SUMMARY OF COMMENTS AND EPA RESPONSES ON

VOLATILE SYNTHETIC ORGANIC CHEMICALS IN DRINKING WATER

October 1985

Criteria and Standards Division
Office of Drinking Water
U.S. Environmental Protection Agency
Washington, D.C. 20460

FOREWORD

This is a comprehensive report providing a summary of comments and EPA's responses on the March 4, 1982 Advanced Notice of Proposed Rulemaking on Volatile Synthetic Organic Chemicals (VOCs) in Drinking Water and the June 12, 1984 Proposed RMCLs for VOCs in Drinking Water. Further discussion of the comments may be found in the Federal Register Final Rule for VOCs in Drinking Water. Comments and EPA's responses on Tetrachloroethylene, from the Advanced Notice of Proposed Rulemaking and the RMCL proposal will be provided in a separate document, after the close ot the additional comment period.

TABLE OF CONTENTS

TABLE OF CONTENTS (Continued)

I. SUMMARY OF COMMENTS AND EPA RESPONSES TO THE MARCH 4, 1982, ADVANCED NOTICE OF PROPOSED RULEMAKING ON VOLATILE SYNTHETIC ORGANIC CHEMICALS IN DRINKING WATER

A. SIGNIFICANCE OF CONTAMINATION BY VOCs

Issue: What is the significance of contamination by VOCs? Does the available occurrence data and/or health effects data warrant action to limit human exposure to VOCs?

1. Comments:

The significance of contamination by VOCs was addressed by 66 commenters. Twenty-five commenters felt that neither the occurrence data, the health effects data nor the combined data demonstrate on a national basis, the significance of VOC contamination in drinking water and, therefore, action to limit human exposure to VOCs is not warranted. Reasons cited by various commenters on the occurrence of VOCs included such statements as the following:

- VOC contamination in drinking water is a localized problem, not a widespread national problem;
- More information is needed on occurrence and health effects especially in order to assess the significance of VOC contamination;
- State data represented emergency spill situations which are not considered to be statistically representative of national occurrence;
- When present, VOCs usually occur at low part per billion concentrations. At this level, significant health risk would not be expected.
- The results of the Ground Water Supply Survey (GWSS) should be considered questionable because the detection limits that were used (i.e., 0.2 ug/L) are extremely sensitive and can rarely be achieved.
- The data concerning the occurrence of VOCs qualitatively indicates their presence in drinking water sources; however, the quantitative reliability and representativeness cannot be determined at the present time because the analytical techniques used to generate such data have not been validated.
- No real difference in ground water vs. surface water (results) can be shown from the randomized samples.
- More than half of the sampling in the drinking water survey was performed on finished water.

Comments on health effects included the following:

- The major shortcomings of the available health effects data are that it is not scientifically established at this time and subject to debate among the scientific community. Some commenters felt that

before the significance of VOC contamination can be evaluated, the National Academy of Sciences (NAS) principles and the following issues need to be reviewed and revised:

- Effects in animals, properly qualified, are applicable to man;
- Methods do not now exist to establish a threshold for long-term effects of toxic agents;
- The exposure of experimental animals to toxic agents in high doses is a necessary and valid method of discovery of possible carcinogenic hazard in man;
- Materials should be assessed in terms of human risk, rather than as "safe" or "unsafe."

Some commenters also felt that scientific issues pertaining to NAS vs. CAG risk assessment, safety factors (70 kg adult vs. 10 kg child), uncertainty factors, and fractional dose estimates should be resolved before regulations are set.

Since "safe" levels of VOCs cannot be determined from existing health effects data these commenters thus felt that MCLs should not be established. The above commenters emphasized the need for more research in the health effects area.

Forty-one commenters felt that VOC contamination of water supplies is a significant national problem because of the frequency of occurrence and potential health risk warranting action to limit exposure to VOCs. Their reasoning is based upon the following:

- local problems of severe VOC contamination in public water supplies;
- State data are more representative than EPA suggests;
- the number of VOCs in drinking water is continually increasing;
- VOCs have been demonstrated to cause serious carcinogenic and non-carcinogenic toxic effects including:
  - carcinogenic effects demonstrated in animal studies and evidence of human carcinogenicity (vinyl chloride);
  - hepatomas in animals, and in some cases in humans;
  - toxicity to the kidneys;
  - serious effects on the reproductive system; and
  - depression of the central nervous system.

Response:

EPA has considered the above comments in its analysis for determining the significance of VOC contamination in drinking waters. A discussion of this analysis, which covers most of the issues raised in the above comments, is available in the Proposal for RMCLs in the June 12, 1984, Federal Register Notice and in the Response to Comment B below. Responses to comments on issues not covered in this Notice are given as follows.

Regarding the issue of questionable data near detection limit levels in the GWSS survey, EPA conducted in-house quality control testing to support the validity of this data. EPA, therefore, believes the GWSS forms a reasonable basis for characterizing the occurrence of VOCs in ground waters in the U.S. Because of the long holding times, there may have been some underestimate of the actual occurrence. However, EPA does not believe that this underestimate would be so significant to disqualify this survey as a national estimate.

Laboratories generating data in all the surveys were required to undergo a quality assurance program. The data generated is considered reliable within the boundaries of the analysis that was considered. This data is available in the Occurrence Documents for each of the VOCs (Occurrence of Volatile Organic Chemicals in Drinking Water, name of VOC, EPA, Criteria and Standards Division).

Regarding the issue of occurrence in ground water vs. surface water, most VOCs, on the basis of data that are available in the above cited documents, are more likely to occur at levels above 5 ug/L in ground waters than in surface waters. Virtually all persistent occurrences of VOCs above 50 ug/L are expected to occur in ground water.

The comment that half of the sampling in the drinking water survey was performed on finished water is incorrect. Most of the occurrence data was based on samples taken from the distribution system.

With regard to the health effects issues, EPA believes that the NAS principles are accepted in the scientific community and present a scientifically acceptable basis for establishing health effects numbers. These principles are widely accepted as forming the basis for chemical risk assessment and have been applied by numerous groups over the years. The Office of Science and Technology Policy's recent review of the science and its associated principles for chemical carcinogens (49 FR 21594) listed principles for risk assessment which included the following:

- Agents found carcinogenic in animal studies, subject to the considerations discussed previously, are considered suspect human carcinogens.

- It is appropriate to use test doses that generally exceed human exposure levels in order to overcome the inherent insensitivity of the traditional design of the long-term animal test.

These principles are very similar to those discussed by the NAS. In addition, EPA's proposed guidelines for carcinogen risk assessment (49 FR 46294) were based upon the same basic principles as outlined above.

Regarding other scientific issues such as carcinogen risk assessment, EPA believes that with the publication of EPA's proposed guidelines for carcinogen risk assessment (49 FR 46294), uniform guidelines for risk assessment have been established and have helped to resolve these scientific issues. In reference to other scientific issues such as safety factors, EPA believes that the science has advanced to the point where relative agreement exists in the scientific community on the calculation of health effects numbers upon which to base regulation.

EPA agrees that more research in the health effects area is desirable and will increase our scientific knowledge of the chemicals; however, EPA believes that sufficient data are currently available upon which to base the MCLs.

B. APPROACH TO DEAL WITH VOCs IN DRINKING WATER

Issue: Which approach should EPA take to deal with VOCs in drinking water?

1. Comments:

117 comments were received that specifically addressed this issue in commenting on either (1) the non-federal regulatory approach, (2) monitoring regulations, or (3) regulations for monitoring and MCLs.

Option 1, the non-federal regulatory approach, was favored by 22 commenters. Several States commented that recent surveys by EPA and their own sampling did not indicate a major VOC contamination problem within their borders; thus, they felt that national requirements for monitoring and MCLs were not warranted. These States felt that problems could be addressed on a case-by-case basis without federal regulations. One of the States emphasized that routine, repetitive monitoring requirements must not be put into regulations because monitoring programs must be flexible and can best be developed by States and utilities.

Option 2, setting monitoring requirements and providing health advisories for State response as appropriate, was favored by 13 commenters. These commenters generally felt that ground water contamination is a problem in some places that must be addressed but:

- contamination was not widespread enough "to require highly formalized and restrictive requirements,"
- available data are insufficient to determine the scope of the problem, or
- only monitoring should be done to determine where problems exist and instead of setting MCLs, guidance should be provided; these commenters generally supported giving States considerable authority for implementation of the monitoring requirements and for determining appropriate action when contamination was found.

One commenter stated that there should be MCLs set for the VOCs but not until there is "some agreement among the scientific community as to an acceptable and meaningful level of concern." In the meantime, this commenter suggested that a monitoring requirement be set at the federal level which would be as flexible as possible such that details of actual monitoring programs could be agreed upon between the States and EPA regional offices. In this way, the monitoring program would address "those communities which are thought to be most vulnerable to contamination."

An additional commenter recommended that contaminants be controlled at their source through EPA's existing statutory authority. This commenter stated that MCLs are not appropriate at this time, since "safe" levels of VOCs cannot be determined from existing health-effects data. However, when the health effects data are evaluated by a recognized independent scientific orgainzation (i.e., National Academy of Sciences [NAS]), MCLs should be established if a significant health risk exists.

This commenter also suggested that national monitoring for specific compound identification should be implemented for all water supplies, preferably using the THM purge and trap procedure (EPA Method 502.1 or equivalent), but requirements for systems serving less than 10,000 people should be at the discretion of the State. The initial monitoring frequency should be similar to the THM rule. In addition, at this time, guidance in the form of contamination levels, and action categories for five of the VOCs should be established for all water supplies. (See Table 1 below)

TABLE 1

Compound	Concentration Levels (ug/L) Categories		
	I	II	III
Vinyl Chloride	>100	10-100	<10
Trichloroethylene	>500	50-500	<50
Tetrachloroethylene	>500	50-500	<50
Carbon Tetrachloride	>500	50-500	<50
1,2-Dichloroethane	>250	25-250	<25

Category I - high concentrations and consequently greater risks. Immediate action warranted to reduce contaminant level.

Category II - intermediate concentration with lower risk. Prompt action warranted to step up surveillance and consider control strategies. Action should reflect whether the concentration is at the higher or lower part of the range.

Category III - very low concentration. Little risk associated with these concentrations. Only routine monitoring needed.

This commenter noted that when extensive monitoring or installation of treatment systems is necessary, the discharger causing the contamination should bear the financial burden of cleanup, not the water utility. However, when the cause of contamination, or the discharger cannot be determined, EPA should use other methods, such as RCRA or Superfund, to provide financial assistance to the water utility. Finally, for the present, health advisories should be used for specific cases of contaminants not previously found in drinking water.

One commenter recommended a national monitoring program with State response based upon guidance on health effects and treatment. Without a consensus on safe levels derived from health effects data of the various VOCs, this commenter felt that there is no basis for the establishment of MCLs.

This commenter noted that the monitoring program should be the same for all water supplies, regardless of size. The initial monitoring should be done at points in the distribution systems representative of the sources of supply. Thereafter, monitoring should be based upon the initial sample results and the levels of action indicated by the severity of the contamination in a program commensurate with the characteristics of each water supply system.

A comment was received which stated that in the absence of a consensus on the dangers of low levels of VOCs in drinking water, a modified regulatory approach was needed. The approach suggested was as follows:

- RMCLs and MCLs should not be developed, except under certain conditions identified below.
- The goal of zero cancer risk should be abandoned in favor of a goal of negligible risk. This should be achieved by the establishment of a risk target level (RTL) of 10^{-5}, in preference to MCLs.
- No action should be taken unless VOCs occur at this level or above in more than one percent of the public water supplies serving at least one percent of the consuming public. If it does, the development of MCLs would be warranted.
- Since the occurrence data indicate that no action is warranted according to the criteria above, EPA should publish a document containing guidance on health effects, treatment technology, analytical methods, and any other significant considerations.

Many commenters specifically suggested that the monitoring option would be appropriate if the data on health effects of VOCs is unclear or insufficient, or if the incidence of contamination is small. These commenters felt that EPA should provide guidance on health effects and treatment. Numerous commenters pointed out that EPA Health Advisories were very helpful to States and public water systems.

Option 3, setting national regulations for monitoring and MCLs, was favored by 82 commenters. Numerous commenters stated that MCLs and monitoring requirements should be set for the VOCs; a number of these commenters

qualified their statements by saying MCLs should be set if it is shown that the occurrence of VOCs is widespread and the health effects data show that VOCs are a health risk. However, most commenters felt that sufficient data were available showing VOCs to be a widespread problem, that data did show a potential health hazard, and that MCLs were needed.

The following related statements were made:

- Problems with organic chemicals have been shown in several States and without enforceable standards, the problems will continue to spread; the

- While Health Advisories (HAs) were noted to have been very useful in addressing incidences of VOC contamination, several commenters commented that the States have adopted widely varying approaches to dealing with VOCs in drinking water. Some States have adopted the HAs as enforceable standards and consequently public water systems have been forced to make permanent and costly decisions on the basis of health guidance.

- One commenter felt that national monitoring requirements, RMCL and MCLs should be set for the VOCs. This was because contamination was widespread and the health effects data showed a potential human health hazard.

- One commenter summarized their argument for MCLs in the following manner:

  - Contamination of water supplies in the U.S. with VOCs is indicative of a national trend. Setting legally enforceable national standards will be important in reversing that trend. It will establish a ceiling on how much contamination of drinking water is acceptable and will trigger remedial action in situations where the ceiling is almost reached or exceeded.

  - Alternatives involving determination of the acceptable levels of contaminants by individual States, based on EPA advisory options, will not be effective.

    - It is likely that EPA advisory opinions on health effects will be misinterpreted and misused as demonstrated by many States that have used the HAs as rigid criteria by which suitability of a water supply is measured. The fact that HAs are developed without consideration for possible carcinogenic properties of a compound and with disregard for economic and technological feasibility of achieving them is forgotten. We are better off with MCLs established in the process involving public participation and intended to be the rigid standards by which quality of drinking water is measured.

    - If left to the States, drinking water guidelines will differ from each other. This will lead to confusion and poor public image for State agencies which recommend guidelines less stringent than others. In addition, leaving the regulatory

activity to States will require more human resources in the area of toxicological evaluation and standard setting. Many States do not have these resources. Thirdly, enforcement will be very difficult, if not impossible, if neighboring States have different drinking water standards. Contamination has no boundaries.

In regard to monitoring requirements, comments ranged from suggesting EPA set requirements for very frequent monitoring to a suggestion that EPA should either set minimal requirements or provide guidance to States to set monitoring to address more closely the situation within each State. Sepecific comments are addressed in the discussion of comments on monitoring.

Response:

EPA has considered the above comments in its analysis of approaches for controlling VOCs. Issues regarding health effects, occurrence data and exposure are addressed in the proposal for Recommended Maximum Contaminant Levels for VOCs in the June 12, 1984, Federal Register Notice. Issues regarding regulatory approach options and monitoring strategies and EPA's proposed action are addressed in the Federal Register proposal for Maximum Contaminant Levels for VOCs.

EPA believes that for the eight VOCs and tetrachloroethylene, there is adequate occurrence and potential occurrence in public water systems to justify a national regulation. EPA has explained elsewhere that these contaminants are currently found in drinking water systems, often at levels above the RMCLs. It is clear that the Safe Drinking Water Act requires EPA to set National Primary Drinking Water Regulations for contaminants that may have an adverse effect on health. Therefore, EPA cannot agree with those commenters who advocate relying on state regulation or combinations of health advisories and monitoring in lieu of any Federal regulation. However, health advisories and monitoring may be appropriate for contaminants whose occurrence or potential occurrence is unknown or unclear to the Agency.

C. WHAT MCL VALUES SHOULD BE ESTABLISHED

Issue: If regulations are determined to be an appropriate approach, what MCL values should be established?

1. Comments:

A total of 14 commenters addressed this issue. Eleven comments were received that addressed the risk rate level: four commenters favored a 10^{-4} risk rate level, one commenter favored a 10^{-5} risk rate level, five commenters favored a 10^{-6} risk rate level, and one commenter favored either a 10^{-4} or 10^{-5} risk rate level depending on economic and technical feasibility.

One commenter stated that risk computations are probably the most feasible alternative available for use in establishing acceptable exposure levels of carcinogens, however:

- the public has a difficult time understanding the concept of risk assessment unless the regulatory agency makes every effort to present the concept clearly and concisely;

- once understood by the public, many people are unwilling to accept any level of risk associated with a drinking water supply; and

- the public is more willing to accept risks as they exercise more control (i.e., choice) over use or non-use of the substance related to that risk. For example, much of the public will readily accept the risks associated with cigarette smoking or driving without a seat belt since the consumer is relatively free to decide the respective course of action in these cases. Conversely, fewer customers will accept a risk associated with drinking water, since they are relatively restricted regarding the choice of water consumption in their own residences.

Two commenters specifically addressed the level of MCLs for VOCs. One commenter felt the level for trichloroethylene should be in the range of 50 to 100 ppb. Another commenter grouped the chemicals as follows:

- Total chlorinated ethylenes (trichloroethylene, tetrachloroethylene, 1,1-dichloroethylene, cis-1,2-dichloroethylene, trans-1,2-dichloroethylene): 5 to 100 ppb.

- Total chlorinated ethanes (1,2-dichloroethane and 1,1,1-trichloroethane): 5 to 100 ppb.

- Total chlorinated benzenes (monochlorobenzene, dichlorobenzenes and trichlorobenzenes): 5 to 100 ppb.

- Vinyl chloride: 1 to 20 ppb.

- Benzene: 1 to 20 ppb.

- Methylene chloride: 5 to 100 ppb.

- Carbon tetrachloride: 5 to 50 ppb.

Response:

RMCLs have been promulgated, as explained in the preamble accompanying the final rule. EPA has proposed MCLs on the basis of the availability and performance of analytical methods and the availability, performance and costs of technologies to achieve levels as close to the RMCLs as possible. A discussion of the rationale used for selecting various MCLs is given in the proposal.

D. GENOTOXIC VS. NONGENOTOXIC CARCINOGENS

Issue: Should different risk models or approaches be used for carcinogens that are not genotoxic? What criteria should be used to classify a compound as "genotoxic" or "n n-gen toxic?"

1. Comments:

Seven commenters addressed the issue of different risk models for genotoxic and non-genotoxic carcinogens. Four commenters stated that different risk models should be used to account for the differentation of carcinogens recognizing different mechanisms. All of these commenters rejected the CAG risk model because it is too conservative in that both the upper and lower bound risks must be taken into account.

According to the above commenters, some of the criteria to classify a compound as "genotoxic" include:

- a reliable, positive demonstration of genotoxicity in appropriate prokaryotic and eukaryotic systems in vitro;
- positive results in studies on binding to DNA; and
- evidence of biochemical or biologic consequences of DNA damage.

One commenter felt EPA should continue to use the CAG model for both genotoxic and non-genotoxic carcinogens. Even though knowledge of the carcinogenic mechanism should be a major factor in selecting the most appropriate risk model, this information is generally not available for environmental carcinogens.

This commenter further stated that a distinction between carcinogenic mechanisms is arbitrary because:

- there is a lack of experimental data establishing a threshold for non-mutagenic carcinogens or showing that the dose-response curve is different in the lower range from that for substances that cause gene mutations, and
- thresholds observed in experiments with an inbred animal population cannot be extrapolated with any degree of certainty to a diverse human population; therefore, no distinction between carcinogenic mechanisms should be made at this time.

Response:

EPA believes that there is an insufficient scientific basis to distinguish classifying chemicals as genotoxic or non-genotoxic carcinogens. The general scientific consensus is that cancer is a multi-stage process involving a variety of events which can include initiation, promotion, and progression. However, the exact nature of the multistage process is not well understood and the available evidence is insufficient to differentiate between carcinogens on the basis of mechanism. This is supported by the Office of Science and Technology Policy's review of the science and associated principles for chemical carcinogens (49 FR 21594). Current views on the mechanisms of carcinogenesis were examined and they concluded that "...cancer development is a multistage process that may involve the genome, both indirectly (frequently termed epigenetic events) and directly, which may include the participation of chemicals or viruses, and which may be modulated by higher order functions, i.e., at the organ and organismic

level." In addition, they stated that "we still lack an in-depth understanding of the mechanisms and stages of cancer induction and expression."

In any event, EPA believes that RMCLs for known and probable human carcinogens by any mechanism should be set at zero, as explained in the final rule preamble.

E. HEALTH EFFECTS CRITERIA DOCUMENTS

Issue: Are the data and conclusions in the Draft Health Effects Criteria Documents scientifically and technically valid?

Comments:

A total of eight commenters addressed the Draft Health Effects Criteria Documents. Of the eight commenters, only four submitted detailed scientific assessments. For the most part, the commenters felt the criteria documents were adequate.

The following is a summary of the comments and EPA's responses concerning issues in the Draft Health Effects Criteria Documents.

General Comments:

1. Comment: There should be more critical analysis of the data in the Criteria Documents.

   Response: Since the ANPRM notice in 1982, more critical analysis of the data has been made in the criteria documents, including further analysis of data in response to public comments, especially on studies used as bases for quantification of toxicological effects.

2. Comment: Better guidance on non-carcinogenic health effects is needed.

   Response: The quantification of toxicological effects sections in the criteria documents have been revised to give more detailed discussions of the methodology behind the quantification, the studies selected, and the rationale for the selection of studies for quantification.

3. Comment: There is a lack of organization in the discussion of combined effects.

   Response: Specific sections consolidating this information have been added to the documents.

4. Comment: EPA should publish only one comprehensive criteria document for agency-wide use.

   Response: At the time that the regulations development process for the VOCs began, the EPA Health Assessment Documents were not available, nor had they been peer-reviewed externally by the Science Advisory Board (SAB). These documents have been peer-reviewed within the Agency and have now been subjected to external comment through the rulemaking process.

5. Comment: The document should provide critical analysis of the individual studies as well as evaluation of the data as a whole.

   Response: Since the ANPRM in 1982, the criteria documents for each contaminant have been revised to include any available studies with a discussion of additive and synergistic effects. However, EPA has determined that due to the conflicting or weak scientific evidence on additive and synergistic effects, RMCLs which reflect this evidence would not be justified. (See also Comment/Response -- III.K.1)

6. Comment: EPA should appoint a panel of recognized scientific experts to provide external review of the documents.

   Response: The SAB is a panel of recognized experts who review criteria documents as resources permit. All criteria documents are widely reviewed within the Agency, by consultant scientists, and through public comments.

7. Comment: Toxicology summaries in the ANPRM are overly brief and simplistic.

   Response: Toxicology summaries in the RMCL proposal and discussion of data in the criteria documents were expanded to include more details, including discussion of Agency reasons for the risk assessments used.

Comments on the Carbon Tetrachloride Criteria Document

8. Comment: The Alumot (1976) study cited is highly incomplete and should be interpreted with caution.

   Response: The revised criteria document indicates the deficiencies in the Alumot study. EPA agrees that the results of this study should be interpreted with caution.

9. Comment: The discussion on teratogenicity is incomplete and uncritical.

   Response: The inhalation exposure teratology studies by Schwetz, et al. (1974) and Gilman (1971) were negative for teratogenesis at high exposure levels. Fetotoxicity was observed; however, discussion of these studies was not expanded since they were not used for quantification of toxicological effects. The statement in the final paragraph in the teratogenicity section has been removed.

10. Comment: The data presented in Table VI-8 on the results of the NCI carcinogenesis bioassay in rats are incorrect and should be recalculated or deleted.

    Response: The data are given as presented in the NCI bioassay report. The influence of mortality on the liver tumor results is discussed in the text of the criteria document.

11. Comment: The daily dose levels given for the Eschenbrenner and Miller (1946) study are incorrect.

Response: The correct daily dose levels are now in the criteria document.

12. Comment: Table VI-11 (on page VI-29) is misleading.

Response: All pertinent information on liver lesions is clearly given in Table V-11 in the final criteria document. Therefore, EPA does not believe that the table is misleading.

13. Comment: The Risk Assessment section (section IX) does not provide a critical assessment of different studies used by CAG and NAS for risk extrapolation. It also ignores serious non-carcinogenic effects.

Response: The criteria document emphasizes the most solid toxicity data with the most sensitive endpoints for quantification based on noncarcinogenic effects. Similarities and differences between NAS and CAG risk assessments are pointed out in the criteria document. However, this comparison may be moot in that the Agency risk assessment in the EPA health assessment document recently approved by the EPA Science Advisory Board is that used in the revised criteria document.

14. Comment: Two sections in the criteria document are missing important studies.

Response: The discussion of the Eschenbrenner and Miller (1946) study has been revised. The Sonich, et al. (1981) study is included in the criteria document.

15. Comment: The 30% inhalation absorption coefficient is inconsistent with the 40% value used in the Agency (OHEA) health assessment document on carbon tetrachloride.

Response: The comment is no longer applicable since only oral dosing studies are considered in the quantification of toxicological effects.

Comments on the Trichloroethylene Criteria Document

16. Comment: The section on carcinogenesis should be revised to include the most recent NCI bioassay results.

Response: The NTP cancer study with epichlorohydrin-free TCE has been included in the document.

17. Comment: The general organization of the document should be improved.

Response: The document has been edited.

18. Comment: The document omits recent studies regarding covalent binding of metabolites to DNA, protein, and lipids.

Response: The following references have been added to the document: DiRenzo, et al., 1982. Microsomal Bioactivation and Covalent Binding of Aliphatic Halides to DNA. Toxicology Letters. 11:243-252; and, Banerjee and Van Duuren, 1978.

19. Comment: The document omits an important recent study of teratogenicity.

Response: The following teratogenicity study has been added to the document: Dorfmueller, M.A., et al., 1979. Evaluation of Teratogenicity and Behavioral Toxicity with Inhalation Exposure of Maternal Rats to Trichloroethylene. Toxicology 14(2):153-166.

20. Comment: The section of mutagenicity could be expanded to include a study of sister chromatid exchange.

Response: The Gu, et al. (1981), study was not included in the criteria document, but its omission does not affect the qualitative and quantitative conclusions because no clear-cut conclusions were obtained in the study due to exposure to other chemicals which may have affected the results.

21. Comment: An important study (Hardell, et al., 1981) has been omitted from the epidemiology section, and inadequate attention is given to the shortcomings of a "negative study" (Axelson, et al., 1978).

Response: The Hardell, et al. (1981) study is not included in the criteria document, but its omission does not affect the qualitative and quantitative conclusions. This is because the epidemiological results are no better than suggestive due to the fact that the subjects were probably exposed to other chemicals. This makes it impossible to identify the specific causative agent(s). The Axelson, et al. (1978) study is discussed in the Criteria Document with the weaknesses of the study highlighted. The major weakness is that there wasn't a sufficient period of time for followup with the subjects in order to see the occurrence of the effects.

22. Comment: How was an absorption factor of 30 percent in the calculation of the adjusted ADI determined?

Response: Although the absorption range has been reported in the literature to range between 36 and 75 percent, there are no precise ways for determining this factor. Consequently, EPA used an absorption factor of 30 percent in the calculation as a conservative estimate of absorption over an extended period of exposure.

23. Comment: The evidence for the carcinogenicity of TCE is questionable and should be reassessed when the (recently completed) NTP bioassay is completed.

Response: The Agency, through its Risk Assessment Forum, as discussed in responses to the RMCL Proposal comments (see Comment/Response II.A.4), has concluded that there is sufficient animal evidence to consider TCE an animal carcinogen. The animal evidence includes the NTP bioassay.

Comments on the Trichloroethylene Health Assessment Document (March 1982)

A commenter submitted a review of the Health Assessment Document for Trichloroethylene (March 1982). This document has since been revised and

finalized; however, some of the issues are still relevant to the final RMCL for trichloroethylene. A summary of the major issues discussed in the review follows, with EPA responses pertaining to the current rulemaking (Comments 24 through 29).

