HSIA
halogenated
solvents
industry
alliance, inc.

March 15, 2013

TSCA Work Plan Chemicals Program
Environmental Protection Agency

Re: EPA-HQ-OPPT-2012-0723; CAS No. 79-01-6

Dear Sirs:

The Halogenated Solvents Industry Alliance, Inc. (HSIA) represents US producers and users of trichloroethylene (TCE, CAS No 79-01-6 ). TCE was identified in an initial group of seven "Work Plan Chemicals" for which the Environmental Protection Agency (EPA) recently completed risk assessments on which it solicits public comment. 78 Fed. Reg. 1856 (January 9, 2013).

HSIA has participated extensively in EPA risk assessments and rulemakings for TCE since its formation in 1980. HSIA welcomes the opportunity to submit these comments, which (i) demonstrate that exposures from use of TCE in small vapor degreasers are already more than adequately regulated under the Clean Air Act (CAA) and other relevant statutory authority, (ii) question the focus on a handful of auto and consumer and hobbyist arts and craft products, and (iii) show that EPA's assessment of the risks posed are based on outdated exposure data and inappropriate inferences as to potential health effects.

Most importantly, HSIA believes that this exercise is *ultra vires* and could lead to a misallocation of EPA and private sector resources away from pressing environmental concerns. As discussed more fully below and in the attached technical comments, the risk assessments are largely based on use and exposure information that predate comprehensive regulation of the most important source of TCE emissions, vapor degreasing. This may be because EPA and its contractors failed to note that this sector is now controlled by emission limits that provide an "ample margin of safety to protect public health" as required by CAA § 112(f)(2).[1] Concern about "bystanders" would appear to be misplaced, as vapor degreasing

[1] 40 CFR Part 63, Subpart T. EPA is required, within eight years of publication of a national emission standard for a particular major source category, to conduct a "residual risk" review for that category to ensure an

1530 Wilson Boulevard, Suite 690 • Arlington, VA 22209
703-875-0684 • Fax 703-875-0675

occurs in occupational settings. And it would be a clear overreach of EPA's authority for it to assert the power to regulate to protect workers in occupational settings when this responsibility has been delegated by Congress to the Occupational Safety and Health Administration (OSHA) for over 40 years since passage of the Occupational Safety and Health Act of 1970.

EPA clearly believes the Toxic Substances Control Act (TSCA) to be in need of revision: "The American public has the right to expect that the chemicals manufactured, imported, and used in this country are safe and the EPA needs an effective law that gives us the tools necessary to provide the public with this assurance. The time is now to fix this badly outdated law. TSCA must be updated and strengthened so that the EPA has the tools to do our job of protecting public health and the environment."[2] TSCA has not been amended by Congress, however, and the language of the current statute cannot be read to give EPA the regulatory authority implicitly asserted in these Work Plan assessments.[3]

That said, we note that EPA recognized that "industrial settings [are] believed to be better controlled and monitored," and appropriately excluded TCE use in large commercial/ industrial solvent degreasing and as an intermediate (mostly in refrigerant manufacturing) from the scope of the Work Plan assessment. EPA might also wish to emphasize the significant reductions in TCE use over the past 25 years, emissions having dropped from 56 million pounds in 1988 to 2.6 million pounds in 2011 (see table at p. 5 of enclosed Technical Comments).

## A. Statutory Framework – Regulation under TSCA § 6

Perhaps for the reasons summarized above, the assessment is silent as to the statutory authority under which EPA might base regulatory action to address the alleged risks from use of TCE in the applications identified. It appears, however, that EPA will be "determining, on the basis of final risk assessments, which chemical or chemicals may be appropriate for restrictions or bans authorized by Section 6 of TSCA."[4]

EPA may regulate a substance under TSCA § 6 only when "there *is* a reasonable basis to conclude" that the substance presents "an unreasonable risk of injury to health" (emphasis added). Thus, regulation under TSCA § 6 must be preceded by a determination that there is

---

ample margin of safety and to adopt more protective standards where a particular standard does not reduce lifetime excess cancer risks to the most exposed individual to less than one in a million. CAA § 112(f)(2).

[2] Testimony of James J. Jones, Acting Assistant Administrator, Office of Chemical Safety and Pollution Prevention, Environmental Protection Agency, before the Committee on Environment and Public Works and the Subcommittee on Superfund, Toxic and Environmental Health, United States Senate (July 24, 2012).

[3] As the Supreme Court has stated, "Congress does not . . . hide elephants in mouseholes." *Whitman v. Am. Trucking Association*, 531 U.S. 457, 468 (2001).

[4] *EPA to Focus on Existing Chemicals in 2013,* BNA Daily Environment Report, p. 2 (January 22, 2013).

an actual risk to health and that the benefits of regulation outweigh its costs. EPA has not identified the metrics it used to determine that TCE presents an "unreasonable risk" under TSCA § 6 and that the benefits of such regulation would outweigh its cost. A review of the evidence demonstrates that neither standard is met in the case of TCE.

In addition, TSCA § 6 requires:

> "If the Administrator determines that a risk of injury to health or the environment could be eliminated or reduced to a sufficient extent by actions taken under another Federal law (or laws) administered in whole or in part by the Administrator, the Administrator may not promulgate a rule under subsection (a) of this section to protect against such risk of injury unless the Administrator finds, in the Administrator's discretion, that it is in the public interest to protect against such risk under this chapter. In making such a finding the Administrator shall consider (i) all relevant aspects of the risk, as determined by the Administrator in the Administrator's discretion, (ii) a comparison of the estimated costs of complying with actions taken under this chapter and under such law (or laws), and (iii) the relative efficiency of actions under this chapter and under such law (or laws) to protect against such risk of injury."[5]

This provision is of special significance as EPA considers use of TCE in small vapor degreasers. EPA has already adopted a national emissions standard under CAA § 112 specifically to regulate emissions of TCE and five other chlorinated solvents from vapor degreasing operations.[6] It required both major and area source batch and in-line cleaning machines to apply maximum achievable control technology (MACT) to meet emission standards.

More recently, EPA adopted facility-wide annual emission limits for these sources, in order to provide an "ample margin of safety to protect public health" as required by § 112(f)(2).[7] These standards impose facility-wide limits based on application of cancer potency factors to estimated emission rates, as follows:

> "To develop the proposed risk-based alternatives, all emission rates in the assessment data base were first converted to MC [methylene chloride]-

---

[5] TSCA 6(c)(1); 15 U.S.C. § 2605(c)(1).

[6] 40 CFR Part 63, Subpart T, initially adopted at 59 Fed. Reg. 61805 (December 2, 1994) (the "degreasing NESHAP").

[7] 72 Fed. Reg. 25138 (May 3, 2007). EPA is required, within eight years of publication of a national emission standard for a particular major source category, to conduct a "residual risk" review for that category to ensure an ample margin of safety and to adopt more protective standards where a particular standard does not reduce lifetime excess cancer risks to the most exposed individual to less than one in a million. CAA § 112(f)(2).

> equivalents based on the relative cancer potency of the [hazardous air pollutants, or HAPs] emitted. The cancer-potency-weighted MC-equivalent emission rate was calculated as the estimated emissions for the HAP in [kilograms per year] or [pounds per year] times the unit risk estimate (URE) for the HAP divided by the URE for MC."[8]

Moreover, the NESHAP limits emissions from batch vapor solvent cleaning machines (the type of open-top degreaser typically used by small facilities) to 150 kilograms per square meter (of the open face) per month.

In sum, CAA § 112(f) requires EPA to adopt standards that reduce lifetime excess cancer risks to the most exposed individual to less than one in a million for vapor degreasing, and EPA has done this. Regrettably, the Work Plan assessment fails to consider the degreasing NESHAP at all. If it had, EPA could have addressed how any TSCA authority realistically could achieve greater public health protection for vapor degreasing sources of TCE than EPA already is required to achieve and is achieving under current law. Before moving forward, in any event, TSCA § 6 requires the Administrator to find "that it is in the public interest to protect against such risk under [TSCA]. . . consider [ing] (i) all relevant aspects of the risk, . . . (ii) a comparison of the estimated costs of complying with actions taken under [TSCA and CAA § 112], and (iii) the relative efficiency of actions under [TSCA and CAA § 112] to protect against such risk of injury."

1. Existence of Health Risk

A principal driver of the instant risk assessment is a mathematical demonstration of risk from data generated from high-dose animal studies. In reliance on conservative policy assumptions, the available human and animal evidence suggesting that such an extrapolation may not reflect reality was accorded no weight. A more solid scientific basis is required to support regulation under TSCA § 6.

