APRIL 1998

APPENDIX

PUBLIC COMMENT SUMMARY & RESPONSE DOCUMENT

Identification and Listing of Hazardous Wastes
Organobromine Production Wastes

(Proposed: 59 FR 24530; May 11, 1994)

Index of Public Comments

Commenter #	Commenter Name
00001	Eastman Kodak Company
00002	Monsanto Company
00003	Rollins Environmental Services, Inc.
00004	Environmental Defense Fund (EDF)
00005	Chemical Manufacturers Association (CMA)
00006	Albemarle Corporation
00007	Great Lakes Chemical Corporation

The U.S. Environmental Protection Agency (EPA) issued a proposed rulemaking (59 **FR** 24530) in which the Agency proposed to list, as hazardous wastes, solids and filter cartridges from the production of 2,4,6-tribromophenol. The Agency also proposed to add 2,4,6-tribromophenol to Appendix VIII of 40 CFR Part 261, the list of hazardous constituents established by EPA under the authority of the Resource Conservation and Recovery Act (RCRA). In addition, the Agency proposed not to list nine waste streams from the production of various brominated compounds and deferred action on the listing determination for waste solids from the production of tetrabromobisphenol-A (TBBPA).

EPA received seven comments on the proposed rulemaking. Comments were received from two members of the bromine industry; one trade association representing industrial chemical producers; two manufacturers of chemical products; one company involved in the treatment and destruction of hazardous and toxic wastes; and one environmental interest group.

OVERVIEW OF MAJOR ISSUES

Use of Quantitative Structure-Activity Relationships (QSARs)

All seven commenters expressed views on the use of QSARs in making hazardous waste determinations:

- Four commenters were opposed to the use of QSARs as the basis for a hazardous waste determination because this approach is generally used as a predictive tool and requires empirical evidence to substantiate the results. Two of these four commenters indicated that the use of QSARs established a new criterion for hazardous waste determinations, which requires the opportunity for public comment before implementing it.

- Two commenters expressed reservations regarding the use of QSARs for hazardous waste determinations, but outlined conditions (peer review, use of more than one commercial software package, structural alerts, validation of QSARs and pharmacokinetic assumptions) under which their use may be acceptable. Both commenters recommended that the Agency require peer review of the results as a standard procedure.

- One commenter supported EPA's proposal to use QSARs for listing determinations in the absence of chemical-specific toxicological data.

Adding 2,4,6-Tribromophenol to Appendix VIII

Two commenters expressed their opposition to EPA's proposal to add 2,4,6-tribromophenol (2,4,6-TBP) to Appendix VIII and simultaneously use its presence on Appendix VIII to justify listing wastes from 2,4,6-TBP production.

Deferring a Listing Determination on Wastes from Tetrabromobisphenol-A Production

Two commenters submitted or identified toxicology data on tetrabromobisphenol-A (TBBPA) and indicated that the Agency has sufficient information to support a decision not to list TBBPA.

Plausible Mismanagement Scenario for 2,4,6-tribromophenol Production Wastes

One commenter disputed the plausible mismanagement scenario used by the Agency to support the proposed listing of 2,4,6-tribromophenol production wastes (disposal in unlined Subtitle D landfills).

SUMMARY OF COMMENTER CONCERNS BY ISSUE

Issue I. Issues Regarding the Use of Quantitative Structure-Activity Relationship (QSAR) Analysis to Support Listing Determinations

I.a. Validity of QSAR Analysis in Supporting the Listing Determination for Wastes from the Production of 2,4,6-TBP

All seven commenters addressed the validity of using a quantitative structure-activity relationship (QSAR) analysis in a listing determination for wastes from the production of 2,4,6-TBP.

The Agency has seriously considered the criticisms and suggestions made by these commenters regarding the QSAR analysis. In light of the quantitative uncertainties raised and other issues, EPA has reevaluated the QSAR analysis and agrees that the available data are insufficient to support such an analysis. However, the significant similarities between 2,4,6-TBP and 2,4,6-TCP show that 2,4,6-TCP is an appropriate surrogate for 2,4,6-TBP, because: 2,4,6-TBP and 2,4,6-TCP are both tri-halogenated phenols with substitutions at the same positions; the physical and chemical properties, such as the octanol-water partition coefficient and the water solubility, of the compounds are similar; available genetic toxicity data show consistent results for 2,4,6-TCP and 2,4,6-TBP; and examples in the literature (e.g. 1,2-dibromoethane and 1,2-dichloroethane) support the idea that if a chlorinated compound is a carcinogen,

the compound formed by substitution of a chlorine with bromine will still be a carcinogen, leading to the prediction that 2,4,6-TBP is likely to be a carcinogen based on the known carcinogenicity of 2,4,6-TCP. Because this issue is central to the rulemaking, each commenter's remarks will be addressed separately.

Commenter # 7

The commenter stated that the specific QSAR analysis performed in support of EPA's proposal is not reliable because the analysis did not conform to standards normally employed for QSAR in four major ways: (1) an oversimplified QSAR analysis based on only one parameter (electronic effects) was used; (2) in comparing chlorine and bromine substitution, no attempt was made to account for the substitution of three chlorine atoms by three bromine atoms; (3) data on structurally similar compounds were not available and could not be used to validate the QSAR analysis; and (4) the carcinogenic mechanism of 2,4,6-TCP is unknown, raising questions about the appropriateness of the QSAR approach. The commenter included, as an attachment, a critical review of EPA's "Development of Provisional Human Health Reference Value for 2,4,6-Tribromophenol." Specific issues raised in this document relative to these four concerns are discussed in more detail below.

The commenter's first major argument was that a classical QSAR analysis defines biological activity in terms of electronic, steric, and hydrophobic effects, and that the Agency's analysis was incomplete in only considering electronic effects. Steric factors can influence the ability of the compound to interact with DNA or enzymes, and hydrophobicity may influence partitioning within a cell or accessibility to membrane-bound enzymes. The commenter noted that a measure of hydrophobicity (log K_{OW}) is available for both 2,4,6-TCP and 2,4,6-TBP. It may be more appropriate to use Hammet sigma values for measuring electronic effects, although the electronic similarity between bromine and chlorine means that this would not make a large difference.

The commenter noted that 2,4,6-TCP and 2,4,6-TBP differ in three halogen atoms, and no attempt was made to account for the multiple substitutions. It is not known if the multiple substituents interact in an additive, synergistic, or antagonistic manner. Since the electronic effects were evaluated on a molecular level, and the biological response is reported in terms of mg of compound, the different molecular weights of the two compounds (331 for 2,4,6-TBP and 197 for 2,4,6-TCP) should be taken into account.

In the third major point, the commenter noted that QSAR analysis is best conducted using a family of related compounds,

particularly if one uses the Hansch mathematical paradigm. In this case, toxicity data were available for only one related chemical (2,4,6-TCP), for which the mechanism of carcinogenesis is unknown. Comparison with only one other compound increases the uncertainty of the analysis.

The commenter also noted that the predictive ability and validity of the QSAR model are limited by the relatively scarce data on the mechanism of 2,4,6-TCP carcinogenicity and the metabolism and potential tumor-inducing mechanisms of 2,4,6-TBP. To illustrate the problems with making carcinogenicity predictions without mechanistic information, the commenter compared the NTP data on the carcinogenicity of other halophenols. For example, 2,4,6-TCP caused dose-related increases in lymphomas or leukemias in male, but not female rats, while pentachlorophenol caused increased incidence of vascular tumors (hemangiosarcomas or hemangiomas) in female mice but not male mice, and pheochromocytomas in male and female mice. (Liver tumors observed with both compounds may have been due to contaminating dioxins.) The reason for the difference in target between these two related compounds is unknown. Furthermore, the related compound 2,4-dichlorophenol is not carcinogenic in rats or mice. In other examples, the commenter noted differences in species specificity and target organ for carcinogenicity of trihalomethanes with varying levels of chlorine and bromine substitution, and noted that methyl chloride causes kidney tumors in mice, but methyl bromide was not carcinogenic in mice in an NTP study (1992).[1]

With regard to the mechanism of 2,4,6-TCP carcinogenicity, the commenter stated that it is not clear whether 2,4,6-TCP acts via a genotoxic or nongenotoxic mechanism. Although the metabolic pathway for 2,4,6-TCP supports a genotoxic mechanism, the commenter stated that 2,4,6-TCP yields equivocal to weakly positive results in genotoxicity assays, and has been proposed to cause cancer by suppressing the immune system.

EPA Response:

The Agency agrees with the comment that the QSAR analysis does not account for a number of important factors. Some of these factors, such as data on a number of related compounds and information on the mechanisms of carcinogenicity, are not accounted for due to the lack of available data. While the commenter did provide some suggestions as to how the calculations of relative electronic effects might be done differently and how

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[1]NTP 1992. Toxicology and Carcinogenesis Studies of Methyl Bromide (CAS No. 74-83-9) in $B6C3F_1$ mice (Inhalation Studies). U.S. National Toxicology Program, Research Triangle Park, North Carolina. NTP-TR No. 385; NIH/PUB 92-2840.

hydrophobic effects might be considered, the Agency notes that the commenter did not suggest an alternative complete quantitative analysis, but rather implied that the data were too limited to develop a supportable QSAR.

Therefore, the Agency is no longer relying on the proposed calculation based on relative electronic effects to adjust the 2,4,6-TCP slope factor in order to develop a slope factor for 2,4,6-TBP. However, a SAR does show that 2,4,6-TCP is an appropriate surrogate for 2,4,6-TBP, leading to the prediction that 2,4,6-TBP is likely to be a carcinogen. Although the qualitative SAR predicts 2,4,6-TBP to be a carcinogen, there is a lack of data to perform a quantitative extrapolation for the 2,4,6-TBP cancer slope factor, and therefore, the slope factor for 2,4,6-TCP is being used as a default for 2,4,6-TBP.