24. Comment: The implications that low ambient air concentrations of trichloroethylene pose a serious health hazard due to toxic effects on the central nervous system and the cardiovascular system, effects seen at high concentrations, are not supported by the available data.

    Response: As discussed in the Criteria Document, trichloroethylene at high dose levels produces anesthesia. EPA agrees that the central nervous system effects are seen at high concentrations in animal studies; however, the fact that these effects are seen at high dose levels does not negate their importance. EPA believes that all effects should be examined and the RMCL based upon the most sensitive endpoint. For trichloroethylene, the RMCL is based upon the potential carcinogenicity of the compound.

25. Comment: The claim that teratology studies are inconclusive and do not provide adequate evidence that trichloroethylene may be teratogenic in humans completely ignores the conclusions reached in the text of the Health Assessment Document that available data indicate no teratologic effect.

    Response: Based on the available data, EPA agrees that trichloroethylene does not appear to be teratogenic in animals. This conclusion is discussed in the Final Criteria Document where several negative teratology studies are discussed.

26. Comment: The Document fails to recognize the transitory nature of toxic exposure to atmospheric breakdown products.

    Response: This comment is not applicable to the current rulemaking, as it deals with atmospheric degradation of trichloroethylene while the rulemaking deals with exposure to trichloroethylene in drinking water.

27. Comment: The Document presents a misunderstanding of the update, retention and elimination of trichloroethylene and implies it accumulates in bodily tissue, particularly fat.

    Response: EPA disagrees with the commenter's conclusion that trichloroethylene does not accumulate in body tissues. The data indicate that trichloroethylene is distributed in tissues according to their fat content (McConnell, et al., 1975). In addition, trichloroethylene has been reported to cross the placental barrier and has been detected in fetal blood (Beppu, 1968).

28. Comment: Epidemiology studies, while limited in size, consistently show no increase in liver cancer. Taken as a whole, these studies support the conclusion that trichlorethylene is not a human carcinogen.

Response: EPA does not agree that the epidemiology studies present sufficient evidence to conclude that trichloroethylene is not a potential human carcinogen. These studies rarely involved an unexposed group for comparison and the description of the studies usually did not include the age and sex distribution of the workers. Worker exposure to other chemical substances in these workplaces is another confounding factor that makes it very difficult to reach firm conclusions regarding these studies.

29. Comment: The preliminary NTP report of the Carcinogenic Bioassay of Trichloroethylene does not support the carcinogenicity of pure trichloroethylene.

Response: The NTP bioassay of trichloroethylene (1982) using $B_6C_3F_1$ mice showed positive results with liver neoplasms being the effects noted. The NTP report, in which trichloroethylene was found to be carcinogenic for both sexes of mice, is final and has been accepted by the NTP Board of Scientific Counselors. This study has been considered, along with other relevant data, in the assessment of the carcinogenicity of the compound (See Comment/Response - II.A.4 and II.A.8).

Comments on the 1,1,1-Trichloroethane Health Assessment Document (January 1982)

A commenter submitted a review of the Health Assessment Document for 1,1,1-Trichloroethane (January 1982). This document has since been revised and finalized; however, some of the issues are still relevant to the final RMCL for 1,1,1-trichloroethane. A summary of the major issues discussed in the review follows, with EPA responses pertaining to the current rulemaking (Comments 30 through 32).

30. Comment: The HAD contains serious misunderstandings of basic and well-recognized physical-chemical factors which influence uptake, storage and excretion of volatile substances. As a result, erroneous conclusions are drawn concerning possible effects of long-term exposure to extremely low environmental levels.

Response: These "serious misunderstandings" were not identified, so EPA cannot specifically address them. However, as noted in the final Criteria Document, 1,1,1-trichloroethane may be absorbed and distributed in the body after inhalation or ingestion exposure, with the potential for adverse health effects. Thus, EPA believes that long-term exposure to 1,1,1-trichloroethane could result in adverse health effects and is setting the RMCL to prevent their occurrence.

31. Comment: There is unwarranted speculation on a reactive intermediate while available data indicate very limited metabolism of methyl chloroform.

Response: Trichloroethanol and trichloroacetic acid are the primary metabolites of methyl chloroform. Human metabolic profiles after skin application of methyl chloroform indicate both trichloroethanol and trichloroacetic acid in urine. However, most methyl chloroform

was found unchanged in the air. Thus, EPA agrees with the commenter that limited metabolism of methyl chloroform occurs.

32. Comment: The HAD selects limited positive mutagenic data, while ignoring a large body of negative data.

Response: Mutagenicity testing of methyl chloroform has proven inconclusive. The results show 2 positive studies, 3 negative studies and 1 inconclusive study. EPA is not considering 1,1,1-trichloroethane to have sufficient evidence of mutagenicity or carcinogenicity in this rulemaking.

Position Paper on Water Quality Criteria for Trichloroethylene

A commenter submitted a review of the Water Quality Criteria Document for trichloroethylene. The following is a summary of those issues related to this rulemaking and EPA responses.

33. Comment: The water quality criterion for protection of human health based upon cancer is more restrictive than necessary. Since tumors in mice exposed to massive doses of trichloroethylene appear to be induced non-genetically, it is appropriate to base the human health criterion for trichloroethylene on non-carcinogenic health concerns.

Response: EPA disagrees that the health-based number for trichloroethylene should be based on non-carcinogenic effects. As discussed in Comment/Response - II.A.8, trichloroethylene has been classified as having sufficient evidence of carcinogenicity in animals, and thus the number should be based upon carcinogenicity as an endpoint.

Comments on the 1,1,1-Trichloroethane Criteria Document

34. Comment: A potential MCL for 1,1,1-trichloroethane of 1000 ug/L is listed in the Criteria Document, based upon the 1977 NCI bioassay. The Criteria Document does not contain an explanation of how the 1000 ug/L MCL was derived from the toxic effects observed in the bioassay.

Response: The RMCL for 1,1,1-trichloroethane is based on an inhalation study and is not based upon the 1977 NTP bioassay. A discussion of the derivation of the RMCL may be found in the Final Criteria Document for 1,1,1-trichloroethane, as referenced in the Federal Register Final Rule for the promulgation of RMCLs.

F. WHICH CONTAMINANTS SHOULD BE REGULATED

Issue: If regulations are determined to be an appropriate approach, for which of the contaminants should regulations be developed?

1. Comments:

Eighty-two commenters were in favor of setting national regulations for VOCs, but did not specifically state which specific VOCs; presumably, these commenters were concerned with the list of six to fourteen VOCs in the ANPRM.

Two commenters addressed the specific contaminants for which regulations should be set. One commenter stated that MCLs should only be established for carbon tetrachloride, trichloroethylene, tetrachloroethylene and vinyl chloride. For non-carcinogens (i.e., 1,1,1-trichloroethane), States should be authorized to require water companies to indicate the concentration of such chemicals in the finished drinking water, the likely risk to the individual at such levels and a list of sites where people can draw drinking water that is free of such chemical compounds. This commenter suggested that this information could be included in the billing statement. One commenter stated that MCLs should be established for the VOCs listed in the ANPRM except for benzene and the chlorinated benzenes.

Response:

EPA believes that at this time there is enough information available to establish MCLs for 9 of the 14 VOCs considered in the ANPRM. The rationale for the selection of those chemicals proposed to be regulated is presented in the Federal Register Final Rule for the promulgation of RMCLs. Other VOCs will be considered for regulation at a later date.

G. MONITORING REQUIREMENTS

Issue: What monitoring requirements should be imposed for determining exposure to VOCs?

1. Comments:

Forty-four commenters addressed the issue of monitoring requirements. The commenters' suggestions can be summarized as follows:

- Eleven commenters suggested that federal monitoring requirements be set in such a manner that would allow States to determine the actual sampling requirements for public water systems within their boundaries. These requirements would be set by the State with concurrence by EPA regional offices and would be targeted for public water systems considered to be "vulnerable" to contamination by VOCs.

- Ten commenters recommended that EPA require an initial round of monitoring for all systems to determine the incidence of contamination. One commenter felt that a sufficient number of laboratories were available and that the initial round of monitoring should be required to be completed within one year, not three as suggested by EPA. This commenter recommended that the initial round of monitoring should require GC/MS analysis for the 113 "priority pollutants" and the identification of other significant peaks. After the initial round, systems could switch to purge and trap GC if they did not find significant concentrations of non-VOCs.

- Another commenter recommended that the initial round of monitoring follow the frequency set by the THM regulations and should be at the discretion of the States for systems serving less than 10,000 people. Following the inital sampling, systems would be required to monitor on a frequency based upon the results of the first round of sampling.

Several commenters recommended that if no contamination was found, monitoring should be set at once every three to five years.

- Twenty comments were received that stated monitoring frequency should be set at least annually with some suggesting that quarterly sampling would be appropriate. One of these commenters recommended the following monitoring requirements:

  - once per year for systems not finding VOCs above detection limits in the initial round of sampling;

  - once per six months for systems finding VOCs above half the MCL; and

  - once per three months for systems finding VOCs at a level above the MCL, at a concentration above 50 ppb, or at a sum of two or more unregulated organic chemicals above 100 ppb.

  This commenter suggested that systems should take a minimum of four samples in the distribution system on each sampling day and that sampling requirements should be for each source.

In regard to differentiation of monitoring requirements for surface waters versus ground waters, commenters generally stated that any regulations should apply to both. However, several of these commenters felt that there may be circumstances that would allow for some distinction such as:

- systems located in "remote, mountainous terrain," and

- systems on surface waters if MCLs are set around 50 ppb since EPA occurrence data shows that levels above 1 ppb are seldom found.

Four commenters felt that monitoring requirements should be modified based upon the size of the system; one of these especially felt that non-community systems should be excluded. One commenter felt that reduced monitoring requirements are not warranted for VOCs since the discharges from the major VOC sources, industrial discharges and landfills, may fluctuate widely.

Response:

EPA has considered the above comments in developing the proposed monitoring requirements for VOCs. Proposed monitoring options and the rationale behind them are presented in the Federal Register Proposed Rule for MCLs for VOCs. EPA is soliciting comments to these options.

Initial monitoring for the 113 priority pollutants is considered inappropriate at this time. Analysis of all the priority pollutants involves many different analytical methodologies, some of which are more widely used than others. Reliable, analytical capability for VOCs has been established in enough laboratories in the U.S. to support national monitoring. In its proposed monitoring requirements, EPA is recommending that monitoring include coverage of all VOCs which can be reliably identified

and quantified under the available analytical methodologies. Monitoring requirements for non-volatile synthetic organic chemicals will be considered in subsequent regulations.

H. ANALYTICAL METHODS

Issue: Are analytical techniques available which can reliably and practically be used in monitoring for VOCs?

1. Comments:

Twenty-three commenters addressed the availability of analytical methods for measurement of VOCs. Most commenters felt that analytical methods were available for measurement of VOCs. The commenters' suggestions are summarized as follows.

Fourteen commenters stated that analytical methods are available to measure VOCs and eight of these recommended the use of EPA Method #502.1 or equivalent. The levels of precision varied among the commenters regarding this method. Three commenters felt the level of precision would be + or - 20%. Another commenter stated the precision level would be + or - 10%. Other commenters felt the inter-laboratory precision at the ppb level would be + or - 50% accuracy when considering the precision within laboratories or between laboratories.

Five commenters recommended that GC/MS is the most suitably accurate method. One commenter felt the precision at the 1 ppb level would be in the range of 1 to 20% and another commenter felt the level of precision would be + or - 10%. This commenter further stated that the GC/MS method is the most suitable method in a large sampling program whereas EPA Method #502.1 and 503.1 are not. Another commenter felt that the GC/MS method could be improved through automation of the analysis.

One commenter felt that analytical methods are available to accurately measure these contaminants. However, they have not yet been fully validated in laboratory testing and have not yet had the results published. This commenter stated that "until that effort is complete, any data from those methods must be considered to have minimal quantitative value. These methods can be improved by completion of the peer review process."

Five commenters criticized the use of EPA Methods #502.1 and 503.1. Three commenters stressed the need for adequate peer review and inter-laboratory validation of these methods. Two other commenters questioned the ability of laboratories to test with reliable results at low concentrations (1 to 5 ppb level).

One commenter submitted detailed comments as to how these analytical methods are not precise, accurate, simple or inexpensive. Their evaluation is summarized below:

"Method #502.1 was developed at the Organic Analysis Section of EMSL which essentially is a research and development laboratory. The precision and accuracy data for a "single laboratory" (EMSL) suggest that at least

e laboratory is what optimistic to expect that any or all other laboratories would be able to employ the method, as currently written, with the same success."

"Section 2.3 of the method indicates that a halogen specific detector is used for measurement. Also, a mass spectrometer may be used in place of the halogen specific detector. It needs to be pointed out that there is a tradeoff which results in different limits of detection. The so-called halogen specific detector is the more sensitive of the two and perhaps allows for low part per billion analyses; however, it lacks the specificity of the mass spectrometer with respect to positive identification. The mass spectrometer, unfortunately, requires more analyte to be present which is reflected in a higher limit of detection. The practical useful range of Method #502.1 is above 10 ug/L and not at low parts per billion levels."

"This method has numerous interference problems such as complex mixtures containing coeluting materials and situations where concentration differences for components are larger than a factor of 10."

In addition, this commenter pointed out that, "it is virtually impossible to establish the presence or quantity of methylene chloride in environmental samples."

Most of the comments for Method #502.1 also apply to Method #503.1. "The only differences would be that Method #503.1 uses a photoionization detector instead of a halogen specific detector and the acceptable range for the EMSL certified standard has been raised to + or - 20% of the true value."

In sum, this commenter questioned "why EPA would propose these methods and solicit comments without providing the necessary supporting data to demonstrate that a particular method is not subject to matrix effects (robustness), has an acceptable level of accuracy (recovery) from the matrix of interest and will generate data with an acceptable and defined level of uncertainty, both within one laboratory (repeatability) and more importantly, between laboratories (reproducibility). Without such data it is impossible to properly evaluate the methods."

Response:

EPA has revised Methods 502.1, 503.1, and 524.1. Additional information on the precision and accuracy of these methods obtained from an interlaboratory method validation study are given in the Federal Register Proposed Rule for MCLs for VOCs. These methods were tested by 20 laboratories using drinking water spiked with VOCs at various levels. Single operator precision, overall precision, and method accuracy were found to be related to the concentration of the analyte. EPA feels that a requirement that analysis of reference standards agree within + or - 20 percent of the certified values above 10 ug/L is a reasonable criterion that has been successfully applied to its drinking water contract laboratories. (This requirement has been modified in the revised version of Method 502.1 since, originally, the requirement was + or - 10 percent of the certified value.) EPA is presently in the process of gathering information to determine what performance criteria are reasonable at concentrations below 10 ug/L.

EPA recognizes that the limits of detection are dependent on the detection system used for the measurement and that there are tradeoffs between the use of a halogen specific detector and a mass spectrometer. An electrolytic conductivity detector was used to gather the information presented in Method 502.1. A separate method using a mass spectrometer as the detection system has been developed by EPA.

Method 524.1 is a gas chromatography/mass spectrometry (GC/MS) method developed by EMSL in recognition of the fact that the electrolytic conductivity and the mass spectrometer detection systems have differences in sensitivity, specificity and that there are specific quality control requirements peculiar to GC/MS methods. Method detection limits (MDLs) are lower for Method 502.1. However, Method 524.1 can measure most VOCs of interest at or below 1 ug/L. Again, these MDLs are achieved not only by EPA's EMSL laboratory but also by its contract laboratories.

The section devoted to interferences provides useful information on precautionary measures to avoid contamination of samples. This section is devoted to pointing out good laboratory practices in quality control to verify that compounds measured were present in the original sample and are not the result of sample contamination. This information is the result of experience with the analytical methodology and in no way detracts from the usefulness of the methodology if the analyst follows the recommendations provided.

Concerns expressed by commenters about Method 503.1 are similar to those already discussed for Method 502.1. This method has been successfully used for the determination of aromatic compounds such as benzene by other laboratories besides EMSL. The revised method provides information on single operator precision, overall precision and method accuracy at various concentration levels. These data were obtained from an interlaboratory method validation study in which 20 contract laboratories participated. The statement related to the decomposition of aromatic compounds in non-sterile samples is followed by the statement that samples can be stabilized by adding a preservative. The revised method recommends the adjustment of pH to <2 and chilling samples on the day of collection until analysis for preservation.

I. ANALYTICAL COSTS OF MONITORING

Issue: What are the analytical costs associated with monitoring for VOCs? TOX?

Comments:

Eleven commenters addressed the issue of analytical costs. Eight commenters estimated the cost for EPA Methods #502.1 and 503.1. Five commenters agreed with the cost estimate stated in the ANPRM to range from $100 to $200 per sample. Another commenter felt the cost would be $80 per sample. Two other commenters believed the estimated costs in the ANPRM were too low. Their reasoning was that EPA's estimate did not recognize the hidden costs, such as: time required to set up the method, calibrat the instrument, analyze the EMSL certified standards, determine detection

and quantification limits, establish precision and accuracy, train technicians and demonstrate that the analyst and laboratory are qualified to analyze samples; a conservative estimate of cost per sample would be $500 to $600.

Six comments were received concerning the GC/MS analytical method estimated costs. Each commenter's cost estimate was different, ranging from $75 to $100 per sample to $300 per sample.

Four commenters estimated the cost for EPA Method #450.1 (TOX). Two commenters agreed with the cost estimate stated in the ANPRM of $100 per sample. Two other commenters felt the cost would be $120 per sample and $40 per sample, respectively. One commenter stated that EPA's estimated analytical costs are a gross underestimation of actual costs per sample for these methods.

Response:

EPA conducted a survey of analytical costs associated with the analysis of VOCs. The survey included 28 commercial laboratories throughout the U.S. The average cost for GC/MS analyses was $197/sample and for GC analyses (Method 502.1 and 503.1) was $187/sample. The range of prices quoted was from $50-$300 for GC/MS and $75-500 for GC analyses. These prices are presently being charged by these laboratories and include the "hidden costs." The prices quoted by the commenters appear to be excessively high from the information obtained by EPA.

J. TOTAL ORGANIC HALOGEN

Issue: Should Total Organic Halogen (TOX) be used as a screening mechanism for VOCs?

Comments:

Of 22 comments received, 12 did not favor using TOX as a screening tool for VOCs. Their reasoning is as follows:

The lack of specificity would not allow determination of specific compounds without re-analysis. These commenters felt that costs were not that much less expensive than VOC analysis. They felt that more information would be provided to public water systems using VOC analysis instead of TOX. Furthermore, they felt that VOC analysis would be more cost-effective. Several commenters pointed out that VOCs would be masked in TOX analysis in systems using chlorination. Benzene would not be detected by TOX analysis.

One commenter submitted detailed comments on the use of TOX. The shortcomings cited were: "If TOX (detection limit 5 ppb) is used as a screening method to determine if samples should be analyzed using Method #502.1 (detection limit <10 ppb), the concentration level where one could reliably quantify the data would be approximately 15 ppb. The differences in detection limits for the two methods would limit the usefulness of TOX, as a screen for Method #502.1, to situations where the sum of chlorinated species exceeds 15 ppb. Furthermore, there are no definitive data to

indicate that TOX will respond to, or is suitably precise or accurate for the compounds of interest cited in the ANPRM. Also, in order to use TOX, the method should specify just how the undissolved solids are to be handled."

Ten commenters felt that TOX should be used as a screen for VOCs. These commenters pointed out that use of TOX would avoid use of the more expensive analytical methods that test for a specific list of compounds. TOX would detect all organic halogens, not just those VOCs listed. Once a positive result has been verified, additional testing to determine the source and nature of the problem could be initiated. It was suggested that EPA should provide either guidance or a standard for TOX as a reference background. These commenters felt that TOX would be the most cost-effective monitoring technique. One commenter suggested that TOX should be used in an initial round of monitoring of all public water systems and that for those systems not finding levels above background, TOX monitoring should be conducted at periodic intervals.

One of the above comments received stated that it might be appropriate to use TOX as a screening analysis. However, TOX has three major disadvantages: (1) it does not give readings for individual compounds; (2) it does not measure non-halogenated VOCs such as benzene (one of the 14 VOCs addressed in the ANPRM); and (3) certain questions remain to be answered about which pollutants are detected with what analytical precision and accuracy.

Response:

EPA has conducted studies to evaluate the feasibility of using TOX as an indicator for VOCs and has decided not to use TOX since it does not measure individual compounds for which the MCLs are proposed and it does not measure compounds such as benzene. In addition, it would not be cost-effective since the individual compounds would have to be analyzed using VOCs analysis in any case to insure the levels are in compliance with the MCL.

K. TREATMENT TECHNOLOGIES

Issue: Are treatment technologies generally available to reliably remove VOCs to appropriate levels?

Comments:

Twelve of the 15 commenters felt that treatment technologies were generally available to remove VOCs. Six commenters favored the use of either GAC or a combination of GAC and aeration on the basis that these are the most costeffective treatment technologies, there is no basis for concern of leaching of any chemical material from GAC, VOC concentration can be reduced to 10 ppb or less, and 90% removal with aeration and 99% removal with GAC can be achieved.

Some of the above commenters differed on the following two issues: (1) small system feasibility (two commenters said small systems will have no difficulty in operating and installing GAC and/or aeration technologies

and two said there would be difficulty) and (2) whether or not air pollution will be significant from aeration (one commenter said no air pollution would result, another said there would be).

Five commenters felt that EPA should not require a specific treatment technique. They recommended that the treatment technology be decided on a case-by-case basis. Suggested factors which determine treatment feasibility were: volatility of the contaminants present, air temperature, price fluctuations for GAC media, availability of operators, efficacy of modification to existing plant facilities, and potential for future contamination.

Two of the above commenters felt that small systems will have difficulty in installing and effectively operating the available treatment technologies. One commenter recommended that small systems should receive preferential treatment such that systems supplying 500 to 1,000 people should be excluded and systems supplying 5,000 to 10,000 people should use the simplest type of aeration treatment.

Three commenters felt that treatment technologies are limited at this time. One commenter stated that there are many unanswered questions concerning the use of GAC as to the actual costs, breakthrough of organics in the bed, and such items as frequency of regeneration. Another commenter suggested the use of either small on-tap water filtration systems or powdered activated carbon and sand and gravel filtration. However, performance data indicates that neither treatment is sufficient to purge VOCs. This commenter further questioned the orientation of the ANPRM's treatment section, in that the section focuses more on cost and less on the willingness of water consumers to accept higher water costs for a greater degree of safety. In addition, this commenter recommended that small systems be consolidated in order to handle the treatment costs.

Response:

EPA addressed the above issues in the Federal Register Proposed Rule for MCLs for VOCs. Although treatment costs per unit volume of water are more expensive for the smaller systems, EPA believes they are affordable and small systems have installed these technologies even in the absence of Federal requirements. For very small systems, on-tap filtration devices may offer the best alternative. An approach for how such systems might be used to meet the MCLs is discussed in the proposal.

L. COSTS OF TREATMENT TECHNOLOGIES

Issue: What are the capital and operating costs of available treatment technologies? Are the costs presented in the ANPRM reasonable?

Comments:

One commenter felt the costs presented in the ANPRM are accurate. However, this commenter expressed concern that there are large uncertainties due to the fact that there is no history of costs for completed and operating facilities.

Three commenters felt the costs presented in the ANPRM are too low. Two commenters stated that the costs were low by a factor of about two.

One commenter felt the costs for GAC in the ANPRM are 2 to 3 times higher than actual costs and that capital expenditures are overstated in Tables IV and V. For example, in the population category of 1,000 to 2,499, capital expenditures of $344,000 are shown. This figure is 7 times higher than their experience indicates. Complete cost estimates were submitted. One commenter felt that cost estimates should be compound specific.

Detailed cost estimates concerning GAC and Packed Tower Air Stripping were submitted by one commenter.

Response:

Based on new information, EPA has updated capital and operating costs in the Federal Register Proposed Rule for MCLs for VOCs. See the proposal for a discussion of the costs used.

M. RISK/BENEFIT ANALYSIS FOR VOCs

Issue: Should a risk-benefit analysis be done concerning VOCs in drinking water?

Comment:

One commenter addressed this issue and did not favor analysis to be done for any regulation that applies to human health.

Response:

EPA presents an analysis of regulatory alternatives in the Federal Register Proposed Rule for MCLs for VOCs. This analysis is conducted in response to Executive Order No. 12291 and discusses risks and costs. The SDWA requires setting RMCLs based upon health effects only and MCLs based upon cost and feasibility factors.

N. DIFFICULTIES OF MONITORING REQUIREMENTS FOR STATES

Issue: Will monitoring requirements impose any difficulties to States and water companies?

Comments:

The two commenters that addressed this issue felt that any monitoring requirements will create monetary difficulties for their respective States, especially in lieu of federal cutbacks.

Response:

In the proposal of MCLs for VOCs, EPA proposed alternatives for conducting monitoring over an extended period to mitigate cost impacts. EPA solicits comments on these proposals.

O. HOME WATER TREATMENT SYSTEMS

Issue: Should EPA encourage the use of home water treatment systems?

Comments:

The two commenters responding to this issue felt that EPA should review and publish information concerning small on-tap water filtration systems. One commenter stated that one water purifier can remove 95% to 100% of 106 organic chemicals.

Response:

EPA discusses the use of on-tap filtration systems for removing VOCs in the Federal Register Proposed Rule for MCLs for VOCs. Literature on the performance of these devices is available in the public docket. Also, the following report is available through NTIS.

> Perry, D.L., J.K. Smith, and S.C. Lynch. 1981. Development of Basic Data and Knowledge Regarding Organic Removal Capabilities of Commercially Available Home Water Treatment Units Utilizing Activated Carbon. Phase 3/Final Report. Performed for Criteria and Standards Division, Office of Drinking Water, United States Environmental Protection Agency.

P. STRATEGY FOR CONTROLLING VOCs

Issue: What strategy should be adopted to control VOCs in drinking water?

Comments:

Eleven comments were received concerning this issue. Eight commenters emphasized control of contaminants at their source instead of remedial action, primarily concerning ground water.

One commenter proposed a regulatory strategy similar to the possible approaches in the ANPRM which is as follows:

- establish a National Drinking Water Quality Assessment Program under Section 1445 of the SDWA to assess the quality of drinking water across the country;
- prepare health and technical guidance documents for all of the VOCs found in drinking water for the use of State or local authorities to determine whether they have a contamination problem;

- develop a contingency plan whereby the Administrator, under the statutory authority of Section 1431 of the SDWA, would take remedial action if a serious threat to public health is being ignored by the responsible State or local authority; and

- reassess the need for national regulations based on data generated from the Drinking Water Quality Assessment Program or other reliable sources.

One commenter was not in favor of a single MCL value since spills and dumps into surface streams or ground water supplies create extremely atypical transient conditions. This commenter recommended setting three MCLs, that is: long-term effect MCL; short-term MCL (cover spills); and emergency response MCL (concentration above which the drinking water is immediately not recommended for use).

Response:

EPA believes that enough information is available to support national regulations requiring monitoring for 9 VOCs at this time by all public drinking water systems and compliance with specific MCLs. Proposed monitoring requirements and MCLs are presented in the Federal Register Prop sed Rule for MCLs. EPA is continuing the preparation of health advisories for numerous VOCs found in drinking water.

In reference to the commenter who favored setting three MCLs, the Safe Drinking Water Act specifies that a single MCL be set for chemicals of concern in drinking water. However, by setting health advisories for short- and longer-term exposures, EPA has developed numbers to take care of emergency and longer-term exposures.