Regulations adopted under TSCA § 6 must be based on "substantial evidence in the rulemaking record . . . taken as a whole," as opposed to the more deferential standard of review prescribed in the Administrative Procedure Act.[9] The decision of the U.S. Court of Appeals for the Fifth Circuit in *Gulf South Insulation v. Consumer Products Safety Commission*,[10] in which the court applied the substantial evidence test to set aside the Commission's ban of urea formaldehyde foam insulation, indicates the degree of certainty in the evidence required to support regulation under this strict standard of judicial review. The court found that a risk assessment based on a single data set, incorporating mathematical

---

[8] 71 Fed. Reg. 47670, 47680 (August 17, 2006).

[9] TSCA § 19(c)(1)(B)(i), 15 U.S.C. § 2618(c)(1)(B)(i).

[10] 701 F. 2d 1137 (1983) ("*Gulf South*").

extrapolation from high levels in rats to low levels in humans, does not constitute substantial evidence. Moreover, the court identified at least two assumptions from the Commission's risk assessment that were "of questionable validity" – that at identical ambient exposure levels the effective dose is the same for rodents as for humans, and that there is no threshold below which the chemical poses no risk of cancer.[11] These same two assumptions form the basis for the risk estimates in the TSCA Work Plan TCE assessment.

"Substantial evidence," then, means more than mathematical calculations based on conservative policy assumptions to the exclusion of all other scientific data. To justify regulation under TSCA § 6, there must be scientific evidence indicating a real risk of injury to health, not the mere possibility of risk. As the Supreme Court held in interpreting the Occupational Safety and Health Act, an agency cannot justify pervasive regulation on the basis of the mere possibility of some human risk.[12]

2. Economic Factors

Under TSCA § 6, the determination that an unreasonable risk is presented requires that any real risk identified be weighed against the costs associated with reducing it:

> "In general, a determination that a risk associated with a chemical substance or mixture is unreasonable involves balancing the probability that harm will occur and the magnitude and severity of that harm against the effect of proposed regulatory action on the availability to society of the benefits of the substance or mixture, taking into account the availability of substitutes for the substance or mixture which do not require regulation, and other adverse effects which such proposed action may have on society."[13]

The higher the cost to society of regulation, the more serious the risk must be before EPA may regulate under TSCA § 6. Section 6(c)(1) requires EPA to consider specifically not only health effects and human exposure, but also the benefits of the substance for various uses, the availability of substitutes, and the economic consequences of any rule, including the effect on the national economy, small business, and technological innovation.

Congress recognized that regulation under TSCA § 6 could have severe economic consequences, and intended that these be accorded great weight in deciding whether to act under § 6:

---

[11] 701 F.2d at 1147, n. 19.

[12] *Industrial Union Dept., AFL-CIO v. American Petroleum Institute,* 448 U.S. 607 (1980).

[13] H. Rep. No. 1341, 94th Cong., 2d Sess. 14, *reprinted in* H. Comm. On Interstate and Foreign Commerce, Legislative History of the Toxic Substances Control Act ("Legislative History") at 422 (1976); *see also* 122 Cong. Rec. S3499 (March 26, 1976), Legislative History at 212 (statement of Sen. Magnuson).

> "[A TSCA § 6] requirement may remove a substance from the market or impose lesser restrictions on its availability and such a requirement is not of limited duration. Thus, the effect on society may be far reaching. As a result regulatory effect will be of greater significance in a determination of unreasonable risk for purposes of section 6 than for a determination for purposes of section 4 or 5(g) . . . . [T]he requirements for a determination of unreasonable risk for purposes of Section 4 or 5(g) are less demanding."[14]

The Work Plan assessment contains none of the economic analysis that would be required to support a TSCA § 6 rulemaking. We note, however, that TCE is the solvent of choice for manufacturing a range of products to specification across the medical, electronics, aerospace, and many other industries. It is the best solution for many cleaning applications, and in some cases is the only solution. Aqueous cleaning, for example, is not an option where there is no tolerance for corrosion, rusting, and pitting of the substrate being cleaned. Alternative cleaning methods may leave residues, which are not acceptable in applications such as medical instruments and implants.

Forced substitution of TCE by aqueous or other solvent cleaners can also harm the environment. TCE is typically recycled as part of a controlled process, leaving only filters and sludge to be disposed of. Aqueous systems require much greater water usage and can produce large amounts of contaminated waste water, which when discharged can cause significant problems for publicly owned treatment works (POTWs).

Furthermore, a number of alternatives to TCE pose greater risks of flammability and/or toxicity. Acetone is highly flammable at room temperature; vapors from acetone in a degreasing machine can readily be ignited by sparks, which are commonly produced when metal parts being cleaned strike one another. Hexane and n-propyl bromide (nPB), also used as substitutes in certain operations, can result in significant risk of neurotoxicity.[15]

Airless degreasers have major operational disadvantages, as a number of equipment manufacturers have commented. Moreover, they are not an option in many applications. A number of companies in Pennsylvania clean the narrow tubes they manufacture in large (40-

---

[14] H. Rep. No. 1341, 94th Cong., 2d Sess. 14-15, Legislative History at 422-23.

[15] "UC Berkeley research scientist Michael Wilson studied auto mechanics disabled by a neurotoxic blend of hexane and acetone used as a brake cleaner. The product had been substituted for chlorinated solvents . . . . The next reformulation was no better: Hexane was swapped out for bromopropane, known to cause sterility, Wilson said." (http://www.universityofcalifornia.edu/news/article/22772, reporting on UC Centers for Occupational and Environmental Health (COEH), Green Chemistry, Cornerstone to a Sustainable California (2008), p. 16; http://coeh.berkeley.edu/docs/news/green_chem_brief.pdf). *See also* Samukawa, M, Ichihara, G., Nobuyuki, O, Kusunoki, S., "A case of severe neurotoxicity associated with exposure to 1-bromopropane, an alternative to ozone-depleting or ozone-warming solvents." *Arch. Intern. Med.* 172: 1257-1260 (2012) (use of nPB in metal degreasing operations identified as causing severe peripheral neuropathy in an exposed worker).

50 feet) custom-built equipment. No airless system is available that meets such requirements. These considerations led EPA to exempt narrow tube manufacturing facilities from the degreasing NESHAP.

B. Statutory Framework – Referral under TSCA § 9

As indicated above, TCE does not appear to present an unreasonable risk of injury to health for purposes of regulation under TSCA. Even if it were deemed to do so, however, TSCA § 9 requires EPA to consult and coordinate with other federal agencies "for the purpose of achieving the maximum enforcement of this Act while imposing the least burdens of duplicative requirements on those subject to the Act and for other purposes."

1. Worker Exposure

The Work Plan TCE assessment addresses potential risks to workers and bystanders as a result of its use in vapor degreasing. As noted above, worker health and safety falls under the jurisdiction of OSHA. In an analysis of TSCA § 9, EPA's Acting General Counsel concluded that "Congress expected EPA – particularly where the Occupational Safety and Health Act was concerned – to err on the side of making referrals rather than withholding them."[16]

OSHA has regulated occupational exposure to TCE for many years. The current workplace limits are 100 parts per million (ppm) as an 8-hour time-weighted average (TWA), 200 ppm as an acceptable ceiling concentration, and 300 ppm as an acceptable maximum peak (5 minutes in any 2-hour period) above the acceptable ceiling concentration for an 8-hour shift.[17] OSHA should be given an opportunity to consider whether a lower workplace standard would be appropriate. Otherwise, if EPA were to go forward with regulation under TSCA, there would be a potential for conflicting and overlapping regulation. OSHA's existing limits would remain in place, regardless of EPA's action, and OSHA's enforcement of its own standards is mandatory (subject to prosecutorial discretion). OSHA may not, however, enforce an EPA regulation under the general duty clause of the Occupational Safety and Health Act, even if the EPA regulation afforded greater protection, as long as an OSHA standard on the same substance is in effect.

It is also significant that EPA is not authorized to establish ambient concentration limits under TSCA § 6.[18] EPA thus cannot limit employee exposure directly, but could only do so indirectly, *e.g.*, by controlling the amount of substance used in a product or prohibiting

---

[16] Memorandum to Lee M. Thomas from Gerald H. Yamada, June 7, 1985, p. 2.

