corresponding to doses of approximately 0, 10, 20, 40, 80, or 150 mg/kg-d). Histopathology was negative in all organs examined at the 1600 ppm dose level. Overall results indicated body weight decreases that appear correlated with food consumption decreases, serum triglyceride and cholesterol reduction, and urine protein elevation with dose and liver and spleen weight increases with dose. In the absence of histopathological changes, these effects are considered to be relatively mild in nature (i.e., adaptive rather than adverse). However, the presence of histopathological changes in the chronic toxicity study (see below) suggest that the identification of liver effects as an appropriate basis for non-cancer risk assessment. Based on the organ weight, a NOEL of 20 mg/kg-d is established in male F344 rats at 200 ppm SAN Trimer in the feed and a NOEL of 40 mg/kg-d for female rats at 400 ppm SAN Trimer in the feed. Based upon the dose-response data for liver weight changes in male and female rats (Table 4), BMDSD and BMDLSD values of 17 and 12 mg/kg-d were predicted by the best fitting model (Hill model AIC = –354.4, Figure 2). AIC values for all other models were greater than –354 (poorer fits), and except for the linear and power models, returned BMDSD values that were similar (within approximately 20%) of the Hill model value. Application of a total uncertainty factor of 300, as defined earlier for the short-term RfD, yields a subchronic RfD of 0.04 mg/kg-d (12 mg/kg-d/300 rounded to one significant figure) for SAN Trimer. The results of this study were used by NTP to set doses for the chronic cancer bioassay.

Chronic RfD NTP conducted a chronic cancer bioassay for SAN Trimer in which groups of 50 male and 50 female rats were given diets of 0, 400, 800, or 1600 ppm SAN Trimer for 2 yr, which correspond to average daily doses of approximately 20, 40, and 75–85 mg/kg-d. To better understand the potential effects associated with perinatal exposures, which were of specific interest due to observations of increased incidence of childhood cancers in near the Reich Farm site, the dams of core and special study rats were fed the same concentrations from gestation day 7 until the pups were weaned. In so doing, animals were exposed to SAN Trimer in utero (gestation day 7 to delivery), lactation (postnatal day 1–20), and through adulthood (104 wk). At the end of the exposure period, effects were observed in the liver (eosinophilic foci, mixed cell foci,), bone marrow (inflammation), and sciatic nerve (degeneration). The chronic cancer bioassay study design does not allow for the proper collection of nerve tissue for appropriate histological

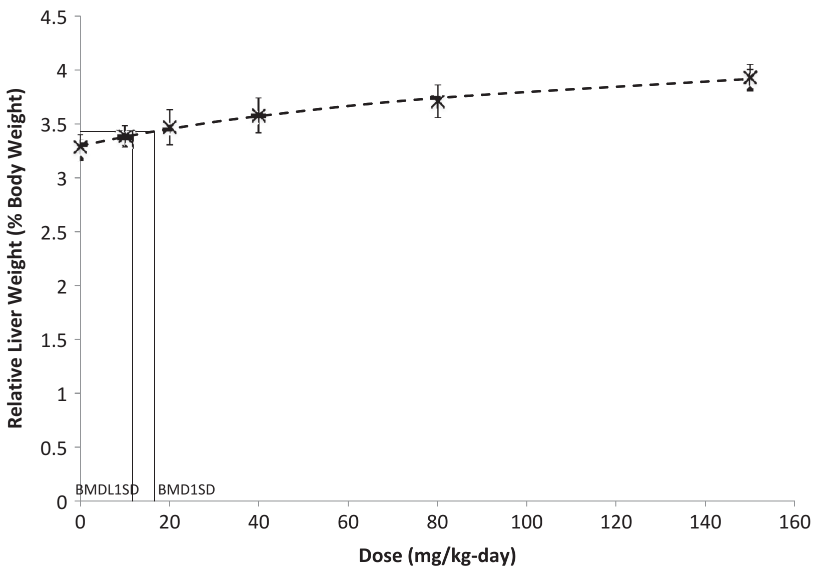

FIGURE 2. Benchmark dose modeling results based on relative liver weight changes in male and female rats exposed to SAN Trimer for 18 weeks (NTP 2011a). X = arithmetic mean; error bars = standard deviation; dashed line = Hill model; solid lines = BMD and BMDL.

