

**ENVIRONMENTAL PROTECTION  
AGENCY**
**40 CFR Parts 141 and 142**
**[WH-FRL-5988-7]**
**National Primary Drinking Water  
Regulations: Disinfectants and  
Disinfection Byproducts Notice of Data  
Availability**
**AGENCY:** U.S. Environmental Protection Agency (USEPA).

**ACTION:** Notice of data availability; request for comments.

**SUMMARY:** In 1994 USEPA proposed a Stage 1 Disinfectants/Disinfection Byproducts Rule (D/DBP) to reduce the level of exposure from disinfectants and disinfection byproducts (DBPs) in drinking water (USEPA, 1994a). This Notice of Data Availability summarizes the 1994 proposal and a subsequent Notice of Data Availability in 1997 (USEPA, 1997a); describes new data that the Agency has obtained and analyses that have been completed since the 1997 Notice of Data Availability; requests comments on the regulatory implications that flow from the new data and analyses; and requests comments on several issues related to the simultaneous compliance with the Stage 1 DBP Rule and the Lead and Copper Rule. USEPA solicits comment on all aspects of this Notice and the supporting record. The Agency also solicits additional data and information that may be relevant to the issues discussed in the Notice.

The Stage 1 D/DBP rule would apply to community water systems and nontransient noncommunity water systems that treat their water with a chemical disinfectant for either primary or residual treatment. In addition, certain requirements for chlorine dioxide would apply to transient noncommunity water systems because of the short-term health effects from high levels of chlorine dioxide.

Key issues related to the Stage 1 D/DBP rule that are addressed in this Notice include the establishment of Maximum Contaminant Level Goals for chloroform, dichloroacetic acid, chlorite, and bromate and the Maximum Residual Disinfectant Level Goal for chlorine dioxide.

**DATES:** Comments should be postmarked or delivered by hand on or before April 30, 1998. Comments must be received or post-marked by midnight April 30, 1998.

**ADDRESSES:** Send written comments to DBP NODA Docket Clerk, Water Docket (MC-4101); U.S. Environmental

Protection Agency; 401 M Street, SW., Washington, DC 20460. Comments may be hand-delivered to the Water Docket, U.S. Environmental Protection Agency; 401 M Street, SW., East Tower Basement, Washington, DC 20460. Comments may be submitted electronically to [owdocket@epamail.epa.gov](mailto:owdocket@epamail.epa.gov).

**FOR FURTHER INFORMATION CONTACT:** For general information contact, the Safe Drinking Water Hotline, Telephone (800) 426-4791. The Safe Drinking Water Hotline is open Monday through Friday, excluding Federal holidays, from 9:00 a.m. to 5:30 p.m. Eastern Time. For technical inquiries, contact Dr. Vicki Dellarco, Office of Science and Technology (MC 4304) or Mike Cox, Office of Ground Water and Drinking Water (MC 4607), U.S. Environmental Protection Agency, 401 M Street SW., Washington DC 20460; telephone (202) 260-7336 (Dellarco) or (202) 260-1445 (Cox).

**SUPPLEMENTARY INFORMATION:**

**Regulated entities.** Entities potentially regulated by the Stage 1 D/DBP rule are public water systems that add a disinfectant or oxidant. Regulated categories and entities include:

Category	Examples of regulated entities
Public Water System.	Community and nontransient noncommunity water systems that add a disinfectant or oxidant.
State Government.	State government offices that regulate drinking water.

This table is not intended to be exhaustive, but rather provides a guide for readers regarding entities likely to be regulated by this action. This table lists the types of entities that EPA is now aware could potentially be regulated by this action. Other types of entities not listed in this table could also be regulated. To determine whether your facility may be regulated by this action, you should carefully examine the applicability criteria in § 141.130 of the proposed rule (USEPA, 1994a). If you have questions regarding the applicability of this action to a particular entity, contact one of the persons listed in the preceding **FOR FURTHER INFORMATION CONTACT** section.

**Additional Information for Commenters.** Please submit an original and three copies of your comments and enclosures (including references). The Agency requests that commenters follow the following format: Type or print comments in ink, and cite, where possible, the paragraph(s) in this Notice to which each comment refers.

Commenters should use a separate paragraph for each method or issue discussed. Electronic comments must be submitted as a WP5.1 or WP6.1 file or as an ASCII file avoiding the use of special characters. Comments and data will also be accepted on disks in WordPerfect in 5.1 or WP6.1 or ASCII file format. Electronic comments on this Notice may be filed online at many Federal Depository Libraries. Commenters who want EPA to acknowledge receipt of their comments should include a self-addressed, stamped envelope. No facsimiles (faxes) will be accepted.

**Availability of Record.** The record for this Notice, which includes supporting documentation as well as printed, paper versions of electronic comments, is available for inspection from 9 to 4 p.m. (Eastern Time), Monday through Friday, excluding legal holidays, at the Water Docket, U.S. EPA Headquarters, 401 M. St., S.W., East Tower Basement, Washington, D.C. 20460. For access to docket materials, please call 202/260-3027 to schedule an appointment.