[17] 29 CFR § 1910.1000 Table Z-2. HSIA members recommend compliance with Threshold Limit Values (TLVs) published by the American Conference of Governmental Industrial Hygienists (ACGIH). For TCE, the current TLVs are 10 ppm as an 8-hour TWA and 25 ppm as a Short Term Exposure Limit.

[18] H. Rep. No. 1341, 94th Cong., 2d Sess. 34 (1976), *reprinted in* Legislative History at 441.

a particular use of the substance under § 6. This is potentially much more burdensome economically than ambient standards, which permit each employer subject to the standards to achieve the necessary reduction in exposure in the most cost-effective manner. Yet Executive Order 13563 requires agencies to achieve their objectives by using the least costly regulatory alternative.[19]

In light of the foregoing, considerations of avoiding unnecessary duplication and utilizing established expertise weigh in favor of invoking the Administrator's referral authority under TSCA § 9(a) even if EPA were to proceed under TSCA. If EPA were to identify a category of exposure deemed to present a risk that is unreasonable, these considerations indicate that referral under § 9(a) would be the appropriate course.[20] It is clear from Section 9(a) that TSCA is to be used only when other statutes fail to provide a remedy for unreasonable risks. Representative James Broyhill of North Carolina indicated that "it was the intent of the conferees that the Toxic Substance Act not be used, when another act is sufficient to regulate a particular risk."[21] EPA applied this statutory directive in determining that the risk from 4,4' methylenedianiline (MDA) could be prevented or reduced to a significant extent under the Occupational Safety and Health Act, and referring the matter for action by OSHA.[22]

---

[19] Improving Regulation and Regulatory Review, 76 Fed. Reg. 3821-3823 (January 21, 2011). In pertinent part, E.O. 13563 states:

"This order is supplemental to and reaffirms the principles, structures, and definitions governing contemporary regulatory review that were established in Executive Order 12866 of September 30, 1993. As stated in that Executive Order and to the extent permitted by law, each agency must, among other things: (1) propose or adopt a regulation only upon a reasoned determination that its benefits justify its costs (recognizing that some benefits and costs are difficult to quantify); (2) tailor its regulations to impose the least burden on society, consistent with obtaining regulatory objectives, taking into account, among other things, and to the extent practicable, the costs of cumulative regulations; (3) select, in choosing among alternative regulatory approaches, those approaches that maximize net benefits (including potential economic, environmental, public health and safety, and other advantages; distributive impacts; and equity); (4) to the extent feasible, specify performance objectives, rather than specifying the behavior or manner of compliance that regulated entities must adopt; and (5) identify and assess available alternatives to direct regulation, including providing economic incentives to encourage the desired behavior, such as user fees or marketable permits, or providing information upon which choices can be made by the public."

[20] Section 9(a) provides that if the Administrator has reasonable basis to conclude that an unreasonable risk of injury is presented, and he determines, in his discretion, that the risk may be prevented or sufficiently reduced by action under another federal statute not administered by EPA, then the Administrator shall submit a report to that agency describing the risk. In the report, the Administrator shall request that the agency determine if the risk can be prevented or sufficiently reduced by action under the law administered by that agency; if so, the other agency is to issue an order declaring whether the risk described in the Administrator's report is presented, and is to respond to the Administrator regarding its prevention or reduction. The Administrator may set a time (of not less than 90 days) within which the response is to be made. The other agency must publish its response in the Federal Register. If the other agency decides that the risk described is not presented, or within 90 days of publication in the Federal Register initiates action to protect against the risk, EPA may not take any action under Section 6 of TSCA.

[21] 122 Cong. Rec. H11344 (Sept. 28, 1976).

[22] 50 Fed. Reg. 27674 (July 5, 1985).

2. Consumer Exposure

Regarding the assessment of home consumer use of TCE-containing products for arts and crafts, EPA action is constrained by the Federal Hazardous Substances Act, which grants jurisdiction over household products containing hazardous substances to the Consumer Product Safety Commission (CPSC). The Labeling of Hazardous Art Materials Act of 1988 added a § 23 to the Federal Hazardous Substances Act (FHSA) by requiring that all art materials be reviewed to determine the potential for causing a chronic hazard and for recommending appropriate warning labels.[23]

According to the CPSC, the term "art material" includes "any substance marketed or represented by the producer or package company as suitable for use in any phase of creation of any work of visual or graphic art of any medium," including products which are closely and intimately associated with the creation of the final work of art, such as brush cleaners, solvents, ceramic kilns, brushes, silk screens, molds or mold making material, and photo developing chemicals.[24] The six Sprayway products listed in the Work Plan assessment would seem to fall within this definition.

CPSC has confirmed that art materials containing TCE must be labeled under the FHSA:

> "[A]t least where there is evidence that the substance is an actual or potential human carcinogen . . .and where the product is intended for use in the household . . . [t]he requirements of section 2(p)(1) automatically apply to hazardous substances intended for use in the household or by children."[25]

Under the FHSA, further regulation of these materials is precluded absent a finding that this mandatory cautionary language is ineffective.

II. The Work Plan TCE Assessment is Based on Erroneous, Outdated, and Inappropriate Hazard and Exposure Assessments

HSIA's comments on the technical aspects of the Work Plan TCE assessment are enclosed.

A. Hazard Assessment

---

[23] 15 USC § 1277.

[24] *See* 16 CFR 1500.135.

[25] http://www.cpsc.gov//PageFiles/108353/309.pdf.

The Technical Comments make very clear that the derivation of hazard values ignored the reference doses/concentrations (RfDs/RfCs) in EPA's own comprehensive IRIS assessment of TCE, published in 2011, in favor of endpoints that were rejected by the EPA authors of that assessment as uncertain or inconsistent with other studies. They also detail how the PBPK model relied upon is inappropriate for the estimation of hazard values for developmental toxicity, and makes other important points.

B. Exposure Assessment

The Technical Comments contain a detailed critique of the methodology used to obtain exposure estimates. EPA relied on reported annual emissions data from two national databases (TRI and NEI) with little attention given to the reliability or relevance of those data to the evaluation of worker exposure. Although neither of these databases contains measured workplace air concentration data for TCE, the reported annual emissions data were manipulated to generate a gram/minute estimate of TCE releases into workplace air. As exposure is such a critical component of any risk assessment, it is unfortunate that the Agency was unable to use air concentrations that reflect actual receptor exposures. Without reliable exposure information, one can have little confidence in the estimation of worker risk.

Perhaps the most telling point in the Technical Comments is the conclusion that the exposures EPA estimates from degreasing operations are similar to those measured in the late 1970s. Such exposure levels are simply not possible today in light of two generations of degreasing NESHAP controls and the ACGIH TLV of 10 ppm as an 8-hour TWA, with which the manufacturers recommend compliance. There is no basis for EPA to assume that TCE is being used throughout the United States in violation of these requirements/ recommendations.

Moreover, an exposure assessment of vapor degreasing conducted by EPA some ten years ago reaches quite different conclusions as to workplace exposure for a different solvent used in vapor degreasing. In support of a proposed determination that nPB would be acceptable as an alternative to methyl chloroform in vapor degreasing, EPA proposed to adopt 25 ppm as an acceptable exposure limit (AEL), in the absence of an OSHA workplace limit for nPB. In this regard, EPA concluded that exposure data from vapor degreasing operations indicated a range of exposure levels from 2 to 24 ppm as an 8-hour TLV.[26] EPA also properly referred to the ACGIH TLVs as establishing industry practice regarding workplace exposure levels.

III. Conclusion

Further development of a Work Plan assessment for TCE in small degreasers and a handful of art materials seems ill-advised, in light of the substantial regulation of TCE

[26] 68 Fed. Reg. 33284, 33288 (June 3, 2003). EPA stated "EPA defers to OSHA in regulating workplace safety. The recommended AEL in today's proposal is an interim measure in the absence of an OSHA PEL. Thus any PEL that OSHA sets would supersede EPA's recommended AEL." *Id.* at 33300.

emissions already in place and the statutory directive that those regulations ensure an "ample margin of safety to protect public health." This clear statutory mandate stands in sharp contrast to TSCA, which indeed requires the Administrator first to look to other authorities available to EPA and to refer any workplace or consumer concerns to OSHA and CPSC, respectively. Should the risk assessment be completed, the issues noted in the enclosed Technical Comments must be given careful consideration.