assessment and statistical analysis. Henceforth, it is not possible to determine a causal association between SAN Trimer exposure and sciatic nerve changes (McConnell 2011), and consequently this observation was not considered as an appropriate basis for the RfD. The incidence data for the liver and bone-marrow effects were considered for the RfD and their incidence data are summarized in Table 5. Inspection of the dose-response data for these endpoints indicated similar responses in male and female animals, and therefore the data were combined to increase the statistical power of the data set. Of the data sets and BMD models considered, the log-logistic model (AIC = 548.8) fitted to the liver effects data (eosinophilic foci) provided the most conservative BMD10 and BMDL10 values (16 and 9.2 mg/kg-d, respectively) (Figure 3). AIC values for alternative models fit to the eosinophilic foci data were greater than 548.9 (poorer fits). Alternative models and endpoints resulted in BMDSD values that were similar (within approximately a factor of 2) of the value for eosinophilic foci with the log-logistic model. Application of a net uncertainty factor of 300, as defined earlier for the acute and subchronic RfD, yields a chronic RfD of 0.03 mg/kg-d (9.2 mg/kg-d/300, rounded to one significant figure) for SAN Trimer.

Oral RfD values derived for SAN Trimer are summarized in Table 6.

Carcinogenicity

The draft NTP report concluded that there was equivocal evidence of carcinogenic activity for SAN Trimer in male rats based upon a small number of astrocytomas and granular-cell tumors in the brain and spinal cord, and that there was no evidence of carcinogenic activity in female rats (NTP 2011a). However, after a review of NTP draft conclusions by the NTP Technical Reports Peer Review Panel on January 26, 2011, it was concluded by a vote of 6 to 1 that there was no evidence of carcinogenic activity in both genders of rats (NTP 2011b).

There were significant decreases in the incidences of pituitary gland pars distalis adenoma in 1600 ppm males and females, and the incidences in both genders occurred with negative trends. The incidences of mammary gland fibroadenoma occurred in females with a negative trend, and the incidences in 800 and 1600 ppm females were significantly less than that in the control group. The incidences of mononuclear-cell leukemia in all exposed groups of males and females were significantly less than those in the controls.

TABLE 5. Incidence of Key Effects Observed in Male and Female Rats Following Chronic Exposure to SAN Trimer (NTP 2011a)

	Eosinophilic foci in liver			Mixed cell foci in liver			Bone marrow hyperplasia		
Dose (mg/kg-d)	M	F	MF	M	F	MF	M	F	MF
0	17/50	23/50	40/100	6/50	4/50	10/100	24/50	16/50	40/100
20	19/50	31/50	50/100	19/50	8/50	27/100	24/50	25/50	49/100
40	22/40	30/50	52/100	12/50	7/50	19/100	24/50	25/50	49/100
80	33/40	29/47	62/100	20/50	13/50	33/100	37/50	38/50	75/100

Note. M = male, F = female, MF = both sexes combined.