However, the Agency believes that one change suggested by the commenter has merit. As the commenter noted, the biological effects of 2,4,6-TCP and 2,4,6-TBP should be compared for similar molar quantities of the compounds. The Agency agrees that the cancer slope factor for 2,4,6-TBP should be adjusted to account for the difference in molecular weight of the compounds (i.e., assuming a 1:1 relationship on a molar basis, rather than on a weight basis). Such an adjustment was also recommended by one of the peer reviewers. Because a bromine atom is heavier than a chlorine atom, one gram of 2,4,6-TBP has fewer molecules in it than does a gram of 2,4,6-TCP, and therefore a gram of 2,4,6-TBP is less potent than a gram of 2,4,6-TCP. Since chemically-induced cancer results from binding of molecules to DNA or to another molecule in the body,[2] a compound's cancer potency is related most directly to the number of molecules administered (rather than the weight alone). Thus, the cancer slope factor (CSF) in $(mg/kg/day)^{-1}$, for 2,4,6-TCP is multiplied by the ratio of the molecular weights of 2,4,6-TCP and 2,4,6-TBP:

$$1.1\times10^{-2}\ (mg/kg/day)^{-1} \times \frac{MW\ TCP\ (197)}{MW\ TBP\ (331)} = 6.5\times10^{-3}\ (mg/kg/day)^{-1}$$

This slope factor may also be applied in a risk analysis, as described in the preamble to the proposed rule. Briefly, the risk analysis was conducted using TCLP leaching data showing concentrations of 760 and 16 mg/L of 2,4,6-TBP in leachate extracts from off-specification product and from filter cartridges, respectively. Using the conservative assumption of a dilution and attenuation factor of 100 to simulate the dilution of the leachate between an unlined landfill and a hypothetical

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[2]Williams, G.M. and J.H. Weisburger. 1991. Chemical carcinogenesis. In: Amdur, M.O., J. Doull, and C.D. Klaassen. Casarett and Doull's Toxicology: The Basic Science of Poisons, 4th ed. New York, NY: Pergamon Press. pp. 127-200.

receptor well, the estimated 2,4,6-TBP concentrations in groundwater are 7.6 and 0.16 mg/L, respectively. Assuming that people drinking from this hypothetical well drink 1.4 L/d of contaminated water every day for a 30-year period, the revised estimated individual risk from exposure to 2,4,6-TBP in groundwater would be 4.2x10-4 and 1.2x10-5 for the off-specification product and the filter cartridges, respectively. These individual risk levels are still above levels of concern.

As part of the support for a SAR analysis, this discussion summarizes the available data related to the carcinogenic activity of 2,4,6-TCP and the genotoxicity of 2,4,6-TCP and 2,4,6-TBP:

2,4,6-TCP Data Summary

The primary study of 2,4,6-TCP carcinogenicity was conducted with male and female F344 rats and B6C3F1 mice.[3] Leukemias were significantly increased in male rats, and there were significant increases in hepatocellular hyperplasia, adenomas, and carcinomas in mice of both sexes. Based on these data, 2,4,6-TCP is classified as a probable human carcinogen (B2), and a slope factor of 1.1E-2 per mg/(kg/day) was calculated based on leukemia in male rats.[4] Due to the possibility of dioxin contamination of the 2,4,6-TCP sample used by NCI, the liver tumors were not used in the estimate of carcinogenic risk. Chlorinated dibenzodioxins do not induce leukemia.

The data regarding the potential genotoxicity of 2,4,6-TCP are equivocal. Positive results were reported for gene mutations in mouse lymphoma cells[5] and in V79 cells.[6] A ***Bacillus subtilis***

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[3]NCI. 1979. Bioassay of 2,4,6-trichlorophenol for possible carcinogenicity. National Cancer Institute, Bethesda, Maryland. NCI-CG-TR-155; DHEW/PUB/NIH-79-1711. As cited in Docket #F-94-OBLP-S0013.

[4]U.S. Environmental Protection Agency (EPA). 1994. Integrated Risk Information Service (IRIS). On-line database. Office of Research and Development (ORD). Cincinnati, OH. As cited in Docket #F-94-OBLP-S0013.

[5]McGregor, D.B., A. Brown, P. Cattanach, I. Edwards, D. McBride, C. Riach, and W.J. Caspary. 1988. Responses of the LS178Y tk+/tk- mouse lymphoma cell forward mutation assay: III. 72 coded chemicals. Environ Mol Mutagen 12: 85-154. As cited in Docket #F-94-OBLP-S0013.

[6]Hattula, M.L. and J. Knuutinen. 1985. Mutagenesis of mammalian cells in culture by chlorophenols, chlorocatechols and chloroguaiacols. Chemosphere 14: 1617-1625. As cited in Docket

DNA damage assay was also reportedly positive, but no quantitative data were reported.[7] All of these tests were only conducted in the absence of exogenous metabolic activation. The McGregor et al. (1988) and the Kinae et al. (1981) studies are limited because they did not provide purity information.

Negative results were reported in a well-conducted *Salmonella typhimurium* reverse mutation assay conducted with a battery of tester strains in the absence of S9 activation and in the presence of rat and hamster S9[8]. The protocol used by Haworth et al. (1983) is similar to that conducted with 2,4,6-TBP and is described in further detail below. 2,4,6-TCP was also negative in another *Salmonella* assay conducted in the presence and absence of rat S9[9], and in assays for sister chromatid exchanges and chromosome aberrations in Chinese hamster ovary cells.[10] Thus, it appears that 2,4,6-TCP is positive in mammalian cell forward gene mutation assays, and negative in the *S. typhimurium* reverse mutation assay and in mammalian cell cytogenetics assays. Based on the available data, it is unclear why the results of the gene mutation assays in bacterial and mammalian cells appear to be inconsistent, and no definitive conclusion can be drawn regarding the mutagenic potential of 2,4,6-TCP.

Summary of 2,4,6-TBP Data

#F-94-OBLP-S0013.

[7]Kinae, N., T. Hashizume, T. Makita, I. Tomita, I. Kimura, and H. Kanamori. 1981. Studies of the toxicity of pulp and paper mill effluents. 1. Mutagenicity of the sediment samples derived from kraft paper mills. Water Res 15: 17-24. As cited in Docket #F-94-OBLP-S0013.

[8]Haworth, S., T. Lawlor, K. Mortelmans, W. Speck, and E. Zeiger. 1983. Salmonella mutagenicity test result for 250 chemicals. Environ Mutagen Suppl 1: 3-142. As cited in Docket #F-94-OBLP-S0013.

[9]Rasanen, L., M.L. Hattula, and A.U. Arstila. 1977. The mutagenicity of MCPA and its soil metabolites, chlorinated phenols, catechols and some widely used slimicides in Finland. Bull. Environ. Contam. Toxicol. 18:565-571.

[10]Galloway, S.M., M.J. Armstrong, C. Rueben, S. Colman, B. Brown, C. Cannon, A.D. Bloom, F. Nakamura, M. Ahmed, S. Duk, J. Rimpo, B.H. Margolin, M.A. Resnick, B. Anderson, and E. Zeiger. 1987. Chromosome aberrations and sister chromatid exchanges in Chinese hamster ovary cells: Evaluations of 108 chemicals. Environ Mol Mutagen 10: 1-175. As cited in Docket #F-94-OBLP-S0013.

Genetic toxicity data for 2,4,6-TBP are limited to a negative result in one well-conducted assay for reverse mutations in *Salmonella typhimurium* strains TA1535, TA1537, TA98, and TA100 using the preincubation protocol.[11] 2,4,6-TBP was tested up to a cytotoxic concentration in the absence of exogenous metabolic activation, and in the presence of Aroclor-induced liver S9 derived from rats and hamsters. While these data indicate that 2,4,6-TBP is not genotoxic, a definitive statement regarding the compound's genotoxicity cannot be made on the basis of a single assay. Typically, results from an *in vitro* mammalian gene mutation assay and a cytogenetics assay (e.g., micronucleus assay) would be necessary to confirm these results.

Comparison of 2,4,6-TCP and 2,4,6-TBP

Although the existing data on 2,4,6-TBP are very limited, they are consistent with the data for 2,4,6-TCP. 2,4,6-TCP was carcinogenic even though it was negative in the *Salmonella* assay. Therefore, the negative results in the *Salmonella* assay conducted with 2,4,6-TBP under similar conditions are not evidence against its carcinogenicity.

Although additional mutagenicity data were not available for 2,4,6-TBP, the finding that *in vitro* hepatotoxicity is comparable for 2,4,6-TCP and 2,4,6-TBP when their concentration in the growth medium is expressed on a molar basis[12] supports the comparison of CSF on a molar basis, as discussed above. Furthermore, as noted by one of the peer reviewers of the SAR analysis, comparison of *in vivo* and *in vitro* developmental toxicity of p-chlorophenol and p-bromophenol shows that the brominated compound is consistently somewhat less toxic than the chlorinated compound when doses are expressed on a molar basis[13],[14]. Calculations by the peer reviewer found the slight

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[11]Zeiger, E., B. Anderson, S. Haworth, T. Lawlor, K. Mortelmans, and W. Speck. 1987. Salmonella mutagenicity tests. III. Results from the testing of 225 chemicals. Environ. Mutagen. 9 (Suppl. 9) 1-109. As cited in Docket #F-94-OBLP-S0013.

[12]Murayama J.-I., M. Ishiwata, M. Fukui, H. Utsumi, and A. Hamada. 1990. Comparative acute cytotoxicities of 37 xenobiotics detected in drinking water to rat hepatocyte primary culture. Eisei Kagaku 36(4): 267-276.