Respectfully submitted,

Faye Graul /WCN

Faye Graul
Executive Director

Enclosure

# TECHNICAL COMMENTS

## GENERAL COMMENTS

The Halogenated Solvents Industry Alliance, Inc. (HSIA) is pleased to provide technical comments on the TSCA Work Plan Risk Assessment (RA) for trichloroethylene (TCE, CAS No 79-01-6) released as an External Draft by the U.S. Environmental Protection Agency (USEPA) on January 9, 2013. The draft RA includes exposure and risk estimates for two general scenarios, including (1) operators and bystanders for open-top vapor degreasers in small industrial /commercial facilities and (2) consumers using TCE-containing products in a home setting.

For open-top degreasers, USEPA estimated exposures in two steps: (1) estimation of emissions from its Toxic Release Inventory (TRI) and National Emissions Inventory (NEI) database, and (2) use of the near-field far-field (NFFF) industrial hygiene exposure model.

For consumers (as well as non-users in the same household), USEPA estimated exposures using its E-FAST Consumer Exposure Model (CEM), a two-zone indoor model that estimates the evaporation rates of surface applied products based on vapor pressure and molecular weight.

In its 2000 Science Policy Council Handbook on Risk Characterization[1], USEPA states that "*[w]hile the Policy calls for TCCR [Transparency, Clarity, Consistency and Reasonableness] in the risk characterization, the principles of TCCR need to be fully applied throughout every aspect of the risk assessment process.*" HSIA is concerned that the RA for TCE (and for the other four chemicals) has not adhered to the principles of TCCR. For example, it is difficult to have confidence in the process used to estimate TCE emissions and subsequent worker exposure when viewed in terms of the principles of TCCR. As will be discussed in the specific comments to follow, USEPA relied on reported annual emissions data from two national databases (TRI and NEI) with little attention given to the reliability or relevance of those data to the evaluation of worker exposure. Although neither of these databases contains measured workplace air concentration data for TCE, the reported annual emissions data were manipulated to generate a gram/minute estimate of TCE releases into workplace air. As exposure is such a critical component of any RA, it is unfortunate that the agency was unable to find/generate air concentrations that reflect actual receptor exposures. Without reliable exposure information, one can have little confidence in the estimation of worker risk.

HSIA has examined the draft RAs for TCE and DCM and is also concerned that the approaches used by the agency have not resulted in the level of consistency endorsed by the principles of TCCR. Without going into specifics, HSIA would recommend that the various contractors

[1] USEPA, 2000, Science Policy Council: Risk Characterization, Office of Science Policy, Washington, DC [EPA100-B-00-002].

involved in generating these assessments be encouraged to use a consistent approach to their estimation of emission and exposure levels, their selection of reasonable exposure scenarios and their interpretation of available dose-response data.

By using worst-case or high-end assumptions that will tend to overestimate risks, USEPA has, in fact, conducted a screening level assessment for TCE. Although HSIA is very concerned that, even at a screening level, there is a lack of reasonableness in the agency approach, a greater concern is that the results of this RA will be used as justification for some regulatory action rather than, at most, as an indication that a more-realistic assessment of TCE's risks is needed.

The studies used to estimate the hazard values for reproductive, neurological, renal and developmental effects either provided only suggestive evidence of adverse effects, introduced a high level of uncertainty into the assessment, or the findings were not supported by other well designed studies. In addition, based on the limitations noted for these studies by both the USEPA and the USEPA SAB, the kidney should not have been considered as an endpoint in the development of MOEs.

The acute hazard values (HECs), derived using the PBPK models, are daily averages computed for a lifetime continuous exposure. As such, they were incorrectly compared in the RA to a single average daily exposure derived for the worker and consumer. The appropriate exposure estimates for the development of acute MOEs should have been the lifetime daily average exposure for the worker and consumer. This incorrect comparison would result in an under-prediction of the MOE.

The use of the PBPK model to estimate HECs for the developmental studies is inappropriate because the PBPK model does not simulate the physiological changes during pregnancy. Physiological and metabolic changes during pregnancy can have a major impact on the estimation of exposures that may be associated with effects and, therefore, on the estimation of acceptable levels of exposure to TCE.

A single benchmark MOE of 30 should not be applied in the determination of TCE exposure concentrations that may be of concern for the degreaser and the consumer. MOE benchmark values depend on the endpoint, the population being evaluated and other factors associated with uncertainty. The development of a MOE should be specific to the uncertainty in the data relied upon for the estimation of a hazard value.

Specific technical comments on the draft RA for TCE are provided in the following sections.

## SPECIFIC COMMENTS

**Note: Unless specifically cited in a footnote, references can be found in the draft TSCA RA**

### I. ESTIMATION OF TCE EMISSIONS FROM SMALL DEGREASERS

**Comment 1.**

The overall methodology used to estimate TCE emissions for small commercial degreasing units is complex and convoluted. USEPA makes use of three separate emissions databases, including the 2008 NEI and the 2008 and 2010 TRI. It is never made clear why all three of the databases need to considered. It would helpful to the reader for USEPA to clearly state its assumptions, the strengths and weaknesses of the databases, and a clear explanation of the process used to estimate current emissions for the source category.

**Comment 2.**

EPA appears to assume that all TCE emissions in the U.S. are associated with 78 industries. The industries were identified through the North American Industry Classification System (NAICS). While industries on this list may use degreasing, there could be other uses of TCE in these facilities.

**Comment 3.**

Table 3-2 is labeled "The Number of TCE-Emitting Emission Points and Corresponding Total Annual Air Emissions of TCE as Reported in the 2008 NEI." We read this to be the total emissions of TCE reported in the NEI, regardless of source. If it is meant to mean only for solvent degreasing, then the table heading should be made clearer.

We downloaded the file "Facility-Level by Pollutant" at USEPA's 2008 NEI website. The total TCE emissions were 4,088,000 lb across 2378 facilities, which are close, but slightly less, than the total provided by USEPA in Table 3-2 of 4,340,000 lb[2]. Later in the discussion there is a reference made to only including emissions from facilities from one of 78 North American Industry Classification Scheme (NAICS) codes. When we only include the 78 NAICS codes, the emissions in the "Facility-Level by Pollutant" are reduced to 2,734,000 lb across 373 facilities. It is not clear where USEPA is getting the 186 TCE point sources and 1,779 nonpoint sources. It is possible that some of the non-point sources are not in the facility file, but it seems that some of them must be since there are more facilities with the 78 NCAIS codes than the 186 quoted by USEPA.

[2] The USEPA file had a significant flaw which required an additional processing step to utilize it. It is a comma-delimited file, but there were extra commas in some of the fields, resulting in problems when loading it to Access. A SAS script was developed to correct the problem.

**Comment 4.**

USEPA estimates that the ratio of TCE totals in the NEI and the TRI, which is used in a future calculation, is 1.7. This apparently comes from comparing the total NEI emissions of 4,340,000 lbs (Table 3-2) and the total TRI emissions of 2,550,000 lbs (Table 3-3), where the ratio is indeed 1.7. However, given the importance of this value in the calculation, further clarification on how the NEI number was derived (see above) would be helpful.

**Comment 5.**

The RA does not include any discussion of the implications of the Halogenated Solvent Cleaning National Emission Standard for Hazardous Air Pollutants (NESHAP), which limits emissions for open-top degreasers. The NESHAP limits emissions from batch vapor solvent cleaning machines (i.e., open-top degreasers used by small commercial manufacturing facilities) to 150 kilograms per square meter (of the open face) per month. When emissions exceed the limit, the NESHAP proscribes a series of control options. The potential impact of the NESHAP on emission estimates needs to be addressed in the assessment.