**Abbreviations Used in This Notice**

AWWA: American Water Works Association  
 AWWARF: AWWA Research Foundation  
 BAT: Best Available Technology  
 BDCM: Bromodichloromethane  
 CMA: Chemical Manufacturers Association  
 CWS: Community Water System  
 DBCM: Dibromochloromethane  
 DBP: Disinfection Byproducts  
 D/DBP: Disinfectants and Disinfection Byproducts  
 DCA: Dichloroacetic Acid  
 ED<sub>10</sub>: Maximum likelihood estimate on a dose associated with 10% extra risk  
 EPA: United States Environmental Protection Agency  
 ESWTR: Enhanced Surface Water Treatment Rule  
 FACA: Federal Advisory Committee Act  
 GAC: Granular Activated Carbon  
 HAA5: Haloacetic Acids (five)  
 HAN: Haloacetonitrile  
 ICR: Information Collection Rule  
 ILSI: International Life Sciences Institute  
 IESTWR: Interim Enhanced Surface Water Treatment Rule  
 IRFA: Initial Regulatory Flexibility Analysis  
 LCR: Lead and Cooper Rule  
 LED<sub>10</sub>: Lower 95% confidence limit on a dose associated with 10% extra risk  
 LMS: Linear Multistage Model  
 LOAEL: Lowest Observed Adverse Effect Level  
 LTESTWR: Long-Term Enhanced Surface Water Treatment Rule

MCL: Maximum Contaminant Level  
 MCLG: Maximum Contaminant Level Goal  
 M-DBP: Microbial and Disinfectants/Disinfection Byproducts  
 mg/L: Milligrams per liter  
 MoE: Margin of Exposure  
 MRDL: Maximum Residual Disinfectant Level  
 MRDLG: Maximum Residual Disinfectant Level Goal  
 MTD: Maximum Tolerated Dose  
 NIPDWR: National Interim Primary Drinking Water Regulation  
 NOAEL: No Observed Adverse Effect Level  
 NODA: Notice of Data Availability  
 NPDWR: National Primary Drinking Water Regulation  
 NTNCWS: Nontransient Noncommunity Water System  
 NTP: National Toxicology Program  
 PAR: Population Attributable Risk  
 PQL: Practical Quantitation Limit  
 PWS: Public Water System  
 q1 \*: Cancer Potency Factor  
 RFA: Regulatory Flexibility Act  
 RfD: Reference Dose  
 RIA: Regulatory Impact Analysis  
 RSC: Relative Source Contribution  
 SAB: Science Advisory Board  
 SBREFA: Small Business Regulatory Enforcement Fairness Act  
 SDWA: Safe Drinking Water Act, or the "Act," as amended in 1986 and 1996  
 SWTR: Surface Water Treatment Rule  
 TCA: Trichloroacetic Acid  
 TOC: Total Organic Carbon  
 TTHM: Total Trihalomethanes  
 TWG: Technical Working Group

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#### I. Introduction and Background

##### A. 1979 Total Trihalomethane MCL

USEPA set an interim maximum contaminant level (MCL) for total trihalomethanes (TTHMs) of 0.10 mg/L

as an annual average in November 1979 (USEPA, 1979). There are four trihalomethanes (chloroform, bromodichloromethane, chlorodibromomethane, and bromoform). The interim TTHM standard applies to any PWS (surface water and/or ground water) serving at least 10,000 people that adds a disinfectant to the drinking water during any part of the treatment process. At their discretion, States may extend coverage to smaller PWSs. However, most States have not exercised this option. About 80 percent of the PWSs, serving populations of less than 10,000, are served by ground water that is generally low in THM precursor content (USEPA, 1979) and which would be expected to have low TTHM levels even if they disinfect.

##### B. Statutory Authority

In 1996, Congress reauthorized the Safe Drinking Water Act. Several of the 1986 provisions were renumbered and augmented with additional language, while other sections mandate new drinking water requirements. As part of the 1996 amendments to the Safe Drinking Water Act, USEPA's general authority to set a Maximum Contaminant Level Goal (MCLG) and a National Primary Drinking Water Regulation (NPDWR) was modified to apply to contaminants that "may have an adverse effect on the health of persons", that are "known to occur or there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern", and for which "in the sole judgement of the Administrator, regulation of such contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems" (1986 SDWA Section 1412 (b)(3)(A) stricken and amended with 1412(b)(1)(A)).

The Act also requires that at the same time USEPA publishes an MCLG, which is a non-enforceable health goal, it also must publish a NPDWR that specifies either a maximum contaminant level (MCL) or treatment technique (Sections 1401(1), 1412(a)(3), and 1412 (b)(4)B)). USEPA is authorized to promulgate a NPDWR "that requires the use of a treatment technique in lieu of establishing a MCL," if the Agency finds that "it is not economically or technologically feasible to ascertain the level of the contaminant" (1412(b)(7)(A)).

The 1996 Amendments also require USEPA to promulgate a Stage 1 disinfectants/disinfection byproducts (D/DBP) rule by November 1998. In

addition, the 1996 Amendments require USEPA to promulgate a Stage 2 D/DBP rule by May 2002 (Section 1412(b)(2)(C)).

### C. Regulatory Negotiation Process

In 1992 USEPA initiated a negotiated rulemaking to develop a D/DBP rule. The negotiators included representatives of State and local health and regulatory agencies, public water systems, elected officials, consumer groups and environmental groups. The Committee met from November 1992 through June 1993.