[13]Kavlock, R.J. 1990. Structure-activity relationships in the developmental toxicity of substituted phenols: In vivo effects. Teratology 41:43-59.

[14]Oglesby, L.A., M.T. Ebron-McCoy, T.R. Logsdon, F. Copeland, P.E. Beyer, and R.J. Kavlock. 1992. In vitro embryotoxicity of a

difference in toxicity between the chlorinated and brominated analogues not to be statistically significant. Although the endpoint evaluated by these papers (reproductive/developmental toxicity) is different from the endpoint of concern for this rulemaking (carcinogenicity), the results on relative potency are likely to be applicable to both endpoints, since toxicity in both cases is likely to be attributable to a toxic metabolite. In addition, toxic potency is roughly correlated with cancer potency. Thus, these studies show that a bromine/chlorine substitution on a halogenated phenol resulted in comparable when doses were expressed on a molar basis, supporting the adjustment of the CSF for 2,4,6-TCP to account for the different molecular weight of 2,4,6-TBP.

Comparison of the Structures of 2,4,6-TCP and 2,4,6-TBP

In the periodic table, the halogen group includes fluorine, chlorine, bromine, and iodine, which react in chemically similar ways. Bromine and chlorine are the most similar halogens; fluorine binds to carbon much more strongly than do chlorine or bromine, while the reactivity of iodine is also influenced by its larger size. When a chemical group, such as a halogen atom replaces a hydrogen atom on an organic molecule (carbon-containing), the molecule is said to be substituted, or in the case of a halogen atom, halogenated. The more similar two substituted molecules are in terms of the type, number, and position of the substitutions, the more closely related the molecules are likely to be in terms of chemical and toxicological properties. This is because both the type and location of the substitution contribute to the electronic, steric (spatial), and other attributes of the molecule.

As can be seen in Figure 1, 2,4,6-TCP and 2,4,6-TBP are both halogenated phenols with substitutions of the closely related halogens chlorine and bromine at the 2-, 4-, and 6- positions. 2,4,6-TCP is thus a close structural analog to 2,4,6-TBP. Furthermore, a key measure of hydrophobicity, the log of the octanol-water partition coefficient (log K_{ow}), is similar for these two chemicals; the values of log K_{ow} are 4.23 for 2,4,6-TBP and 3.69 for 2,4,6-TCP.

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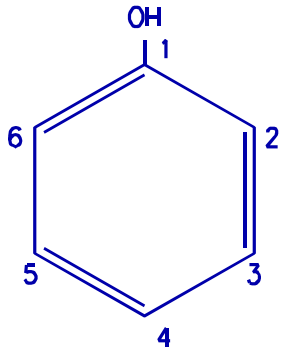
series of para-substituted phenols: Structure, activity, and correlation with in vivo data. Teratology 45:11-33.



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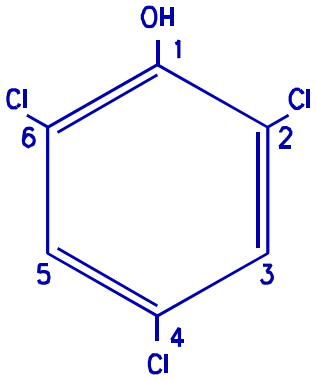
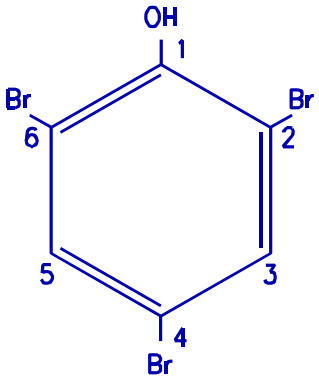


2,4,6 – TCP



2,4,6 – TBP

Conclusion

The first step in any structure-activity analysis is the identification of structurally-related compounds. The validity of a SAR analysis is related to the degree of similarity of the candidate (the compound for which adequate toxicity information are lacking) and the surrogate (the chemical used as the basis for the analysis), and the amount of information available on how any differences between the two chemicals affects their activity. Should sufficient data be available on both the candidate and surrogate chemical(s), it may then be possible to perform a QSAR.

The validity of using 2,4,6-TCP as a appropriate surrogate for 2,4,6-TBP rests on four factors. One, 2,4,6-TCP is a close structural analogue to 2,4,6-TBP as described above. Two, the physical properties of the compounds are also similar, with similar octanol/water partition coefficients and solubility in the same solvents. Three, the available genetic toxicity data also show consistent results for 2,4,6-TCP and 2,4,6-TBP, although data for the latter compound are quite limited. Finally, examples in the literature support the idea that if a chlorinated compound is a carcinogen, the compound formed by substitution of a chlorine with bromine will still be a carcinogen. Based on this line of reasoning, the Agency believes that a SAR is appropriate in this case, and the very strong chemical similarities between 2,4,6-TCP and 2,4,6-TBP justify the use of the cancer slope factor for 2,4,6-TCP as a default value for 2,4,6-TBP, with the molar adjustment described above.

Response to Specific Issues Raised by Commenter #7

This section addresses each of the specific issues raised by the commenter. Because the QSAR has been replaced by an SAR, the commenter's specific concerns regarding quantitative

extrapolation aspects of the QSAR are not addressed here. Similarly, detailed information about the carcinogenic mechanism of 2,4,6-TCP is not addressed since it is not used for a QSAR. EPA agrees with the commenter that further mechanistic information would be necessary if a quantitative comparison were being used. Although QSAR analysis is typically conducted using a group of chemicals and statistical methods, it may also be possible to use QSAR analysis for pairs of chemicals that are extremely similar chemically and physically. Both the chemical and physical properties of the "surrogate" and the "candidate" are taken into account in making any predictions. The Agency believes that comparison with a single compound is acceptable for a SAR analysis in cases such as this, when the structural similarities between the two compounds are so strong. Comparisons across multiple chemicals are needed for larger structural differences.

One commenter believed that the analysis should have compared 2,4,6-TBP to an entire class of compounds rather than to a single chemical compound. The Agency believes that comparison with a single compound is acceptable for SAR analysis in cases such as this, when the structural similarities between the two compounds are so strong. Comparisons across multiple chemicals are needed for larger structural differences. This commenter also stated that the QSAR/SAR analysis disregarded documented differences between the carcinogenicity of chlorinated and brominated analogues. For example, the commenter noted differences in the species and tissue (e.g., kidney or liver) in which tumors develop following administration of trihalomethanes ranging from chloroform ($CHCl_3$) to bromoform ($CHBr_3$). The compounds in the series represent a series of replacements of chlorine atoms by bromine atoms (i.e., 3 chlorines; 2 chlorines and 1 bromine; etc.).

EPA believes that this example may be relevant to a quantitative analysis, but does not diminish the validity of the qualitative SAR analysis used here. A quantitative analysis would involve extrapolation of the cancer slope factor from the surrogate to the candidate. All available information on the chemical and physical properties of the compounds, as well as on their metabolism, distribution in the body, and mechanism of action should be incorporated into such an analysis. Because the trihalomethanes are such small molecules, the three halogen atoms constitute a relatively large percentage of the total volume of the molecule. Thus, substituting bromine for chlorine would be expected to have a larger effect than the same substitution in the large 2,4,6-TCP/2,4,6-TBP molecules. This difference in size may explain the observed differences in target organs among the trihalomethanes. Nonetheless, differences in target organs are not of concern for the 2,4,6-TBP qualitative SAR, where a direct quantitative extrapolation was not made. The important point is

that all four trihalomethanes are carcinogens, regardless of the target tissue.

Regarding the issue of the appropriateness of SAR analyses based on analogues in which a chlorine is substituted by a bromine, the Agency notes that there are additional well-studied examples in which substitution of a chlorine by a bromine has resulted in retention of carcinogenic activity. For example, both 1,2-dichloroethane and 1,2-dibromoethane (ethylene dibromide) are multi-target carcinogens, causing tumors in the lung, the forestomach, the circulatory system, and the mammary gland. As noted above, a commenter cited differences in cancer target for trihalomethanes. The Agency recognizes that examples of bromine/chlorine substitutions in which both the chlorinated analogue and the brominated analogue are carcinogens are not sufficient to show that such substitutions in general will not change a carcinogen into a noncarcinogen. However, based on these examples and in light of the carcinogenicity of 2,4,6-TCP in animal testing, it is plausible to conclude that 2,4,6-TBP is a potential carcinogen.

There are other examples in which the bromine and chlorine analogs were both carcinogenic. For example, both PCBs[15] and PBBs[16],[17] are liver carcinogens. Based on the strong chemical similarity between these compounds (i.e., both are polyhalogenated biphenyls with chlorine or bromine substitutions) and the fact that they have the same carcinogenicity target organ, it is likely that they have similar mechanisms of carcinogenesis. Similarly, both 1,2-dichloroethane[18] and 1,2-

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[15]Reviewed in: ATSDR. 1992. Toxicological Profile for Polychlorinated Biphenyls. Agency for Toxic Substances and Disease Registry. U.S. Department of Health and Human Services.

[16]NTP. 1983. Carcinogenesis Study of Polybrominated Biphenyl Mixture (Firemaster FF-1) (CAS No. 67774-32-7) in F344/N Rats and $B6C3F_1$ Mice (Gavage Studies). U.S. National Toxicology Program, Research Triangle Park, North Carolina. NTP-TR No. 244; NIH/PUB 83-1800.

[17]Kimbrough, R.D., D.F. Groce, M.P. Korver, and V.W. Burse. 1981. Induction of liver tumors in female Sherman strain rats by polybrominated biphenyls. J National Cancer Institute 66: 535-542.