Q. MISCELLANEOUS

1. Comment:

EPA did not address a "cost-cutoff," the point where the cost of improving the water is higher than the health benefits resulting from the improvement. One commenter proposed three factors which may help establish cost-cutoffs: public pressure, the cost of imported water, and the cost of other residential utilities. Supporting documentation was submitted.

Response:

EPA does not establish MCLs based on "cost-cutoff" points. However, the SDWA requires setting MCLs based upon cost and feasibility factors, including reasonable costs for public water systems. MCLs are established as close to RMCLs as is feasible taking costs into consideration. A benefit-cost analysis for various regulatory approaches, including "cost-cutoff" points, is available in the Economic Impact Analysis in the Public Docket for Proposed MCLs for VOCs.

2. Comment:

EPA is ignoring the fact that VOCs are only one of several groups of organic chemicals which contaminate many drinking waters. Furthermore, EPA conducted a biased analysis comparing the total cost of treatment to only part of the benefits (ignoring non-volatile organics, PCBs, and taste and odor). EPA should avoid a benefit-cost approach to controlling VOCs and adopt a technology-based approach.

Response:

EPA is developing regulations which will consider other groups of organic chemicals. The extent of secondary benefits in treating to remove VOCs will depend on the technology that is used (different for GAC vs. aeration). If the contaminants of concern can be economically and technologically measured, as is the case for VOCs, EPA is required under the Safe Drinking Water Act to develop MCLs rather than a treatment regulation.

3. Comment:

A major failure of EPA's risk assessment procedure is the attempt to use a mathematical exercise as a substitute for sound scientific data (supporting documentation was submitted).

Response:

EPA's risk assessment procedure involves a qualitative analysis of the data to determine the strength of evidence of carcinogenicity and subsequently a quantitative analysis consisting of mathematical extrapolation, if the quality of evidence has been determined to be sufficient. EPA believes that all appropriate data should be considered in the risk assessment process.

4. Comment:

The Ground Water Supply Survey (GWSS) is biased in the way the samples were selected. The 500 samples should have been randomly selected rather than arbitrarily deciding 200 should be from systems serving under 10,000 people and 300 systems serving greater than 10,000 people.

Response:

In the GWSS, 500 samples were selected at random following a stratified community population base to assure national representation of all community sizes.

5. Comment:

GWSS study results are probably significantly lower than what is actually present in the water supplies sampled because the samples were analyzed 1-2 years after being collected. There are probably a number of false negatives.

Response:

This problem with the GWSS data was discussed in the occurrence assessment reports. The national estimates of occurrence for those substances for which long holding times in the GWSS (and other surveys) leads to a reduction in the measured contaminant level are recognized as potentially underestimating actual occurrence levels.

6. Comment:

EPA needs to do in-depth studies on exposure to VOCs from all routes, taking into account geographic variations and socioeconomic factors in order to characterize the significance of exposure to VOCs from drinking water across the general population.

Response:

The existing body of data and available resources are inadequate to develop national occurrence and exposure data to account for variability among different subpopulations.

II. SUMMARY OF COMMENTS AND EPA RESPONSES ON JUNE 12, 1984 RMCL PROPOSAL ON TECHNICAL ISSUES

A. TRICHLOROETHYLENE

1. Comment:

Two commenters selected two studies to calculate the RMCL for trichloroethylene: Kimmerle and Eben (1972) and Adams, et al. (1951). They also provided step by step derivations to calculate the RMCL as follows:

"For the purpose of risk assessment, a NOEL of 100 ppm is justified. Calling 100 ppm a NOEL is a scientific judgment reflecting the fact that 200 ppm for 6 months was a no-observed-adverse-effect level (Adams, et al., 1959) for four species, while taking into account the broad range over which liver weight increases were observed by Kimmerle and Eben (1971) and Adams, et al. (1951).

In converting this NOEL based on the Wistar rat to a dose expressed in mg/kg/day, two factors must be taken into account that are absent from the calculation in the draft criteria document. These are the minute volume (0.225 1/min) and the average body weight of the male (0.35 kg) Wistar rat. These factors are necessary because the rodent inhales a greater volume of air per unit of body weight than the human. Adding these factors to the assumptions used in the criteria document, the NOEL for the Wistar rat may be expressed in mg/kg/day as follows:

$$\frac{100 \text{ ppm} \times 0.0054 \text{ mg/1}^{*} \times 0.225 \text{ 1/min} \times 480 \text{ min/day} \times 0.3^{**} \times 5^{***}}{0.35 \text{ kg} \times 7^{***}}$$

$$= 31.2 \text{ mg/kg/day}$$

* Conversion factor (1 ppm v/v in air = 0.0054 mg/1 at 25°C and 760 torr)
** Absorption rate
***Conversion of 5-day to 7-day exposure

Thus, using the methodology and the thousand-fold safety factor suggested by EPA, the AADI for man may be computed as follows:

$$\frac{31.2 \times 70 \text{ kg}}{1{,}000 \times 2 \text{ L/day}} = 1.09 \text{ mg/L}$$

Again using the methodology suggested by EPA, this AADI may be converted into an RMCL by dividing by 5, on the assumption that drinking water contributes 20 percent of the total daily intake. This results in an RMCL for tri of 0.22 mg/L."

Response:

The Adams, et al. (1951) study is a summary of toxicological data and therefore cannot be used for the derivation of an RMCL. There is not enough raw data available from the Adams study to determine its validity. EPA selected the Kimmerle and Eben (1973) study for the calculation as it

is not a summary of toxicological data; it is a well designed and well conducted study and is therefore an acceptable study available to make calculations.

The EPA and the commenters' approaches to calculating the ADIs are similar, the major difference being the dose conversion from inhalation to ingestion exposure. EPA has used the approach of Olson and Gehring (Olson, K.J., and P.O. Gehring. 1976. Basis for Estimating Acceptable Levels of Organic Contaminants in Drinking Water Employing Inhalation Data. Unpublished report prepared for the National Academy of Science's Safe Drinking Water Committee) in which it is believed that the dose for the human would be the same as it is for the experimental animal because the lung volume to body weight ratio is the same across species, including man. Thus, one can substitute the parameters for the human into the equation. It is difficult to find consensus on exactly what values are correct for minute volume and body weight for various strains and species and, thus, EPA believes it is more appropriate to use the Olson and Gehring approach.

2. Comment:

It is very difficult to comment on this draft CD since it neglects so many key references that should have been included. A comparison of the bibliography of the draft HAD with this CD quickly illustrates that many more references are available than have been used.

Response:

In response to this comment, EPA reviewed all the references in the draft HAD. EPA added only the reports which were considered relevant in deriving the AADI. Particular attention was directed toward the utilization of primary references for the assessment of health effects. Secondary references were rarely used.

The object of the CD is to assess the health effects information on trichloroethylene in drinking water for the purpose of proposing an RMCL. To achieve this objective, data on pharmacokinetics, assessment of human exposure, acute and chronic health effects in animals, human health effects (including epidemiology) and mechanisms of toxicity were evaluated.

3. Comment:

The CD does not present a balanced summary of the data on mutagenesis. Page I-2, Line 16 "Trichloroethylene is mutagenic in bacterial test systems utilizing liver microsomal fractions for activation." As the CD states, it is not possible to rule out the possibility that pure TCE caused a slight increase in mutant yields in Salmonella. However, it is important to consider criteria for positive mutagenic response in this assay. Among the most commonly accepted requirements for a positive result are a dose-response relationship, replication of results, exceedance of spontaneous rates by 100% and indications of less than an overwhelming degree of cytotoxicity from the chemical exposure. The reported studies are quite deficient in these respects. Thus, it is appropriate to use them to support contentions of positive mutagenic activity. See de Serres and Shelby, Sciences 203, 563 (1979) for a discussion of recommended criteria

for positive responses in Salmonella tests. The Criteria Document suggests that mutagenic responses in bacteria and other organisms were dependent on metabolic activation systems and, thus, stabilizers were not responsible for activity seen. However, a clear demonstration of the active role of stabilizers in Salmonella reversions was demonstrated by Shimada and Williams (1983). This should be reflected in the CD.

Response:

The comment relates to the Summary Section of the criteria document. This section provides pertinent information concerning the health effects of trichloroethylene. Appropriateness or validity of the studies, in this case mutagenesis, is discussed in the body of the document. The EPA has accepted the conclusions, and thus the criteria, of the investigators who reported the studies for positive mutagenic responses to the trichloroethylene samples tested in bacterial, as well as in other test systems.

Despite the commenter's arguments on commonly accepted requirements for mutagenicity findings, we believe there is adequate qualitative evidence of mutagenicity.

EPA accepts that the Shimada and Williams study shows that there is a demonstration of the active role of the stabilizers. However, there is evidence that pure TCE is mutagenic (See Greim, et al. 1975, 1977 and Bartsch, et al. 1979).

4. Comment:

The CD fails to present a balanced summary of the probable mode of carcinogenic action. It is noteworthy that prominent members of the EPA Science Advisory Board, after reviewing the data on trichloroethylene, concluded that it was not appropriate to calculate a unit risk assessment for trichloroethylene. The mode of toxic action was most likely non-genetic and the increase in tumors in the mouse was due to repeated tissue injury.

The last sentence on page I-2 needs to be revised or eliminated since it is not consistent with current information. "This intermediate is thought to be responsible for the mutagenic and carcinogenic potential of trichloroethylene." There is now a considerable body of data which indicates trichloroethylene increases tumors in mice by a non-genetic mechanism. A large number of scientists and several organizations recognize that repeated injury and the resultant repair can enhance the onset of "normally" occurring tumors. Hepatocellular carcinomas in mice livers are a commonly cited example of a non-genetic mechanism. Hence, the epoxide is not "thought to be responsible for the mutagenic and carcinogenic potential of trichloroethylene," as stated in the CD.

Furthermore, the CD should not refer to the current NTP study until the NTP has issued a final report. It has been necessary for NTP to withdraw certain draft reports in order to make significant changes We have also become aware of a very recent paper (attached) by Henschler, Elsasser, Romen and Eder (1984) in which they reported no increase in tumors in male and female Swiss (ICR/HA) mice given 2400 and 1800 mg/kg daily by gavage in corn oil for two years.

Response:

The sentence, "This intermediate is thought to be responsible for mutagenic and carcinogenic potential of trichloroethylene," has been taken out of context. This sentence provides accurate information if read along with, "However, interaction of the epoxide with the nuclear material - a step towards carcinogenesis - has not been studied."

The current NTP study is final and has been accepted by the NTP Board of Scientific Counselors. This study (1984) has been added to the Criteria Document. The recently published study by Henschler, et al. (1984) does not offset the conclusion of sufficient animal evidence, which has been obtained with different experimental systems, for the carcinogenicity of trichloroethylene by the EPA. The NTP studies and the Fukuda study are better tests and outweigh the Henschler study. The Henschler study used mice that are known to be less responsive to hepatocellular carcinomas.

Although some members of the SAB questioned the risk assessment, the SAB as a group accepted the study. The risk assessment is based on the best available evidence; we recognize there are flaws. However, we are not basing regulation on it. Its information is useful to decisionmakers even with limitations.

EPA rejects the distinction between epigenetic/genetic mechanisms (See Comment/Response I.D.1). It is possible that both epigenetic and genetic mechanisms are active here; the fact that epigenetic mechanisms occur doesn't preclude the possibility that genetic mechanisms are also occurring. Since there appears to be sufficient evidence that TCE is a carcinogen, the exact mechanism is unimportant for purposes of regulation under the SDWA. There certainly is not enough evidence to establish a threshold of carcinogenic effects from the data suggesting an epigenetic mechanism.

5. Comment:

"It has been used in...dry cleaning shops..." TCE has extremely limited use in industrial dry cleaning of shop uniforms, gloves and towels, but has no use in retail cleaning machines or coin-operated machines in the U.S. While it may have had some experimental use in the early 1930's, it was quickly found to be an unsatisfactory solvent for personal clothing since it removed colors and damaged certain fabrics and plastics.

Response:

The EPA accepts the comment.

6. Comment:

"After entering the blood stream, it distributes into various tissues and organs. The extent of distribution depends largely on the fat content of the organ." This paragraph fails to indicate that a significant portion of ingested trichloroethylene will be rapidly expired unchanged from the lungs. The extent of distribution of the remaining trichloroethylene depends upon several factors including the fat content of the organs. As written, the reader is led to associate distribution with accumulation (or

bioaccumulation) and long-term storage, as is the case with certain large, nonvolatile chlorinated and non-chlorinated substances (i.e., DDT, PCBs, etc.). This cannot be the case for a volatile substance such as trichloroethylene which has a relatively rapid partitioning into and out of body organs.

Response:

The sentence in the Criteria Document appropriately discusses the mechanism of transfer of trichloroethylene in body. It has nothing to do with the bioaccumulation of trichloroethylene in the body. Bioaccumulation of a chemical depends upon the physical and chemical properties, dosing regimen, metabolism and other factors.

We agree that a significant portion of ingested TCE will be expired from the lungs. However, the remaining TCE in the system will be distributed as described.

7. Comment:

"This intermediate (cis 2,2,3-trichlorooxirane) is thought to be responsible for the mutagenic and carcinogenic potential of trichloroethylene." There is not agreement as to what role a potential TCE-epoxide may play in the toxicity of TCE or whether it even represents an obligate intermediate in the metabolism of TCE to the observed excretion products. Miller and Guengerich (1982, 1983), and Henschler, et al. (1979) have provided substantial evidence that several alternative metabolic schemes for TCE exist which do not involve obligatory formation of a TCE-epoxide. It is also noteworthy that in vitro TCE-epoxide has been detected in incubation of TCE with mouse and rat liver microsomes, but not when human microsomes were used (Miller and Guengerich 1983). Further, it has been suggested, with a considerable amount of supportive data, that TCE may cause tumors in mice as a result of trichloroacetic acid-induced proliferation of peroxisomes (subcellular organelles primarily involved in fat metabolism) (Elcombe, et al., 1983a, 1983b). This latter mechanism of tumorigenicity would not involve any interaction of TCE with DNA (Reddy 1983). The statement should more accurately reflect the available TCE metabolism data and not present theories regarding TCE tumorigenicity.

Response:

There is not substantial evidence of alternative metabolic schemes, as suggested by this commenter, only some evidence to support the hypothesis offered by the commenter. EPA agrees that there are several possible mechanisms for TCE metabolism. Several new metabolism studies were noted by the commenters and are discussed in the final criteria document, e.g., Miller and Guengerich (1982, 1983), Elcombe, et al. (1983a, 1983b). EPA also included the Dekant, 1984 study in the criteria document. These studies do not affect EPA's conclusions. Tumorigenicity appears to be one result of the possible mechanisms. Therefore, the above statement in the criteria document has been changed to read, "This intermediate (cis 2,2,3-trichlorooxirane) may be responsible for the mutagenic and carcinogenic potential of trichloroethylene."

9. Comment:

"Trichloroethylene was found (to be) carcinogenic in $B_6C_3F_1$ strain mice: however, it was not carcinogenic in Osborne-Mendel rats." Four other oncogenicity bioassays of TCE are not mentioned.

a. Henschler, et al. (1980) did an inhalation study using NMRI mice, Syrian hamsters and Wistar rats. No treatment-related tumors were noted in any sex or species exposed to TCE. An observed increased incidence of lymphomas in female mice was of viral origin which is endemic in this strain of mouse.

b. Fukuda, et al. (1983) did an inhalation study using female ICR mice and Sprague-Dawley rats. An increased incidence (not dose-related) of lung adenocarcinomas was observed in mice, while no tumorigenic response was seen in rats. This strain of mouse has been observed to normally have a high (up to 30%) incidence of benign lung tumors. These results with the ICR mice thus appear to be analogous to the results obtained with the B6C3F1 mouse, in which TCE exposure increased the incidence of a tumor which may already occur at a high incidence in control animals. IARC does not consider either lung or liver tumors in mice to be indicative of a carcinogenic risk to man.

c. An increased incidence of tumors was not observed in ICR mice receiving dermal applications of 1 mg/kg TCE 3 times a week for nearly 2 years, nor was TCE found to be an initiator in a skin initiation/promotion bioassay by Van Duuren, et al. (1979).

d. Henschler, et al. (1984) reported no tumor increase in male mice fed 2400 mg/kg/day in corn oil for two years or in female mice fed 1800 mg/kg/day for the same period. The mice were ICR/HA Swiss.

Response:

Trichloroethylene (TCE) appropriately belongs to group B2, indicating that there is sufficient evidence of it producing cancers in animals.' This is the classification for carcinogenicity concluded by a technical panel of EPA's Risk Assessment Forum (RAF) using the recently Proposed EPA risk assessment guidelines for carcinogens (FR 49 (227):46294-46301). The RAF considered all four of these studies. It has been shown to be carcinogenic in different strains of mice utilizing the inhalation as well as the oral route of exposure. The National Cancer Institute (1976) and the National Toxicology Program (1982) conducted two separate studies with TCE contaminated with epichlorohydrin and with TCE free of epichlorohydrin. In these studies, $B_6C_3F_1$ mice were used, and the results were unequivocally positive, showing liver neoplasms. In the inhalation study cited, Henschler, et al. (1980) reported dose-related malignant lymphomas in female mice (NMRI strain). However, the authors downplayed the significance of this observation, indicating that this strain of mice has a high incidence of spontaneous lymphomas. EPA questions this conclusion by the authors as it appears to be speculative. Fukuda, et al. (1983), found pulmonary adenocarcinomas in female ICR mice on exposure to TCE vapor. Although there is an elevated incidence of lung tumors in this mouse, EPA still believes that the evidence is suggestive, as it does for studies using the $B_6C_3F_1$

mouse. The EPA classification scheme does give some weight to studies using species with normally elevated incidences of the effect (e.g., the $B_6C_3F_1$ mouse and liver tumors). Henschler, et al. (1984) tested Swiss (ICR/HA) mice and reported that when the animals were gavaged with TCE in corn oil, no statistical differences were observed in the incidence of cancers. The results of this study can be questioned because dosing and the dose levels were changed throughout the experiment. Therefore, it is ditficult to assess the actual doses given to the animals. A slight increase in tumors was found in all groups treated with TCE but did not approach statistical significance. The Van Duuren study (1979) with skin applications of TCE in ICR/HA mice does not negate the positive findings with other strains of mice and other routes of exposure. The indicated bioassays in the comment have been added to the criteria document. EPA believes that these data, taken together and despite their weaknesses, support classification in the sufficient evidence category.

There is other evidence to support the classification of TCE in group B2. In addition to the long-term bioassays discussed above, TCE has been reported to be weakly mutagenic and to have a low order of binding with DNA.

9. Comment:

This section should include the very relevant information included in papers by Henschler, et al. (1979), Miller and Guergerich (1982, 1983) and Dekant, et al. (1984) Further, metabolism data for TCE inhaled by rats and mice, with evidence of metabolic saturation in rats, presented by Stott, et al. (1982) was also omitted.

Response:

These new references have been discussed in the TCE criteria document.

10. Comment:

Quoting from the Criteria Document: "From the NAS model, it is estimated that at the 95% confidence limit, consuming two liters of water having trichloroethylene concentrations of 45 ug/L, 45 ug/L or 4.5 ug/L per day over a lifetime would increase the risk of one excess cancer per 10,000, 100,000 or 1,000,000 people exposed, respectively".

In reviewing the data on trichloroethylene, members of the EPA Science Advisory Board clearly indicated their lack of confidence in these calculations. The use of an inappropriate animal model (the $B_6C_3F_1$ mouse liver) and the 95% confidence limit are inappropriate.

Response:

The EPA is utilizing state-of-the-art concepts which are consistent with the NAS model in estimating excess cancer risk due to trichloroethyl ne exposure. These concepts include use of the most sensitive animal model and the 95% upper bound with the multistage model. The above calculations present concentrations or TCE in drinking water at which appropriate risk can be expected.

In 1984, the SAB accepted the Agency's health assessment document on trichloroethylene, including the risk assessment based on mouse liver tumor data and the 95% upper limit with the multistage model.

11. Comment:

"Based on the mechanism of toxicity-specifically mutagenesis and carcinogenesis-trichloroethylene has the potential of being carcinogenic. TCE has been reported to bind with mouse liver DNA in an in vivo experiment".

The DNA binding and mutagenicity data do not provide support for the carcinogenicity of TCE. Indeed, these data indicate that TCE is not at all similar to several known potent carcinogens. The in vivo DNA binding data suggest a very minor degree of DNA alkylation occurs in $B_6C_3F_1$ mice dosed with a high or low dosage of TCE (Stott, et al., 1982), and its very weak mutagenicity suggest that TCE does not increase tumors via the direct interaction with genetic material but, rather, increases tumors via some nongenetic mechanism. This statement should be modified to accurately reflect the data.

Response:

The EPA disagrees that the DNA binding and mutagenicity data do not support carcinogenicity. The data on TCE need not be similar to other potent carcinogens.

The Office of Science and Technology Policy reviewed current views on the mechanism of carcinogenesis and concluded that ". . .cancer development is a multistage process that may involve the genome, both indirectly (frequently termed epigenetic events) and directly, which may include the participation of chemicals or viruses, and which may be modulated by higher order functions, i.e., at the organ and organismic level." Thus, it appears that chemicals may act by genetic and nongenetic mechanisms. EPA concludes that the sentence need not be modified. Many scientists believe that DNA binding and mutagenic responses provide data supporting the carcinogenic potential of compounds. Various mechanisms for carcinogenicity have been proposed, and epigenetic and genetic mechanisms are among them.

12. Comment:

Data presented by Stott, et al. (1982) regarding the hepatotoxic effects of repeatedly administered TCE was omitted.

Response:

See Comment/Response II.A.14 below.

13. Comment:

The findings of three oncogenicity studies (see comments on Section 1-2) were omitted.

Response:

See Comment/Response II.A.14 below.

14. Comment:

The Stott, et al. (1982) reference should be discussed. The extensive hepatic and renal macromolecular binding data for inhaled (and orally administered-mouse) TCE in rats and mice which was presented in this paper are omitted.

Response:

These references are included with discussion of the data in the criteria document.

15. Comment:

There is insufficient scientific evidence to conclude that trichloroethylene is a carcinogen and the RMCL should not be set at zero.

Response:

EPA believes that there are sufficient toxicologic data to conclude that trichloroethylene is a probable human carcinogen. A repeat bioassay by the NCI found an increase in hepatocellular carcinomas in both sexes of mice using purified trichloroethylene in corn oil, while the initial bioassay using commercial grade trichloroethylene was also reported to induce hepatocellular carcinomas in male and female mice by oral gavage (See Federal Register Final Rule on RMCLs - Appendix A for a discussion of mouse liver tumors and EPA's response concerning their relationship to human cancer risk and see Comment/Response - II.A.8).

16. Comment:

A biological based approach to quantitative risk assessment which consists of establishing an ADI on the basis of the experimentally derived no-observed-effect level with the application of a safety factor should be used. The safety factor should range from 100 to 1000, based upon a consideration of the mechanism of carcinogenesis, the number and type of tumors induced, the spontaneous incidence of the tumor and other factors.

For those animal cancer studies which did not employ lower dose levels to define a NOAEL, the most sensitive cancer response extrapolated linearly down to a dose equaling with a one percent increase above the spontaneous incidence for the particular type of tumor associated with exposure to the chemical should be used. This dose would be comparable to a NOAEL and a safety factor would be applied based on the same considerations outlined above.

Response:

In regard to the biological-based approach, EPA believes that the primary issue centers on the mechanism(s) of action of the compounds. A

great deal of research and discussion has been forthcoming in recent years which addresses the issue of differing mechanisms for carcinogenesis. At the present time, however, EPA neither classifies nor quantitatively characterizes the risk of exposure to compounds for which carcinogenic potential has been identified on ther basis of their hypothesized mechanism(s) of action. As previously discussed, (see Comment/Response - II.A.11) EPA accepts the view of the Office of Science and Technology Policy that chemicals may act by genetic and nongenetic mechanisms. Consideration of the possibility of the existence of differences is incorporated indirectly in the weight of evidence classification scheme for carcinogenic potential recently proposed by the Agency (49 FR 46294). While data from long term human epidemiologic or experimental animal studies contribute most to the determination of the placement of a reputed carcinogen into one of the five groups, results in short term studies, some of which may give information on potential carcinogenic mechanisms, may result in the compound being placed in a category higher or lower than the longer-term study data would ordinarily suggest.

As described elsewhere, a three-tiered approach for the derivation of the RMCLs is being used. This approach is based, to a significant degree, upon the information available on the carcinogenic potential of each of the compounds for which regulatory action is being considered. The reader is referred to the Federal Register Final Rule for RMCLs for a detailed discussion of this strategy.

17. Comment:

It is very possible that, particularly in humans, at low dosage levels, the metabolic pathway which leads to the proximate carcinogen is not employed; and therefore, at low concentration levels, trichloroethylene and perhaps other volatile organic chemicals would not be carcinogenic, particularly in humans. (See attached draft paper, "Trichloroethylene: An Update," by Renate Kimbrough, Frank Mitchell and Vernon Houk.)

A summary of this paper follows:

AUTHORS' ABSTRACT

In this paper, recent studies that deal with metabolism and carcinogenicity of trichloroethylene (TCE) are examined. In reviewing the publications on metabolism of TCE, we determined that differences exist in its metabolism. If low doses are compared with high doses in animals, there may also be a difference in the metabolism of TCE between different species -- namely, mice, rats, and humans. TCE has not been shown to be a potent carcinogen in rats, and it only seems to be a potent carcinogen in one specific strain of mice -- namely the $B_6C_3F_1$ mouse. Epidemiology studies have been rather limited. The number of persons examined so far for chronic toxic effects is small, compared with the enormous size of the work force that is exposed to TCE over prolonged periods. On an empirical basis, the occupational experience with TCE does not suggest that this compound is a potent carcinogen. The risks associated with exposure to trace amounts (parts per billion) of

TCE concentrations in water appear to be minimal or perhaps negligible.

Because there are differences in the metabolism of TCE, it is important that theoretical risks attributed to TCE in the past be re-examined. It is highly possible that in humans, the metabolic pathway leading to the formation of the proximate carcinogen is not activated at low doses where TCE is excreted by first order kinetics.

Response:

EPA does not agree that trichloroethylene should not be considered a potential human carcinogen for the reasons discussed in the Federal Register Final rule. With regard to the nature of the carcinogenic action of trichloroethylene, EPA believes that there is insufficient scientific data to justify classifying chemicals as epigenetic or genetic carcinogens, as discussed in Comment/Response - II.A.16 above).

18. Comment:

Use of data from all three phases of the NOMS survey employed in projecting the national occurrence of TCE in public water supplies had the effect of skewing the projections in a way so that a larger percentage of water supplies were projected to contain some measureable amount of TCE.

Response:

In combining the results of all surveys to produce the national estimates, the results for supplies measured in more than one survey, or in the case of the NOMS more than one phase, were averaged so that the results would not be significantly skewed by multiple inclusions of the same supply.

19. Comment:

The TCE occurrence document fails to point out that there is a possibility of the TCE concentrations in samples increasing during the holding period due to the biodegradation or reductive dehalogenation of PCE to TCE.

Response:

EPA is unaware of any data that suggests that this had occurred. Since the commenter did not provide any specific data on this point, it is reasonable to assume that this was not the case.

20. Comment:

With reference to the tri, perc and methyl chloroform occurrence documents, it is questionable that any contamination was actually detected in food in the United Kingdom studies where the values obtained approached the limits of detection.

Response:

The United Kingdom data were noted because no other food studies were available but were not used to project levels of exposure.

21. Comment:

In the tri, perc and methyl chloroform occurrence documents, sources of exposure terminology should be defined (e.g., rural/remote, urban/suburban, source dominated and maximum).

Response:

These terms were used as presented in Brodzinsky and Singh (1982); the terms were not further defined in that source.