Early in the process, the negotiators agreed that large amounts of information necessary to understand how to optimize the use of disinfectants to concurrently minimize microbial and DBP risk on a plant-specific basis were unavailable. Nevertheless, the Committee agreed that USEPA should propose a D/DBP rule to extend coverage to all community and nontransient noncommunity water systems that use disinfectants. This rule proposed to reduce the current TTHM MCL, regulate additional disinfection byproducts, set limits for the use of disinfectants, and reduce the level of organic compounds from the source water that may react with disinfectants to form byproducts.

One of the major goals addressed by the Committee was to develop an approach that would reduce the level of exposure from disinfectants and DBPs without undermining the control of microbial pathogens. The intention was to ensure that drinking water is microbiologically safe at the limits set for disinfectants and DBPs and that these chemicals do not pose an unacceptable risk at these limits.

Following months of intensive discussions and technical analysis, the Committee recommended the development of three sets of rules: a staged D/DBP Rule (proposal: 59 FR 38668, July 29, 1994), an "interim" Enhanced Surface Water Treatment Rule (IESWTR) (proposal: 59 FR 38832, July 29, 1994), and an Information Collection Rule (final 61 FR 24354, May 14, 1996). The IESWTR would only apply to systems serving 10,000 people or more. The Committee agreed that a "long-term" ESWTR (LTESWTR) would be needed for systems serving fewer than 10,000 people when the results of more research and water quality monitoring became available. The LTESWTR could also include additional refinements for larger systems.

### D. Overview of 1994 DBP Proposal

The proposed D/DBP Stage 1 rule addressed a number of complex and

interrelated drinking water issues. The proposal attempted to balance the control of health risks from compounds formed during drinking water disinfection against the risks from microbial organisms (such as *Giardia lamblia*, *Cryptosporidium*, bacteria, and viruses) to be controlled by the IESWTR.

The proposed Stage 1 D/DBP rule applied to all community water systems (CWSs) and nontransient noncommunity water systems (NTNCWSs) that treat their water with a chemical disinfectant for either primary or residual treatment. In addition, certain requirements for chlorine dioxide would apply to transient noncommunity water systems because of the short-term health effects from high levels of chlorine dioxide. Following is a summary of key components of the 1994 proposed Stage 1 D/DBP rule.

#### 1. MCLGs/MCLs/MRDLGs/MRDLs

EPA proposed MCLGs of zero for chloroform, bromodichloromethane, bromoform, bromate, and dichloroacetic acid and MCLGs of 0.06 mg/L for dibromochloromethane, 0.3 mg/L for trichloroacetic acid, 0.04 mg/L for chloral hydrate, and 0.08 mg/L for chlorite. In addition, EPA proposed to lower the MCL for TTHMs from 0.10 to 0.080 mg/L and added an MCL for five haloacetic acids (i.e., the sum of the concentrations of mono-, di-, and trichloroacetic acids and mono- and dibromoacetic acids) of 0.060 mg/L. EPA also, for the first time, proposed MCLs for two inorganic DBPs: 0.010 mg/L for bromate and 1.0 mg/L for chlorite.

In addition to proposing MCLGs and MCLs for several DBPs, EPA proposed maximum residual disinfectant level goals (MRDLGs) of 4 mg/L for chlorine and chloramines and 0.3 mg/L for chlorine dioxide. The Agency also proposed maximum residual disinfectant levels (MRDLs) for chlorine and chloramines of 4.0 mg/L, and 0.8 mg/L for chlorine dioxide. MRDLs protect public health by setting limits on the level of residual disinfectants in the distribution system. MRDLs are similar in concept to MCLs—MCLs set limits on contaminants and MRDLs set limits on residual disinfectants in the distribution system. MRDLs, like MCLs, are enforceable, while MRDLGs, like MCLGs, are not enforceable.

#### 2. Best Available Technologies

EPA identified the best available technology (BAT) for achieving compliance with the MCLs for both TTHMs and HAA5 as enhanced coagulation or treatment with granular activated carbon with a ten minute

empty bed contact time and 180 day reactivation frequency (GAC10), with chlorine as the primary and residual disinfectant. The BAT for achieving compliance with the MCL for bromate was control of ozone treatment process to reduce formation of bromate. The BAT for achieving compliance with the chlorite MCL was control of precursor removal treatment processes to reduce disinfectant demand, and control of chlorine dioxide treatment processes to reduce disinfectant levels. EPA identified BAT for achieving compliance with the MRDL for chlorine, chloramine, and chlorine dioxide as control of precursor removal treatment processes to reduce disinfectant demand, and control of disinfection treatment processes to reduce disinfectant levels.

#### 3. Treatment Technique

EPA proposed a treatment technique that would require surface water systems and groundwater systems under the direct influence of surface water that use conventional treatment or precipitative softening to remove DBP precursors by enhanced coagulation or enhanced softening. A system would be required to remove a certain percentage of total organic carbon (TOC) (based on raw water quality) prior to the point of continuous disinfection. EPA also proposed a procedure to be used by a PWS not able to meet the percent reduction, to allow them to comply with an alternative minimum TOC removal level. Compliance for systems required to operate with enhanced coagulation or enhanced softening was based on a running annual average, computed quarterly, of normalized monthly TOC percent reductions.

#### 4. Preoxidation (Predisinfection) Credit

The proposed rule did not allow PWSs to take credit for compliance with disinfection requirements in the SWTR/IESWTR prior to removing required levels of precursors unless they met specified criteria. This provision was modified by the 1997 Federal Advisory Committee (see below).