[18]NCI. 1978. Bioassay of 1,2-dichloroethane for possible carcinogenicity. National Cancer Institute, Bethesda, Maryland. NCI-CG-TR No. 66; DHEW/PUB/NIH-78-1361.

dibromoethane[19] (ethylene dibromide) are multi-target carcinogens, causing tumors in the lung, the forestomach, the circulatory system, and the mammary gland. It is interesting to note that, in this case, the carcinogenic potency is higher for the brominated compound. The commenter stated that methyl bromide is a counter-example, since it was not carcinogenic in mice in an NTP (1992) study, whereas methyl chloride has been reported to cause kidney tumors in mice by the inhalation route. However, squamous cell carcinomas of the forestomach were reported in rats gavaged with methyl bromide for 90 days.[20] Although this was a preliminary study, the observed tumors suggest that methyl bromide may be carcinogenic in a 2-year bioassay via the oral route. Based on these examples, it is plausible to conclude that 2,4,6-TBP is a potential carcinogen, in light of the carcinogenicity of 2,4,6-TCP in animal testing.

The Agency agrees with the commenter that the mechanism of carcinogenicity for 2,4,6-TCP is not known. However, the available data on potential genotoxic and nongenotoxic mechanisms of carcinogenicity for 2,4,6-TCP do not suggest that 2,4,6-TBP would differ markedly from 2,4,6-TCP.

Commenter # 1

The commenter questioned the use of QSAR analysis as a basis for a hazardous waste listing because QSAR methodology can be subject to predictive errors. The commenter indicated that "in the absence of pharmacokinetic data, errors in predicting the potential toxicological properties of untested compounds based on chemical structure alone can occur. These errors occur even for chemicals that are structurally very similar." The commenter illustrated the point by providing five cases in which predictive errors occurred based on SAR analysis performed with structurally similar chemicals (benzene/toluene; 1-/2-naphthylamine; methanol/ethanol; n-hexane/n-heptane; MnBK/MIBK).

Furthermore, the methodology should be subjected to peer review and thorough validation before using it as a basis for hazardous waste listing determinations.

EPA Response:

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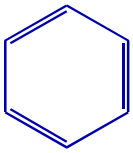
[19]NTP. 1982. Carcinogenesis bioassay of 1,2-dibromoethane for possible carcinogenicity F344 rats and B6C3F$_1$ mice. U.S. National Toxicology Program, Research Triangle Park, North Carolina. NTP-TR No. 210; NIH/PUB 87-1766.

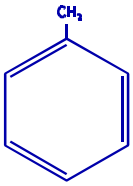
[20]Danse, L.H.J.C., F.L. van Velsen, and C.A. van der Heijden. 1984. Methylbromide: Carcinogenic effects in the rat forestomach. Toxicology and Applied Pharmacology 72: 262-271.

The Agency recognizes the limitations to SAR analysis and agrees that the choice of surrogate needs to carefully take into account the degree of similarity between the chemical of interest (the "candidate") and the surrogate from which predictions are made. Structural similarities are not sufficient; the surrogate should also resemble the candidate chemically and physically (e.g., octanol/water partition coefficient, solubility, electronic properties). The structural and chemical similarities between 2,4,6-TCP and 2,4,6-TBP are greater than those in the pairs cited by the commenter. The pairs cited by the commenter differ in having/not having a substituent group (benzene/ toluene), or are positional isomers (1-/2-naphthylamine), homologues (methanol/ethanol, n-hexane/n-heptane), or structural isomers (MnBK/MIBK). These differences in the cited pairs, as shown in Figure 2, have greater potential to change the chemical properties of the molecule. Toluene is converted (metabolized) to compounds with low toxicity (e.g., benzoic acid) that are easily dissolved in water and removed from the body. Benzene's structure does not allow the use of this pathway for removing the chemical. Instead, benzene is converted and removed via a pathway that creates cancer-producing compounds.[21] Similarly, the position of the amino group in 1-/2-naphthylamine has a marked effect on the molecule's ability to be metabolically activated.

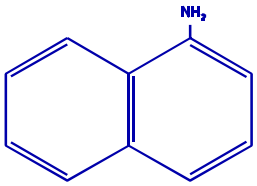
[21]Andrews, L.S. and R. Snyder. 1991. Toxic effects of solvents and vapors. In: Amdur, M.O., J. Doull, and C.D. Klaassen. Casarett and Doull's Toxicology: The Basic Science of Poisons, 4th ed. New York, NY: Pergamon Press. pp. 681-722.



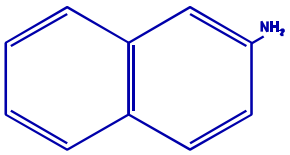
Benzene



Toluene

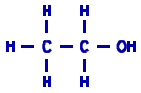


1-Naphthylamine



2-Naphthylamine

Methanol

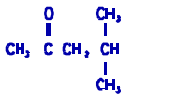


Ethanol

n-Hexane

n-Heptane

Methyl n-butyl ketone
(MnBK)



methyl isobutyl ketone
(MIBK)

EPA has subjected its analysis to both internal Agency review and external peer review. The peer review comments have been placed in the docket.

Commenter # 2

The use of QSARs to predict biological activity is a complex and multivariable problem, and no one predictive model approaches the level of prediction appropriate for regulatory decision-making. Many variables must be considered when predicting biological activity based on structure, including hydrophobicity, electronic effects, and steric properties. The Agency should use more than one commercial software package for predictive purposes so as to compare and understand the possible differences between

models. The results of the predictive models should be reviewed by a group of senior Agency scientists and then by external peer reviewers.

A hazardous waste determination based on SARs should be given less weight than a listing based on actual data. The Agency should simplify the delisting procedures for wastes that were listed based on QSAR analysis such that if actual data are provided to refute the QSAR conclusions, the Agency could delist the waste. This scenario should also lead to delisting of the constituent from Appendix VIII.

EPA Response:

In light of the suggestions by this and other commenters, the Agency has decided that the strong chemical and toxicological similarities between 2,4,6-TCP and 2,4,6-TBP are sufficient to predict that 2,4,6-TBP is a potential human carcinogen. EPA is therefore adding the constituent to Appendix VIII. Since the Agency does not have sufficient information to quantitatively adjust the 2,4,6-TCP CSF, EPA is using the 2,4,6-TCP value directly as a default value for 2,4,6-TBP. Because 2,4,6-TCP is such a close analogue of 2,4,6-TBP, EPA did not find it necessary to use any of the existing SAR/QSAR software.

As stated above, the SAR analysis has undergone both internal and external peer review. The comments submitted in response to the Proposed Rule have also been taken into account in the preparation of the SAR analysis.

In terms of weighing toxicity values based on SARs differently than data-based values, the Agency agrees with the commenter and notes that, where chemical-specific toxicological data are available, an evaluation based on these data would supersede the use of a SAR analysis. If appropriate toxicity data for 2,4,6-TBP become available at some point in the future, and these data refute or modify the results of the Agency's SAR analysis for this rulemaking, EPA will take the new information under advisement regarding whether to revisit the listing investigation for these wastes, including the listing of 2,4,6-TBP on Appendix VIII.

Commenter # 3

QSARs provide the best approach for estimating the toxicity of structurally similar compounds, but they have significant limitations. Results are extrapolated from animal studies to humans and from in vitro studies to in vivo, which leaves significant room for error. In addition, some structurally similar compounds are shown to have diverse properties. Based on such limitations, QSAR alone should not be used to make hazardous waste determinations.

EPA Response:

The Agency is aware of the limitations inherent in the QSAR approach. The decision to use a qualitative approach based on the chemical similarities of 2,4,6-TBP and 2,4,6-TCP and the known carcinogenicity of 2,4,6-TCP instead of a quantitative approach was based partially on these limitations, as well as on the recognition that the data are insufficient in this case for a quantitative extrapolation. Where chemical-specific toxicological data are available, an evaluation based on these data would supersede the use of an SAR analysis. If toxicity data for 2,4,6-TBP become available at some point in the future, and these data refute or modify the results of the Agency's SAR analysis for this rulemaking, EPA will take the new information under advisement regarding whether it is appropriate at that time to revisit the listing investigation for these wastes.

EPA notes that the proposal to list 2,4,6-TBP-containing residuals as hazardous wastes was not based solely on the SAR analysis for 2,4,6-TBP. Other factors were included in the risk assessment, including the concentrations of 2,4,6-TBP in the waste, the volumes of waste generated, the mobility of the toxic constituent, management practices and plausible mismanagement scenarios, and potential receptors.

Commenter # 4

The Agency's use of QSARs in this context is appropriate and the inference that 2,4,6-TBP and 2,4,6-TCP are similar is a scientifically well-justified presumption. The Agency should use QSARs to support RCRA listing determinations under the same general conditions that prompt the use of SARs and QSARs under TSCA, specifically: 1) the lack of chemical- or isomer-specific toxicologic data; 2) an understanding of the toxicity of related structures and the quantitative relationship between structural changes and biological activity; and perhaps 3) the availability of evidence indicating a plausible basis for similar mechanisms among similar structures.

The commenter was not aware of a way, other than QSARs, to characterize the risk potential of wastestreams for which there is a lack of toxicity data on the sole or primary constituent in the wastestream. The commenter noted that SARs enable the Agency to take appropriate action to control chemicals that are structurally related to known toxicants in the absence of chemical-specific toxicity data.

EPA Response:

The Agency appreciates the commenter's support for the QSAR analysis conducted for this rulemaking. EPA agrees with the conditions cited by the commenter; in the future, a listing

determination could be based on a QSAR analysis. Despite insufficient data on the mode of carcinogenic action of 2,4,6-TCP and related compounds, the Agency has decided that a SAR analysis is appropriate based on the similarities of 2,4,6-TBP and 2,4,6-TCP in this case to predict that 2,4,6-TBP is a carcinogen.