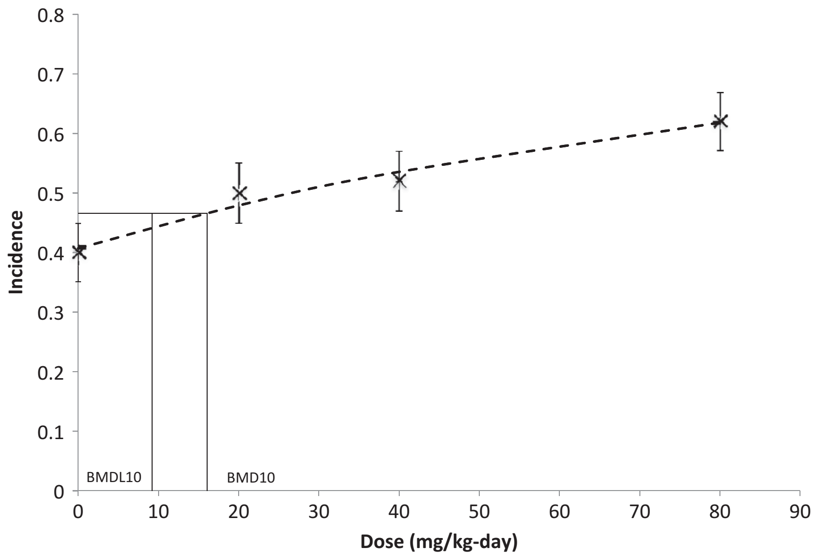

FIGURE 3. Benchmark dose modeling results based on eosinophilic foci data in male and female rats exposed to SAN Trimer for 2 years (NTP 2011a). X = incidence; error bars = standard deviation; dashed line = log-logistic model; solid lines = BMD and BMDL.

TABLE 6. Proposed Reference Doses (RfDs) for SAN Trimer

	Short-term RfD	Subchronic RfD	Chronic RfD
Endpoint	Increased liver weight (Huntington, 1999)	Increased liver weight (Battelle, 2004)	Liver effects, eosinophilic foci (NTP, 2011a)
POD (mg/kg-d)	BMDSD = 63[a] BMDLSD = 41[a]	BMDSD = 17[b] BMDLSD = 12[b]	BMD10 = 16[c] BMDL10 = 9.2[c]
UFh	10	10	0
UFa	10	10	10
UFl	1	1	1
UFs	1	1	1
UFd	3	3	3
UFtotal	300	300	300
RfD (mg/kg-d)	0.1	0.04	0.03

[a]BMD values based on the best fitting model for the short-term data set (exponential, Figure 1).
[b]BMD values based on the best fitting model for the subchronic data set (Hill, Figure 2).
[c]BMD values based on the best fitting model for the chronic data set (log-logistic, Figure 3).

SAN Trimer is only one of several chemicals identified in the well water, and the human epidemiology studies reported equivocal evidence for cancer with "considerable uncertainty in the findings" (ATSDR 2003; NJDHSS 2001). While the carcinogenicity of SAN trimer was not formerly examined in occupational studies where the potential for exposure would be much higher, there have been two large studies of acrylonitrile workers that have a portion of the workers exposed to SAN where the SAN trimer would be a contaminate. While the cancer rates for the SAN workers are not presented separately, these large studies of acrylonitrile workers found no increased risk of leukemia, brain cancer or any other cancer or cause of death (Blair et al. 1997; Swaen et al. 2006). SAN Trimer is readily metabolized in animals, having a half-life in blood of 3–4 h following oral exposure (Gargas et al. 2008). Based on these findings, there is no evidence to indicate that SAN Trimer is carcinogenic, and therefore it is inappropriate to characterize potential cancer risks to potentially exposed human populations.

Risk Characterization

HI values for each of the scenarios are summarized in Table 7 and depicted in Figure 4. HI values for the CTE evaluations range from 0.000008–0.007, while HI values for the RME evaluations range from 0.0001–0.03. Based on HI results that are well below a value of 1, adverse effects are unlikely to be observed from potential human exposures to SAN Trimer in soil and groundwater at or near the site.

DISCUSSION/CONCLUSIONS

An increase in the incidence of childhood cancers including leukemia or central nervous system in Toms River, coupled with the detection of SAN Trimer in soil and groundwater at the Reich Farm site, prompted the conduction of a cancer bioassay in rats by the NTP. In 2011, the NTP published the technical report on the toxicology and carcinogenesis study of SAN Trimer (NTP 2011a). The findings from the studies conducted by the NTP along with those conducted by Union Carbide were that SAN Trimer exerts low toxicity in animals, with the most prominent and consistent effect observed being liver weight increases. It is rapidly eliminated following oral exposure with a half-life of 3–4 h (Gargas et al. 2008). The weight of evidence indicated that SAN Trimer is not genotoxic (NTP 2011a), and the NTP cancer bioassay conclusively demonstrated SAN Trimer is not a carcinogen (NTP 2010 2011b). Of particular note, the incidence of central nervous system tumors was not significantly increased in exposed rats, while the incidence of mononuclear-cell leukemia was significantly decreased in all treated animals when compared to controls (NTP 2011a). Given the lack of significant carcinogenic response in the NTP bioassay, risk assessments for SAN Trimer are based, instead, on noncancer endpoints. Reference dose values were derived based on the liver weight increases reported in exposed rats. Extensive soil and groundwater sampling at the Reich Farm Superfund Site since the 1980s created a robust database that can be used to model potential human exposures to be used for a screening-level risk assessment. Based upon the results of this screening-level assessment, adverse effects are unlikely to be observed from potential human exposures to