#### 5. Analytical Methods

EPA proposed nine analytical methods (some of which can be used for multiple analyses) to ensure compliance with proposed MRDLs for chlorine, chloramines, and chlorine dioxide. EPA proposed methods for the analysis of TTHMs, HAA5, chlorite, bromate and total organic carbon.

#### 6. Effect on Small Public Water Systems

The Regulatory Flexibility Act (RFA), as amended by the Small Business

Regulatory Enforcement Fairness Act (SBREFA), requires federal agencies, in certain circumstances, to consider the economic effect of proposed regulations on small entities. The agency must assess the economic impact of a proposed rule on small entities if the proposal will have a significant economic impact on a substantial number of small entities. Under the RFA, 5 U.S.C. 601 *et seq.*, an agency must prepare an initial regulatory flexibility analysis (IRFA) describing the economic impact of a rule on small entities unless the agency certifies that the rule will not have a significant impact.

In the 1994 D/DBP and IESWTR proposals, EPA defined small entities as small PWSs—serving 10,000 or fewer persons—for purposes of its regulatory flexibility assessments under the RFA. EPA certified that the IESWTR will not have a significant impact on a substantial number of small entities, and prepared an IRFA for the DBP proposed rule. EPA did not, however, specifically solicit comment on that definition. EPA will use this same definition of small PWSs in preparing the final RFA for the Stage 1 DBP rule. Further, EPA plans to define small entities in the same way in all of its future drinking water rulemakings. The Agency solicited public comment on this definition in the proposed National Primary Drinking Water Regulations: Consumer Confidence Reports, 63 FR 7606, at 7620–21, February 13, 1998.

#### *E. Formation of 1997 Federal Advisory Committee*

In May 1996, the Agency initiated a series of public informational meetings to exchange information on issues related to microbial and D/DBP regulations. To help meet the deadlines for the IESWTR and Stage 1 D/DBP rule established by Congress in the 1996 SDWA Amendments and to maximize stakeholder participation, the Agency established the Microbial and Disinfectants/Disinfection Byproducts (M-DBP) Advisory Committee under the Federal Advisory Committee Act (FACA) on February 12, 1997, to collect, share, and analyze new information and data, as well as to build consensus on the regulatory implications of this new information. The Committee consists of 17 members representing USEPA, State and local public health and regulatory agencies, local elected officials, drinking water suppliers, chemical and equipment manufacturers, and public interest groups.

The Committee met five times, in March through July 1997, to discuss issues related to the IESWTR and Stage

1 D/DBP rule. Technical support for these discussions was provided by a Technical Work Group (TWG) established by the Committee at its first meeting in March 1997. The Committee's activities resulted in the collection, development, evaluation, and presentation of substantial new data and information related to key elements of both proposed rules. The Committee reached agreement on the following major issues that were discussed in the 1997 NODA (USEPA, 1997a): (1) Maintaining the proposed MCLs for TTHMs, HAA5 and bromate; (2) modifying the enhanced coagulation requirements as part of DBP control; (3) including a microbial bench marking/profiling to provide a methodology and process by which a PWS and the State, working together, assure that there will be no significant reduction in microbial protection as the result of modifying disinfection practices in order to meet MCLs for TTHM and HAA5; (4) credit for compliance with applicable disinfection requirements should continue to be allowed for disinfection applied at any point prior to the first customer, consistent with the existing Surface Water Treatment Rule; (5) modification of the turbidity performance requirements and requirements for individual filters; (6) issues related to the MCLG for *Cryptosporidium*; (7) requirements for removal of *Cryptosporidium*; and (8) provision for conducting sanitary surveys.

#### **II. Significant New Epidemiology Information for the Stage 1 Disinfectant and Disinfection Byproducts Rule**

The preamble to the 1994 proposed rule provided a summary of the health criteria documents for the following DBPs: Bromate; chloramines; haloacetic acids and chloral hydrate; chlorine; chlorine dioxide, chlorite, and chlorate; and trihalomethanes (USEPA, 1994a). The information presented in 1994 was used to establish MCLGs and MRDLGs. On November 3, 1997, the EPA published a Notice of Data Availability (NODA) summarizing new information that the Agency has obtained since the 1994 proposed rule (USEPA, 1997a). The following sections briefly discuss additional information received and analyzed since the November 1997 NODA. This new information concerns the following: (1) Recently published epidemiology studies examining the relationship between exposure to contaminants in chlorinated surface water and adverse health outcomes; (2) an assessment of the Morris et. al. (1992) meta-analysis of the epidemiology studies published prior to 1996; (3)

recommendations made by an International Life Science Institute (ILSI) expert panel on the application of the USEPA Proposed Guidelines for Carcinogen Assessment (USEPA, 1996b) to data sets for chloroform and dichloroacetic acid; and (4) new laboratory animal studies on bromate and chlorite (also applicable to chlorine dioxide risk). This Notice presents the conclusions of these supplemental analyses as well as their implications for MCLGs, MCLs, MRDLGs, and MRDLs. The new documents are included in the Docket for this action.