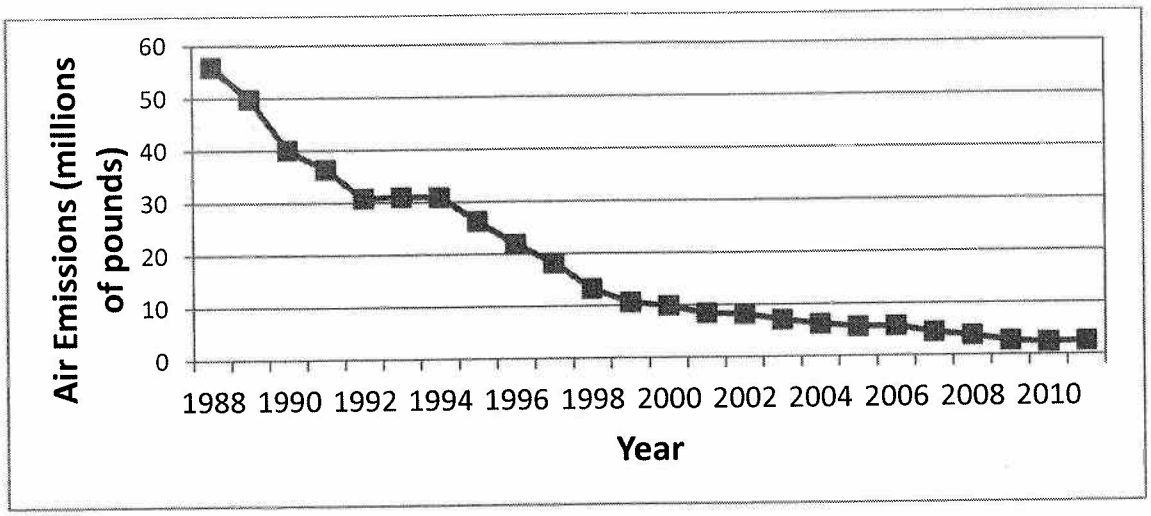
## II. Estimation of Occupational Exposure to TCE from Degreaser Use

**Comment 6.**

There appears to be a serious flaw in USEPA's use of TRI and NEI data to estimate worker exposure to TCE. Although both of these databases contain annual air emissions release data, neither provides information on ambient air concentrations at any on-site location. In the current RA, USEPA has made the assumption that reported annual emissions data for TCE can be directly converted into estimates of TCE emission fluxes into the breathing zones of on-site workers. The RA presents a stepwise progression of calculations and assumptions starting with NEI and TRI data and ending with an estimated TCE emission rate into workplace air of 16.73 grams/minute (Table 3-7). That emission rate is then used to model inhalation exposure for a hypothetical worker (appendix D). USEPA should provide additional justification for this approach (i.e., that all reported TCE emissions end up in the breathing zones of workers) as it appears to be inappropriately conservative and unreasonable.

**Comment 7.**

USEPA cites a survey conducted by NIOSH from 1981 to 1983 as stating that there were 401,000 workers employed at 23,225 plants sites potentially exposed to TCE in the United States. This estimate includes both workers directly involved in vapor degreasing and bystanders that may be exposed. However, TCE emissions have dropped substantially since the 1980s. According to the TRI, TCE emissions in 1988 were 56 million lb, but dropped to 2.6 million lb by 2011. The figure below shows the downward trend from 1988 to 2011.




Referencing the values from the 1981 to 1983 without any qualification is misleading. The actual exposed population today is likely much smaller. In Table 3-8, USEPA cites smaller figures of 7,415 for the exposed population using degreasers and 17,796 for the bystander population. There does not appear to be any explanation for these values.

**Comment 8.**

USEPA appears to estimate exposure for a 2 hour period, assuming a 2 hour use of the degreaser. However, it reports 8-hour time-weighted average (TWA) exposures. From attempting to reproduce the calculation, it appears that USEPA simply divided by four to derive its values (i.e., assuming zero exposure for 6 hours). This assumption is reasonable, but USEPA needs to explain that it made the assumption in the text.

**Comment 9.**

Using the near-field far-field model, USEPA estimates TCE concentrations in the near-field (i.e., exposure for the operator) of 17 ppm (typical case) and 63 ppm (worst-case) for conditions without local exhaust ventilation (LEV). When there is LEV, the near-field exposure was estimated at 2 ppm (typical case) and 6 ppm (worst-case). USEPA provides no indication on the relative prevalence of LEV, which may leave the reader to wonder whether the 17-63 ppm values are more typical or the 2-6 ppm values are more typical.

**Comment 10.**

USEPA assumes that small industrial/commercial degreasers operate for 2 hours per day and for 260 days per year. The basis for this assumption is a draft USEPA internal memo from 2001. It is referenced as "USEPA (2001a). Draft generic scenario – use of vapor degreasers. U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Chemical Engineering Branch." As the 2-hour assumption is one of the most critical assumptions in the assessment, its derivation should be fully described.

**Comment 11.**

The OSHA Permissible Exposure Limit (PEL) is 100 ppm for an 8-hour time-weighted average exposure. It is the operative exposure limit that these facilities must meet. The PEL is only mentioned in the risk assessment once, and that reference is in a footnote. As the estimated air concentrations meet the OSHA PEL, but USEPA finds risks at much lower levels with its alternative methods, it is important to mention in the assessment that the estimated time-weighted average concentrations meet the relevant occupational exposure standard for the facilities.

**Comment 12.**

The free surface area (FSA) value in Table D-1 is listed as 180 $ft^2$. However, following equation (5), the FSA should be 340 $ft^2$. It appears that USEPA actually used 340 $ft^2$ in the calculations, but mistakenly listed the value as 180 $ft^2$ in the document.

**Comment 13.**

Although the Shipman and Whim survey was conducted with measurement data from the 1970s, there is not another recent measurement survey that can be used. While the Shipman and Whim data are within the range of the levels estimated by USEPA, industrial hygiene standards have significantly improved in the last 30-40 years decreasing confidence in the applicability of those data.

## III. Estimation of Exposures From Consumer Use of TCE-Containing Products

**Comment 14.**

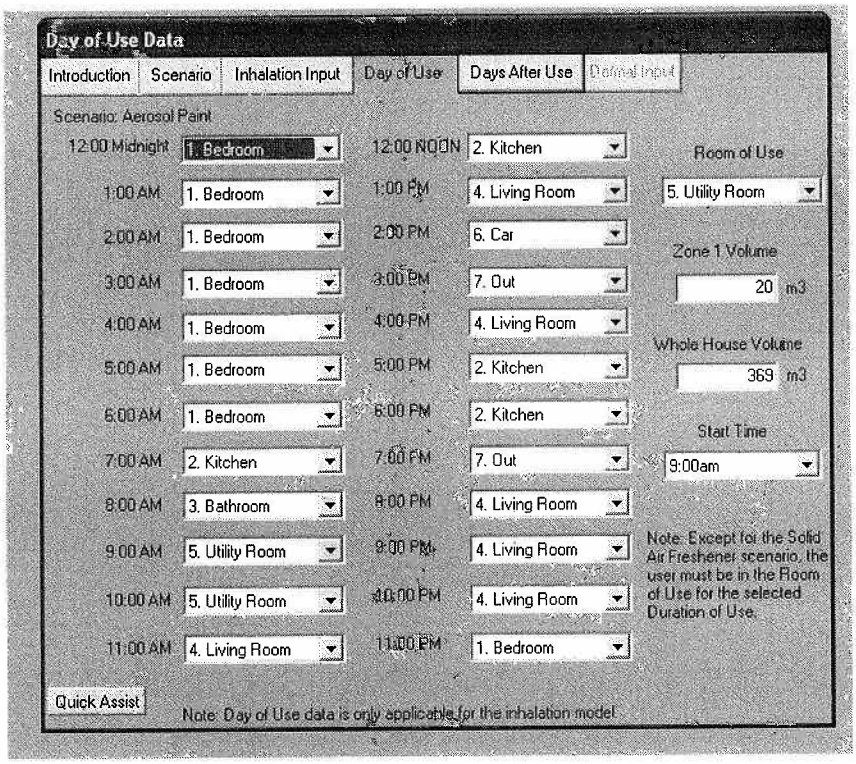
Table 3-9 lists the products containing TCE that may be used in households. There are only six products listed, and they are all from the same manufacturer, Sprayway. A review of the Sprayway website found that there is no longer a Sprayway 205 Film Cleaner listed. This should be reflected in Table 3-9.

**Comment 15.**

The E-FAST/CEM model does not provide a time-weighted average concentration over 24 hours, which is needed to compare to the toxicity levels USEPA derived. The first equation in Appendix E is for the "potential acute dose rate ($ADR_{pot}$)." However, it includes terms for the frequency of product use per year and years of product usage. These terms are not appropriate for an acute dose, which should only consider the hours of exposure in a day. The equation also includes a value for the duration of an event. This is unclear because an event would normally be for the duration of product usage, but E-FAST/CEM calculates the duration of exposure as including both during product usage and the remaining hours of the day when one is exposed to the residual vapor in the home after the event.

The E-FAST/CEM model estimates the exposure during the event, models the transport of the gas within the house and the loss through ventilation since the event, and then assumes, on an hourly basis, that the resident moves around within the house or leaves it all together. The daily average exposure is estimated as the sum of the exposures for each of the hours in the day.