22. Comment:

Source-dominated exposures for tri, perc and methyl chloroform appear to be 4 to 5 orders of magnitude lower than those generally recognized as safe for occupational exposures.

Response:

The evaluation of human exposure to these chemicals was carried out in order to derive a drinking water level which considers total human exposure. It was not intended to evaluate safe levels for occupational exposure.

23. Comment:

In the tri, perc, and methyl chloroform occurrence documents, a minimum quantification level of 0.5 ug/L was used in combining data from various surveys while each survey had a specific MQL ranging from 0.05 to 5 ug/L. It is not clear whether sources designated as positive were based on the MDL of 0.5 ug/1 or on the MQL of each survey.

Response:

The column designated "No. of positive systems" in the tables presenting the combined results of all surveys included positives both above and below 0.5 ug/1; the total number of positives below 0.5 ug/L are also detailed in a separate column in those tables.

B. 1,1,1-TRICHLOROETHANE (METHYL CHLOROFORM)

1. Comment:

"Repeated exposure to methyl chloroform has been shown to increase the excretion of metabolites in both animals and man, probably by the mechanism of enzyme induction." Available data indicate that methyl chloroform exposure does not result in enzyme induction. It should be

further noted that massive, nonphysiological doses were used in the studies cited in the CD.

Response:

EPA agrees that the Schumann study cited by the commenter suggests that enzyme induction does not occur. However, the Platt and Cockrill (1969) study cited in the Criteria Document showed enzyme induction. Thus, there are conflicting data. In any event, there is not sufficient evidence to draw a definite conclusion. The statement in the Criteria Document reads "probably by the mechanism of enzyme induction" which is correct and, therefore, the Criteria Document has not been changed. The significance of the second comment on massive doses is unexplained by the commenter and EPA is therefore unable to respond.

2. Comment:

Page I-7, Line 8. "The CAG has calculated an upper limit cancer risk estimate based on the 1983 NCI bioassay ...respectively." This entire paragraph should be deleted, as it was from the final HAD after Science Advisory Board review. No acceptable scientific data are available to calculate such an estimate.

Response:

As stated in the Criteria Document, this information is included to inform the reader as to the CAG calculations and is not being used to determine the RMCL, which is based on non-carcinogenic effects. EPA believes that, despite the fact that this bioassay is under audit and is being questioned, a risk assessment can be useful as long as the fact that the study is under question is borne in mind.

3. Comment:

Page I-7, Line 21. "Although a number of studies have indicated chronic changes in the heart, nervous reflex activity, respiratory function, and hepatic changes resulting from 'long-term' exposure..." Data do not exist to support the statement that methyl chloroform exposure causes chronic changes in the heart or nervous reflex activity. Such changes, caused by high exposures, have been acute in nature and not chronic.

Response:

EPA agrees and has deleted the word "chronic" from the text.

4. Comment:

Reference to the latest NTP study should be limited to a statement similar to that found on pages VIII-19. This study has not been reported or peer-reviewed and cannot be used at this time for any purpose. Given the scientific quality of the study, NTP found it necessary to withdraw the draft report Based on the results of audits of this study, a report may never be released.

Response:

Information concerning the carcinogenicity results on the NTP repeat draft bioassay in animals is not being considered in determining adverse health effects from methyl chloroform, as the final NTP report is not yet available and is under question. It is not being used to determine the RMCL.

5. Comment:

Page I-9, Line 6 and III-31, Line 19. "Ingestion of ethanol was shown to increase the hepatotoxicity of methyl chloroform." This statement should be amplified to indicate the massive doses used to cause the slight effect that was found. Page III-31, Line 19, also fails to note the massive doses and, in fact, describes the limited effect as "readily" attained.

Response:

The dose of ethanol administered was 5 mg/kg. This dose is now cited in the Criteria Document.

6. Comment:

Page III-10, Line 3 and Page III-11, Line 1. "These results showed that humans and rats differ in any or all of the parameters of absorption, elimination, or retention." "Comparison studies of rat and human responses indicate that both species differ in parameters of absorption, elimination, or retention of methyl chloroform." While these statements are basically true, differences between species appear to be the result of size, rate of respiration and rate of blood circulation. Hence, data on animals can be realistically extrapolated to humans provided proper adjustments for these differences are made. It is particularly important to note that all species metabolize methyl chloroform to a very limited extent and consistently excrete a large portion unchanged.

Response:

EPA agrees with the commenter that the differences between the species may be the result of size, rate of respiration and rate of blood circulation. EPA also agrees that data on animals can be extrapolated to humans. EPA adjusts for size differential and for rate of respiration, but not for rate of blood circulation.

7. Comment:

Page III-18, Line 19. "...and 130 ppm trichloroethylene, 7 hours/day for 5 days (Stewart, et al., 1969)." The reference cited does not appear to be correct since the article does not refer to trichloroethylene.

Response:

The error in the reference cited (Stewart, et al., 1969) in the criteria document has been changed to provide the correct citation (Rowe, et al., 1963).

8. Comment:

Page III-20, Line 1. "Krantz, et al. (1959) estimated the dosage... halothane." This entire section fails to note one of the most important aspects of these studies: the quick and complete reversibility of the effects without sequelae.

Response:

EPA has included the statement concerning the reversibility of the effects without sequelae in the Criteria Document.

9. Comment:

Page III-22, Line 4. "Impairment of motor control after exposure t methyl chloroform has been demonstrated in humans at concentrations as low as 250 ppm...." This sentence appears to refer to the work of Gamberale and Hultengren (1973), who used a very artificial experimental technique in which subjects breathed menthol to cover the odor of methyl chloroform. Furthermore, the subjects wore masks during the exposure period. As noted in the CD, studies done under more realistic physiological conditions by other investigators failed to show a similar effect even at 500 ppm and with repeated exposures.

Response:

The fact that the technique used methanol and involved masks does not affect the validity of the study, and the commenter did not show how EPA's conclusions would be changed. Stewart (1969) found no effects at 500 ppm but Gamberale found effects at 250 ppm and Salvini found effects at 450 ppm. Therefore, impaired motor control has been demonstrated at these low levels in some tests, and the statement in the Criteria Document is correct and no change appears necessary.

10. Comment:

Page III-24, Line 19 and Page VI-1, Line 18. "Human autopsy reports have mentioned tissue congestion following deaths due to methyl chloroform,..." "...an adema typically found in fatalities (sic) result from inhalation of methyl chloroform (Bonventre, et al., 1977; Caplan, et al., 1976)." Congestive changes often accompany death and are not specific to methyl chloroform. Furthermore, changes of this type after exposure to thousands of parts-per-million have no relationship to exposure at occupational levels or, particularly, ambient levels.

Response:

EPA agrees with the commenter's statement; however, no change is needed in the statement in the Criteria Document. This comment does not affect the RMCL.

11. Comment:

Page III-36, Summary. "The possibility of increased pneumotoxicity due to 'additive' exposure to various levels of methyl chloroform from food and drinking water...and feces." The suggestion of pneumotoxicity due to ingestion of methyl chloroform in water and food is inconsistent with long-term repeated exposure to substantial concentrations of the material. It is not a significant concern and should be dismissed.

Response:

The comment refers to pneumotoxicity resulting from ingestion of food and water, and the statement has been modified in the CD to indicate that additive effects on pneumotoxicity from exposure to 1,1,1-TCE through these sources cannot be quantified because there is no evidence that pneumotoxicity is or is not consistent with long-term exposure to 1,1,1-TCE.

12. Comment:

Page V-1, Last Line and Page V-2, First Line. "...little other toxicological data involving oral ingestion are available." This section should cite Lane, et al. (1982) which appears on Page V-21.

Response:

Agree; the Criteria Document has been modified to cite Lane, et al. (1982).

13. Comment:

Page V-10, Line 18 and Page V-18, Line 8. "Two lifetime feeding study (sic)...1983)." and "In the repeat NCI...in those groups." As indicated previously, the second (NTP) study is not yet reported and is of such doubtful quality that it may never be reported. References to this study need to be deleted.

Response:

The second NTP study is reported only for the information of the reader and has not been used to derive the risk calculations or the RMCL.

14. Comment:

Page V-19, Line 11. "Price, et al. (1978) demonstrated..." All references to this unconfirmed report should be deleted. Price also studied methylene chloride at the same time and found an alleged effect. However, he was not able to reproduce the effect. Neither could Sivak, who also attempted transformation with methylene chloride. It can only be concluded that Price's method gives such irreproducible results as to be of dubious value.

Response:

Price, et al. (1978) is a published study of findings of the experiments in a scientific journal "In Vitro;" it is not unconfirmed. Price's and Sivak's works on methylene chloride are not at issue here. It is speculation that his study of methyl chloroform is not reproducible.

15. Comment:

Page V-19, Summary. The entire summary, which refers to the unreported NTP study, must be deleted for the reasons set forth above.

Response:

The information is provided for the purpose of informing the reader on the study and has not been used to derive the risk calculations or the RMCL.

16. Comment:

Page V-20, Line 14. "...and contained 5.5% or about 50 ppm inhibitors." The sentence is inconsistent; 5.5% is not equivalent to 50 ppm.

Response:

Agree. The Criteria Document has been corrected.

17. Comment:

Page VI-4, Last Sentence and Page VI-5, First Sentence. "Their tests of psychophysiological function are certainly more sensitive and objective than the indices used in the earlier studies of Torkelson, et al. (1958) and Stewart, et al. (1961, 1969)." Comment has already been made about the artificial exposure technique via masks with menthol used to cover the odor. This alone raises serious questions about this study. Moreover, the most comprehensive study is that of Stewart, et al. (1975) conducted for NIOSH. This report of repeated 7-hour exposures of men and women showed no objective changes at 500 ppm, although the female subjects did complain of the odor.

Response:

See Comment/Response - II.B.9 above.

18. Comment:

Page VI-12, Line 3. "Collection of data does not appear to have been standardized to avoid bias." This sentence needs to be deleted or an explanation offered for it.

Response:

Agree. The statement has been deleted.

19. Comment:

Page VII-1, Line 4. "...4.5 million are exposed to 1,2 dichloroethane or methyl chloroform (Table VII-1)." There is no association between 1,2-dichloroethane and methyl chloroform. This sentence should be deleted.

Response:

Agree. The statement has been deleted.

20. Comment:

Page VII-1, Last Line. "...exposures to 1,2-dichloroethane do not exceed 5 ppm..." Since the CD addresses methyl chloroform and no relationship has been established to 1,2-dichloroethane, this sentence should be deleted.

Response:

Agree. The statement has been deleted.

21. Comment:

Page VIII-6, Line 13. "Epidemiological evidence...is worth mentioning." The epidemiological data of Ott, et al. are of excellent quality and significance. They suggest the lack of effect in humans and should be cited in this paragraph.

Response:

EPA has searched published scientific literature to locate the reference "Ott, et al.," concerning epidemiological studies. The Agency has contacted the commenter to obtain this specific reference, but the study report has not yet been provided.

22. Comment:

Page VIII-7, Line 3, VIII-9, Line 5, and VIII-14, Line 4. "In the second NCI (sic) bioassay study (1983)..." Delete reference to this incomplete NTP study as in all previously discussed locations.

Response:

See previous responses concerning NCI study.

23. Comment:

Page VIII-15, Line 3. "There are two shortcomings of this study:..." The Agency has been supplied extensive information in regard to this study. The observation period was 19 months, not 12 months. Hence, these rats have a longer study period than in any of the other studies. Data have been supplied to the Agency which clearly show that exposure concentrations were adequate to be considered maximum tolerated dose by current definition.

Response:

The Criteria Document has been changed to note that the observation period was 19 months. EPA has received no evidence in this record that the concentrations were considered to be at the maximum tolerated dose.

24. Comment:

If further evidence shows 1,1,1-Trichloroethane to be a carcinogen, the RMCL should be reproposed at zero.

Response:

EPA will repropose the RMCL for 1,1,1-trichloroethane, if further evidence is available which would change the classification of the compound based on strength of evidence of carcinogenicity.

25. Comment:

The proposed RMCL of 200 ug/l is too high on the basis that the NTP studies suggest the compound is a carcinogen, emerging evidence that 1,1,1-trichloroethane is an animal teratogen and because the compound is stabilized with dioxane - a known carcinogen.

Response:

The available evidence does not support the commenter's statement that 1,1,1-trichloroethane is a carcinogen or an animal teratogen. The NCI has carried out two animal bioassays on the compound; in the first bioassay only 3 percent of the animals survived to the end of the experiment and thus it was concluded that carcinogenicity could not be determined from this study. The results of the second bioassay are presently being audited. The compound has not been shown to have teratogenic effects in animal studies.

EPA recognizes that 1,1,1-trichloroethane may be stabilized with other compounds that could contaminate drinking water and is examining each compound on an individual basis. If a stabilizer is found to be in drinking water and to pose a threat to public health, EPA will propose a standard for that chemical on an individual basis.

26. Comment:

Attached is a copy of the final report of a lifetime carcinogenicity study in mice entitled "Chlorothene VG: A Chronic Inhalation Toxicity and Oncogenicity Study in Rats and Mice - Part 1. Results of Findings in Mice," by J. F. Quast, L. L. Calhoun and M. J. McKenna, Dow Chemical Company. Note that there was no evidence of adverse effect of any kind in mice exposed to 1500 ppm, 6 hours/day, for two years.
The following is a summary of the report:

> Groups of male and female $B_6C_3F_1$ mice (80/sex/group) were exposed to vapor concentrations of 0, 150, 500, or 1500 ppm 1,1,1-trichloroethane formulation, hereafter referred to as CHLOROTHENE

VG*, for 6 hours/day, 5 days/week for 2 years. Ten mice/sex from each group were predesignated for interim sacrifices after 6, 12, and 18 months of exposure. Fifty mice/sex from each group were assigned to the study to be terminated after 24 months. Parameters measured during the study included mortality, in-life clinical signs of toxicity, hematology, clinical chemistry, body weight, organ weights (liver, kidneys, brain, heart, testes), gross pathology, and histopathology.

Inhalation exposure of male and female $B_6C_3F_1$ mice to 1500 ppm or less of CHLOROTHENE VG vapor for 2 years did not result in any toxic or oncogenic effect considered due to the test chemical.

Response:

EPA has concluded that there are insufficient data to classify 1,1,1-trichloroethane as a probable or possible human carcinogen and thus is regulating the compound as a non-carcinogen. This classification is consistent with the results of the submitted report in regard to the oncogenicity findings. With regard to chronic toxicity, other studies have demonstrated adverse health effects from exposure to 1,1,1-trichloroethane and EPA is basing the RMCL upon these effects.

27. Comment:

"Calculations based on toxicological data indicate that the RMCL for methyl chloroform should be based on taste and odor rather than toxicity. A no-observed-adverse-effect level for toxicity of methyl chloroform has been defined in a 14-week inhalation study by McNutt, et al. (1975). Mice exposed continuously to 250 ppm experienced only minimal, reversible liver effects. We agree with EPA that this study may appropriately be used to compute an AADI for human exposure. However, 250 ppm should be considered a NOEL, not a LOAEL, because several long-term studies, including a lifetime study, demonstrated NOELs at much higher concentrations."

Response:

EPA does not agree with the commenter's suggestion that the RMCL for methyl chloroform should be based on taste and odor rather than toxicity. The RMCL, according to the SDWA, must be based on health considerations only. EPA may set secondary standards based on taste and odor. However, for the purpose of setting primary standards, an RMCL must be set for chemicals which may cause adverse health effects. Methyl chloroform falls in this category.

The commenter agrees with EPA that the McNutt, et al. (1975) study is an appropriate study upon which to base the AADI. EPA believes that 250 ppm should be considered a LOAEL because exposure at this level resulted in adverse effects; significant changes in the centrilobular hepatocytes of the animals were seen. These changes consisted of vesiculation of the rough endoplasmic reticulum with loss of attached polyribosomes, increased smooth endoplasmic reticulum, microbodies and triglyceride droplets. The fact that other studies demonstrated NOAELs at much higher concentrations does not invalidate the results of the McNutt Study. EPA believes that

this study clearly demonstrated a LOAEL at 250 ppm and thus should be used as the basis for the AADI.

28. Comment:

The commenter suggested the following approach for deriving the RMCL for 1,1,1-trichloroethane, based upon the McNutt, et al. (1975) study.

In converting the NOEL based on the animal data to a dose expressed in mg/kg/day, the minute volume (0.05 L/min) and average body weight of the male (0.025 kg) mouse used by McNutt assumptions used in the criteria document, the NOEL may be expressed in mg/kg/day as follows:

$$\frac{250 \text{ ppm} \times 0.0055 \text{ mg/L}^{*} \times 0.05 \text{ L/min} \times 360 \text{ min/day} \times 0.3^{**}}{0.025 \text{ kg}} = 297 \text{ mg/kg/day}$$

* Conversion factor (1 ppm v/v in air = 0.0055 mg/L at 25°C and 760 torr)

**Absorption rate

Thus, using the methodology and the thousand-fold safety factor suggested by EPA, the AADI may be computed as follows:

$$\frac{297 \times 70 \text{ kg}}{1{,}000 \times 2 \text{ L/day}} = 10.40 \text{ mg/L}$$

Again using the methodology suggested by EPA, this AADI may be converted into an RMCL by dividing by 5. This results in an RMCL for methyl chloroform of 2.1 mg/L. This concentration limit, while sound toxicologically, would in our view need to be lowered in order to be aesthetically acceptable.

Response:

This approach is basically the same as that used by EPA in deriving the RMCL, with the exception of the approach used to convert from inhalation exposure to oral exposure (the use of the minute volume and body weight of the animal). The response to comment II.A.1 above addresses EPA's approach in converting exposures.

29. Comment:

A similar calculation for the RMCL could be made based upon the Quast, et al. (1984) study as follows:

$$\frac{500 \text{ ppm} \times 0.0055 \text{ mg/L} \times 0.05 \text{ L/min} \times 360 \text{ min/day} \times 0.3}{0.040 \text{ kg}} = 371 \text{ mg/kg/day}$$

$$\frac{371 \times 70 \text{ kg}}{100 \times 1 \text{ L/day}} = 130 \text{ mg/L}$$

Response:

The commenter agreed that the McNutt, et al. study is appropriate for deriving an RMCL. EPA's preliminary review of the Quast, et al. study suggests that there are several unexplained findings in the study. These findings are as follows: (1) the livers of some male mice in the 1500 ppm group appeared to have developed nodules; (2) the death of the female mouse (150 ppm) predesignated for the 6-month interim sacrifice prior to the scheduled sacrifice; (3) the death of several mice (1 male, 500 ppm; 1 female, 150 ppm) prior to the scheduled sacrifice at 12 months; (4) the gross observations suggestive of lymphoreticular neoplastic response in all groups of male mice which the researchers claimed were not related to the chemical exposure; and (5) the increased incidence of cystitis and dilation of the renal pelvis in the 500 ppm group of male mice which the researchers claimed were not related to the chemical exposure. These unexplained findings, taken as a whole, suggest that there may be problems with this study. Thus, EPA believes it is preferable to base the RMCL upon the McNutt, et al. study.

C. 1,2-DICHLOROETHANE (ETHYLENE DICHLORIDE)

1. Comment:

After reviewing the 1,2-Dichloroethane Criteria Document the commenter came to the following conclusions: (1) there was undue reliance on Russian literature; (2) toxicity data are either not germane, inadequate or of questionable quality; (3) the document overemphasizes literature published prior to 1971; (4) mutagenicity studies cited are inadequate to draw firm conclusions; (5) evidence for binding to DNA is weak; (6) evaluation of carcinogenicity of EDC must be more balanced; and (7) the estimate of human exposure is overstated.

While the OHEA HAD of April 1984 has deficiencies in the commenter's estimation, the HAD should be used as the scientific data base for RMCL development, since it contains discussion of some more recently published pertinent information, which is not contained in the drinking water document.

Response:

We agree with the first six conclusions. Particularly because of the first four conclusions, EPA will use the HAD document as the background document instead of its draft criteria document. Both documents, in EPA's estimation, came to the same conclusions concerning the qualitative assessment of both noncarcinogenic and carcinogenic effect data. EPA will use the OHEA HAD as the background document with inclusion of a revised Quantification of Toxicological Effects (QTE) section which presents the quantitative risk assessment. The OHEA HAD has been received and accepted in substance by the EPA Science Advisory Board.

EPA agrees that the improvements indicated by the commenter, specifically points 1-4, are in order for the criteria document. Our response recommends use of the OHEA HAD in place of the criteria document as the background document for EDC, particularly because it contains a more

complete discussion of the scientific literature; however, we also note that the qualitative assessment conclusions between the two documents are the same. In the HAD, EPA concludes that: (1) there is not undue reliance of the Russian literature for assessing health effects, and limitations in the data on health effects from Russian literature are acknowledged; (2) the toxicity data in animals are of adequate quality to support the conclusions on health effects, but the human toxicity data are too limited for conclusive assessment of health effects; (3) the overall literature through 1983 is considered on the merit of each study in drawing the conclusions made, without date of publication being a critical factor in the assessment; (4) the overall evidence for mutagenicity is concluded by EPA to be adequate support for EDC as a weak mutagen; (5) EPA concludes that the evidence for binding of EDC and/or its metabolites to DNA is adequate; (6) EPA concludes that its assessment and conclusions on carcinogenicity, which the EPA Science Advisory Board has accepted, are in order.

2. Comment:

In the occurrence document for ethylene dichloride, there are inconsistencies in the treatment of the date. Table 15: NORS surface water data shows 22 positive systems, whila the text indicates that 16 of these positives are below the minimum quantifiable level, dafined in Appendix A as "the level below which it cannot be determined whether a VOC is present and if so, at what concentrations." Thus, Table 15 should indicate 6 positive systems.

Response:

The NORS data indicated that in 16 of the 22 positives for 1,2-dichloroethane, the contaminant was present above the detection limit of 0.1 ug/L in the GC/MS confirmation analysis but below the minimum quantifiable concentration range of 0.2-0.4 ug/L in the primary analysis using GC with an electrolysis conductivity detector.

3. Comment:

Review of the occurrence document reveals inconsistencies in the treatment of data. The NORS surface water data shown in Table 15 indicate 22 positive systems, while the test indicates that for this survey, 16 of these "positive" systems were below the minimum quantifiable concentration ("MQC"). Reference to Appendix A of the occurrence document indicates that the MQC is the "level below which it cannot be determined whether a VOC is present and, if so, at what concentration." Accordingly Table 15 should indicate only 6 positive systems.

Response:

The text, perhaps confusing to the commenter, is in agreement with Table 15. As noted in the text, 16 of the 22 systems had detectable (but unquantifiable) levels below 0.4 ug/L and two had quantifiable levels below 0.8 ug/L, as indicated in Table 15. Appendix A and the definition of the MQC is incorrect to the extent that it precludes identifying the presence of a contaminant. The MQC is the level below which an accurate statement cann t be made c ncerning the levels (quantification), but it is often possible to determine that a contaminant is present.

4. Comment:

In the EDC occurrence document, only 9 positive systems in 1,059 groundwater supplies were found for an incidence of 0.8%. This is fairly close to the 9 positive systems in the 1,001 groundwater supplies as shown in Table 22, although it is unclear which groundwater sources were deleted as being duplicative. Therefore, the projected national occurrence of EDC in groundwater supplies indicates that 99.7% of groundwater sources contain either no EDC or only levels below 0.5 ug/L.

Response:

The commenter is correct that, based on the available studies, approximately 99.7% of supplies with groundwater sources are expected to contain either no 1,2-dichloroethane or levels below 0.5 ug/L.

5. Comment:

Regarding surface water supplies, the occurrence document is much less clear. After the correction to Table 15 and based on the text, Tables 15-21 indicate 11 positive sources, i.e., greater than 0.5 mg/L, out of 575 surface water sources, for an occurrence rate of 1.9 percent. Reference to Table 26 shows an entirely different picture. The 575 surfac water sources have decreased to 301 while the number of positive sources, i.e., greater than 0.5 ug/L, has swelled from 11 to 18. The seven sources indicated as being less than 0.5 ug/l should not be included in Table 26 at all, since they are below the MQC.

Response:

A total of 575 systems were sampled during five different surveys. Some of these systems were sampled multiple times. A total of 301 different systems were adequately sampled. EPA agrees that the averaging process moved 7 systems which contained 1,2-dichloroethane into a category of slightly higher quantity because subsequent analyses, though "negative," had an elevated minimum quantification limit. The averaging methodology is described on pages A-22 and A-23 of the Occurrence Document and explained in the next comment.

6. Comment:

Table 26 shows the 301 supplies and a total of 25 positives, 7 of which were below the common minimum quantifiable concentration of 0.5 ug/L and 18 at or above 0.5 ug/L. The apparent inconsistency in positives above 0.5 ug/L is an artifact of the averaging process used where a given supply was sampled in more than one survey with both positive and negative results, where the positive values are lower than the minimum quantifiable concentrations of negative values in other surveys. In the case of EDC, several supplies with positives in NORS at values below 0.5 ug/L were averaged with negatives from NORS having a minimum quantifiable concentration of 1.0 ug/L[3]; in which case the negatives from NORS were considered to be positives.

Response:

EPA agrees.

7. Comment:

The projected occurrence of EDC in surface water sources as illustrated in Table 27 does not correspond with Tables 15-21. There are no incidents of contamination in system sizes 25-3,300, yet Table 27 shows 67 systems in this size category as containing 0.5-5 ug/L and 67 surface water systems containing 10-20 ug/L EDC. This is a totally unreasonable interpretation of the data.

Response:

The data set for EDC was so small that stratification by categories of system sizes was statistically impossible. System sizes were collapsed until they were statistically workable, then expanded to the original 11 categories using a simple proportional relationship. This methodology was explained in the appendix of the occurrence document (pages A-23 - A-27 and Appendix B).

EPA believes that absent a complete data set, it is incumbent on the Agency to make reasonable estimates of occurrence. Since the EPA believes this methodology is reasonable to derive a stratified population, it is kept in the Occurrence document unchanged.

8. Comment:

In Table 27 of the EDC occurrence document, the same numbers appear in the columns 0.05-5 and 10-20 up to a system size of 10,000. This suggests an error in transposing data to the table or an incorrect model being used.

Response:

The numbers are correct -- that they are the same is coincident; again, separate estimates were made for the supplies serving ≤10,000 and >10,000 people.

9. Comment:

For the reasons given in comments 7 and 8 above, the estimation of 5.7% of the population being exposed to drinking water containing 0.5-5 ug/L must be recalculated and the estimates of 143,000 persons being exposed to >5 ug/L must be redone.

Response:

The responses to comments 7 and 8 answer this comment. No change in the estimates is required.

10. Comment:

1,2-Dichloroethane should not be considered a probable human carcinogen based upon deficiencies in the NCI bioassay. In addition, negative results obtained by other researchers need to be considered, such as the potential for cross contamination between the mice gavage studies being conducted on other chemicals in the same room, high and early mortality in rats and the presence of pneumonia in both rats and mice. There was also a problem of early mortality and low survival in both male and female mice. The MMCL for 1,2-dichloroethane should be based upon an ADI derived from non-carcinogenic data.

Response:

EPA believes that there are sufficient toxicological data to classify 1,2-dichloroethane as a probable human carcinogen. The chemical has been shown to be carcinogenic in both rats and mice when administered by gavage. The negative carcinogenicity data consists of several inhalation studies (NCI, 1978; Maltoni, et al., 1980; Theiss, et al., 1977). Since 1,2-dichloroethane was shown to be carcinogenic by the oral route, which is the same route by which individuals would be exposed to the compound in drinking water, EPA believes that the positive oral data should outweigh the negative inhalation data in the analysis of the compound's potential carcinogenicity.