As a result of this new information, the EPA requests comment on the following: (1) Revisions to estimates of potential cancer cases that can be attributed to exposure from DBPs in chlorinated surface water (USEPA, 1998a); (2) revisions to the noncancer assessment for chlorite and chlorine dioxide (USEPA, 1998b); (3) revisions to the cancer quantitative risks for chloroform (USEPA, 1998c); (4) updates on the cancer assessment for bromate (USEPA, 1998d); and (5) updates on the hazard characterization for dichloroacetic acid (USEPA, 1998e).

As in 1994, the assessment of public health risks from chlorination of drinking water currently relies on inherently difficult and incomplete empirical analysis. On one hand, epidemiologic studies of the general population are hampered by difficulties of design, scope, and sensitivity. On the other hand, uncertainty is involved in using the results of high dose animal toxicological studies of a few of the numerous byproducts that occur in disinfected drinking water to estimate the risk to humans from chronic exposure to low doses of these and other byproducts. In addition, such studies of individual byproducts cannot characterize the entire mixture of disinfection byproducts in drinking water. Nevertheless, while recognizing the uncertainties of basing quantitative risk estimates on less than comprehensive information regarding overall hazard, EPA believes that the weight-of-evidence represented by the available epidemiological and toxicological studies on DBPs and chlorinated surface water continues to support a hazard concern and a protective public health approach to regulation.

#### *A. Epidemiologic Associations Between Exposure to DBPs in Chlorinated Water and Cancer*

The preamble to the 1994 proposed rule discussed several cancer epidemiology studies that had been conducted over the past 20 years to

examine the association between exposure to chlorinated water and cancer (USEPA, 1994a). At the time of the 1994 proposed rule, there was disagreement among the members of the Negotiating Committee on the conclusions that could be drawn from these studies. Some members of the Committee felt that the cancer epidemiology data, taken in conjunction with the results from toxicological studies, provided ample and sufficient weight of evidence to conclude that exposure to DBPs in drinking water could result in increased cancer risk at levels encountered in some public water supplies. Other members of the Committee concluded that the cancer epidemiology studies on the consumption of chlorinated drinking water to date were insufficient to provide definitive information for the regulation. As a response, EPA agreed to pursue additional research to reduce the uncertainties associated with these data and to better characterize and project the potential human cancer risks associated with the exposure to chlorinated water. To implement this commitment, EPA sponsored an expert panel to review the state of cancer epidemiology research (USEPA, 1994b). As discussed in the 1997 NODA, EPA has implemented several of the panel's recommendations for short- and long-term research to improve the assessment of risks, using the results from cancer epidemiology studies.

The 1994 proposed rule also presented the results of a meta-analysis that pooled the relative risks from ten cancer epidemiology studies in which there was a presumed exposure to chlorinated water and its byproducts (Morris *et al.*, 1992). A conclusion of this meta-analysis was a calculated upper bound estimate of approximately 10,000 cases of rectal and bladder cancer cases per year that could be associated with exposure to chlorinated water and its byproducts in the United States. The ten studies included in the meta-analysis had methodological issues and significant design differences. There was considerable debate among the members of the Negotiating Committee on the extent to which the results of this meta-analysis should be considered in developing benefit estimates associated with the proposed rule. Negotiators agreed that the range of possible risks attributed to chlorinated water should consider both toxicological data and epidemiological data, including the Morris *et al.* (1992) estimates. No consensus, however, could be reached on a single likely risk estimate.

For purposes of estimating the potential benefits from the proposed rule, EPA used a range of estimated cancer cases that could be attributed to exposure to chlorinated waters of less than 1 cancer case per year up to 10,000 cases per year. The less than 1 cancer case per year was based on toxicology (the maximum likelihood cancer risk estimate calculated from animal assay data for THMs). The 10,000 cases per year was based on epidemiology (estimates from the Morris *et al.* (1992) meta-analysis).

#### 1. Assessment of the Morris *et al.* (1992) Meta-Analysis

Based on the recommendations from the 1994 expert panel on cancer epidemiology, EPA completed an assessment of the Morris *et al.* (1992) meta-analysis which comprises three reports: (1) A Report completed for EPA which evaluated the Morris *et al.* (1992) meta-analysis (Poole, 1997); (2) EPA's assessment of the Poole report (USEPA, 1998f); and (3) a peer review of the Poole report and EPA's assessment of the Poole report (USEPA, 1998g). Each of these documents is briefly discussed below. The full reports together with Dr. Morris's comments on the Poole Review (Morris, 1997) can be found in the docket for this Notice.

*a. Poole Report.* A report was prepared for EPA which made recommendations regarding whether the data used by Morris *et al.* (1992) should be aggregated into a single summary estimate of risk. The report also commented on the utility of the aggregated estimates for risk assessment purposes (Poole, 1997). This report was limited to the studies available to Morris *et al.* (1992) plus four additional studies that EPA requested to be included (Ijsselmuiden *et al.*, 1992; McGeehin *et al.*, 1993; Vena *et al.*, 1993; and King and Marrett, 1996). Poole observed that there was considerable heterogeneity among the data and that there was evidence of publication bias within the body of literature. When there is significant heterogeneity among studies, aggregation of the results into a single summary estimate may not be appropriate. Publication bias refers to the situation where the literature search and inclusion criteria for studies used for the meta-analysis indicate that the sample of studies used is not representative of all the research (published and unpublished) that has been done on a topic. In addition, Poole found that the aggregate estimates reported by Morris *et al.* (1992) were sensitive to small changes in the analysis (e.g., addition or deletion of a single study). Based on these

observations, Poole recommended that the cancer epidemiology data considered in his evaluation should not be combined into a single summary estimate and that the data had limited utility for risk assessment purposes. Many of the reasons cited by Poole for why it was not appropriate to combine the studies into a single point estimate of risk were noted in the 1994 proposal (Farland and Gibb, 1993; Murphy, 1993; and Craun, 1993).