The default E-FAST/CEM scenario for the movement of the resident is shown below from a screen capture of the model. The application occurs in a "utility room" at 9:00 am. The resident stays in the utility room for an hour before moving out of the house. Notably, between 3:00-4:00 pm and 7:00-8:00 pm the resident is out of the house and not being exposed.




After presenting the first equation, USEPA states that by "Rearranging and simplifying this equation" they derive another equation that is "*an approximation* for $C_{air}$" (italics theirs). The rearranging and simplification does not make any sense because they end up dropping several terms without explanation, including *FQ* (frequency of product use, events per year), *DEv* (duration of event, hour/event), and *ED* (exposure duration, years of product usage). As noted above, these terms were not appropriate for an acute exposure scenario anyway, but it is very confusing how USEPA goes from the first to the second equation.

The second equation is as follows:

$$C_{air} \approx \frac{ADR_{pot} \times BW}{InhR \times 24}$$

where $BW$ is body weight and $InhR$ is the inhalation rate. The '24' is referred to as a 24-hour averaging time. However, the $ADR_{pot}$ is already an average value over 24-hours. The '24' value is used to adjust the inhalation rate to derive the air volume over the exposure period. However, since the resident is only exposed for 22 hours (they are not home for the other 2 hours), then this value should be 22.

**Comment 16.**

The default E-FAST/CEM scenario appears to include a one hour exposure (between 2:00-3:00 pm) inside a car. The user's guide for E-FAST provides an assumed volume (2.4 $m^3$) and an air exchange rate (12 per hour). If the modeling conducted in this assessment included that exposure, it needs to be explained/discussed.

**Comment 17.**

The evaporation rate is the key variable in the E-FAST/CEM model for products applied to a surface. E-FAST/CEM uses a bi-exponential equation to estimate the evaporation rate of a chemical applied to a surface.

The evaporation rate is estimated from equation (3-42 in the E-FAST manual) that provides an estimate of the time for 90% evaporation of a "pure chemical film" based on the vapor pressure and molecular weight. The equation appears empirical (i.e., likely derived from experimental data fit to a statistical model). The units for the vapor pressure are not specified in the E-FAST manual. The citation for the equation is: "Chinn, K.S.K. 1981. A Simple Model for Predicting Chemical Agent Evaporation, Technical Report, U.S. Department of Defense, Defense Technical Information Center, Cameron Station, Alexandria, VA." The reference is unpublished and unavailable and it is not clear if it was ever peer-reviewed.

It is important to note that the TCE in the Sprayway product is not in "pure chemical" form. The implications for modeling TCE evaporation need to be discussed.

## IV. Studies and Endpoints used to Determine Hazard Values/Points of Departure

**Comment 18.**

Hazard values (HECs) based on the kidney toxicity reported in the available studies should not be used in the development of MOEs due to limitations noted in the IRIS document and by the USEPA Science Advisory Board (SAB).

- The HEC99 values based on kidney toxicity endpoints (Maltoni and Cottie 1986; Woolhiser et al. 2006) are the lowest values applied in the RA (Figure 1) and are three

fold lower than the IRIS derived RfC, which is based on oral studies. This reflects a greater reliance in the RA on kidney toxicity endpoints than in other USEPA assessments including the current IRIS document and the SAB.

- The USEPA Science Advisory Board (SAB) specifically identified limitations in reliance on kidney toxicity endpoints and recommended that USEPA not use this endpoint as the primary basis for toxicity value derivation. USEPA SAB (2011) states: "*For many of the subchronic inhalation studies (Kjellstrand et al. 1983a,b; Kjellstrand et al., 1981), issues associated with whole-body exposures make determination of dose levels more difficult. The focus of the long-term studies of TCE is primarily detection and characterization of liver tumor formation.*" Pg. 4-239

- The SAB reviewed the 2009 draft IRIS assessment of TCE and indicated that USEPA should not rely on kidney endpoints as the basis for the RfD/RfC stating: "*The Panel supported the selection of an RfC and an RfD based on multiple candidate reference values that fell within a narrow range rather than reliance on a single most sensitive critical endpoint. Although recognizing the kidney hazards of TCE, the Panel was concerned about the use of three candidate RfD/RfCs [referring to toxic nephropathy (NTP 1988); toxic nephrosis (NCI 1976); increased kidney weights (Woolhiser et al. 2006)] based on kidney effects as the primary basis for the RfD and RfC because of uncertainties regarding the relative rate of formation of toxic metabolites in humans vs. animals. The Panel recommends that EPA derive RfD/RfC values based on immunological endpoints and cardiac malformations.* "(U.S. SAB 2011)

- Ultimately, the IRIS document states the following regarding kidney endpoints: "*For kidney effects (USEPA 2011, Section 5.1.2.2), there is high confidence in the evidence for a nephrotoxic hazard from TCE. Moreover, the two lowest candidate RfDs for kidney effects (toxic nephropathy [referring to an oral NTP 1988] and increased kidney weight [referring to Woolhiser et al. (2006) here]) are both based on benchmark dose (BMD) modeling and one is derived from a chronic study. However, as discussed in USEPA (2011), Section 3.3.3.3, there remains substantial uncertainty in the PBPK model-based extrapolation of glutathione (GSH) conjugation from rodents to humans due to limitations in the available data. In addition, the candidate RfD for toxic nephropathy had greater dose-response uncertainty since the estimation of its POD involved extrapolation from high response rates (>60%). Therefore, kidney effects are considered supportive but are not used as a primary basis for the RfD.*" USEPA 2013, with bracketed text with references added.

Thus, the final IRIS document does not rely on kidney endpoints as the basis for development of a hazard value, such as the RfD or RfC, due to uncertainties in relating data from rodent to human kidney metabolism and other uncertainties in the studies.

**Comment 19.**

Chia et al. (1996) should not be relied upon for the determination of the chronic hazard value for male reproductive effects, as it provides only suggestive evidence of an adverse effect from TCE exposure and is inconsistent with the available evidence in humans.

- Table 3-21 in the RA provides MOEs of 0.3 to 0.008 associated with a HEC99 of 0.5 for reproductive effects in male workers (Chia et al. 1996). They evaluated 124 workers exposed to TCE in an electronics factory to examine the effects of TCE on spermatogenesis. The authors evaluated semen parameters including volume, sperm density, viability, motility, and morphology. The study reported a minimal decrease in normal sperm morphology in three workers exposed to TCE at levels resulting in urinary measures above the biological index level (i.e., urinary metabolite trichloroacetic acid (TCA) was greater than 100), and a decrease in sperm density relative to the low exposure group. However, sperm density even in the high exposure group was within a normal range increasing the uncertainty as to whether these effects could be considered adverse. The authors did not identify a specific NOAEL or LOAEL and instead grouped workers based on broad subjective exposure categories based on air measures for some workers and urinary measures of exposures in others. No fertility information was collected for this group. In discussing this study, USEPA (2011) notes: "*For the human study by Chia et al. (1996), as discussed above, there are uncertainties in the characterization of exposure and the adversity of the effect measured in the study.*"

- In addition, the RA hazard value based on the Chia et al. (1996) study is in direct contrast with the authors' statement regarding their study findings: "*Based on the study's findings, workers exposed to TCE at a mean environmental concentration of 29.6 ppm and a mean urine TCA concentration of 22.4 mg/g creatinine are unlikely to affect their sperm volume, density, and motility.*"

  This statement by the study authors can be contrasted with the hazard values provided in Table 3-21, which suggest the potential for reproductive effects at air concentrations greater than 0.5 ppm.

- In considering the Chia et al. (1996) study USEPA (2011) notes: "*For the human study by Chia et al. (1996), as discussed above, there are uncertainties in the characterization of exposure and the adversity of the effect measured in the study.*"

This statement indicates a lower emphasis on Chia et al. (1996) in the IRIS document, which is similar to conclusions reported by NYDOH (2006)[3] in their review of this study. Similarly, the IRIS document does not cite Chia et al. (1996). In addition, Rasmussen et al (1988)[4], another study of metal workers exposed to TCE during the use of degreasers for more than 20 hours per week reported no effect on sperm morphology or density in TCE exposed workers. The reliance of the RA on the Chia et al. (1996) study points to the need for additional weight of evidence evaluation in selecting hazard values used in the human health risk characterization.

**Comment 20.**

Reliance on findings from Arito et al. (1994) for the acute hazard value for neurotoxicity (Table 3-21) is inconsistent with the weight of evidence.