Commenter # 5

The use of QSAR analyses to support listing decisions is invalid and lacks statutory and regulatory authority under RCRA. The RCRA regulations do not include, as a factor for EPA to consider, "the availability of data on similar substances or compounds," unlike several other regulatory regimes (e.g., Clean Water Act programs). QSARs serve as one means of determining whether additional toxicity testing should be conducted or required for a constituent. They do not provide definitive toxicity data on which regulatory decisions should be based.

In response to EPA's question concerning other ways to characterize the risk potential of wastestreams for which there is a lack of toxicity data on the sole primary constituent in the wastestream, the commenter suggested the Agency evaluate whether these wastestreams have caused adverse health or environmental effects. If historical evidence does not suggest such adverse effects, the logical conclusion is that the waste is not hazardous.

EPA Response:

EPA is aware of the limitations of the QSAR approach for this chemical. In cases where direct chemical-specific toxicity data are lacking, however, and where appropriate analog chemicals exist to allow valid comparisons to be drawn, SAR analysis represents a scientifically valid approach for assessing the potential toxicity of a chemical. For these reasons, EPA regards SARs as "scientific studies."

In evaluating the risk potential of wastestreams, it is important to differentiate between toxicity and exposure. A chemical may be highly toxic without having caused adverse health or environmental effects, because the chemical was properly managed and no human or environmental exposure occurred. However, this does *not* mean that the waste itself is not hazardous, or that it would not cause adverse effects if it were improperly handled (i.e., "plausible mismanagement"). The Agency used the SAR analysis to assess the potential toxicity of 2,4,6-TBP, and evaluated exposure based on a plausible mismanagement scenario (disposal in an unlined Subtitle D facility).

Commenter # 6

Due to inconsistencies inherent in the approach, SAR results must be used cautiously and with discretion in making hazardous waste listing determinations. In particular, the commenter noted that brominated compounds often differ toxicologically from the corresponding chlorinated compounds. As an example of a situation in which a QSAR analysis can lead to inaccurate results, the commenter noted the structural similarities between decabromodiphenyl oxide (DBDPO) and polychlorinated and polybrominated biphenyls (PCBs and PBBs), which might have suggested that they have similar properties. However, the commenter presented data documenting differences between DBDPO and PCBs in physical properties, metabolism, and resulting toxicity. For example, PCBs are much more soluble than DBDPO in organic solvents. Similarly, PCBs bioaccumulate, whereas DBDPO is metabolized and cleared at an appreciable rate, with little bioaccumulation potential.

EPA Response:

EPA agrees that SAR/QSAR results should be used with discretion, and that physical and chemical characteristics should be evaluated in addition to structural similarities. 2,4,6-TCP and 2,4,6-TBP are much more chemically similar than are DBDPO and PCBs; 2,4,6-TCP and 2,4,6-TBP differ only in the halogen substituent on the phenol ring. By contrast, DBDPO contains an ether linkage that is lacking in PCBs. As the commenter mentions, the ether linkage of DBDPO affects its physical properties. For example, the commenter states that DBDPO is only soluble in cottonseed oil up to 600 ppm, while Aroclor 1242, a sample PCB, can be mixed with cotton-seed oil in a 1:1 ratio. By contrast, both 2,4,6-TCP and 2,4,6-TBP are soluble in alcohol and ether. This strengthens the argument that 2,4,6-TCP is an appropriate surrogate for 2,4,6-TBP. Furthermore, some of the differences between DBDPO and PCBs/PBBs may be related to the fact that PCBs/PBBs are heterogenous mixtures of different congeners. Even among PCBs and PBBs, there are differences in toxicity, depending on whether the congener is planar and can bind to the aryl hydrocarbon (Ah) receptor.

I.b. The Use of QSARs Represents a Departure from Agency Policy

Commenters # 1, 7

The use of QSAR methodology in this rulemaking is a departure from previous Agency policy. EPA has established a new precedent in using QSAR analysis as the basis for a hazardous waste listing determination. The commenters recognized that EPA has used QSAR analysis in the past as a screening mechanism to determine whether additional toxicity testing should be

conducted. However, the Agency has never used QSAR analysis as the basis for a hazardous waste listing determination. Furthermore, the Agency has used SAR evaluations in the past to estimate the potential for a constituent to produce a given toxicological response, not to develop quantitative estimates of potency. The commenters also stated that this process is a departure from previous EPA practices. Thus, the use of QSARs in making a hazardous waste determination establishes a new criterion for identifying a hazardous waste. The commenters objected to the implementation of this new criterion without providing the opportunity for public comment.

EPA Response:

The Agency agrees that this listing represents a new element in the Agency's policy in that this is the first listing to use SAR as a basis for listing a wastestream as hazardous. The Agency was specifically exploring the establishment of a precedent in using other than Agency-verified toxicity data when it issued the organobromines listing proposal. EPA takes the position that, depending on the strength of the evidence, SAR-based listings are appropriate to use for the hazardous waste listings program because SAR is an available tool that can solve a problem the Agency will regularly face: making risk-based regulatory decisions (such as listing determinations) in the absence of Agency-verified or provisional health benchmarks (e.g., reference dose [RfD], reference concentration [RfC], or cancer slope factor [CSF]).

SAR is one approach that was designed to specifically address this problem. The use of SAR is particularly compelling in the organobromines listing determination. The constituent has an extremely close structural analog (2,4,6-TCP) for which direct toxicity data are available. Because of this, the Agency specifically solicited comment on the policy implications of the use of QSAR in the organobromines proposal.

In light of the public comments, the Agency has decided to use a SAR analysis in this rulemaking. No specific comments were received that invalidate the use of SAR in this listing determination. No direct toxicological data on 2,4,6-TBP were submitted to modify or replace the QSAR-based toxicity values used in this listing and, importantly, no alternative to SAR was provided. Therefore, EPA and has concluded that SAR is currently a viable approach for making a human health impact determination for the wastestream of concern. The strong technical argument involved, that the principal toxicant of concern, 2,4,6-TBP, is a highly similar analog of 2,4,6- TCP, makes this listing the appropriate place to use SAR.

In this analysis, the Agency is using the SAR to establish the potential for 2,4,6-TBP to produce a carcinogenic response.

Based on this SAR analysis, EPA has concluded that 2,4,6-TBP is a potential human carcinogen. The analysis follows Agency procedures previously used under Section 5 of TSCA. Using SAR-generated estimates is an approach that allows the Agency to list chemicals that can be anticipated to cause toxic effects, but for which no direct test data are available. Given the lack of test data for 2,4,6-TBP, the Agency believes that an analysis of the structure-activity relationships between 2,4,6-TBP and its nearest congeneric neighbor, 2,4,6-TCP, affords the most scientifically defensible basis for predicting the toxic effects of 2,4,6-TBP. As described in further detail in other places in this document, the evidence in this case rests on four points: 2 4,6-TCP is a close structural analogue to 2,4,6-TBP; the physical and chemical properties of the compounds are similar; the available genetic toxicity data also show consistent results for 2,4,6-TCP and 2,4,6-TBP; and examples in the literature support the idea that if a chlorinated compound is a carcinogen, the compound formed by substitution of a chlorine with bromine will still be a carcinogen.

Regarding the issue of notice and comment, the public and the regulated community had ample opportunity to review and comment on the Agency's proposed criteria for listing hazardous wastes (December 18, 1978; 43 FR 58946). The Agency considered all these comments and used some of the information received therein to revise the listing criteria from proposal to final rule (May 19, 1980; 45 FR 33106). Furthermore, for the reasons discussed above, EPA regards both SAR and QSAR analyses as valid "scientific studies" (40 CFR 261.11(a)(3), as promulgated on May 19, 1980), upon which Appendix VIII listings may be based.

I.c. Use of QSARs to Support Listing Constituents on Appendix VIII

Commenters # 5, 7

Quantitative structure-activity relationships (QSARs) cannot support listing a substance on Appendix VIII or listing a waste as hazardous. Regarding Appendix VIII listings, 40 CFR 261.11(a)(3) states that EPA may list substances on Appendix VIII "only if they have been shown in scientific studies to have toxic, carcinogenic, mutagenic, or teratogenic effects on humans or other life forms." QSARs are not equivalent to empirical evidence and do not represent "scientific studies." Therefore, QSARs do not meet the requirement of the regulation to base Appendix VIII listings on the results of scientific studies. For the same reason, specifically, the absence of scientific data showing the constituent to have toxic or other adverse effects, QSARs may not be used to justify listing a constituent on Appendix VIII.

EPA Response:

Although EPA usually uses controlled animal studies or epidemiological studies of human exposure as the basis for its regulations, 40 CFR 261.11(a)(3) does not preclude the use of other types of scientific studies. For example, some sophisticated statistical analyses might be considered a scientific study that is one step removed from a laboratory study. EPA has used meta-analyses, a statistical tool for combining the data from multiple studies, in several risk assessments, including the risk assessment for environmental tobacco smoke.[22] Similarly, the scientific principles on which SAR analyses are based were developed from many years of chemical review and analysis and, more recently, toxicity studies on related compounds. For example, the SAR analysis for 2,4,6-TBP rests not only on the chemical similarity of 2,4,6-TBP and 2,4,6-TCP, but also on toxicity studies showing structurally similar brominated and chlorinated compounds to be related in terms of whether they are carcinogens.

EPA recognizes that the SAR analysis for 2,4,6-TBP does not *directly* "show" that 2,4,6-TBP is a carcinogen as it would in an animal feeding laboratory study, which is the usual way EPA shows toxic effects in its regulations. However, 40 CFR 260.11(a)(3) does not specify that the experimental laboratory or epidemiological studies must directly implicate the precise chemical. In this case, the finding that 2,4,6-TCP is carcinogenic in animal studies, together with the SAR analysis demonstrating the close chemical similarity of 2,4,6-TCP and 2,4,6-TBP, indirectly shows that 2,4,6-TBP is expected to be carcinogenic.