With regard to the NCI bioassay, the NCI report is final, with the following conclusions:

> "Under the conditions of this bioassay there was a statistically significant association between increased dosage and elevated mortality in both male and female rats and in female mice. During the second year of the study, mortality rates in the male mice were higher for low dose and untreated control than for high dose mice. Despite this accelerated mortality, positive associations were established between 1,2-dichloroethane administration and the incidences of several neoplasms."

These conclusions have been accepted by IARC and used in their evaluation of the carcinogenicity of 1,2-dichloroethane and also by the SAB in their review of the Health Assessment Document for 1,2-dichloroethane.

The deficiencies in the NCI bioassay cited by the commenter do not appear to have played a role in influencing the final results. The potential for cross-contamination with other chemicals is minimal, as th exposure the animals received from other compounds would be so much lower than the dose of 1,2-dichloroethane that it would not negate the effects noted. Also, the presence of pneumonia in the animals would affect the mortality rate but would not affect the carcinogenic response. The mortality rate of the animals was noted in the NCI report but does not invalidate the results of the study in any way. As stated in the report, "Despite this accelerated mortality, positive associations were established between 1,2-dichloroethane administration and the incidences of several neoplasms."

1,2-Dichloroethane has been classified in EPA's Group B2 (probable human carcinogen) and the IARC has classified 1,2-dichloroethane in Group 2B; sufficient evidence of carcinogenicity in animals. Thus, EPA feels that the RMCL should be based upon carcinogenic effects and set at zero, and should not be set using the ADI.

D. VINYL CHLORIDE

1. Comment:

The animal cancer data is weak since neither angiosarcomas nor hepatocellular carcinomas are significantly increased in the low dose groups of the Feron, et al. (1981) study. The only tumors detected at the low dose were liver neoplastic nodules, which have not been proven to be precursors of cancer.

Response:

This study is not considered to be weak because angiosarcomas/carcinomas are significantly increased at medium and high doses. In addition, neoplastic nodules are treated as predictive of carcinomas and they were significantly increased at low doses. The highest dose level used was considered acceptable for assessment of cancer risk because the activation pathways were not saturated, and secondly there was little evidence of chronic toxicity. Since the higher doses were considered acceptable and since a marked carcinogenic response was seen at these doses, the evidence for carcinogenicity in animals was adequate. The evidence is strengthened further by the marked carcinogenic response noted during inhalation exposure to a wide range of VC concentrations.

2. Comment:

The magnitude of risk is greatly overstated because (1) the use of the upper 95% confidence interval does not represent a most probable risk, and (2) the computer program ignores negative results.

Response:

The risk is overstated, but EPA is unable to estimate by how much given the cited factors. The methodology used has been peer reviewed and published by the EPA. This methodology has been designed to provide a conservative estimate of risk because of the many unknown factors in the assessment procedure, i.e., the possibility of unusually sensitive subgroups, uncertainty regarding the shape of the dose-response curve at low doses, differences in metabolic pathways affecting responsiveness between human and test animals. The EPA provides the risk assessment for general information for public and Agency use. The RMCL is not based on the risk assessment.

3. Comment:

In the study in which VCM was fed to rats in PVC powder, the unexpectedly high incidence of liver cell tumors may be due to unusual sensitivity

of the liver as a consequence of an altered metabolic state caused by reduction of daily food intake time to only 4 hours.

Response:

While it can be postulated that sensitivity may be altered by the feeding regime, there is no experimental evidence to prove this. Until such evidence is provided, it is assumed that sensitivity is normal in the experimental animals.

4. Comment:

Since both Feron and Maltoni found no observable effect levels for exposure to VC and since the no-threshold concept has not been proven, it would be better to determine a NOEL with a safety factor to derive a safe exposure level.

Response:

See item 5 below.

5. Comment:

Another commenter provided information on additional carcinogenicity data from Feron and associates where a "no-observed-adverse-effect level" for tumor induction in rats was reported.

Response:

The most widely accepted view of carcinogenesis, based on evidence that a single molecule of a xenobiotic chemical can react with DNA to genetically alter a cell, supports the no-threshold concept. Moreover, the best available epidemiological and animal evidence, especially those studies involving radiation exposure support the no-threshold concept.

EPA believes this single contaminant-specific test showing a threshold is outweighed by the best available scientific evidence on many contaminants, showing no observable thresholds. In addition, this approach errs on the side of safety and protection of public health, given some degree of scientific uncertainty.

6. Comment:

In the development of the quantitative estimate of risk, the total number of tumors were assumed to be the same as the number of animals with tumors. This may result in an overly conservative risk estimate, since some animals may have multiple tumors.

Response:

A q_1^* of 2.3 was derived for female rats based upon the incidences of neoplastic nodules and hepatocellular carcinomas in the liver plus angiosarcomas of the lung and liver. For neoplastic nodules alone, the most common tumor type, the q_1^* was 1.3. Thus, even with the maximum possible

incidence of animals with multiple tumors, the q_1^* would not be decreased to less than 1.3. If it is assumed, on the other hand, that each tumor type evolves independently, the likely number of animals with multiple tumors would be small enough to result in only a minor decrease in q_1^* below 2.3. The quantitative estimate of risk was based on the best available evidence. While possible error as discussed above is undoubtedly small, it is recognized that a more accurate estimate could be made if the tumors present in each individual animal were known. An attempt is, therefore, being made to obtain this data. However, this data does not affect the conclusion that it is carcinogenic and presents an adverse health effect.

7. Comment:

In general, the document provides a competent review of the literature through about 1981. More recent documents are omitted and some of the more recent reports may be of interest.

Response:

EPA agrees and has discussed the following references identified by the commenter in the Criteria Document:

- Hatch, Lein and Stein. 1981. Environ. H. Perspect. 41:195.
- Hanstein, et al. 1981. Mut. Res. 78:211.
- Anderson, et al. 1981. Mut. Res. 83:137.
- Chiazze, et al. 1980. J. Occup. Med. 22:677.
- Falk, et al. 1981. Environ. H. Perspect. 41:107.

All these studies do not affect EPA's findings of adverse health effects. There are sufficient positive mutagenicity data such that these negative studies do not outweigh the overwhelming number of positive studies.

8. Comment:

On Page II-1 it is stated erroneously that VC dissolved in water rises to the surface because the specific gravity of the solute is less than that of the solvent. VC escapes from the surface of water because of the concentration gradient present there, not the pull of gravity.

Response:

EPA has removed that statement from the Criteria Document.

9. Comment:

The document contains no details of the "new" risk assessment by CAG which is necessary in order to comment on the assessment.

Response:

Details on the CAG risk assessment have been added to the Criteria Document. However, because the risk assessment is not crucial to the

conclusion that the contaminant poses adverse health effects, there is no need for additional comment on this assessment. It is merely provided for the Agency's and the public's general information.

10. Comment:

EPA should not consider vinyl chloride to be a non-threshold carcinogen, as EPA has supported this position on the basis that the thresholds for carcinogens are not testable, and the use of absence of available proof as a reason for acceptance of a theory is not acceptable scientifically or philosophically. Very few cases of cancer would be averted with a vinyl chloride regulation and the small number of cases and low occurrence do not justify regulating the compound. If further consideration showed the need for a standard, the RMCL should be based upon a 10^{-5} lifetime risk level.

Response:

EPA believes that any exposure to a carcinogen may present some finite risk, since scientists have been unable to experimentally verify a threshold for carcinogens, including vinyl chloride. EPA believes that it is better to err on the side of safety in regard to the mechanism of action of carcinogens and treat carcinogens as non-threshold contaminants rather than to assume a threshold and perhaps place the public at risk.

EPA has determined that there are sufficient health effects information and occurrence data to justify regulating vinyl chloride. Vinyl chloride is a known human carcinogen which has been detected by several States at various levels. EPA agrees that the State data are not representative of national occurrence; however, these data indicate that vinyl chloride is present in a number of drinking water supplies and EPA believes that this detection is sufficient to warrant action. In addition, information suggests that vinyl chloride may be found in drinking water as a breakdown product of trichloroethylene or other chlorinated hydrocarbons under certain conditions. (Parsons, et al., 1984, Transformation of Tetrachloroethylene and Trichloroethene in Microcosms and Groundwater, J.A.W.W.A., Vol. 26, No. 2; Parsons and Lage, Chlorinated Organics in Simulated Groundwater Environments, J.A.W.W.A., Vol. 27; Vogel and McCarty, 1985, Biotransformation of of Tetrachloroethylene to Trichloroethylene, Dichloroethylene, Vinyl chloride and Carbon Dioxide under Methanogenic Conditions, Applied and Environmental Microbiology, Volume 49, No. 5.)

11. Comment:

The National Drinking Water Advisory Council did not recommend regulating vinyl chloride.

Response:

The National Drinking Water Advisory Council has met several times to discuss the VOCs proposal. At the first meeting they concluded that due to the low occurrence, an RMCL should not be set for vinyl chloride. However, at the second meeting they reversed their initial decision and concluded that an RMCL should be set for vinyl chloride due to the carcinogenicity of the compound.

E. BENZENE

1. Comment:

One commenter felt that EPA's AADI for benzene was calculated using an extremely conservative approach based upon (1) the use of 10 ppm as a NOAEL in the Chang study despite the fact that no hematological toxicity was observed in the 18 workers exposed to 10 to 20 ppm benzene in the study and (2) use of an uncertainty factor of 1,000 despite the fact that the 10 ppm NOAEL reflects human data.

Response:

EPA believes that it is appropriate to use 10 ppm (Chang study) as th NOAEL, as no effects were observed at this level, while cytopenic effects were noted at 20 ppm. EPA further believes that the application of an uncertainty factor of 1000 for the Chang study is appropriate due to deficiencies in the study. These deficiencies include the fact that many details of the exposure were not provided, an unspecified industrial area was used in the study, and no definition was provided of work exposure concentrations for individual employees.

2. Comment:

Use of an uncertainty factor of 10 to account for less than lifetime exposure in the animal study by Wolfe may also be nigh, since the benzene was administered over 187 days rather than the 90 days to which an uncertainty factor of 10 might typically be applied in a study of rats.

Response:

The use of an additional factor of 10 in studies that are less than lifetime applies in the case of the Wolfe study, since the study was for 187 days, which is only one-quarter of the expected lifetime of the animals.

3. Comment:

One commenter noted problems with the calculation of the cancer risk estimate for benzene. They felt that the calculation for risk estimates should be decreased by 8%. The following justification was provided:

> "The first thing that must be said is that this inhalation-derived potency factor (cited in the EPA Criteria Document on Benzene) is outdated. In its most recent actions regarding the regulation of benzene under the Clean Air Act, EPA has revised this potency factor downward from 0.024/ppm to 0.022/ppm, a reduction of 8% (see 49 FR at 23488). Even if everything else in EPA's methodology were unobjectionable, this would mean that the benzene concentrations associated with risk levels of 10^{-6} and 10^{-5} would have to be increased by 8% to 0.73 ug/L and 7.3 ug/L, respectively."

The EPA risk levels of 10^{-6} and 10^{-5} are at 0.68 ug/L and 6.8 ug/L, respectiv ly.

Response:

EPA agrees with the comment that the risk estimate calculation should be decreased by 8% and this has been done by EPA's Carcinogen Assessment Group (CAG).

4. Comment:

Benzene is not present in a sufficient number of drinking water supplies to characterize it as a national problem and the average daily intake of benzene from drinking water constitutes a negligible percentage of the total daily water intake from all sources. No justification is found for adapting a drinking water standard.

Response:

EPA believes regulation is appropriate because the contaminant has been found in drinking water; the occurrence information suggests that around 500 public water supplies would be expected to contain benzene. Benzene is also classified as having sufficient evidence as a human carcinogen. In addition, benzene may be a contaminant from waste disposal as well as from leaking underground gasoline tanks. EPA believes that a standard for benzene will promote uniform action among states when the contaminant is detected and will help prevent future exposure to the chemical.

5. Comment:

On a worst case basis, we estimate that approximately 100,000 people nationwide are exposed to a lifetime risk of 10^{-5} as a result of benzene in drinking water supplies, and that approximately 2.5 million people nationwide are exposed to a lifetime risk of 10^{-6}. This amounts to 0.036 cancers per year nationwide. These estimates greatly overstate the true risk, which is likely to be one to two orders of magnitude lower.

Response:

EPA is required, under the Safe Drinking Water Act, to set RMCLs for those chemicals which may have an adverse effect on health and to set the RMCLs solely based on health. EPA is regulating such chemicals if they are found or are likely to be found in drinking water. The number of cancer cases avoided is not a criteria for setting RMCLs; EPA examines this in the Economic Impact Analysis for the MCLs as part of the overall regulatory analysis.

6. Comment:

The average daily intake of benzene in drinking water represents a negligible percentage of the total daily intake of benzene from all sources. The public health impact of a national primary drinking water regulation in these circumstances also would be negligible.

Response:

EPA does not agree with the commenter that a primary regulation should not be set when drinking water does not constitute the major route of exposure for that chemical. EPA believes that all routes of exposure should be considered in the analyses and a primary regulation should be set when exposure to the chemical is shown to result in adverse health effects and the chemical is known to occur in drinking water or has the potential for occurrence in drinking water.

F. 1,1-DICHLOROETHYLENE

1. Comment:

One commenter responded to the question of whether or not 1,1-dichloroethylene is a carcinogen. The commenter stated that the toxicological evidence does not warrant classification as a carcinogen. The commenter presented an option by which an ADI and AADI for 1,1-dichloroethylene can be derived, then, in turn, used to develop the RMCL for this substance. The option is based upon data gathered in two studies in rats, one via inhalation at exposure levels of 25 or 75 ppm (Rampy, et al. 1977, McKenna, et al. 1980) and one via drinking water at nominal doses of 50, 100 or 200 mg/L (Rampy, et al. 1977, Quast, et al. 1983). 25 ppm was considered by the investigators to be a LOAEL in the former study and at 50 ppm in the drinking water study. Using the LOAEL of 25 ppm from the inhalation study, the commenter suggested an ADI of 0.68 mg/day and an AADI of 0.068 mg/L, if 20% contribution from drinking water were assumed.

Response:

EPA agrees that the toxicological evidence does not warrant classification of this chemical as a carcinogen. EPA has classified 1,1-dichloroethylene in EPA's Group C ("possible" human carcinogen) based upon the mutagenic potential of the compound, the results of mouse and rat inhalation data and the compounds's structural similarity to vinyl chloride.

For derivation of an ADI for noncarcinogenic effects, the Agency used the data from the drinking water study. The drinking water study is used instead of the air study, as drinking water studies are generally more appropriate for calculating drinking water ADIs. In this case, a drinking water study is available and the LOAEL from this study is very close to the LOAEL from the air study. Using the Agency's calculations, the ADI was derived at 0.7 mg/day which yielded an AADI of 0.070 mg/L, assuming a 20% contribution from drinking water. This AADI is essentially identical to the commenter's AADI.

2. Comment:

The occurrence data shows 1,1-dichloroethylene to be the least common (considering 1,1,1-trichloroethane, methylene chloride and 1,1-dichloroethylene) of these three compounds in drinking water. Therefore, questions may be raised concerning the need for an RMCL for this compound.

Response:

EPA did not propose an RMCL for methylene chloride (dichloromethane) in this phase of the Revised Regulations due to problems with the quality of the available occurrence information and insufficient toxicological information. This compound will be considered in a later phase of the Revised Regulation. An RMCL was proposed for 1,1,1-trichloroethane based upon non-carcinogenic effects because questions were raised concerning the latest bioassay data on the compound. The RMCL is based upon the most current valid data for the compound. An RMCL was proposed for 1,1-dichloroethylene based upon the compound's possible carcinogenic effects and non-carcinogenic effects.

G. p-DICHLOROBENZENE

1. Comment:

The reference to Girard, et al. (1969) should be deleted or modified to accommodate for the possible coincident exposure to other compounds.

Response:

The summary reference (Page I-2) to the Girard study has been modified to add a sentence reading: "In three of those cases, it is likely that the individuals were exposed to other compounds as well. Thus, from this study it is not possible to state with any degree of certainty that there is a link between DCB exposure and the disease state."

2. Comment:

The discussion of anemia following DCB exposure should note that the observed cases of anemia were induced only after large exposures and were reversible.

Response:

The Summary reference to this effect (page I-3) has been modified to include the following sentence: "These cases reflect exposure to significant amounts of the agent. When exposure was curtailed, there appeared to be recovery."

3. Comment:

Commenter claims that the Summary statement which states that granulocytopenia is a precursor to leukemia (page I-5) is unsound and suggests that this relationship is entirely speculative. They provide undocumented information to substantiate their belief.

Response:

Since, at the moment, EPA does not have the primary references to support the statement in the Criteria Document, it has been removed from the document.

4. Comment:

The commenter addresses the section in the document that states that the maximum tolerated dose (MTD) may not have been reached in the bioassay with o-DCB. The commenters assert that the NTP Board of Scientific Counselors, in its public review of the bioassay, felt that the dosing regimen was adequate.

Response:

The purported view of the Board of Scientific Counselors has not been documented as being other than that which appears in the draft report. The draft report states that the MTD may not have been utilized. The ODW Health Effects Criteria Document will be modified to make it clear that it is the NTP's draft report opinion that was described in the document, and when a final report on the bioassay becomes available, any change in opinion will be duly noted.

5. Comment:

The commenter mentions that the document should be altered to reflect the existence of teratogenicity studies for o- and p-DCB that were conducted by the Chlorobenzene Producers' Association.

Response:

These studies have been acquired from the Office of Toxic Substances and are described in detail in the Final Health Effects Criteria Document.

6. Comment:

The commenter refers to the Summary statement (page I-1) that suggests that increasing use of o- and p-DCB as deodorizers will lead to increasing amounts being present in waters in the future.

Response:

As the commenter points out, these chemicals have been used for this purpose for many years, and yet, the concentrations found in waters have been small. The sentence in the document has been modified to read: "The use of o- and p-DCB as deodorizers in industrial wastewaters and toilet bowl waters would suggest that there is a potential for these substances to be found in water, particularly surface, around the country."

7. Comment:

One commenter criticized the derivation of the RMCL for p-dichlorobenzene based on data identifying the NOAEL from a subchronic study stating that the exposure duration is too short for defining a "safe" level for possible lifetime exposure. Their concern was based upon two sources of information: (1) NAS's reiteration of an ADI of 0.0134 mg/kg/day and (2) the report about the threshold odor concentration of 0.03 mg/L.

Response:

The Agency feels that the use of the particular study described was appropriate for the generation of the ADI, AADI and the RMCL for p-dichlorobenzene. To accommodate for the possibility that effects may be seen after lifetime exposure at doses that in the subchronic study were without effect, an extra uncertainty factor of 10 was applied to the data.

The Agency disagrees that the NAS (1983) reassessment of an ADI, etc. for p-dichlorobenzene is the correct one. Their assessment was based upon the 1956 Hollingsworth study which employed three gavage doses, each an order of magnitude apart. The 90-day study which the Agency employed in deriving the RMCL used five treatment doses, over a narrower range. In the Agency's judgment, this study better defined the highest NOAEL.

It is agreed that if p-dichlorobenzene actually were present in the drinking water at levels near the RMCL, the water would not be aesthetically pleasing to the consumer. At this time, however, EPA's first priority is to set revised primary drinking water regulations; secondary drinking water regulations will be updated later.

8. Comment:

There is no need for an RMCL for p-dichlorobenzene because the compound is not generally present in drinking water at significant concentration levels or at levels to which significant populations are exposed. Even if the compound was detected in drinking water, the proposed RMCL is far in excess of any concentration level at which the compound has been found in drinking water. Thus, there is no need for the costly monitoring and recordkeeping requirements to be imposed as part of a national standard.

Response:

EPA agrees that the frequency and levels of detected contaminants are quite low, however, since the contaminant may have an adverse effect on health and has been detected in drinking water, EPA believes that a standard is appropriate and consistent with Congressional intent. In addition, it may now be occurring at higher levels in systems that were not sampled by EPA or the States; it may also occur at higher levels in the future. EPA rejects the notion that a contaminant must be detected at levels which are likely to cause adverse health effects before a regulation is justified. The SDWA endorses a protective philosophy which EPA is implementing through regulation of contaminants such as p-dichlorobenzene.

9. Comment:

The NOMS survey, GWSS, and NSP surveys used for exposure estimates of pDCB were not made available for outside review or comment; it is therefore impossible to evaluate the accuracy of EPA's exposure estimates.

Response:

All EPA surveys were available for outside review and comment before the proposed rule and were included in the rulemaking record available to

the public. In addition, the data from these surveys have been summarized and tabulated in the individual Occurrence documents on each chemical.

10. Comment:

The following comments were made concerning specific studies cited in the draft Criteria Document:

- On page I-4, line 6, the dose reported for the Varshavskaya study should be 3,220 mg/kg. At line 10, the reference to 2 cc/m^3 is an inappropriate description of atmospheric concentration. It would be more appropriate to refer to mg/L or mg/m^3.
- The description of the Varshavskaya study at V-10 and V-11 should state data in terms of mg/kg rather than mg/L.
- Table VIII-1 should be revised to reflect that the LD_{50}s for the Varshavskaya study were stated in mg/kg.
- The Burstone (1965) citation is not listed among the references. It is, therefore, impossible to evaluate the claim that tissue DPN, TPN, glucose-6-phosphate and alkaline phosphatase activity is indicative of carcinogenicity.
- The description of the Guerin and Curzin (1961) data at V-58 should be supplemented with the scores for control mice.

Response:

All of the above cited studies have been removed from the Final Criteria Document for the following reasons:

The Burstone (1965) study inadequately supports the claim that enzymes assessed in the Varshavskaya study are indicative of carcinogenesis; the Guerin and Curzin (1961) study is a short-term skin test which does not adequately characterize the carcinogenic potential of dichlorobenzene, and; there is inadequate information in the Varshavskaya study to convert LD_{50}s from mg/L to mg/kg. Elimination of these studies does not affect the conclusions in the Criteria Document.

REVIEW OF p-DICHLOROBENZENE HEALTH ASSESSMENT DOCUMENT

A commenter submitted a detailed review of the Health Assessment Document for chlorinated benzenes (External Review Draft, May 1, 1984). This document has since been revised and finalized; however, some of the issues are still relevant to the final RMCL for p-dichlorobenzene. A summary of the issues relevant to the current rulemaking and EPA responses follows. (Comments 11 through 29)

11. Comment:

Each of the chlorobenzenes is quite distinct from other chlorobenzenes in use, in environmental properties and effects and in toxicologic effects.

Any assessment of these chemicals must clearly differentiate among the several compounds that have been considered in the EPA draft.

Response:

EPA agrees and the Criteria Document for o-dichlorobenzene, m-dichlorobenzene and p-dichlorobenzene considers each of the isomers as a distinct compound.

12. Comment:

It is an error to contend that all chlorobenzenes bioaccumulate in animal and human tissues from ambient air, water and food. EPA cannot conclude that the lower chlorobenzenes accumulate and persist on the basis of partition coefficients. The EPA Draft should limit its conclusions to those chlorobenzenes that are present.

Response:

The Criteria Document states that the ortho- and para-dichlorobenzenes have been shown to be quite lipophilic, and can be expected to bioaccumulate in tissues with high fat content during prolonged, continuous exposure. para-Dichlorobenzene has been detected in human adipose tissue and all three isomers have been detected in blood. The Criteria Document only addresses the dichlorobenzenes and thus does not address the relative persistence of all the chlorinated benzenes.

13. Comment:

Several specific comments were provided concerning production data from the chlorinated benzenes such as incorrect descriptions of the production of the compounds and problems with tables.

Response:

These comments are not directly applicable to the RMCL proposal. The discussion in the Criteria Document on production data states, "only two U.S. companies produce m-dichlorobenzene and in 1974, 31,000 pounds were imported."

14. Comment:

The Environmental Transport and Fate chapter overlooks Monsanto data on bioaccumulation and photogradation. In addition, the chapter postulates that chlorinated compounds are likely to be resistant to biotransformation. This is not demonstrated in the data which show lower chlorobenzenes exhibiting relatively rapid biotransformation.

Response:

The focus of the Criteria Document is upon the health effects of the dichlorobenzenes and thus only minimal data on the environmental transport and fate were included in the document. The Criteria Document did not discuss environmental biotransformation of the chlorinated benzenes.

15. Comment:

Throughout the ecological effects section, the report states that chlorobenzenes are toxic or have adverse effects on reproduction of invertebrates and fish. Most chemicals have these properties at some concentration. No attempt was made to put the toxic effects in perspective.

Response:

These comments are not applicable, as the Criteria Document discusses health effects in animals and humans and not ecological effects.

16. Comment:

Detailed comments were provided on monochlorobenzene.

Response:

These comments are not applicable as the Criteria Document deals with the dichlorobenzenes and not the monochlorobenzenes.

17. Comment:

The description of the Hawkins, et al. (1980) rat study reveals that the data do not support the conclusion drawn by EPA. The Agency cannot conclude that "1,4-dichlorobenzene appears to be well absorbed," on the basis of a study in which no quantitative measures of absorption were attempted.

Response:

EPA agrees; however, the Criteria Document does not include this conclusion. The Hawkins, et al. study described the tissue distribution of p-dichlorobenzene in adult female rats following inhalation, oral or subcutaneous exposure. This study showed that most of the ^{14}C activity (91-97%) was eliminated in the urine within five days after cessation of exposure, while small amounts were found in the feces and expired air. About 50-60 percent was excreted in the bile during the first two days, suggesting reabsorption in the enterohepatic circulation.

EPA agrees that it is not possible to conclude that the compound was "well absorbed" on the basis of this study alone. Since there have not been studies reported which determine the percentage of a dose of dichlorobenzene absorbed following oral or inhalation exposure, EPA is basing its assumed absorption of p-dichlorobenzene (100% from oral exposure and 60% from inhalation exposure) upon the absorption characteristics of benzene and the smaller chlorinated ethanes and ethylenes (Astrand, 1975; Dallas, et al., 1983). This is reasonable based upon the similar molecular weights of the compounds and the fact that there does not appear to be any reason why the absorption characteristics would be markedly different between benzene and these compounds.

18. Comment:

It should be observed that the metabolism data generated by dosing the animals with dichlorobenzenes in oil may have been affected by the vehicle. Studies have shown that oil affects metabolism.

Response:

The commenter did not cite any studies or explain how oil might have affected metabolism or EPA's conclusions. Therefore, EPA cannot fully address the comment. However, EPA is basing its conclusions on metabolism on studies in which p-dichlorobenzene was administered through inhalation, oral and subcutaneous exposure. EPA is unaware of any studies suggesting that oil has affected the results of studies on dichlorobenzene; however, since EPA is not relying totally on corn oil studies, the conclusions would not change even if this were shown to be the case.

19. Comment:

It should also be noted that, like monochlorobenzene, dichlorobenzenes do not bioaccumulate but are instead rapidly biotransformed and eliminated (Hawkins, et al., 1980).

Response:

There have not been studies reported which determine the percentage of a dose of dichlorobenzene absorbed following oral or inhalation exposure. (See Comment/Response 16, above.) However, p-dichlorobenzene has been shown to accumulate in human blood and adipose tissue (Morita and Ohi, 1975; Dowty, et al., 1975).

20. Comment:

Mention of the lethality of dermally applied 1,2-dichlorobenzene in the Reidel (1941) study is not meaningful without a description of the methodology, the dose applied and the degree of lethality. Without such information, there are too many unknowns to conclude anything substantive about the study.

Response:

The Reidel (1941) study is not discussed in the final Criteria Document since dermally applied 1,2-dichlorobenzene is not directly relevant to the possible health effects of the compound through drinking water.

21. Comment:

It is stated that 1,2-dichlorobenzene is more active in its liver toxicity and protein binding than is 1,4-dichlorobenzene. However, the last line of the Summary discusses this activity for 1,4-dichlorobenzene only, suggesting that 1,4-dichlorobenzene is quite active, while 1,2-dichlorobenzene is less so. In fact, Tables 8-4 and 8-5 show that neither compound is very active.