TABLE 7. Hazard Index Values for SAN Trimer Exposure Scenarios

On-site/off-site	Duration	Scenario	Hazard index (HI)	
			CTE	RME
On-site	Short-term	Excavation worker	0.00001	0.0001
		Pica child	0.002	0.003
	Subchronic	Child visitor	0.000008	0.0002
	Chronic	General worker	0.0007	0.01
Off-site	Subchronic	Child resident	0.007	0.03
	Chronic	Child/adult resident	0.007	0.02

Note. A hazard index greater than or equal to 1 indicates that exposure is equivalent to or greater than the reference dose. A hazard index greater than or equal to 300 indicates that exposure is equivalent to or greater than the point of departure.

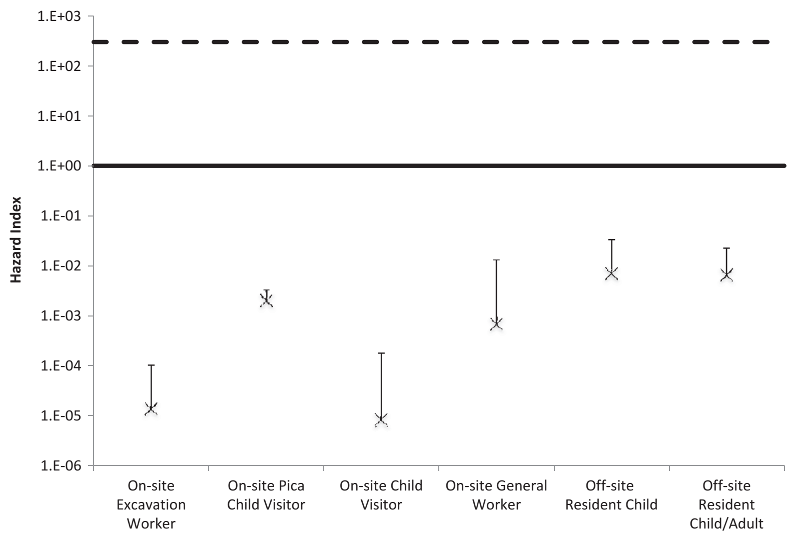

FIGURE 4. Summary of hazard index values calculated for SAN Trimer exposure scenarios. X = CTE value; error bars = RME value; solid line = exposure equivalent to the RfD value; dashed line = exposure equivalent to the BMDL value.

SAN Trimer in soil and groundwater at or near the site

As a screening-level assessment, a number of assumptions and decisions made in this assessment are conservative in nature, intended to be protective (and not predictive) of potential human health hazards. Sources of uncertainty and conservative assumptions are discussed briefly next.

- *Soil concentration*—For this screening-level assessment, the concentration of SAN Trimer in total soil used to assess exposures in the Excavation Worker Scenario included samples collected at depths of 29 ft (8.8 m) below grade. Although samples collected from these depths contained the highest concentrations of SAN Trimer detected (up to 29 mg/kg), they are unlikely to serve as points of contact for most excavations. Limited the sample depth to 20 ft (6.1 m) for the excavation worker scenario would result in mean concentration of 0.48 mg/kg (approximately threefold lower than the value of 1.6 mg/kg used here). For the RME short-term exposure scenarios (i.e., excavation worker, pica child), a case could be made for using the maximum soil concentration rather than the UCL. This is a reasonable assumption for acute (single day) exposures, but becomes much less likely for exposures of 2 wk in duration. Based upon a review of the soil concentrations (Table 1), use of the maximum detected soil concentrations for the RME short-term scenarios would result in HI values that are approximately twofold higher than depicted here using the UCL. Based upon a review of the soil concentrations (Table 1), use of the maximum detected soil location (7.3 mg/kg) or sample depth interval (29 mg/kg) concentrations for the RME excavation worker scenario would result in HI values that are respectively twofold (HI = 0.0002) and ninefold (HI = 0.0009) higher than depicted here using the UCL (HI = 0.0001).
- *Groundwater concentration*—The arithmetic mean and UCL values for SAN Trimer in surface soil, total soil, on-site groundwater, and off-site groundwater serve as exposure point concentrations for the screening-level risk assessment. In calculating exposure point concentrations for on-site and off-site groundwater, the maximum value detected for each location in 2010 was used. This is a conservative assumption since the maximum value is as much as ninefold higher that the arithmetic mean for some locations. UCL values could be calculated for all media except for on-site groundwater, which was highly influenced by a single