I.d. Types of Data Appropriate to Support or Refute QSAR or SAR Predictions

Commenters # 2, 5, 7

QSARs have been useful in predicting the activity of a structure based on information on a series of structurally related compounds. However, this approach should be used in conjunction with empirical confirmation. Furthermore, empirical data must be considered superior to QSAR predictions.

Commenter # 3

The Agency should consider other information in addition to QSAR, such as worker exposure and health data, and studies of

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[22]USEPA. 1992. Respiratory health effects of passive smoking: Lung cancer and other disorders. ORD, USEPA, Washington DC, 20460. EPA/600/6-90/006F.

residents living in close proximity to facilities producing these chemicals.

Commenter # 4

For purposes of this rulemaking, the Agency does not require additional data to support the use of QSAR. Specific toxicological data are required to refute the QSAR approach and these are currently lacking.

EPA Response:

EPA appreciates the commenters' response to its request for information on the types of data appropriate for supporting or refuting QSAR/SAR results. As stated above, EPA recognizes that empirical data, when available, supersede predictions based on QSAR/SAR analyses. If toxicity data for 2,4,6-TBP become available at some point in the future and these data refute the results of the SAR analysis used in this rulemaking, EPA will take the information under advisement regarding whether to revisit listing 2,4,6-TBP as a hazardous constituent. Data on health effects in exposed workers or in residents living near facilities producing the chemicals were not available. As with other risk assessment data, if such data become available, they will be considered in EPA's overall analysis.

Issue II. Addition of 2,4,6-TBP to Appendix VIII

Commenters # 5, 7

Two commenters stated that EPA cannot simultaneously propose to list a constituent on Appendix VIII and propose to list a waste as hazardous because it contains that constituent. The commenters contended that this approach is illegal and violates the procedures established in 40 CFR 261.11(a)(3), which requires the Agency to list a constituent on Appendix VIII based on the results of "scientific studies" demonstrating that the substance has toxic or other adverse effects. Following the listing of a constituent on Appendix VIII, the Agency may use that constituent to justify a hazardous waste listing. The commenter indicated that EPA clarified this procedure of first listing a constituent on Appendix VIII and then citing the Appendix VIII listing as a basis for a hazardous waste listing in 51 FR 28296 (August 6, 1986). EPA's approach in this case violates the Agency's own procedures and does not allow the public an opportunity to comment on the proposed Appendix VIII listing before that constituent is used as the basis to list certain wastes.

EPA Response:

EPA disagrees with the commenters and finds no basis in the regulations to support the contention that the Agency cannot simultaneously propose to add a constituent to Appendix VIII and propose to list a waste as hazardous because it contains the constituent. Furthermore, this practice is long-standing. Other simultaneous listings are found at 59 FR 24530 (May 11, 1994), 59 FR 458 (Jan. 4, 1994), 54 FR 50968 (Dec. 11, 1989), and 51 FR 6537 (Feb. 25, 1986).

The plain language of 40 CFR 261.11(a)(3) provides that a waste shall be listed if it contains an Appendix VIII constituent and the Administrator concludes it poses a hazard after considering the eleven factors cited in the regulations. Neither the August 1986 preamble text to which the commenter makes reference nor the regulatory language of § 261.11(a)(3) suggests that a sequential determination is required. In the August 1986 rule, the Agency stated that the significance of placing a constituent on Appendix VIII includes the fact that the constituent can then be cited as a basis for listing toxic wastes (51 FR 28296). Nothing in this statement suggests that an Appendix VIII listing must be proposed for public comment and finalized separately from an associated hazardous waste listing. The public was given ample opportunity to comment on all relevant issues concerning both the proposed hazardous waste listing and the Appendix VIII listing on which it was based. The scientific basis for adding 2,4,6-TBP to Appendix VIII is justified under Issue Ia. above.

Issue III. Other Issues Regarding the Listing Determination for Waste Solids from the Production of 2,4,6-TBP

Commenter # 4

The commenter strongly supported the listing of waste solids from the production of 2,4,6-TBP. The extremely high concentrations of 2,4,6-TBP found in floor sweepings independently warrant listing these solids as hazardous wastes, in light of the potential for environmental and occupational exposure.

EPA Response:

EPA agrees with the commenter that the high concentration of the toxic chemical, 2,4,6-TBP, is a major concern. However, EPA did not consider this factor in isolation, but also considered the mobility of the waste an equally important factor. The risk assessment predicts TBP leaching from unlined landfills to receptor drinking-water wells at concentrations far above health-based levels of concern.

Commenter # 7

One commenter disputed the plausible mismanagement scenario used by the Agency to support the proposed listing of 2,4,6-TBP production wastes (disposal in unlined Subtitle D landfills), and noted that the proposed rule contained errors in the description of 2,4,6-TBP waste quantities and management practices. The commenter stated that it was the sole generator of TBP wastes covered by the proposed listing and that all of its solid streams containing TBP are shipped to a Subtitle C disposal facility. The generator subsequently submitted information showing that it disposed of these wastes in Subtitle C facilities for many years. (See letter to Anthony Carrell, EPA, from Stephen M. Wallace, Great Lakes Chemical Corporation, dated April 23, 1997). The commenter noted that the only waste from 2,4,6-TBP production disposed in a Subtitle D landfill consists of 10 tons of empty soda ash bags that do not contain any TBP. The commenter stated that the other combined waste solids from TBP production (floor sweepings, off-specification product and spent carbon from filters) total approximately 34 tons annually. The commenter argued that EPA's selection of unlined a Subtitle D landfill as a plausible mismanagement scenario is erroneous and, therefore, EPA's risk analysis significantly overstates the risk.

The assumptions used by EPA in its risk assessment do not reflect observed conditions. In the proposal, EPA stated that sampling at a landfill where organobromine production wastes had been disposed for years showed the absence of any brominated materials in the leachate. Actual leachate sampling results refute the assumptions about 2,4,6-TBP concentrations in landfill leachate used in EPA's risk analysis. EPA is not justified in basing a listing decision on such a risk assessment.

EPA Response:

Based on the information provided by the commenter, EPA agrees that the quantity of waste solids from 2,4,6-TBP production that contain 2,4,6-TBP levels of concern should be approximately 34 tons, and should not include the 10 tons of empty bags. The Agency also acknowledges that the generator apparently has a long record of disposing the wastes with high 2,4,6-TBP content in a lined Subtitle C hazardous waste landfill. However, EPA continues to believe that the waste solids from production of 2,4,6-TBP should be listed as hazardous. EPA considered several critical factors in deciding to list this wastestream.

First, as shown by the SAR analysis, the waste contains a highly toxic chemical, 2,4,6-TBP, which may present significant carcinogenic risk even at low concentrations. This chemical was also found to be present in the wastes of concern at extremely

high concentrations. EPA's analytical data show levels up to 40% (equivalent to 400,000 ppm) in the waste solids. Thus, while the volume of wastes generated (approximately 34 tons) may not be very large, the extremely high levels of 2,4,6-TBP render this waste highly toxic. (Note that the amount of 2,4,6-TBP is so high, that the wastes could be diluted a hundred fold to 2400 tons and still contain 4000 ppm of the this toxic chemical).

Furthermore, EPA's data show that 2,4,6-TBP is relatively mobile and will leach out of the waste at high concentrations. In the proposal, EPA used the TCLP method to estimate the potential concentration of waste constituents that could be in leachate generated from disposal of the waste in a landfill, and found up to 760 mg/L of 2,4,6-TBP in the TCLP leachate. This level is 76,000 times the health-based limit of 0.01 mg/L that corresponds to the 10^{-6} cancer risk level for ingestion. The proposed rule estimated risks of 7×10^{-4} from migration to groundwater, if this waste were placed in an unlined landfill (see the proposed rule, 59 FR 24538). Although the generator has sent this waste to a lined Subtitle C facility in the past, EPA believes that the risks estimated from migration from an unlined landfill provide an indication of the potential risks that could occur if 2,4,6-TBP is released from the lined landfill due to failure of unit to contain the waste leachate. The Agency concedes that the liner/leachate collection system in a Subtitle C unit would serve to contain the waste over the short term, and may lessen the risk even in the case of liner failure. However, EPA believes that the uncertainty in the long term integrity of this containment is high, and that significant risks may result.

As the commenter noted, EPA's risk estimate based on an unlined landfill may overstate the risk for disposal in a lined landfill. To evaluate the extent of this overestimate, EPA examined recent attempts to estimate the effectiveness of Subtitle C containment (landfill covers and liners). In the Regulatory Impact Analysis of Land Disposal Restrictions for Newly Identified Wastes and Hazardous Soil --Final Phase II Rule (page 5-10))[23], EPA assumed that 30 years after closure of a Subtitle C landfill, about 15% of the water infiltrating the unit would pass through the landfill and enter the groundwater. Thus, multiplying infiltration by 0.15 would reflect the effect of Subtitle C containment that is no longer at peak effectiveness. (This assumes that the landfill cover is not replaced or repaired 30 years after closure.) If the Agency used this efficiency factor for Subtitle C landfills to lower the risks estimated for

[23]The original source of these estimates is a draft Technical Guidance Document, "Indexing of Long-Term Effectiveness of Waste Containment Systems for a Regulatory Impact Analysis", Office of Solid Waste, November 1992.

disposal of 2,4,6-TBP wastes in an unlined landfill, the reduced risk would still be significant (i.e., multiplying the 7×10^{-4} risk by 0.15 gives a reduced risk of 6×10^{-5}). Therefore, even after trying to account for the added protection of a Subtitle C landfill, EPA believes that the risks presented by this waste warrant listing.