Response:

This comment addresses the relative liver toxicity and protein binding of 1,2-dichlorobenzene (the ortho-isomer) versus 1,4-dichlorobenzene (the para-isomer). For the purpose of this rulemaking, only p-dichlorobenzene is being addressed and thus the relevant issue is the liver toxicity and protein binding of the para-isomer. p-Dichlorobenzene has been shown to exhibit histological alternatives in the liver in rats by gavage (Battelle-Columbus, 1978a, b; 1980a, b) and histopathological changes in the liver in inhalation studies (Hollingsworth, et al., 1956).

22. Comment:

The summary of epidemiologic data notes that the data are insufficient to evaluate dose-response relationships. This conclusion suggests that the epidemiologic data are sufficient to evaluate general toxicologic relationships. In fact, the data are limited to case studies in which exposures were mixed with other chemicals. It is thus uncertain whether the effects noted were related to dichlorobenzene exposure.

Response:

EPA agrees that the human data are limited to case studies in which other chemicals may have been involved. Thus, EPA is not basing the RMCL upon human data but is basing it upon animal data.

23. Comment:

The alleged associations between dichlorobenzenes and blood-forming tissue toxicity and between 1,2-dichlorobenzene and chromosomal alterations in humans must be questioned on several grounds. First, there is no valid experimental evidence that chlorobenzenes have mutagenic/clastogenic activity in test systems relevant to mammals. Indeed, a bone marrow chromosomal test in rats was negative. Second, the activities described are those expected for benzene which may have been a factor in many of these observations. Third, the recent NTP subchronic and chronic test in two species failed to demonstrate effects on the blood-forming tissues.

Response:

EPA agrees that exposure to p-dichlorobenzene has not been shown to result in blood-forming tissue toxicity and thus liver toxicity and not blood-forming toxicity was used as the endpoint in the derivation of the RMCL. With regard to the association between p-dichlorobenzene and chromosomal alterations in humans, the data indicate that p-dichlorobenzene is mutagenic in certain of the test systems, such as its ability to interact with and damage bacterial DNA in the E. coli differential toxicity assay system. No evidence of mutagenic activity in animals has been published.

24. Comment:

Table 8-5 claims that the Domenjaz (1946) inhalation study used a dose of 10^5 mg/m^3 of 1,4-dichlorobenzene. Such a high concentration would be almost impossible to generate in an inhalation chamber.

Response:

This comment is not relevant as the Domenjaz (1946) study is not discussed in the final Criteria Document.

25. Comment:

The observation that the dichlorobenzenes have not been extensively studied for mutagenic activity is inaccurate. EPA overlooked the unscheduled DNA synthesis assay and the cell transformation assay performed by Williams, et al. All tests reported that the dichlorobenzenes were without mutagenic activity.

Response:

The mutagenicity data on p-dichlorobenzene has shown mixed results, demonstrated as follows: p-Dichlorobenzene has been shown to induce abnormal mitotic division in plants and to increase the frequency of back mutation in the fungus, Aspergillus nidulane (Prasad and Pramar, 1968; Prasad, 1970). The compound was not mutagenic when tested in a culture of histidine-requiring mutants of Salmonella typhimurium or in the E. coli WP2 system (Anderson, et al., 1972; Anderson, 1976; Simmon, et al., 1979). p-Dichlorobenzene has not been shown to be mutagenic in animals (Anderson, et al., 1976; Anderson and Hodge, 1976).

26. Comment:

The EPA Draft contends that the NTP rat study on 1,2-dichlorobenzene was not conducted at an appropriately high dose level (120 mg/kg) and that the bioassay may not have been sufficiently sensitive to detect potential carcinogenicity. This is not a supportable contention since the NTP Board of Scientific Counselors indicated that the dose selection was appropriate.

Response:

This comment is not relevant since the draft report of the results of the NTP studies with 1,4-dichlorobenzene (para-) has not been made available as yet. EPA will not make a final assessment of the compound's carcinogenic potential until the results of the study becomes available.

27. Comment:

The EPA draft notes that no data on reproductive or teratogenic effects were available for review. It should note that teratogenicity studies on monochlorobenzene, 1,2-dichlorobenzene and 1,4-dichlorobenzene have been performed by the Chlorobenzene Program Panel and the results have been submitted to the EPA Test Rules Development Branch.

Response:

EPA has cited several teratogenicity studies in the final Criteria Document (Hodge, et al., 1977; Hayes, et al., 1985; Hayes, et al., 1982).

28. Comment:

The EPA draft should be revised to delete repeated references to bioaccumulation as there are no available data that demonstrate bioaccumulation in human tissues.

Response:

p-Dichlorobenzene has been shown to accumulate in human blood and adipose tissue (see Comment/Response 18, above).

29. Comment:

Specific comments were submitted on the trichlorobenzene, tetrachlorobenzene, pentachlorobenzene and hexachlorobenzene chapters.

Response:

These comments are not relevant to this rulemaking since they do not discuss p-dichlorobenzene.

H. TREATMENT FOR CONTROL OF VOCs

These comments are being addressed here as a courtesy to those who commented and as a further explanation of the basis for EPA's proposed MCLs. Final comments and responses will be provided when the MCL is promulgated.

1. Comment:

A treatment device, consisting of a combination of ozone and ultraviolet light, will significantly reduce concentrations of VOCs. (Commenter provided promotional material on the device.)

Response:

This material does not directly impact the RMCL and thus will not be addressed in this package. EPA will consider this material with the MCL proposal comments.

2. Comment:

Granular activated carbon (GAC) units or systems using reverse osmosis and activated carbon are effective point-of-use devices and should be considered generally available technology (GAT) by EPA. Point-of-use treatment presents a cost-effective and reliable alternative to central water treatment for removal of VOCs in drinking water.

Response:

EPA agrees with this comment and is considering authorizing point-of-use treatment devices under certain circumstances. See the Fed ral Register MCL Proposal for a further discussion of this issue.

3. Comment:

VOCs should be controlled at the source, not at the tap. There are problems with various treatment techniques for removing VOCs; GAC only weakly removes VOCs and air stripping of VOCs is unfeasible.

Response:

EPA agrees that VOCs should be controlled at the source and is working through a variety of programs to control their releases. However, because they are not always controlled at the source, drinking water systems must treat the water they serve. GAC is effective for the removal of all VOCs to low levels except vinyl chloride. Aeration is also an effective treatment method.

4. Comment:

EPA should provide performance standards to meet the statutory requirements of the SDWA, allowing utilities in cooperation with the primary agency to select the most effective treatment process. Treatment techniques are extremely site specific and effectiveness is dependent on numerous factors.

Response:

The definition of "performance standards" is unclear, but EPA is setting MCLs to meet the requirements of the SDWA. EPA agrees that the effectiveness of treatment techniques is dependent on numerous factors. EPA does not intend to require any system to use special treatment techniques to control VOCs; systems may select treatment techniques that are efficient at the specific site.

5. Comment:

The level of contaminant removal should be a function of the cost-effectiveness of the removal technology. Increments of VOC removal should be compared to incremental increases in treatment cost for setting the MCL.

Response:

EPA agrees that the level of contaminant removal should be a function of the cost-effectiveness of the removal technology and has examined incremental increases in treatment costs for setting the MCLs (see the Federal Register MCL proposal).

6. Comment:

A limit of technology or limit of detection approach to setting the MCLs should be used, not an approach based on quantitative risk assessment. GAC can bring the concentration of most VOCs down to 0.1 ppb or the limit of detection and thus technology availability is not a limiting factor in setting the MCLs.

Response:

EPA agrees that a limit of technology or detection approach should be used to set the MCLs and has applied this approach in the analysis (see the Federal Register MCL Proposal). EPA also agrees that technology availability is not a limiting factor in setting the MCLs.

7. Comment:

Biological degradation, ozonation and reverse osmosis are practical and cost-effective technologies for VOC removal.

Response:

EPA feels that insufficient data are available to analyze the technologies of biological degradation, ozonation and reverse osmosis for practical application and cost-effectiveness. The current literature does not support the claim that these technologies are practical and cost-effective. There are indications that natural biological activity may convert one VOC to another (i.e., trichloroethylene to vinyl chloride) which must be considered in an evaluation of biological degradation as a treatment technology.

I. COSTS OF TREATMENT

These comments are being addressed here as a courtesy to those who commented and as a further explanation of the basis for EPA's proposed MCLs. Final comments and responses will be provided when the MCL is promulgated.

1. Comment:

Operating and maintenance costs, as well as capital cost, should be compared in any table comparing costs of alternative treatment methodologies. This appears to be missing in Table 8 in the June 12 FR Notice.

Response:

EPA agrees that operating and maintenance costs should be factored in an analysis of treatment methodologies. This was included in Table 8 (p. 24349) in the calculation of unit cost (cents per X gallons) even though the annual operating and maintenance costs were not presented in the table.

2. Comment:

The estimates of cost of GAC and aeration should be substantially higher than those developed by EPA and presented in the Federal Register Notice.

Response:

There are several reasons for the differences in cost. For aeration, the cost for buildings and pumping facilities were added to the commenter's cost, but were not used in developing EPA's cost. The operating and maintenance cost is very sensitive to the electric power rate. The commenter's rate is $.10 per KWH while EPA used a rate of $.07 per KWH. The commenter included the cost of replacing the well pumps which may not always be necessary and was not included by EPA. In addition, the commenter's design is based on treating average daily flow, but actual flows are one-third of this. This results in the capital portion of the rate appearing three times higher than if design flow is used in the denominator. For GAC, the commenter's design is based on treating average daily flows, but actual flows are approximately one-third of this. The commenter's equipment costs are high compared to EPA's estimates. One major expense in the commenter's system is a backwash recycling system, while the EPA cost estimate assumed discharge to a sewer. EPA feels that this recycling system is probably not cost-effective considering that backwash occurs for 10-15 minutes every 39 days. The electric power cost assumption used by the commenter is $.10/KWH versus $.07/KWH used by EPA. The commenter assumes a GAC cost of $.40 per pound versus $.50 per pound assumed by EPA. In addition, the commenter shows cost for replacing well pump and motor. EPA's costs do not include this assumption, since existing well pumps and motors would likely be suitable.

3. Comment:

Cost of treatment may come down due to development of new technologies and increased utilization of existing techniques.

Response:

EPA agrees that there is a logical basis to the assumption that costs of contaminant removal may come down due to development of new technologies. However, there is no direct evidence to support this conclusion and EPA must consider the current costs of technology in the development of MCLs.

III. SUMMARY OF COMMENTS AND EPA RESPONSES TO THE JUNE 12, 1984 RMCL PROPOSAL: ADDITIONAL TECHNICAL ISSUES

A. STRENGTH OF EVIDENCE OF CARCINOGENICITY

1. Comment:

EPA should not refer to a substance as "almost" an IARC Group 2B and use this as a basis for regulation. In addition, if major new data have been developed since the last IARC review and EPA reclassifies a substance, the evidence and reclassification should be reviewed by EPA's Science Advisory Board.

Response:

EPA's Science Advisory Board reviews major new information on chemicals and has reviewed EPA's classification of several of the VOCs based on carcinogenicity. EPA agrees that a substance should be placed into an IARC category based upon the best available scientific information.

2. Comment:

Distinguishing between carcinogens on the basis of mechanism is not warranted by the scientific information at this time. This is demonstrated in the following attached article, Frederica Perera. The Genotoxic/Epigenetic Distinction: Relevance to Cancer Policy. Environmental Research, Volume 34, 1983.

A summary of this article follows:

AUTHOR'S ABSTRACT:

Should federal agencies use separate, less stringent guidelines for regulating epigenetic or nongenotoxic carcinogens on the assumption that thresholds are likely to exist for these agents? This article reviews recent initiatives by the Environmental Protection Agency that either propose or informally adopt this approach in light of responses from the scientific community and a review of the recent literature. Relevant background is provided by current research concerning the role of chromosomal damage and oncogene activation in carcinogenesis along with findings that classical promoters or "epigenetic" agents can induce both DNA damage and chromosomal rearrangements. The conclusion is that such a revision of cancer policy is not now supported by available scientific data concerning chemical carcinogenesis.

"Genotoxic" may be broadly defined as "having the potential to cause a heritable change in the structure or sequence of the genetic material at the level of the nucleic acid, the gene, or the chromosome. A distinction can be made between "direct" genotoxicity (in which the parent compound or its metabolite interacts with the genetic material) and "indirect" genotoxicity (in which the actual damage is inflicted by a reactive agent or

factor induced by the genotoxin). "Epigenetic" may be equated with "nongenotoxic."

AMPLIFICATION:

Attempts to distinguish types of carcinogens have important implications for regulation of these agents. The concept of a clear distinction between epigenetic and genotoxic agents could affect the interpretation of experimental data with these results:

1) Reconsideration of linear extrapolation of dose-response curves, and new emphasis on thresholds and "hockey-stick type" curves.

2) Strengthening the idea of reversibility of activity below a certain threshold level, because of the mechanisms of epigenetic activity (tissue injury, immunosuppressive effects, etc.)

3) Reinterpreting curves on the basis that "the carcinogenic effect in experimental animals was likely to be secondary to physiological effects triggered only at high levels."

Proponents of the distinction have classified many important chemicals as epigenetic. These include asbestos, the insecticide permethrin, formaldehyde, diethyl stilbestrol (DES), and others.

With regard to its effect on regulation, the arguments for and against the distinction came to a head in the Comments on the Draft Carcinogen Assessment Group Proposal (EPA, 1982). "While there was some qualified support, the majority were negative on the genotoxic-epigenetic regulatory distinction."

A large body of specific information is cited to show that the distinction should not be used in developing regulations.

With regard to the mechanisms of carcinogenic action, the genotoxic and epigenetic mechanisms are not mutually exclusive. "It may be preferable, therefore, to think of the carcinogenic process as comprising three general stages--initiation, promotion, and progression--each involving a variety of mechanisms, both genetic and non-genetic."

Response:

EPA agrees with the substance and conclusions of this article that there is insufficient scientific basis to distinguish classifying chemicals as genotoxic or non-genotoxic carcinogens. As explained in the final rule preamble, EPA is classifying chemicals according to the strength of evidence of carcinogenicity and is not classifying chemicals according to mechanism. (See Comment/Response - I.D.1).

B. MOUSE LIVER TUMORS

1. Comment:

Mouse liver tumor data are inadequate to serve as the basis for a meaningful quantification of human cancer risk. The report by the International Expert Advisory Committee to the Nutrition Foundation entitled "The Relevance of Mouse Liver Hepatoma to Human Carcinogenic Risk" confirms this view. The following is a summary of this report:

> The complexity and difficulty of identifying and classifying liver tumors in mice are clearly displayed. These tumors occur in several forms, both benign and malignant, with various subdivisions. Classification depends largely on morphology. Functional criteria also apply, including effects on enzyme reaction and other chemical reactions. Types of biological behavior used as criteria include invasions of adjoining tissues, metastases, and growth of transplants.
>
> The report enumerates factors affecting the incidence of tumors. These include genetic factors (with wide variations among strains), dietary and related factors, sex and sex related conditions, and age. In one instance, a laboratory-to-laboratory variation was reported for spontaneous hepatomas in the same strain of mice.
>
> One special difficulty with the use of mice in assays is the large number of spontaneous neoplasms observed. Morphological differences between spontaneous and induced neoplasms occur in some cases and not in others. The variation of types of spontaneous tumors occurring in different strains of mice is complex.
>
> With respect to tests on suspected carcinogens, one instance is reported in which different agents produced quite different distributions of the various type of tumors.
>
> A broader view is provided by the National Cancer Institute Bioassay results for 85 chemical agents. A tablulation shows the occurrence of cancer types (liver and non-liver) for different sexes and for different animal species (mice and rats). The occurrences for different chemicals are widely distributed between cancer types and between species. They are less widely distributed for sex, within each species.
>
> These considerations lead to a cautious conception of regulation. "From a regulatory point of view, caution is necessary in making judgments based upon tumor pathogenesis alone, since we do not have a full understanding of carcinogenic mechanisms." Patently genotoxic chemicals should be strictly regulated. "Less concern is warranted in the case of chemical induction of tumors only in mouse liver, particularly if the tumors are benign neoplasms, that are associated only with high exposure levels that produce additional biological effects such as chronic tissue injury."

However, a more conservative course would be warranted when additional toxicological data suggest an increased potential for human risk.

Response:

EPA's policy regarding mouse liver tumors and their relation to human cancer risk is discussed in the Federal Register Final Rule (Appendix A). EPA agrees with the report that "caution is necessary in making judgments based upon tumor pathogenesis alone, since we do not have a full understanding of carcinogenic mechanisms." EPA also agrees that less concern is warranted where a chemical induces tumors only in mouse livers and that a more conservative course is justified when other toxicological data suggest carcinogenicity.

2. Comment:

The work of Roe and others (Proc. Nutr. Soc. 40:57, 1981) demonstrated that ad libitum feeding substantially affects the hormonal status of rodents and produces highly statistically significant effects on survival and on several varieties of spontaneous tumors. In one instance the crude incidence of SPF mice with liver tumors was reduced from 14% in males fed ad libitum to 2% when fed on restricted diets. Lung, pituitary and lymph or thymus tumors were correspondingly reduced. Therefore, liver tumors in male mice who have a substantial spontaneous incidence of such tumors should not be the sole basis for assessing potential carcinogenicity.

Response:

This comment concerns the weight of evidence issue on mouse liver tumors, including conditions under which mouse liver tumors along with any other evidence for carcinogenicity are interpreted as either sufficient or limited evidence for carcinogenicity, as discussed in EPA's Proposed Guidelines for Carcinogen Risk Assessment (49 FR 46294). In such a case, EPA looks carefully at short-term test results and does not rely only on liver tumors in mice with spontaneous incidence of such tumors. The commenter cites evidence for reduced formation of spontaneous tumors in mice fed restricted diets as opposed to ad libitum diets. EPA agrees that caloric intake could play a role in the occurrence of tumors. However, the Agency does not believe that there are sufficient data at this time to incorporate this parameter into the Agency Guidelines for Carcinogenic Risk Assessment. Since ad libitum feeding is the usual procedure in carcinogenicity studies, and until more data consisting of comparisons with ad libitum and restricted feeding become available for consideration, EPA will continue to weigh evidence for carcinogenicity as stated in the guidelines mentioned above.

C. AADI APPROACH

1. Comment:

The development of RMCLs for non-carcinogens based upon human epidemiology or animal studies to determine the "no effect" levels for chronic

There is, however, a constant need to review and revise the no-observed-adverse-effect level (NOAEL) for each compound regulated.

Response:

EPA agrees that the NOAELs for each compound regulated should be updated as new information becomes available and EPA plans to continually review the scientific literature and update the numbers, as needed.

2. Comment:

We can certainly agree that for compounds where human ingestion studies have been used to determine the NOAEL, the use of an uncertainty factor of 10 may be well justified. There is, however, significant question as to the need for a safety factor of 100 where long-term animal studies have been used and of 1,000 where inadequate animal studies were used as the basis for determining the NOAEL.

Response:

EPA bases its uncertainty factors upon the NAS guidelines (Drinking Water and Health, Vol. I, 1977) which state that an uncertainty factor of 10 should be used with valid results from studies on prolonged ingestion by man; an uncertainty factor of 100 should be used with valid results of long-term feeding studies on experimental animals in the absence of human studies; an uncertainty factor of 1,000 should be used with scanty results on experimental animals. EPA believes that these uncertainty factors have been protective in the past and adequately account for uncertainties in the data. According to the NAS, "When the quality and quantity of data are high the uncertainty factor is low and when data are inadequate or equivocal, the uncertainty factor must be larger." (Drinking Water and Health, Vol. I, 1977, p. 804.)

3. Comment:

In deriving RMCLs, EPA should consider all potential routes of human exposure to volatile organics via drinking water, and routinely include these factors in their calculations of AADIs. Based upon Dr. Brown's paper, an additional reduction of at least 50% after the 80% reduction recommended by the NAS, would appear to be indicated.

The following is a summary of Dr. Brown's paper (Brown, et al. 1984 The Role of Skin Absorption as a Route of Exposure for Volatile Organic Compounds [VOCs] in Drinking Water. American Journal of Public Health, Volume 74, No. 5):

> Contaminants in drinking water may operate through avenues other than ingestion, in particular through skin absorption.
>
> The authors analyze literature data on skin absorption for aqueous solutions of ethylbenzene, styrene, toluene, and xylene. They use Fick's Law to extrapolate absorption rates to the low levels which could be present environmentally.

The authors proceed to calculate total quantities of the hydrocarbons absorbed from very dilute solutions by adults and children under various assumed conditions of exposure (in bathing and swimming). Using these results together with reasonable estimates of drinking water ingested, they calculate that absorption can account for 29-91 percent of the total hydrocarbon transferred. (The high figure is extreme, being based on immersion of a small child for 1 hour.)

Response:

EPA agrees that all sources of human exposure to VOCs should be considered in the calculation of AADIs. However, EPA believes that an 80% reduction is sufficient to account for other sources of exposure, including inhalation and dermal exposure. EPA does not believe that an additional reduction of at least 50% after the 80% reduction is warranted.

4. Comment:

For VOCs, by definition, air will be the primary source and even that source is miniscule by comparison with the waterborne source, even where air pollution is high. At the highest contamination site recently reported for methyl chloroform in the air (H.B. Singh, et al., Environ. Sci. & Tech. 16:872, 1982) the concentration averaged 4 ug/m^3. If that concentration (i.e., 4 ug/m^3) were inhaled for 24 hours a day it would still represent under 5% of an RMCL calculated for drinking water as the sole source of this material. For the occupationally-exposed working population this RMCL represents less than 0.003% of the TLV and is insignificant.

Response:

EPA does not believe that the RMCLs should be set based upon a comparison with the TLVs, for the two values are set based upon totally different factors. RMCLs are designed to be protective of the entire population over a lifetime exposure while TLVs are occupational standards designed to be protective for a particular subset of the population (workers) over a specified time period (5-day work week).

5. Comment:

The application of the 100-fold factor to the highest no-adverse-effect dose measured in animal studies to establish ADIs for humans was one of the key steps in deriving food tolerances. The expert committees of the FAO/WHO believed that a steadfast, indiscriminate use of the 100-fold factor would not provide due consideration to species, strain, and sex differences among animals, to variations in susceptibility among exposed individuals and inadequate human and animal data, among others and, therefore, recommended the employment of a range of safety factors depending on the quality and nature of the data under review.

Response:

EPA agrees that a steadfast, indiscriminate use of the 100-fold uncertainty factor is not warranted. EPA believes that a range of uncertainty

factors, depending on the quality and quantity of the data, should be applied.

6. Comment:

I urge the EPA to re-evaluate its common practice of using safety factors of 10, 100, and 1,000 steadfastly and should consider the incorporation of appropriate safety factors based on FAO/WHO recommendations. Such an approach would reduce the arbitrary nature of safety factors thereby lending more scientific support to the AADIs derivation process.

Response:

EPA accepts the recommendations of the NAS Safe Drinking Water Committee (Drinking Water and Health, Vol. I, 1977) and applies uncertainty factors of 10, 100, and 1,000 as the data indicate. However, EPA will apply other uncertainty factors if the data suggest an intermediate uncertainty factor may be more appropriate.

7. Comment:

I believe that the literature contains sufficient information, although not precise, for the EPA to assess the contribution of inhalation exposure and, possibly, oral exposure for some contaminants instead of reducing the AADIs by an arbitrary 80% or 99% to establish RMCLs and MCLs.

Response:

EPA agrees that for certain contaminants, information is available on the contribution from inhalation exposure. When data are available and reliable, EPA believes it is appropriate to factor this into the ADI. However, EPA does not believe that sufficient data are available on all the VOCs at this time, and thus believes that it is appropriate to reduce the AADIs by a set value for these compounds.

8. Comment:

A study suggests that petroleum-product vapor buildup in the bathroom resulting from volatilization as one takes a shower may be sufficiently high so as to cause or contribute to mucous membrane irritation. The predicted bathroom air concentrations are consistent with those measured in gasoline-contaminated homes whose residents have complained of headaches and eye, nose and throat irritations.

Response:

EPA agrees that volatilization is one route for inhalation exposure to VOCs.

9. Comment:

For acute exposure, the use of low level chemically contaminated water for showering purposes can generate vapor in the confined area of the bathroom at levels sufficient to cause or contribute to mucous tissue

irritation commonly reported in affected homes. High temperatures and humidity may also contribute to these effects especially in the bathroom. For chronic exposure, the use of chemically contaminated water at EPA recommended guidelines for all purposes in an affected home may result in inhalation, oral, and dermal exposures leading to cumulative doses exceeding EPA's recommended total daily body burdens for an adult and a child.

Response:

EPA does not agree that cumulative doses exceeding the ADI commonly occur in homes. However, there is undoubtedly some exposure through showering and EPA believes that by reducing the ADI by 80% to account for exposures from inhalation, oral and dermal exposure, the public should be sufficiently protected against all routes of exposure.

10. Comment:

"Non-carcinogens" will have RMCLs chosen by using safety factors applied to a NOAEL. We question the adequacy of such safety factors in certain circumstances. Since risk analysis is being applied to "carcinogens", why is a similar approach not taken towards the "non-carcinogens"?

Response:

EPA believes that it is appropriate to assume a threshold approach for non-carcinogens and to calculate the RMCLs using safety factors applied to a NOAEL. This approach is recommended by the National Academy of Sciences (Drinking Water and Health, Vol. 3, 1980) and by numerous other scientific organizations. EPA is not using risk analysis to set the RMCLs for carcinogens.

D. RMCLS FOR CARCINOGENS AT ZERO

1. Comment:

Although the health effects work groups studying the drinking water problem believed there was sufficient data to cause concern, every group qualified its recommendation by saying, variously, that the data were limited, more studies were needed, and that the difference between genotoxic and nongenotoxic carcinogens should be addressed by EPA. Until such questions are resolved by further information, we believe the RMCLs should not be set unduly low and certainly not at the zero level.

Response:

EPA believes that there are sufficient data available to make a judgment on the carcinogenic and non-carcinogenic effects of the nine VOCs. Additional research will add to current knowledge on these chemicals; however, EPA believes that the current data show sufficient reason for concern over the adverse health effects of the chemicals. (See the RMCL Proposal for a discussion of the adverse health effects of the VOCs and Comment/Response - I.D.1 for a discussion of genotoxic versus non-genotoxic carcinogens.)

2. Comment:

If you must develop RMCLs, none of them should be 0. The word "none" would be preferable to using "0". It would be even better to adopt a policy which would say "It is the goal of all water suppliers and regulators that there be no contaminants in the drinking water."

Response:

The comment does not identify why this issue is important or how it should affect the MCL. The SDWA requires that RMCLs be established and states that an RMCL is a health goal. EPA recognizes that "none" is equivalent to "zero" and has chosen to use the word "zero". While it is ideal that there be no contaminants in drinking water, some contaminants have thresholds for adverse health effects, and it is important to set RMCLs that reflect these adverse health effect levels. Carcinogens will have RMCLs of zero.

3. Comment:

Section 1412(b)(1)(B) of the Safe Drinking Water Act requires the Administrator to determine the lowest level at which health effects may occur, plus a margin of safety, in establishing RMCLs. This requirement mandates a risk assessment method. Setting RMCLs at zero or at analytical detection limits would fail to fulfill this statutory requirement.