*b. EPA's Evaluation of Poole Report.* EPA reviewed the conclusions from the Poole report and generally concurred with Poole's recommendations (USEPA, 1998f). EPA concluded that Poole presented reasonable and supportable evidence to suggest that the work of Morris *et al.* (1992) should not be used for risk assessment purposes without further study and review because of the sensitivity of the results to analytical choices and to the addition or deletion of a single study. EPA agreed that the studies were highly heterogeneous, thus undermining the ability to combine the data into a single summary estimate of risk.

*c. Peer Review of Poole Report and EPA's Evaluation.* The Poole report and EPA's evaluation were reviewed by five epidemiologic experts from academia, government, and industry (EPA, 1998g). Overall, these reviewers agreed that the Poole report was of high quality and that he had used defensible assumptions and techniques during his analysis. Most of the reviewers concluded that the report was correct in its assessment that these data should not be combined into a single summary estimate of risk.

#### 2. New Cancer Epidemiology Studies

Several cancer epidemiological studies examining the association between exposure to chlorinated surface water and cancer have been published subsequent to the 1994 proposed rule and the Morris *et al.* (1992) meta-analysis (McGeehin *et al.*, 1993; Vena *et al.*, 1993; King and Marrett, 1996; Doyle *et al.*, 1997; Freedman *et al.*, 1997; Cantor *et al.*, 1998; and Hildesheim *et al.*, 1998). These studies, with the exception of Freedman *et al.* (1997), were described in the "Summaries of New Health Effects Data" (USEPA, 1997b) that was included in the docket for the 1997 NODA.

In general, the new studies cited above are better designed than the studies published prior to the 1994 proposal. The newer studies generally include incidence cases of disease, interviews with the study subjects and better exposure assessments. Based on the entire cancer epidemiology database, bladder cancer studies provide

better evidence than other types of cancer for an association between exposure to chlorinated surface water and cancer. EPA believes the association between exposure to chlorinated surface water and colon and rectal cancer cannot be determined at this time because of the limited data available for these cancer sites (USEPA, 1998a).

### 3. Quantitative Risk Estimation for Cancers From Exposure to Chlorinated Water

Under Executive Order 12866 (58 FR 51735, October 4, 1993), the EPA must conduct a regulatory impact analysis (RIA). In the 1994 proposal, EPA used the Morris *et al.* (1992) meta-analysis in the RIA to provide an upper-bound estimate of 10,000 possible cancer cases per year that could be attributed to exposure to chlorinated water and its associated byproducts. EPA also estimated that an upper bound of 1200–3300 of these cancer cases per year could be avoided if the requirements for the Stage 1 DBP rule were implemented (USEPA, 1994a). EPA acknowledged the uncertainty in these estimates, but believed they were the best that could be developed at the time.

Based on the evaluations cited above, EPA does not believe it is appropriate to use the Morris *et al.* (1992) study as the basis for estimating the potential cancer cases that could be attributed to exposure to DBPs in chlorinated surface water. Instead, EPA is providing for comment an analysis based on a more traditional approach for estimating the potential cancer risks from exposure to DBPs in chlorinated surface water that does not rely on pooling or aggregating the epidemiologic data into a single summary estimate. Based on a narrower set of improved studies, this approach utilizes the population attributable risk (PAR) concept and presents a range of potential risks and not a single point estimate. As discussed below, there are a number of uncertainties associated with the use of this approach for estimating potential risks. Therefore, EPA requests comments on both the PAR methodology as well as on the assumptions upon which it is based.

Epidemiologists use PAR to quantify the fraction of the disease burden in a population (e.g., cancer) that could be eliminated if the exposure was absent (e.g., DBPs in chlorinated water) (Rockhill, *et al.*, 1998). PARs provide a perspective on the potential magnitude of risk associated with various exposures. The concept of PAR is known by many names (e.g., attributable fraction, attributable proportion, etiologic fraction). For this Notice, the term PAR will be used to avoid

confusion. A range of PARs better captures the heterogeneity of the risk estimates than a single point estimate.

In the PAR analysis of the cancer epidemiology data and the development of the range of potential cancer cases attributable to exposure to DBPs in chlorinated surface water, EPA recognizes that a causal relationship between chlorinated surface water and bladder cancer has not yet been demonstrated by epidemiology studies. However, several studies have suggested a weak association in various subgroups. EPA presents potential cancer case estimates as upper bounds of suggested risk as part of the Agency's analysis of potential costs and benefits associated with this rule. EPA focused its current evaluation on bladder cancer because the number of quality studies that are available for other cancer sites such as colon and rectal cancers are very limited.