sample, resulting in the use of the maximum detected concentration (0.034 mg/L) as the exposure point concentration for the RME on-site worker scenario. This concentration is not consistent with the remaining on-site water collected (the next highest concentration detected in on-site groundwater was 0.00006 mg/L), and is not expected to be sustained for the 25-yr exposure duration evaluated for the RME on-site worker. Using the next highest on-site groundwater concentration would result in ADD and HI values for the on-site groundwater pathway that are more than 500-fold lower than evaluated in this screening-level assessment.

- *Exposure scenarios*—As an industrial site, the general worker and excavation worker scenarios are expected to reasonable depictions of potential human exposures. However, the child visitor scenarios (including short-term pica exposure) are not expected to occur at an industrial site. The child visitor scenarios are expected to overestimate the potential exposures and hazards for a more likely exposure scenario, such as a youth trespasser scenario, since children would be expected to contact more SAN Trimer (on a milligrams per kilogram per day basis) due to differences in body weights and contact rates.
- *Exposure pathways*—Exposure pathways for on-site and off-site groundwater were assumed to be complete in this screening-level assessment, despite the fact that potable use of groundwater within the historic plume is prohibited by municipal ordinance and a state administrative control. The groundwater pathway contributed 100% of potential exposure to the off-site resident scenarios, and 98% of the potential exposure to the on-site worker. Therefore, excluding the groundwater pathway, off-site resident exposures to SAN Trimer would be zero, while on-site worker exposures to SAN Trimer would be negligible (i.e., only 2% of the total HI calculated here). For the on-site excavation worker scenario, the potential for use of personal protection equipment (PPE), which would greatly reduced the fraction of skin surface area exposed to soil, was conservatively ignored. If PPE were to effectively eliminate the dermal pathway, the HI for the RME excavation worker would drop to 0.00003.
- *Combined exposure scenarios*—The possibility remains that multiple exposure scenarios can apply to a single individual (i.e., a worker who lives near the site). To account for this possibility, the HI values for multiple scenarios can be summed. However, this is best accomplished using the CTE values, since combining RME scenarios, which are already conservative by themselves, will likely result in unrealistic exposure assumptions. For example, the CTE HI values for the general worker scenario (0.0007) and the off-site resident child/adult scenario (0.007) can be summed (0.008, rounded to one significant figure) to assess the potential hazards to an off-site resident who works at the site. Consistent with a screening-level assessment, this approach is conservative due to overlapping assumptions for the two exposure scenarios (e.g., 250 d/yr for the worker, 350 d/yr for the resident).
- *Reference doses*—For the short-term and subchronic RfD values, an endpoint (liver weight changes) that may be considered to be an adaptive change rather than evidence of toxicity was selected. These organ weight changes following short-term exposure were assumed to be a conservative precursor event to the histopathological changes noted in the liver following chronic exposures. For the chronic RfD value, the endpoint selected (eosinophilic foci) provided more conservative POD values than the other chronic endpoints considered (mixed cell foci, bone marrow hyperplasia), but were generally within a factor of 2. In addition, the dose-response models selected as providing the best overall fit to the key data sets yield POD values that are similar (i.e., generally within a factor of 2) to alternative models. For all three RfD values, default uncertainty factors were used to account for inter-and intra-species variation.

For the reasons just discussed, the hypothetical exposures and potential HI discussed for the scenarios presented are expected to overestimate actual exposures and hazards at the site. Based upon these small HI values, along with the conservative nature of this screening-level assessment, adverse effects are unlikely to be observed from potential human exposures to SAN Trimer in soil and groundwater at or near the site.

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