Finally, the fact that wastes from the production of 2,4,6-TBP currently are being disposed in Subtitle C landfills does not preclude the possibility of disposal in unlined Subtitle D units at some point in the future. EPA believes that disposal in a Subtitle D facility remains a possible mismanagement scenario because this is the lowest cost disposal option, based on information obtained through RCRA Section 3007 surveys of current management practices in the organobromine industry. In addition, any new generators that may produce the waste in the future may not choose to send it to a Subtitle C facility, but rather may decide that the less costly option of disposal in a Subtitle D landfill is appropriate. EPA believes listing of this waste is necessary for the other reasons noted above, however, the uncertainty over future management practices (and possible future management in an unlined landfill) provides an additional concern for such a high risk waste.

To respond to the commenters concern related to waste solids that do not contain 2,4,6-TBP, EPA is revising the regulatory language to clarify that the wastes covered in the listing are those of concern, i.e., those containing high levels of 246-TBP. This avoids capturing the empty soda ash bags, and possibly other waste solids downstream from the production unit that EPA did not intend to cover in the listing. Therefore, the final listing reads as follows:

> K140---Floor sweepings, off-specification product, and spent filter media from the production of 2,4,6-tribromophenol.

In response to the comment that sampling of leachate generated at an on-site landfill refutes EPA's risk analysis, EPA notes that the landfill in question is not at the generator's site and does not contain, as far as EPA could determine, the 2,4,6-TBP waste solids that the commenter generates. EPA noted in the proposal (59 FR 24537) that leachate from a landfill that received *another* waste, solids from the production of tetrabromobisphenol-A, showed the absence of brominated materials in the leachate. EPA does not believe that this provides any useful information on the mobility of constituents in the 2,4,6-TBP waste solids.

Issue IV. Proposed Deferral of Listing Determination for Waste Solids from the Production of TBBPA

Commenter # 6

The commenter submitted information regarding characterization of the commercial tetrabromobisphenol-A (TBBPA) product, the characterization of floor sweepings, and the leachability of brominated phenols from the product matrix.

Regarding the toxicology of commercial TBBPA product, the commenter stated that adequate health-based data exist and that TBBPA's toxicology has been well-characterized in various tests. The commenter included a brief summary of test data as an appendix. The appendix, entitled "Toxicology of Saytex RB-100 Flame Retardant," concludes that "TBBPA's toxicology data show the product does not pose a health hazard to mammals." Additionally, the commenter indicated that the Interagency Testing Committee (ITC) reviewed TBBPA in 1985. Based on the existing data, the ITC found no need to conduct health effects testing, but recommended ecological testing be performed. EPA requested that certain environmental effects tests be conducted based on ITC's recommendation. The Brominated Flame Retardant Industry Panel submitted the results of these tests to EPA. The commenter stated that, based on the TBBPA information submitted, TBBPA waste solids should not be listed as hazardous.

Commenter # 7

In response to EPA's decision to defer a listing determination on TBBPA due to insufficient data, the commenter recommended that the Agency not list TBBPA as a hazardous waste. The commenter cited the Interagency Testing Committee's (ITC) report on the toxicity of TBBPA and test data submitted to EPA by the Brominated Flame Retardant Industry Panel of the Chemical Manufacturers Association (CMA), indicating that the Agency has

sufficient data supporting a decision not to list TBBPA wastes as hazardous.

EPA Response:

EPA appreciates the data submitted by the commenter on the concentration of 2,4,6-tribromophenol in the TBBPA product. In determining potential risk from 2,4,6-TBP in the TBBPA waste (spilled product and floor sweepings), the Agency considered data submitted by the commenter and data collected during record sampling. In considering whether to list spilled product and floor sweepings from the packaging of TBBPA, EPA assumed that the 2,4,6-TBP concentration in the spilled product and floor sweepings is not greater than the 2,4,6-TBP concentration in the TBBPA product. The commenter reported that commercial TBBPA has less than 1% impurities, and the primary impurities are isomers of tribromobisphenol A, not 2,4,6-TBP. The concentration of 2,4,6-TBP in the TBBPA product reported by the commenter is more than 100 times less than the concentration of 2,4,6-TBP EPA found in the off-spec 2,4,6-TBP product. This appears to be a worst case assumption because 2,4,6-TBP is not handled in the packaging area, thus the spilled product should not be contaminated with any further 2,4,6-TBP (the commenter confirmed that waste solids from production of TBBPA are floor sweepings generated from spills in the packaging area, and not the production area).

The TCLP leaching data presented in the proposed rule show a maximum concentration of 760 mg/l of 2,4,6-TBP in leachate extracts from the off-specification 2,4,6-TBP product. In the absence of TCLP leaching data for the TBBPA solids, EPA assumed the TCLP leaching efficiency of 2,4,6-TBP from the spilled TBBPA product and floor sweepings would be comparable to the leaching efficiency of 2,4,6-TBP measured for the off-specification TBP product. Thus, the TCLP level for 2,4,6-TBP from the TBBPA solids was assumed to be more than 100-fold less than the TCLP level found in the TBP off-specification product. As described in the proposed rule, the level of estimated individual risk from exposure to 2,4,6-TBP in groundwater for disposal of the off-specification 2,4,6-TBP product in an unlined Subtitle D landfill was 7×10^{-4} (using the SAR-based health number after correction for molecular weight differences of 2,4,6-TCP and 2,4,6-TBP as noted in today's notice, the risk would be 4.2×10^{-4}). Using this analysis, any risk posed by TBBPA solids under the same disposal scenario would be more than a 100-fold less, or less than 10^{-6}. Therefore, this waste is not a candidate for listing as hazardous based on the presence of 2,4,6-TBP.

In addition, the results of the ecological testing submitted to the Agency by the Brominated Flame Retardant Industry panel do not indicate an unacceptable margin of safety for aquatic organisms. Ecological effects data indicate that TBBPA is not particularly toxic to aquatic test species (e.g., fathead minnow,

bluegill, daphia); no long-term aquatic effects are observed with tetrabromobisphenol-A in water at levels below 0.22 mg/L (the Maximum Acceptable Toxicant Concentration [MATC] for fathead minnows exposed continuously for 35 days). Using the data on fish and assuming that the waste was placed in an unlined landfill close to a stream into which ground water discharged, the Agency made a worst-case assumption that leachate from the landfill would be saturated with tetrabromobisphenol-A at the chemicals solubility level (4.16 mg/L). Dilution of this leachate by a factor of 100 before reaching the nearby stream yields a maximum concentration entering the stream of below 0.042 mg/L. Further dilution in the stream will readily reduce TBBPA levels further, to far less than the above-stated long-term aquatic effect level of 0.22 mg/L.

EPA has monitoring data that also indicate TBBPA wastes do not present a significant risk. As stated in the proposed rule, record sampling of an on-site landfill at one plant where TBBPA solids formerly were disposed for a number of years showed the absence of TBBPA and any brominated compounds in the landfill leachate. Therefore, based on the data submitted by the commenter, the available data on the limited toxicity of TBBPA noted above, and the monitoring data, the Agency has decided not to list waste solids from the production of TBBPA.

Issue V. Relationship of a Listing Decision for TBBPA Wastewaters to the Existing K131 Listing

Commenter # 6

The commenter objected to the language used in the proposed rule to describe the process step that generates wastewaters. The proposal reads "process wastewater originates from the distillation step where methyl bromide is recovered." The commenter stated that the wastewater originates from a distillation step where methanol is recovered. The commenter suggested that the language in the proposed rule is inconsistent with the existing listing description for K131 and expressed concern that EPA is attempting to amend the K131 listing as part of this rulemaking.

EPA Response:

The Agency concedes that the language used in the proposed rule was misleading. Indeed, the distillation step is where methanol, or both methanol and methyl bromide, can be recovered, as described in the Listing Background Document. The Agency was not referring to a specific process at any one facility; rather, the Agency was attempting to make the point that TBBPA and methyl bromide are produced in the same process and the wastewaters arising from that process meet the existing listing description

for K131. As a result, there is no need for further action on a hazardous waste listing for wastewaters from TBBPA production.

In response to a petition filed by the Ethyl Corporation for judicial review of the K131 listing, the Agency stayed the K131 listing as it applies to the "liquid material exiting the reactor producing methyl bromide located at Ethyl Corporation's production facility." This facility currently recycles the wastewaters, after solids removal, to the bromine plant for recovery of bromine values. As directed by the terms of the stay, the Agency is in the process of "determining whether [the wastewater stream generated at this facility] contains a solid waste and, if so, whether it is eligible for an exemption or variance." EPA clarifies that this rulemaking does not affect the Agency's ongoing effort to respond to this petition. EPA is not attempting to reach a decision on the applicability of the K131 listing to Ethyl's wastewater stream as part of the listing determination for wastes from organobromines production.

Issue VI: Use of Toxicity Equivalent Factors (TEFs)

Commenter # 7

Regarding the Agency's request for comment on the use of toxicity equivalent factors (TEFs) in the analysis of possible effects of brominated dibenzofurans (BDFs), the Agency should not use TEFs for regulatory evaluation. The commenter stated that the adequate scientific consensus necessary for successful application of TEFs for regulatory purposes does not exist. The commenter provided a copy of the comment submitted to EPA by the Brominated Flame Retardant Industry Panel of CMA on the use of TEFs for regulatory purposes, which expresses CMA's opposition to using TEFs for regulatory evaluation until definitive procedures have been developed and reviewed. The commenter also attached a copy of a letter submitted to the TSCA Receipt Office in August 1991 by CMA, in which similar concerns were raised.