EPA estimated PARs for the best bladder cancer studies that provided enough information to calculate a PAR (USEPA, 1998a). In addition, EPA selected studies for inclusion in the quantitative analysis if they met all three of the following criteria: (1) The study was a population based case-control or cohort study conducted to evaluate the relationship between exposure to chlorinated drinking water and incidence cancer cases, based on personal interviews (no cohort studies were found that met all 3 criteria); (2) the study was of high quality and well designed (e.g., good sample size, high response rate, and adjusted for confounding factors); and (3) the study had adequate exposure assessments (e.g., residential histories, actual THM data). Based on the above selection criteria, five bladder cancer studies were selected for estimating PARs: Cantor *et al.*, 1985; McGeehin *et al.* 1993; King and Marrett, 1996; Freedman *et al.*, 1997; and Cantor *et al.*, 1998. PARs were derived for two exposure categories: years of exposure to chlorinated surface water; and THM levels and years of chlorinated surface water exposure.

The PARs from the five bladder cancer studies for the two exposure categories ranged from 2–17%. The uncertainties associated with these PAR estimates are large as expected, due to the common prevalence of both the disease (bladder cancer) and exposure (chlorinated drinking water). Based on 54,500 expected new bladder cancer cases in the U.S., as projected by NCI (1998) for 1997, the upper bound estimate of the number of potential bladder cancer cases per year potentially associated with exposure to

DBPs in chlorinated surface water was estimated to be 1100–9300.

EPA made several important assumptions when evaluating the application of the PAR range of estimated bladder cancer cases from these studies to the U.S. population. They include the following: (i) The study population selected for each of the cancer epidemiology studies are reflective of the entire U.S. population that develops bladder cancer; (ii) the percentage of bladder cancer cases exposed to DBPs in the reported studies are reflective of the bladder cancer cases exposed to DBPs in the U.S. population; (iii) the levels of DBP exposure in the bladder studies are reflective of the DBP exposure in the U.S. population; and (iv) the possible relationship between exposure to DBPs in chlorinated surface water and bladder cancer is causal.

EPA believes that these assumptions would not be appropriate for estimating the potential upper bound cancer risk for the U.S. population based on a single study. However, the Agency believes that these assumptions are appropriate given the number of studies used in the PAR analysis and for gaining a perspective on the range of possible upper bound risks that can be used in establishing a framework for further cost-benefit analysis. In addition, EPA believes these assumptions are appropriate given the SDWA mandate that "drinking water regulations be established if the contaminant may have an adverse effect on the health of persons" (SDWA—Section 1412(b)(1)A). Because of this mandate, EPA believes that when the scientific data indicates there may be causality, such an analytical approach is appropriate. EPA believes the assumption of a potential causal relationship is supported by the weight-of-evidence from toxicology and epidemiology. Toxicology studies have shown several individual DBPs to be carcinogenic and mutagenic, while the epidemiology data have shown weak associations between several cancer sites and exposure to chlorinated surface water.

EPA notes and requests comment on the following additional issues associated with basing an estimate of the potential bladder cancer cases that can be attributed to DBPs in chlorinated surface water from the five studies selected for this analysis. The results generally showed weak statistical significance and were not always consistent among the studies. For example, some reviewers believe that two studies showed statistically significant effects only for male smokers, while two other studies showed higher effects for non-smokers.

One study showed a significant association with exposure to chlorinated surface water but not chlorinated ground water, while another showed the opposite result. Furthermore, two studies which examined the effects of exposure to higher levels of THMs failed to find a significant association between level of THMs and cancer. The Agency notes that it is not necessary that statistical significance be shown in order to conduct a PAR analysis as was stated by peer-reviewers of this analysis.

#### 4. Peer-Review of Quantitative Risk Estimates

The quantitative cancer risks estimated from the five epidemiology studies derived through the calculation of individual PARs has undergone external peer review by three expert epidemiologists (USEPA, 1998a). Two peer reviewers concurred with the decision to derive a PAR range. This approach was deemed more appropriate than the selection of a single study or aggregation of study results. One reviewer indicated significant reservations with this approach based not on the method, but the inconclusivity of the epidemiology database and stated that it was premature to perform a PAR analysis because it would suggest that the epidemiological information is more consistent and complete than it actually is. To better present the degree of variability, this reviewer suggested an alternative approach that involves a graphical presentation of the individual odds ratios and their corresponding confidence intervals. Two reviewers agreed that there is not enough information to present an estimate of the PAR for colon and rectal cancer.

EPA understands the issues raised regarding the use of PARs and recognizes there may be controversy on using this approach with the available epidemiology data. However, as stated above, EPA believes the PAR approach is a useful tool for estimating the potential upper bound risk for use in developing the regulatory impact analysis. EPA agrees with two of the reviewers that there is not enough information to present an estimate of colon and rectal risk at this time using a PAR approach.

#### 5. Summary of Key Observations

The 1994 proposal included a meta-analysis of 10 cancer epidemiology studies that provided an estimate of the number of bladder and rectal cancer cases per year that could be attributed to consumption of chlorinated water and its associated byproducts (Morris *et*

*al.*, 1992). Based on the evaluations previously described, EPA does not believe it is appropriate to use the Morris *et al.* (1992) study as the basis for estimating the potential cancer cases that could be attributed to exposure to DBPs in chlorinated surface water. Instead, EPA has focused on a smaller set of higher quality studies and performed a PAR analysis to estimate the potential cancer risks from exposure to DBPs in chlorinated surface water that does not rely on pooling or aggregating the data into a single summary estimate, as was done by Morris *et al.* (1992). EPA focused the current evaluation on bladder cancer because there are more appropriate studies of higher quality available upon which to base this assessment than for other cancer sites. It was decided to present the potential number of cancer cases as a range instead of a single point estimate because this would better represent the uncertainties in the risk estimates. The number of potential bladder cancer cases per year that could be associated with exposure to DBPs in chlorinated surface water is estimated to be an upper bound range of 1100–9300 per year.