- Arito et al. (1994) investigated the brain activity and cardiac activity in male JCL-Wistar rats (5/group) exposed to TCE 8 hrs/day, 5 days/wk for 6 weeks to 0, 50, 100 or 300 ppm (0, 269, 537 or 1612 mg/m$^3$). The authors reported no changes in gross appearance or behavior in exposed rats, but in rats at all exposure levels a statistically significant, dose related decrease in the amount of time spent in wakefulness ($p < 0.01$) was reported during the 8-hour exposure period. Rats exposed to 50 ppm or higher also had statistically significant decreases in time averaged heart rates during stages of wakefulness ($p < 0.05$), slow wave sleep ($p < 0.01$) and paradoxical sleep ($p < 0.01$) during the 22-hour post exposure period. The Lowest Observed Effect Level (LOEL) in this study for decreased wakefulness during the exposure period and lower heart rates during the post exposure period was identified as 50 ppm (269 mg/m$^3$). This can be contrasted with the RA use of a HEC99 of 4.8 ppm derived by USEPA (2011) from this study assuming continuous exposure.

- In the IRIS document, Arito et al. (1994) is described as a study that has lower confidence than the other neurotoxicity studies reviewed with a more sensitive endpoint. No other study reviewed in the RA, IRIS document or the current IRIS file, notes the change in wakefulness as an endpoint. It is notable that this finding is at levels below the current OSHA standard of 100 ppm which is based on central nervous system effects, a primary target endpoint protected by the standard. For these reasons, use of this study introduces uncertainties into the assessment and is inconsistent with the weight of the evidence.

---

[3] New York Department of Health (NYDOH). (2006). *Final Report Trichloroethene Air Criteria Document.* Available at: http://www.health.ny.gov/environmental/chemicals/trichloroethene/docs/cd_tce.pdf

[4] Rasmussen et al.(1988). *A Genotoxic Study of Metal Workers Exposed to Trichloroethylene. Sperm Parameters and Chromosome Aberrations in Lymphocytes.* Int Arch Occup Environ Health. 60:419.

**Comment 21.**

Healy et al. (1982) which is relied upon in the RA for the acute hazard value for developmental toxicity for TCE has findings that are inconsistent with other large well designed inhalation studies.

- The RA relies on a hazard value derived from Healy et al. (1982) to evaluate the potential for acute developmental hazards in exposed individuals (RA Table 3-21). The six studies evaluating the potential for developmental effects following inhalation exposure to TCE (USEPA 2011) provided only limited evidence of adverse effects. Healy et al. (1982) was the only inhalation study in which adverse developmental effects were reported following TCE exposure. Healy et al. (1982) identified increased incidence of resorptions, decreased fetal body weight, and what the authors described as 'minor ossification variations" in Wistar rats exposed to a single test dose of 100 ppm TCE for 4 hours per day from day 8 to day 21 of gestation. In contrast, Schwetz et al. (1975)[5] and Hardin et al. (1981)[6] did not report any developmental effects in Sprague-Dawley rats exposed to 300 ppm or 500 ppm TCE for up to 7 hours per day during gestation. This finding may represent differences in sensitivity between strains, with Wistar rats representing a sensitive strain. The relevance to human health of these effects may be questionable.

- The use of only one exposure concentration in the Healy et al. (1982) study significantly limits the ability to interpret the shape of the dose-response curve and therefore, the potential for adverse effects at lower concentrations.

- The report of two animals dying (one on day 13 and another on day 8) in the Healy et al. (1982) study raises concerns about the methodological problems or limitations. . Healy et al. notes: "*The two rats died because of an obstruction in the air supply system leading to a trichloroethylene overdose.*"

  In considering this finding, NYDOH (2006) raised concerns about this aspect of the study stating: "*However, the authors reported that two exposed rats died due to a TCE overdose after the air supply malfunctioned. This raises concerns about the potential influence of methodological problems (excess exposure concentrations) on the study results.*"

---

[5] Schwetz B, Leong B, Gehring P. (1975). *The Effect of Maternally Inhaled Trichloroethylene, Perchloroethylene, Methyl Chloroform, and Methylene Chloride on Embryonal and Fetal Development in Mice and Rats.* Toxicol Appl Pharmacol 32: 84-96.

[6] Hardin B, Bond G, Sikov M, Andrew F, Beliles R, Niemeier R. (1981). *Testing of Selected Workplace Chemicals for Teratogenic Potential.* Scand J Work Environ Health. 7(4):66-75.

Additional concerns regarding the Healy et al. (1982) study were raised by the European Union (2004), stating: *"The number of females with total litter loss was significantly higher in the trichloroethylene exposed group (7/32 compared with 2/31 in the control group).It is, however, difficult to interpret this finding because it is possible that the authors may have described animals showing pre-implantation loss, which would have occurred before exposure commenced, and even non-pregnant animals as having total litter loss. In the exposed group foetal weight was significantly less than the control values (by about 9%) and there was an increased incidence of minor skeletal variants, such as absent or bipartite centres of ossification. However, the results of this study have been discounted because they are inconsistent with the other inhalation studies, all of which showed no evidence of developmental toxicity at higher exposure levels*".

- Two other single exposure inhalation studies (Dorfmueller et al. 1979[7]; Westergren et al. 1984)[8] provided limited evidence of developmental effects following inhalation exposure to TCE. Dorfmueller et al. (1979) reported skeletal abnormalities in offspring of Long Evans rats exposed to 1,800 ± 200 ppm, but the use of a single very high dose limits interpretation of these findings. In contrast, a large well-designed study by Carney et al. (2006) evaluated developmental toxicity in Crl:CD rats exposed by inhalation to 0, 50, 150, and 600 ppm TCE for 6 hours per day, 7 days per week, during gestational days 6-20. Offspring were examined for skeletal and visceral malformations, including heart malformations. No significant dose related increases in any malformations were found in any of the treatment groups. The NOAEL for developmental effects in this study was the highest dose of, 600 ppm and no LOAEL was determined for offspring. The authors also identified 600 ppm as a LOAEL for maternal effects based on a slight but significant reduction in maternal body weight in the 600 ppm group at gestation day 9 only, with a NOAEL of 150 ppm. No effect was seen on body weight in any other dose groups at any time point.

  Thus, reliance on data from Healy et al. (1982) is not supported by findings in other inhalation studies evaluating these endpoints. Moreover, the study by Carney et al. (2006)[9] would provide a more comprehensive basis for developmental endpoints following inhalation exposure.

---

[7] Dorfmueller M, Henne S, York R, Bornschein R, Manson J. (1979). *Evaluation of Teratogenicity and Behavioral Toxicity with Inhalation Exposure of Maternal Rats to Trichloroethylene*. Toxicology. 14:153-166.

[8] Westergren I, Kjellstrand P, Linder L, Johansson, B. (1984). *Reduction of Brain Specific Gravity in Mice Prenatally Exposed to Trichloroethylene*. Toxicol Lett. 23: 223-226.

[9] Carney, E; Thorsrud, B; Dugard, P; Zablotny, C. (2006). *Developmental Toxicity Studies in Crl:CD (SD) Rats Following Inhalation Exposure to Trichloroethylene and Perchloroethylene*. Birth Defects Res B Dev Reprod Toxicol. 77: 405-412.

**Comment 22.**

The studies and endpoints considered in the development of hazard values/PODs should not be given equal weight in the estimation of Margins of Exposure (MOEs) and an evaluation of the weight of evidence is needed in selecting endpoints for comparison.

- The RA presents a broad range of inhalation hazard values (i.e., 0.28-190 for HEC50 and 0.013-67 for HEC99) in Table 3-19 that could serve as the basis for evaluating inhalation hazards of TCE. Ultimately, the RA then selects the lowest of the inhalation HEC99 values as the hazard value for deriving MOE estimates in the risk characterization. Because some of the studies relied upon in the IRIS document were merely suggestive of a potential effect while others provided a more robust basis for establishing a causal link between TCE exposure and an adverse effect, this approach leads to an undue emphasis on studies with lower confidence and/or greater uncertainty. Ultimately, selection of the lowest HEC99 as the basis for MOE derivation leads to conclusions that are not supported by consideration of the weight of evidence.

- As shown in Table 3-17, the lowest HEC99 values are those for kidney weight relative to body weight reported by Kjellstrand et al. (1983a,b) and male reproductive effects based on short term exposure in the study by Chia et al. (1996). Neither of these studies or endpoints is used by USEPA for the RfC in the current IRIS file (USEPA 2013). The current IRIS file indicates that reproductive and kidney effects as among those caused by TCE, but does not include reproductive effects among the most sensitive endpoints and does not cite either of these studies in the summary file.