EPA Response:

The Agency appreciates the commenter's apprehension regarding the use of TEFs for regulatory decision-making and recognizes that this is still an area of considerable debate. However, TEFs were used in the proposed rule to justify *not* listing the waste from the production of octabromodiphenyl oxide, which contains dibenzofurans. The proposed rule noted that available data indicate that brominated dioxins and furans appear to be approximately 30% to 100% as toxic as their chlorinated counterparts. Even making the conservative assumption that the brominated compounds are 100% as toxic as the chlorinated ones, the estimated exposure is sufficiently low to indicate that the waste stream would not pose a threat to human health and the

environment. While the use of TEFs to support a decision *to regulate* may be more controversial, the Agency believes that the scientific basis for TEFs is sufficiently well established to support their use when other data are not available, as part of a conservative risk assessment resulting in a decision *not to list*.

Issue VII. Accuracy of Sampling Data

Commenter # 7

The commenter questioned the accuracy of the analytical tests conducted on samples obtained during two site visits to their plant in May 1992. The commenter included a copy of a letter to EPA dated January 8, 1993, listing the company's concerns about the quality and accuracy of the analytical results. The commenter recommended that the Agency withdraw its proposal due to the inaccuracies of the data on which the proposal is based.

EPA Response:

The Agency prepared a complete response to the issues that were enumerated in the referenced letter of January 8, 1993. A copy of the original letter from the commenter and the Agency's full response have been placed in the public docket for today's rulemaking. EPA notes that none of the questioned data were used as a basis for the proposal to list wastes from the production of 2,4,6-tribromophenol. Therefore, the questioned data are not addressed in detail in this document.

Issue VIII. Definition of "production"

Commenter # 2

The commenter requested that the Agency provide a detailed definition of the term "production" as it is used in the proposed listing description for K140. The commenter suggested that production be defined to limit the reach of the listing to wastes resulting from the actual synthesis of 2,4,6-TBP (i.e., the listing should not encompass wastes from processes that isolate an intermediate or a product other than 2,4,6-TBP).

EPA Response:

In general the Agency does not believe it is necessary for a rule to define “production” because the majority of wastes listed in 40 CFR 261.32 contain the unambiguous term "production". The fact that intermediates or co-products may arise from the same process that produces 2,4,6-TBP would be irrelevant to the basis

for listing the process wastes from the production of 2,4,6-TBP. If listings were constructed so narrowly as to capture wastes from production of a given product only when the process produced that product alone, vast amounts of process waste containing similarly hazardous constituents would remain unregulated. In this case, by manipulating the process, a producer of tribromophenol may be able to co-produce di-, tetra-, or penta-brominated phenols along with tribromophenol from the same process. If a listing was crafted the way the commenter suggests, the operator of such a process would escape the intent of a regulation, while still producing a particular chemical (e.g., 2,4,6-TBP).

Issue IX. Bromine Recovery Units (BRUs)

Commenter # 7

The commenter contended that the proposed rule may have the unintended effect of increasing the land disposal of streams containing 2,4,6-TBP by providing disincentives to their use as BRU feedstocks. The commenter noted that two of its plants operate BRUs. These BRUs are halogen acid furnaces, but they do not require RCRA permits. The commenter noted that some of the streams currently fed to the BRUs may contain 2,4,6-TBP. However, in accordance with the EPA technical correction to the Boiler and Industrial Furnace (BIF) regulations regarding BRUs, the feedstocks are not considered listed or characteristic hazardous wastes, because none of the BRU feedstocks contain Appendix VIII constituents in concentrations >1%. The commenter expressed concern that listing 2,4,6-TBP in Appendix VIII could drive the concentration of Appendix VIII constituents in some streams above the 1% threshold, resulting in the stream being deemed a hazardous waste. If this occurred, the commenter would be required to either seek a RCRA permit for the affected BRU, or to send the stream to an off-site facility. In light of the relatively small volume of the 2,4,6-TBP streams, the commenter stated that it would be more likely to seek other management alternatives than to apply for a RCRA permit. The commenter also stated that the management of BRU feedstocks at the commenter's plants is in compliance with all applicable regulations and does not pose a risk to human health and the environment.

EPA Response:

As the commenter noted, EPA issued a correction notice on August 27, 1991 that excluded certain brominated materials from regulation when combusted in halogen acid furnaces (56 FR 42504). As stated in § 261.2(d)(2)(i) - (iii), brominated materials containing at least 45% bromine, and less than 1% of compounds listed in Appendix VIII are excluded, as long as the material is processed via direct conveyance. The 1% ceiling was included in

the correction notice in order to limit the burning of waste containing higher percentages of hazardous materials to facilities with RCRA permits. As the commenter recognizes, listing 2,4,6-TBP in Appendix VIII would not preclude the use of BRU feedstocks containing 2,4,6-TBP. Such feedstocks could still be used if the 2,4,6-TBP levels are kept low (total Appendix VIII components below 1%). The Agency believes that burning wastes containing >1% 2,4,6-TBP may be hazardous and should not be conducted in a facility lacking a RCRA permit. Finally, EPA notes that the sole generator of 2,4,6-tribromophenol production solids did not attempt to use this material as feedstock for the BRU.

Issue X. Waste Minimization Data

Commenter # 7

In response to the two potential waste minimization opportunities identified by EPA in the proposed rule, the commenter provided detailed information about its waste minimization efforts. The first opportunity identified by EPA refers to a stream that leaves the process hot and contains up to 15,000 mg/L (15,000 ppm) 2,4,6-TBP. EPA suggested that a large fraction of the 2,4,6-TBP in the first stream could be recovering by cooling and filtering the hot wastewater, since the solubility of 2,4,6-TBP is 70 ppm. The commenter had two criticisms of this suggestion. First, the commenter was unable to locate the origin of the 70 ppm figure, and the commenter stated that the solubility of 2,4,6-TBP is higher than 70 ppm. Secondly, the commenter described unsuccessful efforts that have been undertaken "for 15 years" to recover the 2,4,6-TBP from the stream under consideration. Such efforts have been hampered by the corrosiveness of the stream, which contains HBr, and the complex solubilities of the other organic compounds in the stream. The commenter stated that research continues in this area, but attempts to date have always resulted in an impure 2,4,6-TBP with no commercial value, even after "various purification steps."

The second waste minimization opportunity identified by EPA was in product packaging. The commenter replied that certain solids contain elevated impurity levels and therefore cannot be recycled. Specific examples mentioned were: (1) Although some of the material spilled in the drumming area is recovered, some of the spilled material is impacted with foreign materials that compromise the quality of the product. For example, a solid adsorbent is combined with the material on the floor to improve its removal from the floor. (2) Small amounts of off-specification material that cannot be blended or reworked, and therefore must be discarded. (3) Inerts, such as gloves, may be included in this waste stream. The commenter stated that the

entire waste stream represents <0.3% of the quantity of 2,4,6-TBP produced at the site.

EPA Response:

EPA appreciates the effort that the commenter has made to recover 2,4,6-TBP from the 15,000 ppm stream, and understands the difficulty of recovering pure product. However, the Agency notes that another commenter is using a process to recover a low-grade material that is a mixture of 2,4,6-TBP and underbrominated bisphenol-A compounds. If this material can be marketed successfully, commenter 7 may also be able to market the impure 2,4,6-TBP from the 15,000 ppm stream.

Because the commenter did not provide a citation or a value for the solubility of 2,4,6-TBP, the apparent inconsistency in this value cannot be explained. However, the data available to EPA indicate that 2,4,6-TBP is soluble in 14,000 parts water at 15°C (i.e., solubility in water is 70 ppm).[24] Differences in the temperature at which 2,4,6-TBP solubility was measured may be a source of the apparent inconsistency in the solubility data. Based on this information, cooling the hot waste stream would lead to 2,4,6-TBP recovery, albeit perhaps in an impure form.

With regard to the second waste minimization opportunity, the commenter stated that the waste stream contains a mixture of (1) off-specification material, (2) spilled product, and (3) inerts. Improved housekeeping measures in the packaging area may reduce the volumes and levels of impurities of these wastes. In addition, keeping the three components of the stream separate may allow for additional product recovery or marketing opportunities.

Issue XI. Modeling and Injection Wells

Commenter # 7

The commenter uses injection wells to dispose of wastewaters and there is no basis to conclude that the 2,4,6-TBP in the injected wastewater presents a hazard to human health and the environment. Supporting this claim, the commenter submitted detailed information on the injection wells located at its plants. The commenter noted that drinking water wells sampled on its property and outside the plant did not indicate a trace of 2,4,6-TBP and that there has been no indication of any contamination by 2,4,6-TBP in the nearly 20 years the plant has

[24]Lewis, Richard J. 1992. Sax's Dangerous Properties of Industrial Metals. Van Nostrand Reinhold, New York. Eighth Edition, Volume 3, p. 3338.

been in operation. Additionally, modeling performed by EPA indicates the use of the injection wells shows no risk of exposure to 2,4,6-TBP. A consultant who reviewed EPA's model indicated that the model is very conservative and that many assumptions used are known not to exist. The commenter provided, as an attachment, a critical review of the Agency's modeling assessment of subsurface contaminant migration at the commenter's underground injection site.

EPA Response:

In response, the Agency notes that the model was intended to represent a conservative scenario in order to identify any *potential* risk if leakage were to occur. The Agency reexamined the record and agrees that the existing data collected for the site suggest that the release scenario modeled is not likely to exist. The information available indicates that the only abandoned wells found in the area of the injection wells that are deep enough to penetrate the injection zone are in fact known to be plugged and should not serve as potential conduits for release of waste constituents from the injection zone to the upper drinking water aquifer. Furthermore, as noted in the proposed rule, sampling of drinking water wells on the plant site and in the vicinity of the plant did not find any trace of tribromophenol in the groundwater, even though disposal has been occurring for nearly twenty years. In any case, the comment is moot, since EPA has decided not to list wastewaters from the production of 2,4,6-TBP.