Response:

EPA does not agree that the SDWA mandates a risk assessment method. Using a risk assessment method to set a risk level and the RMCL would not fulfill the statutory mandate that RMCLs are to be set to prevent adverse health effects with a margin of safety. The risk calculations consider levels at which a specified concentration of a chemical results in a certain excess cancer risk in the population. These risk calculations do not consider the no-effect level with a margin of safety. Rather, they approve of some risk and some projected level of occurrence of the adverse effect.

4. Comment:

RMCLs are by definition based on health and safety considerations, but this approach is not based on such considerations. Most compounds have a concentration beneath which health risks are not identified. As a result, selection of zero for an RMCL would not provide significant additional protection of health beyond that provided by a higher, finite, level.

Response:

EPA disagrees. EPA believes that chemicals which are known and probable human carcinogens should be classed along with other carcinogens which are believed to have no threshold and thus have no safe level of exposure. As such, selection of zero as an RMCL does provide additional protection beyond that provided by a higher, finite level.

5. Comment:

Setting RMCLs at zero would also present a misleading picture to the public, since most of the compounds for which RMCLs are currently proposed are also ingested daily via inhalation, food intake, or smoking. Attempts to reduce concentrations to zero would not necessarily reduce daily exposure to any given compound.

Response:

EPA agrees that most of the compounds for which RMCLs are proposed are also ingested daily to some extent via inhalation, food intake or smoking. However, EPA believes that it is appropriate to reduce the intake of potential human carcinogens via drinking water as it should ultimately lead to an overall reduction in the daily exposure to a compound.

6. Comment:

If the EPA sets RMCLs at zero for each carcinogen, then they provide no information and guidance. The potency of carcinogens varies ten million fold to one from agents like saccharin and 1,1,1-trichloroethane to agents like aflatoxin B^1 and dioxin. Surely Congress did not mean that EPA set the same level for saccharin as for dioxin.

Response:

The goal of RMCLs is not to provide information and guidance; it is to set a health goal for the MCL rulemaking. EPA has considered strength of evidence in setting the final RMCLs for carcinogens so that the RMCLs for chemicals with sufficient evidence of carcinogenicity are set at zero and the RMCLs for chemicals with equivocal evidence of carcinogenicity are set at a non-zero level. Thus, chemical potency is considered in the evaluation of the strength of evidence.

7. Comment:

It is currently impossible to label any material as definitely not a carcinogen, since a test with improved sensitivity or better experimental design may subsequently show that the material is carcinogenic. Indeed such a case is quoted within this notice of proposed rulemaking.

Response:

The Agency agrees. EPA classifies chemicals according to the weight of evidence of carcinogenicity at the current time. The Agency recognizes that new data may become available in the future which would result in the reclassification of the chemical and in such a case, EPA would repropose the standard for that chemical.

8. Comment:

The use of zero for an RMCL is essentially based on the belief in a linear dose-response curve at low doses -- so that any amount of material might cause some irreparable damage. However, choosing zero RMCL as a

policy decision denies the possibility that the dose-response relationship is not linear, as is plausible and perhaps likely with some materials. Thus an automatic choice of zero for the RMCL of any "carcinogen" prevents the use of other information which may be available.

Response:

EPA believes that it is appropriate to follow a conservative approach, in order to be protective of human health, and believes, based on best scientific judgment and review of many cancer studies, that the dose-response curve is probably linear at low doses. EPA does not agree that by setting an RMCL at zero, other information on the chemical may not be used. The Agency is aware that evidence of non-linear dose-response curves may become available and will consider any such evidence when it becomes available.

9. Comment:

It seems odd that a material which has been shown to provoke a carcinogenic response should be specially singled out for having a zero RMCL. There are other responses which could also be irreversible and caused by very low doses (i.e., have no threshold) -- especially in certain groups of sensitive individuals. Much less is known about the mutagenic and teratogenic effects of most materials, for example, especially at low doses, and low doses of some materials might have feto-toxic or neurological effects, especially if they bioaccumulate.

Response:

EPA considers all effects (including mutagenicity and teratogenicity) in the analysis of the chemicals and has set RMCLs of zero for those chemicals showing a carcinogenic response since this response has not been shown to exhibit a threshold. Mutagenicity is factored into the classification of the chemical for carcinogenicity, according to the EPA Proposed Guidelines for Carcinogen Risk Assessment and can result in a chemical being classified in a different category than it would have been had the mutagenicity data not have been available. The EPA Proposed Guidelines for the Health Assessment of Suspect Developmental Toxicants (49 FR 46325) considers teratogenicity to be a threshold effect and proposes that a safety factor approach be used to assess developmental toxicants. The commenter does not explain how this comment should affect EPA's decision-making for these VOCs.

10. Comment:

The proposal appears to assume, even if not explicitly stating so, that achieving a zero level of these pollutants in our water supplies will achieve a zero level of risk. This is not true. We know that the pollutants currently exist in at least some supplies, and so some action would be required to reduce their levels. Associated with any such actions will be concomitant risks. Thus, for example, adding aeration stages or activated charcoal filters to water supplies will have some effect on the levels of bacteria within the water supplies -- possibly leading to increased risk. Even the construction of such filters or

aeration plants has associated with it a risk. Such effects have to be considered -- or at least shown negligible -- in setting the RMCL so as to have negligible adverse health effects.

Response:

EPA has proposed RMCLs at zero as a health goal and recognizes that it is not possible to achieve "zero" level of these pollutants in our water supplies, or in society generally. There will be other risks from VOC control in drinking water, for example from aeration or transfer of VOCs from water to granular activated carbon. However, those risks and risks from bacteria in water supplies are already regulated to protect health; VOCs in drinking water are not. Thus, EPA does not believe that an RMCL of zero will achieve a zero level of risk.

11. Comment:

Setting the RMCLs to zero is foolish. It may also be dangerous. Some materials (e.g., selenium is a possible candidate) may be both carcinogenic and also essential components of a human's diet. If the major source of such a material is water, and it is also possible to reduce the level in water to low levels, then an RMCL of zero will be mischievous.

Response:

EPA agrees that it may not be appropriate to set RMCLs at zero for those compounds which are essential elements. However, this is not the case for any of the nine VOCs in the proposal.

12. Comment:

We favor a new MCL when considering the significance of the Woburn study by the Harvard School of Public Health. A summary of this study follows:

> The authors performed a health survey in Woburn, Massachusetts, in 1982-1983. The objective was to investigate health hazards associated with contamination of certain wells in the city's water supply.
>
> The major finding was "a consistent pattern of positive associations between availability of water from wells G and H and the incidence of childhood leukemia, perinatal deaths, and some classes of birth defects and childhood disorders."
>
> The population surveyed for leukemia comprised 4,978 children (in 1982). Children with leukemia had an average 21.1 percent of their yearly water supply coming from wells G and H, compared with an expected availability of 9.5 percent. The pattern of incidence of leukemia was as follows:

Period of Observation	1969-1979	1980-1983
Cases observed:	12	4
Cases expected*:	5.3	2.3

*From a matched population of Woburn children

The association with use of water from wells G and H[1]) is significant.

Other conditions associated with water from the contaminated wells were perinatal deaths and some classes of birth defects. There was no evidence of association for spontaneous abortions or low birthrate.

Among the observed group of children, there were no demonstrable associations between well water use or place of residence and anemia, diabetes, heart/blood pressure disorders, learning disabilities and other disorders. However, elevated risks for the exposed groups were found for lung/respiratory, kidney/urinary, allergy/skin and neurologic/sensory disorders.

No analyses for water contaminants were reported in the study. However, the following data are available from another source:

Contaminants in Wells G and H in 1979

	ppb
Chloroform	1.1 - 11.8
Trichloroethylene	63 - 267
Tetrachloroethylene	9.0 - 20.8
Trichlorotrifluoroethane	22 - 23
Dichloroethylene	28
Dichlorotrifluoroethane	<5
1,1,1-Trichloroethane	0.6 - 2.1
Dibromochloromethane	2.0
Arsenic	2

Response:

The water analysis data from the Woburn study identifies trichloroethylene as the primary agent of concern. EPA believes that there are sufficient toxicologic data to consider trichloroethylene to be a probable human carcinogen, as discussed in the Federal Register Final Rule. However, the data from the Woburn study are not conclusive and thus this data will not be factored into the analysis of the carcinogenicity of trichloroethylene.

13. Comment:

The Safe Drinking Water Act does not require that RMCLs be set at zero. Although the House Committee suggested that an RMCL should be set at zero where there is no safe threshold for a contaminant, it did not

state that "safe" means entirely free of risk. To the contrary, the House Report uses relative terms in describing what is intended by the "adequate margin of safety" provision. Consequently, under the Safe Drinking Water Act, the presence of a carcinogen at very low levels does not mean that the drinking water is "unsafe."

EPA has interpreted the term "safety" and the concept of "margin of safety" as not requiring the elimination of all risk under the other regulatory programs. As there is no legal requirement that EPA set RMCLs at zero for carcinogens, EPA should use the "significant risk" approach to set RMCLs.

Response:

The Safe Drinking Water Act does not provide a "relative standard of safety" approach to setting RMCLs. Section 1412(b)(1)(B) states that "each such recommended maximum contaminant level shall be set at a level at which, in the Administrator's judgment based on such report, no human or anticipated adverse effects on the health of persons occur, and which allows an adequate margin of safety." The statute itself states that EPA shall determine the level which meets these criteria, including allowing for an adequate margin of safety.

It is clear that zero for carcinogens best meets these criteria. This position is most consistent with Congressional intent and with the most explicit statement given to EPA, i.e., that where there is no safe threshold for a contaminant, the RMCL should be set at zero. In the opinion of the Agency, there is no safe threshold for carcinogens, i.e., every level of exposure to a carcinogen presents some degree of risk and thus the RMCLs should be set at zero.

14. Comment:

RMCLs should not be set at zero, as zero level RMCLs are not in accord with the views of Federal agencies on risk assessment. For example, in considering regulatory action under the Toxic Substances Control Act, risks in the range of 10^{-6} to 10^{-4} have been regarded as insignificant by EPA. The Nuclear Regulatory Commission has adopted a policy designed to limit carcinogenic radioactive exposures to risk which would be reasonable when compared to risks posed to society by day-to-day living and by comparable technologies. Other advisory groups and experts also agree with a risk approach.

Response:

EPA acknowledges that other Federal agencies and offices within EPA have used a risk approach to setting regulations. However, EPA does not believe that a risk approach for carcinogens is appropriate under the Safe Drinking Water Act. The Safe Drinking Water Act has its own legislative history and statutory language which clearly states that if a threshold cannot be demonstrated for a chemical, then the RMCL should be set at zero. EPA believes that the direct language of the legislative history and statute is preferable over interpretations imported from other statutes.

E. RMCLs FOR CARCINOGENS AT THE ANALYTICAL DETECTION LIMIT

1. Comment:

Risk may be defined as exposure at a concentration level which causes toxicity. The fact that a chemical substance can be detected at a very low level, such as its "limit of detection," does not necessarily mean that the chemical substance represents a risk at that concentration.

Response:

EPA agrees that the fact that a chemical can be detected at a certain level does not necessarily mean that the chemical represents a risk at that concentration. EPA has not set the RMCLs based upon the analytical detection limits. EPA has set the RMCLs for known and probable human carcinogens at zero based upon the SDWA, which states that RMCLs are to be set at a level at which no known adverse or anticipated adverse health effects occur, with a margin of safety. For non-carcinogens, EPA has determined RMCLs based upon conventional toxicological principles which assume a threshold of effect.

F. RMCLs FOR CARCINOGENS BASED ON RISK CALCULATIONS

1. Comment:

As is noted in various places in the proposed rulemaking, EPA's Carcinogen Assessment Group (CAG) uses a 95 percent upper-confidence bound on a linearized multistage model to assess cancer risks. This is a highly conservative method which typically overestimates actual cancer risks significantly.

Response:

EPA agrees that the 95 percent upper confidence limit on the linearized multistage model is a conservative method which can overestimate actual cancer risks. However, it is not possible to state the extent to which the actual cancer risks whould be overestimated.

2. Comment:

In addition to the biological uncertainties in interspecies comparisons, there are also severe uncertainties in mathematical extrapolation from high-to-low dose risks in the test species themselves. With respect to carcinogenesis, there are several dose-dependent differences which current mathematical models do not take into consideration.

Response:

EPA agrees that there are many uncertainties in mathematical extrapolation. However, EPA has not based the RMCLs for known or probable human carcinogens upon risk models.

3. Comment:

The risk assessment model currently employed uses only one part of available data: tumor incidence. Other relevant data, such as pharmacokinetics, comparative metabolism, and competing risks should, as mechanisms become more understood, be evaluated and appropriately reflected in risk characterization. Current models, while based on "informed logic," are not biologically validated, leading to potential differences between extrapolated results and observed results that differ by orders of magnitude.

Response:

The risk assessment models are not being used to set the RMCLs for known or probable human carcinogens. EPA agrees that the current models are not biologically validated. However, to wait for such validation in the face of sufficient evidence to indicate that there may be adverse effects on health is inconsistent with the Act. Current models represent the best methods currently available to evaluate cancer risk.

4. Comment:

For clearly identified carcinogens, a variety of models exist, of approximately equal validity, with which maximum likelihood estimates of carcinogenic risk can and should be made.

Response:

EPA agrees that there are a variety of models with which maximum likelihood estimates of carcinogenic risk can be made. The Agency employs a variety of models to estimate carcinogenic risk, emphasizing the linearized multistage model, as this model is presently believed to be the most biologically plausible of the various risk models. The reason why the linearized multistage model is considered to be the most biologically plausible is that this model has been used to support the somatic mutation hypothesis of carcinogenesis (Armitage and Doll, 1954; Wittemore, 1978; Wittemore and Keller, 1978). This model is consistent with linearity dose-response evidence and the fact that carcinogenicity progresses through a number of stages (NAS, 1977).

5. Comment:

The range of additional lifetime risks commonly referenced by regulatory bodies and experts lies in the range of 10^{-4} to 10^{-6}. Legislative precedent focuses on the higher end of the range. EPA and other regulatory agencies historically have developed such *ad hoc* thresholds for carcinogenic risk. In addition to these precedents, numerous outside commentators have recommended threshold values of acceptable risk. Although these sources do not provide the Agency with a single unique recommendation, they agree on the general range of such risk values.

Response:

EPA agrees that the range of lifetime risk commonly referenced by regulatory bodies and experts lies in the range of 10^{-4} to 10^{-6}. However, EPA believes that the RMCLs for compounds with sufficient evidence of carcinogenicity should be set at zero, not based upon risk calculations. EPA does use such risk estimates for contaminants which present known or anticipated non-cancer effects but also have equivocal evidence of carcinogenicity as a means of accounting for this equivocal evidence.

6. Comment:

Arbitrary selection of one quantitative risk assessment model, say the most conservative, is unjustified scientifically and is contrary to recent legal precedent which ruled against the exclusive use of extreme risk modeling procedures. We recommend the use of several applicable models to represent the range of estimated risk. The following models merit consideration: Logit, probit, multistage, Weibull and multihit.

Response:

EPA's CAG, in the derivation of numbers based upon risk models, uses several models to derive risk. CAG emphasizes the multistage model as the most biologically plausible model, but does derive numbers based on other models.

7. Comment:

The exposure levels should be extrapolated from the small laboratory animal to man using at least two extrapolation methods. The first is on a mg/kg body weight basis which ignores any influence of metabolic rate and suggests that the toxic effect is a direct function of the amount of compound present in a unit body weight. The second method for dose rate extrapolation includes a consideration of metabolic rate and can be based on a direct comparison of metabolic rate or one of the indirect indicators of metabolic rate such as body surface area. We recommend at least these two methods in order to better define the likely range of risk by using all the available information.

Response:

Extrapolations from animals to humans could also be done on the basis of relative weights rather than surface areas. The latter approach, used here, has more basis in human pharmacological responses; it is not clear which of the two approaches is more appropriate for carcinogens. In the absence of information on this point, it seems appropriate to use the most generally accepted method, which also is more conservative.

8. Comment:

Unless there is information to the contrary, all models provide risk estimates with an equal probability of being correct. A process that tak s into consideration all of this information is one in which the geometric mean of all of the risk estimates is obtained. This is a rational and

systematic method which is recommended to develop an estimate of the central tendency of the likely risk that is neither arbitrarily conservative nor arbitrarily liberal.

Response:

EPA examines each chemical on a case-by-case basis and for those chemicals where a valid study by the appropriate route is available, a risk estimate is determined using the multistage model. For other chemicals where several studies by the appropriate route are available and all have been determined to be of equal validity, EPA will use the geometric mean of all these studies using the multistage model. This was the case for carbon tetrachloride where the geometric mean of four studies was used to determine the cancer risk.

9. Comment:

The stronger and more reliable the evidence, the less risk one takes. If the evidence is weak and does not appear to support a strong case for adverse effects in man, then the higher the estimated risk one is likely to find acceptable.

Response:

EPA agrees with this comment and has followed this philosophy by setting the RMCLs for known or probable human carcinogens at zero (allowing less risk) and setting the RMCLs for those compounds with less evidence of carcinogenicity at a finite level (allowing more risk).

10. Comment:

The commenter does not endorse "risk assessment" as a regulation-setting tool at this time. Despite its analytical elegance, risk assessment is laden with uncertainties -- some of which are addressed in the proposed rule -- and these require value judgments by the analyst.

Response:

EPA agrees that it is not appropriate to use risk assessment for setting regulations for all chemicals. RMCLs for chemicals with "sufficient" evidence for human carcinogenicity have been set at zero and not based upon risk calculations. EPA also agrees that risk assessment has many uncertainties associated with it which require value judgments by the analyst.

11. Comment:

If the notion of acceptable risk were accepted, it would be necessary to set risk at a level of magnitude higher than 1 in 100,000, in order to take into account the effects of a carcinogen in combination with other chemicals present in drinking water.

Response:

In the past, regulations have generally been set in the general range of 10^{-4} to 10^{-6}. However, EPA has not selected an "acceptable" risk level as the basis for all regulations.

12. **Comment:**

A one in a million per year risk level is also seen to be reasonable when we look at the true legislative requirement that the level be set at a level that no adverse health effects be observed with a suitable margin of safety (wording not exact). We suggest that this be interpreted using the language commonly used by medical men and others at that time, and not by the more precise language of risk analysts who must assume that anything poses a risk even at small doses. The key here is 'observed' health effects. The level at which an epidemiological study can just detect a risk, in favorable circumstances, is about 0.1% annual risk (5% of canc r incidence). This could be called a No Effect Level in Man, and 1 in 10^6 annual risk gives a 3 orders of magnitude safety factor -- more than often demanded.

Response:

The SDWA specifies that the RMCLs are to be set at a level "at which, no known or anticipated adverse effects on the health of persons occur and which allows an adequate margin of safety." EPA does not believe that a risk level is consistent with the legislative mandate, since a risk level corresponds to a concentration where effects occur, and not to the no-effect level with an adequate margin of safety.

13. **Comment:**

For the "non-carcinogens," it is possible to assume a toxicological model (e.g., the probit - log (dose) model which assumes a lognormal distribution of thresholds in the population) and estimate the risks from the various levels of materials obtained after applying the safety factors. Why has this not been done, in order to show that the non-carcinogens are to be regulated as much (or as little) as the "carcinogens" (see below - section G)? The absence of a calculation or the absence of data does not imply the absence of risk!

Response:

The potential utility of dose-response extrapolation methodology for noncarcinogenic human risk assessment does exist but has been found to be of limited value for contaminants in drinking water. The models used to estimate risk require lifetime feeding studies which use appropriate numbers of animals of each sex and demonstrate some dose response. As noted above, this type of information is not now available for many of the contaminants of drinking water. While both the risk estimate and ADI approach require some degree of value judgment, it is the belief of the EPA that the ADI methodology is the most useful for noncarcinogenic hazards given the general deficiencies in available data. In situations for which high-quality toxicological data are available, the risk estimate approach

would be appropriate for the assessment of noncarcinogenic hazards. Consequently, in the absence of such data the application of safety factors to no-observed-effect levels that have been derived from laboratory animal toxicity data is the most feasible and currently acceptable method for the determination of human exposure limits to noncarcinogenic environmental contaminants.

14. Comment:

When information is available other dose response relationships should be considered. The information here will necessarily be indirect. For as must be emphasized, there is no data which can prove the absence of a threshold for any type of health effect at sufficiently low doses. This might change at some future time when EVERY possible mechanism for ANY effect can be elucidated, but currently, even when thresholds are apparent at some dose levels, one cannot deny the possibility of some other mechanism operating down to very low doses.

Response:

EPA agrees that it is not possible to prove the absence or presence of a threshold at sufficiently low doses. Thus, EPA is following a conservative philosophy and assuming a nonthreshold philosophy for carcinogens at low doses.

15. Comment:

The EPA has not considered risk in context, nor realized that to carry useful risk analysis and assessment ALL effects of actions must be factored in, not just a single effect of that action.

A summary of four articles which were provided on the subject of risk assessment follows:

1) Richard Wilson. Commentary: Risks and Their Acceptability. Science, Technology and Human Values, Volume 9, Issue 2, 1984.

Risks are ever-present and necessary. In the conduct of their lives, people are continually forced to trade off risks. Their perceptions lead them to overstate many risks while ignoring others of much greater magnitude.

For an objective evaluation, hazards may be quantified and ranked in terms of deaths produced per year of exposure. Using this measure, risks above some boundary in the neighborhood of one in one million, or 10^{-6}, are generally considered acceptable. Many common causes (all industrial work, traffic accidents, etc.) create risks which are far higher. "Most occupational risks of 10^{-5}/year are usually ignored."

Legal indecision over the regulation of saccharin as a carcinogen suggests that the average ingestion of saccharin leads to a risk which is near the borderline of acceptability. This estimated value is 2×10^{-6}/year.

The economic risk of hazards is also evaluated by a method which calculates the cost per fatality averted implied by various societal activities.

2) E.A. Crouch, R. Wilson and C. Zeise. The Risks of Drinking Water. Water Resources Research, Volume 19, No. 6, 1983.

AUTHORS' ABSTRACT:

Exposures to the low levels of organic compounds found in drinking water might cause a variety of health effects, cancer being one of great concern. The estimation of cancer risk is uncertain, which may in part explain why cancer risk is not properly considered in establishing drinking water standards. Current standards for a given chemical or class of chemicals do not account for the presence of other pollutants, chemicals which have not been tested in long term oral bioassays are generally ignored, and the uncertainties of risk calculations are not explicitly considered. To better quantify risks from drinking waters, we apply procedures which incorporate measures of uncertainty into the risk calculation and consider all chemicals included in a water analysis. This procedure is demonstrated by calculating risks for several U.S. water supplies. Our results show that some might pose moderately high risks.

3) Edmund Crouch and Richard Wilson. Regulation of Carcinogens, Risk Analysis. Volume 1, Number 1, 1981.

AUTHORS' ABSTRACT:

We propose a procedure, suitable for regulatory use, for estimating individual and societal risks of carcinogenic materials by using information on interspecies comparisons of carcinogenic potency. The consistent treatment of uncertainties allows evaluation of confidence limits and hence regulatory measures of risk which incorporate safety factors and incentives for better information. Numerical examples are given, together with discussion of the treatment of undetected carcinogens. Applications of the procedure to setting priorities for carcinogenicity testing and to product substitution are mentioned.

4) Lauren Zeise, Richard Wilson and Edmund Crouch. Use of Acute Toxicity to Estimate Carcinogenic Risk. To be published in Risk Analysis.

AUTHORS' ABSTRACT:

Data on the effects of human exposure to carcinogens are limited, so that estimation of the risks of carcinogens must be obtained indirectly. Current risk estimates are generally based on lifetime animal bioassays which are

expensive and which take more than two years to complete. We here show how data on acute toxicity can be used to make a preliminary estimate of carcinogenic risk and give an idea of the uncertainty in that risk estimate. The estimates obtained are biased upwards, and so are useful for setting interim standards and determining whether further study is worthwhile. A general scheme which incorporates the use of such estimates is outlined, and it is shown by example how adoption of the procedures suggested could have prevented regulatory hiatus in the past.

Response:

EPA has examined the data presented on risk assessment and agrees that risk assessment is a useful tool in the health assessment of chemicals present in the environment. However, EPA does not agree that the RMCLs should be set for all chemicals using risk assessment. For those chemicals which are potential human carcinogens, EPA believes that an RMCL of zero is most consistent with the legislative mandate of the SDWA.

Article #4 presents a scheme by which data on acute toxicity can be used to make a preliminary estimate of carcinogenic risk. This approach appears to be worth further investigation; however, EPA does not believe that this approach should be incorporated into the methodology for screening chemicals for carcinogenicity at the present time. The main drawback is that this approach further compounds the uncertainty of risk by adding one more conversion to the chain of conversions and projections already used. In addition, the authors noted several glaring exceptions to the predicted behavior of the chemicals. These exceptions need further investigation before this method can be fully accepted.

16. Comment:

It is important that risk assessment is used in a way that is unbiased and accepted from a toxicological perspective. In using the multistage model, I think that there are certain things that we feel should be proposed for guidance before we would use that model and the procedure. For example, if the agent was shown to cause either a benign or malignant tumor, and if this was found to be in a dose-dependent manner, and if the study was deemed acceptable by a peer review committee, that would be the first basic criterion.

Response:

EPA agrees that risk assessment should be used in an unbiased and toxicologically acceptable manner. EPA bases its risk assessment upon studies which it deems to be acceptable, i.e., those studies which show benign or malignant tumors in a dose-dependent manner and which have been carried out in a scientifically acceptable manner. The studies and resulting risk levels are reviewed by the SAB.

17. Comment:

If the carcinogenic effect occurred only at the highest dose of several dose levels, or it was not significant at the lower levels, then I would recommend that further toxicologic studies be carried out to ensure that the reason why the toxicologic effect was occurring wasn't because of some type of dose-dependent kinetics, whereby saturation was occurring and detoxification mechanisms may have been overwhelmed.

Response:

EPA agrees that in the situation described above, it is desirable that further studies be carried out to confirm the toxicologic effect. However, EPA does not agree that further studies should be required before the original study could be used for risk assessment purposes. Since the original study did show an effect at a dose level, even if the reason for that effect was due to saturation or another mechanism, EPA believes that that study should be considered, only with all other relevant data, in the risk assessment process. See also the Response to Comment 18 below.

18. Comment:

If something is shown to be a carcinogen but it occurred because of the saturation phenomenon, that would be the basis for not using quantitativ risk assessment.

Response:

EPA disagrees. If a compound is shown to be a potential human carcinogen, regardless of the mechanism which induces the carcinogenicity, EPA believes that it is appropriate to perform a risk assessment. However, as previously discussed, EPA is not setting the RMCLs for potential human carcinogens based upon risk levels but is setting the RMCLs at zero.

19. Comment:

Something should be considered a carcinogen if it was positive in one animal species and positive in a genotoxic screen. On the other hand, if it was carcinogenic in the long-term bioassay but negative in a genotoxic screen, I would not recommend its use in quantitative risk assessment using the multistage model. However, I would still recommend using quantitative risk assessment, but I would use a less conservative model, typically a tolerance distribution model.

Response:

EPA follows the criteria outlined in EPA's Proposed Guidelines for Carcinogen Risk Assessment in order to determine whether a compound should be considered a carcinogen. Those criteria are discussed in 49 FR 46300, Nov. 23, 1984.

EPA does not agree that different risk models should be used depending on the strength of evidence of carcinogenicity for the compound as th re is no rational basis for choosing one risk model ov r another with regard

to strength of evidence. EPA believes that it is appropriate to do risk calculations using several models, but the multistage model is emphasized as this is the most biologically plausible model.

20. Comment:

In a study involving a summation of the literature, I have found that sex-specific occurrences are known for over 200 different pollutants and drugs, and that with respect to the human, about 2 dozen sex-specific responses occur. So it is not uncommon in animal studies to find that the agent causes cancer or some adverse effect just in one sex. I do not believe that a study shouldn't be used for quantitative risk assessment because the effect only occurs in one sex.