**Comment 23.**

The RA identifies unacceptable MOEs for workers at concentrations far below the current OSHA standards (Table 3-21).

- RA Table 3-21 identifies unacceptable MOE values for workers at exposure concentrations ranging from 2 to 63 ppm, all of which are well below the current OSHA standard of 100 ppm based on central nervous system effects (ATSDR 2007[10]; OSHA 2013[11]).

---

[10] ATSDR. (2007). *Trichloroethylene Toxicity What Are the U.S. Standards for Trichloroethylene Exposure?* http://www.atsdr.cdc.gov/csem/csem.asp?csem=15&po=8

[11] Occupational Safety and Health Administration (OSHA). (2013). Available at: http://www.osha.gov/dts/sltc/methods/mdt/mdt1001/1001.html

## V. USE OF PBPK MODELING TO DERIVE HAZARD VALUES/POINTS OF DEPARTURE

**Comment 24.**

The USEPA reported having low confidence in the kidney dose metrics, so HEC values derived from those dose metrics should not be used in a non-cancer evaluation.

- In addition to the problems with the kidney studies noted in the comments above there are problems associated with the use of the PBPK model to estimate the dose metrics used in deriving hazard values for the kidney. The dose metrics (ABioactDCVCBW34, AMetGSHBW34) associated with GSH metabolism were used to determine HEC values for the kidney studies and were reported to be highly uncertain in rodents with predictions of GSH conjugation and renal bioactivation of S-dichlorovinyl-L-cysteine (collectively, the 1,2- and 2,2- isomers) (DCVC) spanning >1,000-fold in mice and 100-fold in rats (USEPA 2011). In addition, although the PBPK model fit for these kidney dose-metrics was deemed to be adequate for rats and humans, "the substantial inconsistencies across studies and methods in the quantification of S-dichlorovinyl-L-glutathione (collectively, the 1,2- and 2,2- isomers) (DCVG) following TCE exposure suggest lower confidence in the accuracy of these predictions" (USEPA 2011). There also remains uncertainty in the interspecies extrapolation of GSH conjugation from rodents to humans.

**Comment 25.**

The PBPK model applied in the development of the HECs is not intended to model pregnancy or gestation and as such application of this PBPK model to estimate dose-metrics for developmental effects is inappropriate.

- The PBPK model used is not a pregnancy model nor is it a lifestage model. Physiological changes during childhood and pregnancy as well as differences in metabolism can have a major effect on the dose-metric estimation in both the mother and the fetus (Gentry et al. 2003[12], Corley et al. 2003[13]) and therefore the estimation of exposures that may be associated with effects.

- For fetal effects, since the PBPK model did not contain a fetal compartment, the maternal internal dose-metric was assumed to be the total amount of oxidative metabolism of TCE scaled by the ¾ power of body weight (TotMetabBW34) in the adult female rat.

---

[12] Gentry P, Covington T, Clewell, III H. (2003). *Evaluation of the p\Potential Impact of Pharmacokinetic Differences on Tissue Dosimetry in Offspring During Pregnancy and Lactation.*" Regul Toxicol Pharmacol. 38(1):1-16.

[13] Corley R, Mast T, Carney E, Rogers J, Daston G. (2003). *Evaluation of Physiologically Based Models of Pregnancy and Lactation for Their Application in Children's Health Risk Assessments.* Crit Review Toxicol. 33(2):137–211.

This dose-metric was used to estimate HECs associated with the reported increase in resorptions and decreases in fetal weight reported in female rats. The USEPA states that "because of the complicated fetus/neonate dosing that includes transplacental, lactational, and direct (if dosing continues postweaning) exposure, the maternal internal dose is no more accurate a surrogate than applied dose in this case" (USEPA 2011). Note that the model used an adult female not a maternal internal dose-metric as the surrogate as it is not a pregnancy model. No scientific justification was provided to support the application of this dose metric in the development of a hazard value for developmental effects.

## VI. Uncertainty and Conservatism Associated with Characterization of Risk/Hazard

**Comment 26.**

The Hazard Values/PODS used in this assessment are chronic HECs estimated from the application of a PBPK model in the IRIS document and are not appropriate for comparison to the acute daily average exposures used in the RA for the development of MOEs for the worker or the hobbyist.

- HECs derived in the IRIS document from the PBPK model are a daily average computed for continuous exposure (USEPA 2011). However the exposures considered for degreasers and hobbyists reported in the TSCA work plan is not continuous, but rather is an 8-hour time-weighted average for the worker and a 24-hour average exposure for hobbyist. In comparing these exposure estimates to the HECs, the appropriate exposure estimate for the development of an MOE would be the lifetime daily average for the worker or the hobbyist. Further adjustments would be needed to reflect the discontinuous lifetime exposure patterns (i.e., once per week for the clear protective spray or twice a month for the degreaser). Therefore the single day of exposure for the hobbyist is far larger than a continuous lifetime average exposure that should be compared to the HEC values for the development of the MOE. Using the same HEC99 values as were used in the RA, the hobbyist MOEs based on the lifetime average daily concentration would range from 39 to 516 for the user of degreaser and 360 to 1,330 for the user of clear coat. For the bystanders, the MOEs would range from 121 to 6,879 for the degreaser and from 117 to 20,472 for the clear coat.

- Use of the internal dose metrics for the development of the MOE would be more appropriate, as the application of the PBPK model in the evaluation of exposure estimates in the worker or hobbyist could take into account any nonlinearities in the pharmacokinetics of TCE in the target tissue. In the hobbyist, the elimination of TCE between exposures is critical in estimating the target tissue dose and therefore, the potential for adverse effects. The internal dose metrics reported in the IRIS document

for the animal (in the supplemental reports), should be used to compare to the internal dose metric for the human considering the exposure patterns for the occupational worker or the hobbyist. The necessary information for the hobbyist would be the exposure during usage and the elimination of TCE and its metabolites over time between usage for both the hobbyist and the bystanders.

- Based on the range of half-lives reported of Table 3-15 of the RA, it is highly likely that TCE would be completely eliminated between exposures for both the hobbyist and the bystanders, and it is also likely, that complete elimination would occur for the occupational workers over a weekend. Therefore, any estimated exposure for the worker or the hobbyist has to consider interim periods with no exposure. This makes the use of the lifetime average daily dose (LADD) from the E-FAST program the most appropriate value to compare to the hazard values (HEC99s) for calculation of a MOE as both values would be representative of the average daily exposure over a lifetime.

**Comment 27.**

The MOE benchmark of 30 was incorrectly applied to all of the MOE's calculated regardless of the study used to estimate the hazard value. A separate benchmark MOE should be used for each hazard value based on the uncertainty associated with the data set and study from which the hazard value is derived.

- As noted in the RA, MOE benchmark values depend upon the endpoint, the population being evaluated, and other factors associated with uncertainty. The development of a MOE should be specific to the uncertainty in the data relied upon for the estimation of a hazard value. Therefore, when the Hazard value is divided by the estimated exposure to derive the MOE, any MOE above the benchmark would indicate no risk of concern. (USEPA 1993). These are the same procedures used in the IRIS document of TCE when estimating uncertainty for each of the hazard values considered for the RfC. The UFs used by USEPA (2011) for the same studies considered in this assessment ranged from 3 times lower to 10 times higher than the MOE benchmark of 30.

- Those studies that would require a benchmark MOE of 30 or greater (Arito et al. 1994; Healy et al. 1982; Woolhiser et al. 2006; Chia et al. 1996) introduce a higher level of uncertainty, and as discussed in section 2.1 are not recommended for use in the development of hazard values for the RA.

MOE benchmarks should be developed for each MOE derived based on the uncertainty in the HEC99 and the study on which it is based.

**Comment 28.**

The inclusion of subchronic data in the estimation of the acute MOE (Arito et al. 1994; Kjellstrand et al. 1987) significantly decreases the confidence level for the acute MOE.

- Using studies of inappropriate duration for the estimation of the acute MOE could overestimate the potential risk and introduces a level of uncertainty that cannot be accounted for using uncertainty factors.

- USEPA (2002) recommends the use of values for risk assessment in which the known or assumed exposure duration approximates the exposure duration in the reference value definition. USEPA (2002) defines acute exposure as exposure by the oral, dermal, or inhalation route for 24 hours or less.