Response:

EPA agrees and considers studies in which effects are seen in only one sex for risk assessment purposes.

G. CRITERIA FOR SETTING RMCLs/MCLs

1. Comment:

In general, prioritization involves an initial determination that a compound poses a "significant" health or environmental risk. For regulation of drinking water, significance should be judged from analyses and interpretation of data on both occurrence and exposure.

Response:

EPA prioritizes chemicals for regulation based upon the analytical ability to detect a contaminant, the potential health risk and the occurrence or potential for occurrence in drinking water. EPA believes that those substances of greatest concern generally should be regulated first but a preventive approach should be taken so that substances which present a risk or potential risk in drinking water are regulated.

2. Comment:

EPA should consider regulating chemicals which fit into one of the following categories:

1) present in 8-10% of randomly selected water supplies.
2) found in 25 or more instances of contamination.

Response:

EPA has set criteria for selection of contaminants for regulation (see RMCL Proposal). However, EPA does not feel that it is appropriate to set a numerical cutoff level based upon percent occurrence in drinking water for deciding whether a compound should be regulated. Many factors enter into the decision on regulation, such as potential for occurrence in drinking water and these factors must be considered in total before a

decision is made. In addition, the suggested criteria would not be preventive: a potentially significant health risk would have to occur before regulation was appropriate. EPA intends to apply the SDWA in a protective fashion.

3. Comment:

RMCLs and subsequent national primary drinking water regulations should be promulgated only when two conditions are met:

1) The contaminant is present in drinking water at a level which, on the basis of epidemiological or toxicological data, may reasonably be expected to have an adverse effect on human health; and

2) The contaminant is present at such a level in a significant number of drinking water supplies nationwide, so that EPA can fairly conclude that the problem is not limited, and localized in nature.

In deciding whether the foregoing conditions are met, EPA also should consider what percentage the average daily intake of the compound in drinking water constitutes of the total daily intake of the compound from all sources.

Response:

EPA does not agree with the commenter that a contaminant should only be regulated if it is found at levels in drinking water which pose a health hazard, on a nationwide basis. EPA believes that a preventive approach is consistent with the Safe Drinking Water Act and contaminants should be regulated if they are found to cause adverse health effects, even at levels below that normally found in drinking water. If EPA were to wait to regulate until contaminants were found at levels in drinking water resulting in adverse health effects, public health would not be protected. EPA also feels that regulation should not wait until a problem goes from localized to nationwide. National primary drinking water regulations should serve the purpose of preventing contamination on a nationwide scale and this can only be accomplished by setting RMCLs and MCLs for those chemicals known to occur in drinking water even on a regional basis, or which have the potential for occurrence in drinking water. However, EPA believes this criteria is met for VOCs as a group. VOCs have been detected at levels that are believed to pose significant risk and they have been detected in a number of drinking water systems across the nation.

In regard to the comment that EPA should also consider what percentage the average daily intake of the compound in drinking water constitutes of the total daily intake from all sources, EPA does not believe that this criteria should be considered in deciding whether or not to regulate. A compound could be present in drinking water and result in adverse health effects and still constitute a small percentage of the total daily intake, e.g., carcinogens. In these situations, EPA feels that it is appropriate to regulate the chemical in order to protect the public against possible toxic effects through drinking water. The other sources of exposure to the chemical, such as air or food, should be regulated under the appropriate statute for that particular medium.

H. SIMULTANEOUS PROPOSAL OF RMCLs AND MCLs

1. Comment:

It is realized that the statutory language of the SDWA (§1412) anticipates the proposal of an MCL on the date an RMCL is promulgated. The inherent delay in this two-step process tends to encourage state and local regulatory bodies to discount costs and feasibility when addressing water quality issues. One way to alleviate this problem without being in derogation of the statute is to issue an advance notice of proposed rulemaking (ANPR) for the MCL which specifically takes costs into consideration, at the same time RMCL goals are announced.

Response:

EPA believes that the issuance of an ANPR for the MCLs at the same time that RMCLs are proposed would add an additional step to the already lengthy and time-consuming process. By proposing MCLs at the same time the RMCLs are promulgated, the public has an opportunity to comment on the MCLs before they are finalized and EPA believes that this process is sufficient without adding an additional ANPR.

I. RISK ASSESSMENT

1. Comment:

In acknowledgment of the lack of convincing evidence for thresholds for carcinogens, including those which do not act directly on the genome, OSTP rejected the use of the No Observed Adverse Effect Level (NOAEL)/ Safety Factor approach in carcinogen risk assessment.

Response:

EPA agrees with the OSTP review of chemical carcinogens and does not use the NOAEL/safety factor approach in carcinogen risk assessment.

J. RMCLs AS STANDARDS

1. Comment:

The case for practical as opposed to theoretical or "ideal" RMCLs is strengthened further when it is recognized that State and local entities use federal recommendations to determine appropriate regulatory response. Nonbinding federal drinking water advisories, Suggested No Adverse Response Levels (SNARLs), have been used as cleanup standards in several states including Florida and Michigan.

Response:

EPA recognizes that non-binding Federal drinking water advisories have been used as cleanup standards in several States. However, RMCLs and other drinking water advisories are not intended for use in this manner and EPA

does not encourage or endorse the adoption of guidance as standards by States or other locales.

K. TOTAL VOCs

1. Comment:

Neither a total VOC regulation nor "supporting guidance" is justified at this time. The limited data that are available indicate that only a small fraction of drinking water systems have more than one VOC present in measurable quantities. Moreover, as EPA itself recognizes, the scientific evidence as to whether health effects from exposure to drinking water containing more than one VOC are additive, synergistic or antagonistic is weak and often conflicting. In addition, type and degree of toxicity are known to vary substantially among VOCs. A total VOC standard, to be meaningful, would have to take into account the specific VOCs that will be present in water and the type of toxicity associated with each of these compounds, both singly and in combination.

Response:

EPA agrees with the commenter that a regulation for total VOCs is not justified at this time due to the conflicting scientific evidence and the varying toxicity data among VOCs. In addition, as a matter of priority EPA is attempting to regulate as many VOCs as possible which meet its criteria for regulation. EPA may reassess additive and synergistic effects at a later date.

L. OTHER ISSUES

1. Comment:

Current RCRA regulations do not allow groundwater as sampled, analyzed, and reported under RCRA, to deteriorate below primary drinking water standards. When the goals of the proposed regulations become incorporated into these standards, they will have a profound effect on the discharge and groundwater monitoring policies at many of our plant sites and on the cost of operating such plants.

Response:

The RMCLs are strictly health-based goals and are not equivalent to primary drinking water regulations. The MCLs, when promulgated, may be incorporated into the RCRA regulations for groundwater. If that action is taken, there will be an opportunity to address the impacts of that regulation through notice and comment procedures.

2. Comment:

We agree with the NAS principle (Drinking Water and Health, Volume I) that states human exposure to carcinogens should be addressed in terms of risk rather than safe or non-safe.

Response:

EPA also agrees with the NAS that human exposure to carcinogens should be addressed in terms of relative risk. However, the RMCLs are to be set at a level at which adverse health effects will not be seen, with a margin of safety, and EPA believes that zero best fulfills this statutory requirement. EPA does not believe that the NAS intended this principle to be interpreted to mean that RMCLs should be set at cancer risk levels.

3. Comment:

EPA should provide national guidance levels for the primacy agency to implement for those VOCs where the quality of evidence concerning the compound's potential to cause cancer in either animals or humans is inadequate. This guidance should be published, along with recommended response actions geared to the level of contamination encountered. A low concentration that represents very little, if any, risk would require only minor action or no action. High concentration would require immediate action to reduce the level of contamination. Compounds between a high and low concentration would require increased monitoring and consideration of other alternatives, according to the severity of the contamination.

Response:

EPA is providing guidance levels for short-term exposure to regulat d compounds in drinking water and short-term and long-term exposure to unregulated compounds in drinking water (Health Advisories). These guidance levels will be provided to interested Agencies for their use in contamination situations.

4. Comment:

One approach to regulation could be structured around types of chemicals instead of individual ones. Such an approach would involve setting a group MCL and regulating specific chemicals within each group as the health data becomes available. These groups should consist of chemicals with similar structures and should include at least two chemicals which have extensive toxicity tests. The groups should be constructed so that every chemical would fit into at least one group. Such a group might consist of halogenated hydrocarbons without double bonds. The numerical value of the group MCL should be based on the highest toxicity of the chemicals within the group which have been tested for toxicity. In the absence of data, EPA should assume the worst in order to be safe.

Response:

EPA believes that chemicals should be examined on a case-by-case basis to determine if it is appropriate to set MCLs for a group or for the individual compounds. In the case of the trihalomethanes, EPA determined that a group MCL was appropriate. For the VOCs, EPA believes that regulation should be done on an individual chemical basis, as it is not possible to extrapolate the toxicity results from one chemical to another.

5. Comment:

EPA needs to devise a scheme for regulating potentially dangerous chemicals which have been detected in drinking water but which have been under-researched or not investigated at all.

Response:

EPA does not believe that regulation by group would be an appropriate response for those chemicals which have not been investigated or under-researched. Regulation by group is an appropriate response when the toxicity of the chemicals have been investigated and they have been shown to resemble each other toxicologically. For those chemicals which have not been investigated, further research to document the toxicity of the chemical is required.

6. Comment:

If the Agency persists in its current approach for setting MCLs based on quantitative risk assessment, however, we strongly urge adoption of the following recommendation. Instead of any of the population incremental risk levels which are presented in the proposal (49 Fed. Reg. 24334), EPA should designate one excess case in 10^7 people as the maximum allowabl risk associated with drinking water. Salient reasons for such a protective stance are (1) the involuntary and universal nature of human consumption of drinking water, (2) the legitimate expectations by the public that drinking water quality should be carefully guarded by government, and (3) the assumption of at least additive risks from numerous compounds to which people are simultaneously and sequentially exposed.

Response:

EPA is not proposing to set MCLs based upon quantitative risk assessment.

7. Comment:

These regulations will result in the downstream consumer bearing the continuing cost of cleanup while the discharger may still release waste into the drinking water supply.

Response:

EPA believes that other EPA and State programs, such as the NPDES program and Superfund program, will help control the release of wastes into water sources which may ultimately be used for drinking water purposes. In addition, there are often common law and tort remedies available to prevent such activities where they can be identified. EPA believes the discharger should bear the cost of cleanup and is working through these programs and others to ensure that the responsible parties clean up their wastes.

8. Comment:

Basically, we propose that drinking water regulation consist of three steps:

1) A regulatory risk ceiling for contaminants in drinking water would be established to assure drinking water quality. Contaminants would be prioritized for regulation against this risk ceiling to assure that those contaminants which pose the greatest national risk in drinking water are regulated first.

2) Recommended Maximum Contaminant Levels (RMCLs) would be set at practicable levels below risk ceilings considering their broad use in other regulatory applications. We believe that a defensible annual threshold for cancer risk is in the region of 10^{-5} to 10^{-6}.

3) Maximum Contaminant Levels (MCLs) would be developed essentially at the same time as RMCLs, and set as close to RMCLs as feasible, taking into consideration the costs related to drinking water applications. Simultaneous issuance of MCLs and RMCLs is desirable to minimize confusion between goals and enforceable standards.

Response:

EPA does not believe that a regulatory risk ceiling should be established for contaminants in drinking water. EPA prioritizes contaminants for regulation based upon: (1) the occurrence of the chemical in drinking water; (2) the potential for occurrence of the chemical in drinking water, and (3) the health effects of the contaminant. EPA believes that this method of prioritization ensures that those chemicals which present the greatest potential for adverse effects in drinking water are regulated first.

Comments (2) and (3) are addressed elsewhere in this document.

9. Comment:

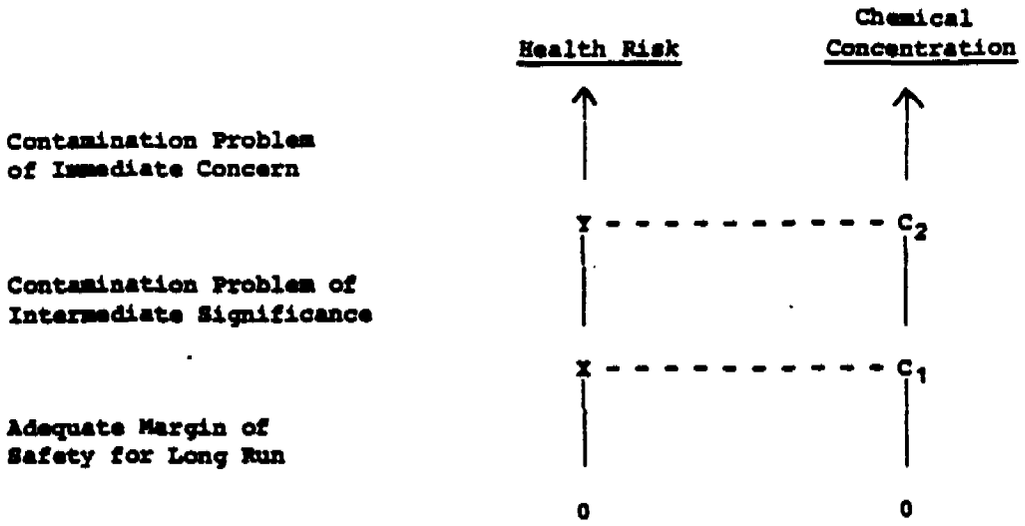
Mutagenicity and teratogenicity should be considered in addition to carcinogenicity in regulating VOCs. We agree that regulation of contaminants should be federal to ensure uniformity and thus equity across states.

Response:

EPA agrees that mutagenicity and teratogenicity should be considered in regulating VOCs. EPA examines all of the available data and calculates a number based upon the most sensitive endpoint.

10. Comment:

EPA, rather than defining only one standard, should define levels which would correspond to increasing seriousness of contaminant problems and needed remedial action. The following model is suggested:



Response:

EPA, according to the Safe Drinking Water Act, must set a single standard (MCL) for each compound that it has determined will result in adverse health effects. Thus, sliding standards or a series of levels are not an appropriate response according to the legislative mandate. How ver, EPA does set nonregulatory health effects guidance (Health Advisories) for different durations of exposure for chemicals in drinking water.

11. Comment:

At the time of the ANPR, several commenters recommended a peer-reviewed survey of drinking water supplies to document the extent of contamination by various compounds and to allow prioritization of regulatory needs. Since the information in this proposed rulemaking is based upon the same data sets as those cited in the ANPR, it is clear that the Agency has not responded to these recommendations for a survey in spite of the two year lapse between the ANPR and this proposal.

Response:

Several EPA surveys have already been conducted. These data form the basis of occurrence/exposure estimates. Survey designs, sampling and quality assurance procedures have been reviewed by govenment work groups, as well as by independent contractors. The regulatory decisions on individual chemicals are made based on the fact that these contaminants occur in drinking water or are likely to occur. The occurrence document provides both the raw data and national estimates. These documents have also undergone review by scientific personnel outside the originating office.

12. Comment:

The balancing of costs and benefits is an essential part of cleanup under CERCLA. As noted by Senator Stafford during debate on the bill:

"The relationship between the costs and the benefits of a particular response action are an essential part of both the national contingency plan to be developed under Section 105 and the selection of remedial and response actions under Section 104..." (Congressional Record: November 24, 1980).

Ideally, the balancing would include a consideration of scientific judgment concerning the hazard, the need to protect exposed populations, and the availability of technologies. Any arbitrary standard, such as an RMCL equalling zero, would appear to be in direct opposition to the goals of CERCLA.

Response:

EPA believes that RMCLs set at zero for potential human carcinogens fulfill the mandate of the Safe Drinking Water Act. RMCLs are not set under the statutory authority of CERCLA and thus are not set balancing costs and benefits. Any use of RMCLs under CERCLA would be subject to notice and comment through revisions to the National Contingency Plan or CERCLA removal or remedial actions and are not the subject of this rulemaking.

13. Comment:

Of the many sampling and analytical deficiencies confounding the interpretation of the existing data, one of the most scientifically troublesome is the statistical treatments used. There is no indication that any sophisticated analyses capable of discerning significant differences were used.

Response:

Data from random and nonrandom segments of the Ground Water Supply Survey were subjected to statistical tests to discern differences. The findings are presented in the occurrence documents for individual chemicals.

14. Comment:

We believe that the full reports of the appropriate surveys should be available for review. The occurrence data should be correlated to the size of the water systems and statistically meaningful population exposures generated for each compound.

Response:

The findings and raw occurrence data from the surveys were placed in the occurrence documents for the individual contaminants. In addition, several of the occurrence surveys have been reported in peer-reviewed literature. Occurrence data are correlated to size of the water systems and population exposures that were generated.

15. Comment:

This proposal completely leaves out the halomethanes, chloroform, bromoform and others. Why? They are volatile. Chloroform is synthetic (it is produced by the action of chlorine on organic matter in chlorination plants). Indeed, the selection method for the VOCs mentioned in this proposed rulemaking is illogical, for it has no relation to possible health risks which is presumably what the whole proposal is about. It is important to go after the large risks and leave the small risks until later, and if the reduction of the large risk reduces the small ones also, so much the better.

Response:

EPA addressed the trihalomethanes in its Final Rule for the promulgation of an MCL for trihalomethanes (44 FR 68624). In the MCL promulgation package, the health risks of chloroform and other trihalomethanes are discussed. EPA agrees that it is important to regulate the large risks first and leave the smaller risks until later. This is the reason why an MCL for the trihalomethanes was promulgated several years ago, before the other VOCs. Other volatile organics will be considered for revised rulemaking in the future.

16. Comment:

Continuing pursuit of establishment of RMCLs represents the expenditure of time and resources on a program directed at managing risks at levels far below what EPA has deemed negligible.

Response:

EPA is required, under the Safe Drinking Water Act, to set RMCLs and MCLs for all compounds that may have an adverse effect upon the health of persons. EPA is also regulating those contaminants that appear in drinking water or are likely to appear. Therefore, EPA cannot say these risks are negligible. EPA is following the legislative mandate in the establishment of RMCLs.

17. Comment:

EPA is proposing RMCLs for several VOCs based upon cancer studies in which VOCs were administered to rats and mice in corn oil (NCI, 1976) ... Use of such studies is wholly inappropriate for assessing cancer risks that might result from the presence of VOCs in drinking water. Recent studies (SRI for EPA) suggest that the corn oil vehicle may have promoted the tumors found in NCI chloroform bioassays.

EPA's reliance on data obtained from studies that do not administer the VOCs to animals in drinking water are totally unreasonable as a basis for setting a zero RMCL.

Response:

The overall finding that chloroform, for instance, is probably carcinogenic for humans is based upon several different sets of data, the mouse liver response via corn oil gavage being only one of these. The positive long-term bioassay data include the following (although other positive, single dose and negative studies also exist):

	Gavage Oil	Drinking Water	Toothpaste or Arachis Oil Gavage
mouse, male	+ liver	not tested	+ kidney
female	+ liver	-	- not tested similarly
rat, male	+ kidney	+ kidney	-
female	- kidney	not tested	-

The uncertainty regarding the possible influence of corn oil upon the tumorigenic responses in the mouse bioassays certainly does not negate the positive finding in the mouse, nor does it render the overall conclusion of "probably carcinogenicity in humans" for chloroform invalid. While some uncertainty remains about the influence of corn oil on liver tumors in the $B_6C_3F_1$ mouse, the interpretative significance of the dose delivery vehicle can be explained by consideration of two sets of factors:

1) The appearance of kidney tumors in male rats in both the corn oil (NCI) and drinking water (EPA/SRI) studies speaks to the reproducibility of the results regardless of carrier vehicle.

2) A pharmacokinetic analysis shows that differences in dosing regimens result in variations in absorption patterns, peak blood and tissue levels, and percent of dose metabolized. The absorption patterns for chloroform have been shown to differ depending upon whether the carrier vehicle is corn oil or water. Also, the rate and possibly the extent of absorption is probably diminished by the corn oil, not increased. However, in the carcinogen bioassays the chloroform administered in corn oil as a single bolus would result in considerably higher peak blood and target tissue levels than those resulting from the multiple intermittent doses due to the drinking water regime. Therefore, the failure to obtain a positive response in the drinking water study (female mouse) may well be a result of the particular pharmacokinetic considerations with or without influence from corn oil itself. The present knowledge of chloroform metabolism and related acute toxicity suggests several general cellular mechanisms that may lead to a carcinogenic effect. Each of these mechanisms is supported by experimental data.

18. Comment:

Available information concerning the metabolic pathway of VOCs including chloroform in rats and mice suggests that these may not be appropriate animal models from which to extrapolate data to humans. There is evidence of species variations in the metabolism of VOCs between rodents, rats, mice, and the non-human primates.

Response:

Experimental data for chloroform show no difference in absorption characteristics among species, including man. There are known qualitative differences among species with regard to metabolic pathways or metabolic profiles.

Metabolism of chloroform produces phosgene and other putative reactive metabolites that covalently bind extensively to cellular lipids and proteins, and also minimally to DNA. Organ localization and binding intensity parallels acute cellular toxicity in liver and kidney of experimental animals, i.e., in mice, covalent binding of chloroform metabolites in both liver and kidney has been demonstrated to be proportional to the dose. This is noteworthy since the liver and kidneys are target organs of carcinogenicity. The irreversible binding of the reactive chloroform metabolites to cellular macromolecules is generally believed to be responsible not only for hepatic and renal damage from chloroform, but also the carcinogenic response, although the mechanism for the latter has not been elucidated.

It is true that even within a species there are strain and sex differences for the susceptibility to liver and kidney toxicity to a fixed dose of chloroform. The human population encompasses a full range of genetic variability in contrast to the inbred strains of laboratory animals, and hence a carcinogenic response observed in only certain species, strains or sexes in laboratory animals may be expressed in the human counterpart.

19. Comment:

The NCI cancer studies upon which EPA relies were never intended t be other than preliminary tests to identify chemicals which needed to be studied more intensely. The animals in the NCI study had their daily doses administered by gavage, which is believed to induce a cancer response significantly different than that obtained when a test compound is administered through drinking water.

Response:

EPA agrees that the NCI studies were carried out as preliminary tests. However, EPA believes that the NCI studies present information which must be considered along with all other data on the chemical in order to make a judgment on the carcinogenicity of the chemicals.

EPA uses oral gavage studies to assess carcinogenicity in the absence of drinking water studies. EPA does not agree that these studies always induce a response different than that obtained through drinking

water exposure and believes that oral gavage studies present a valid method of toxicological analysis. (See Comment/Response - III.L.17 above).

20. Comment:

The promulgation of the proposed RMCLs as a final rule exceeds EPA's statutory authority under the SDWA, since Section 1412(e) of the Act requires EPA to arrange with the NAS or other independent scientific organization to study the potential health effects of contaminants in drinking water.

Response:

Section 1412 of the Safe Drinking Water Act provides that the Administrator shall establish Revised Drinking Water Regulations incorporating Maximum Contaminant Levels (MCLs). Such regulations are to be developed after consultation with the National Academy of Sciences (NAS) and promulgation of RMCLs. Under section 1412(e), the Administrator is required to arrange with the NAS for a study to determine appropriate RMCLs. This study is to contain (1) evaluations of relevant publications, (2) a statement of methodologies, (3) a statement of methodologies for estimating the margin of safety, (4) proposals for RMCLs, (5) a list of contaminants whose levels cannot be determined, and (6) recommended studies and test protocols for future research. The NAS was also to consider morbidity and mortality data, the existence of susceptible groups in the population, synergistic effects, total contamination from all media sources, and total body burden. The NAS report was to provide proposals for RMCLs which EPA would then be required to publish within 10 days (Section 1412(b)(1)(A)).

The NAS responded by providing a comprehensive study of the health effects of drinking water contaminants on June 20, 1977. Subsequent reports were provided in 1980, 1982 and 1983. The study represented an exhaustive effort and, for most of the contaminants it addressed, provided most of the data necessary to determine RMCLs. The items NAS omitted were proposed RMCLs and the list of contaminants that could not be measured.

It is clear that the NAS substantially complied with the statutory directive. NAS has provided the Agency with significant data and much f the information that would be necessary to determine RMCLs. For this reason, we believe that NAS' omission did not excuse the Agency from the responsibility of proposing and promulgating RMCLs. Rather, the NAS omission merely excused EPA from meeting the statutory deadlines for proposing and promulgating RMCLs and Revised Regulations. Since 1977, EPA has completed sufficient data gathering to initiate rulemaking on the Revised Regulations.

There is no legitimate argument that NAS' failure to provide RMCLs precludes promulgation of RMCLs or the Revised Regulations. The statute contemplated that EPA would propose and promulgate RMCLs based on the study supplied by NAS. The RMCLs were merely one part of the study that Congress directed NAS to provide. To preclude the Agency from promulgating Revised Regulations -- a major feature of the Act -- because of the minor failure of the NAS is totally inconsistent with the statute.

21. Comment:

The granular activated carbon in existing filter beds at water treatment plants -- a technology likely considered by EPA to be the best available technology for reducing the levels of VOCs in drinking water -- may present its own health problems. Bacteria and pathogenic microorganisms attached to GAC particles can contaminate treated water.

Response:

EPA recognizes that activated carbon may protect organisms against disinfection. However, there have been no documented outbreaks associated with microbiological growth on GAC. Sufficient post-chlorination would control microbiological growth and protect public health against microbiological outbreaks.

22. Comment:

The NAS principles from Drinking Water and Health, Volume I, 1977, must be carefully considered in light of the available data as regards the VOCs.

Response:

EPA believes that the NAS principles are valid. These general principles are in agreement with the Office of Science and Technology Policy's review of chemical carcinogens (49 FR 21594) and with the EPA Guidelines for chemical carcinogens.

23. Comment:

There are problems with reproductibility of the GWSS data. Thirty-seven supplies were resampled and 25 of the positive samples did not recur.

Response:

Follow-up analyses on GWSS sampling sites have indicated that individual wells serving a community may be contaminated while those in adjacent well fields are not. The apparent negatives detected upon resampling of systems initially found to be positive has been ascribed to differential pumping rates for individual wells and changes in sampling locations rather than error in initial chemical analysis.

24. Comment:

There are problems with precision in the GWSS study. Forty-three of 99 positive samples were < 1 ppb. The analytical variability of less than 5 ppb is 100%. This leaves open the possibility of false positives.

Response:

The possibility of false positives was not a problem with the GWSS; the chemicals were detected in the analysis. The quantitation of the

chemicals, in terms of the exact levels detected, is another issue not addressed in this comment.

25. Comment:

State data were used which were often collected in response to emergency spills and, therefore, are not representative of statewide concentrations.

Response:

EPA agrees. For that reason, state data were not used to project national occurrence.

26. Comment:

The statistics used in interpreting data in the GWSS are open to question. The study used only the highest concentration reported at a given water supply in their statistical variation ignoring the analytical and actual variability.

Response:

Only one sample was collected for each water supply during the GWSS; thus there was only one data point for each water supply. EPA used the only concentration available in their statistics.

27. Comment:

Data contained in occurrence documents indicate that the vast majority (> 95%) of public water systems are either not contaminated or contain levels below the limit of detection. Exposure at these levels is not a major public health problem.

Response:

EPA believes that a sufficient number of public water supplies have been shown to be contaminated with VOCs to warrant action in this area. The SDWA does not require that "a major public health problem" be demonstrated before regulation; in fact, the SDWA is a preventive statute in which the approach is to err on the side of safety.

28. Comment:

Data compiled in the occurrence documents have not received any independent scientific review.

Response:

The documents have been widely reviewed within EPA, including the Office of Air and Radiation and the Office of Drinking Water staff and are open to public comment.