In the PAR analysis of the cancer epidemiology data and the development of the range of potential cancer cases attributable to exposure to DBPs in chlorinated surface water, EPA presents the estimates as upper bounds of any suggested risk. As was debated during the 1992–1993 M/DBP Regulatory Negotiation process, EPA believes that there are insufficient data to conclusively demonstrate a causal association between exposure to DBPs in chlorinated surface water and cancer. EPA recognizes the uncertainties of basing quantitative estimates using the current health database on chlorinated surface waters and has identified a number of issues that must be considered in interpreting the results of this analysis. Nonetheless, the Agency believes that the overall weight-of-evidence from available epidemiologic and toxicologic studies on DBPs and chlorinated surface water continues to support a hazard concern and thus, a prudent public health protective approach for regulation.

#### 6. Requests for Comments

EPA is not considering any changes to the recommended regulatory approach contained in the 1994 proposal, and discussed further in the 1997 NODA, based on the upper bound risk analysis issues discussed above. Nonetheless, EPA requests comments on the conclusions from the Poole report

(Poole, 1997), EPA's assessment of the Poole report (EPA, 1998f), the peer-review of the Poole report and EPA's assessment of the Poole report (EPA, 1998g); and Dr. Morris comments on the Poole review (Morris, 1997). EPA also requests comments on its quantitative analysis (PAR approach) to estimate the upper bound risks from exposure to DBPs in chlorinated surface water, the methodology for estimating the number of cancer cases per year that could be attributed to exposure to DBPs in chlorinated surface water, and any alternative approaches for estimating the upper bound estimates of risk. In particular, EPA requests comment on the extent to which the approach used in the PAR analysis addresses the concerns identified by Poole and others regarding the earlier Morris meta-analysis. EPA also requests comments on the peer review of the PAR analysis.

#### B. Epidemiologic Associations Between Exposure to DBPs in Chlorinated Water and Adverse Reproductive and Developmental Effects

The 1994 proposed rule discussed several reproductive epidemiology studies. At the time of the proposal, it was concluded that there was no compelling evidence to indicate a reproductive and developmental hazard due to exposure to chlorinated water because the epidemiologic evidence was inadequate and the toxicological data were limited. In 1993, an expert panel of scientists was convened by the International Life Sciences Institute to review the available human studies for developmental and reproductive outcomes and to provide research recommendations (USEPA/ILSI, 1993). The expert panel concluded that the epidemiologic results should be considered preliminary given that the research was at a very early stage (USEPA/ILSI, 1993; Reif *et al.*, 1996). The 1997 NODA and the "Summaries of New Health Effects Data" (USEPA, 1997b) presented several new studies (Savitz *et al.*, 1995; Kanitz *et al.* 1996; and Bove *et al.*, 1996) that had been published since the 1994 proposed rule and the 1993 ILSI panel review. Based on the new studies presented in the 1997 NODA, EPA stated that the results were inconclusive with regard to the association between exposure to chlorinated waters and adverse reproductive and developmental effects (62 FR 59395)

### 1. EPA Panel Report and Recommendations for Conducting Epidemiological Research on Possible Reproductive and Developmental Effects of Exposure to Disinfected Drinking Water

EPA convened an expert panel in July 1997 to evaluate epidemiologic studies of adverse reproductive or developmental outcomes that may be associated with the consumption of disinfected drinking water published since the 1993 ILSI panel review. A report was prepared entitled "EPA Panel Report and Recommendations for Conducting Epidemiological Research on Possible Reproductive and Developmental Effects of Exposure to Disinfected Drinking Water" (USEPA, 1998h). The 1997 expert panel was also charged to develop an agenda for further epidemiological research. The 1997 panel concluded that the results of several studies suggest that an increased relative risk of certain adverse outcomes may be associated with the type of water source, disinfection practice, or THM levels. The panel emphasized, however, that most relative risks are moderate or small and were found in studies with limitations of their design or conduct. The small magnitude of the relative risk found may be due to one or more sources of bias, as well as to residual confounding (factors not identified and controlled). Additional research is needed to assess whether the observed associations can be confirmed. The panel considers a recent study by Waller *et al.* (1998), discussed below, to provide a strong basis for further research. This study was funded in part by EPA as an element of the research program agreed to as part of the 1992/1993 negotiated M/DBP rulemaking.

### 2. New Reproductive Epidemiology Studies

Three new reproductive epidemiology studies have been published since the 1997 NODA. The first study (Klotz and Pynch, 1998) examined the potential association between neural tube defects and certain drinking water contaminants, including some DBPs. In this case-control study, births with neural tube defects reported to New Jersey's Birth Defects Registry in 1993 and 1994 were matched against control births chosen randomly from across the State. Birth certificates were examined for all subjects, as was drinking water data corresponding to the mother's residence in early pregnancy. The authors reported elevated odds ratios (ORs), generally between 1.5 and 2.1, for the association of neural tube defects with TTHMs. However, the only

statistically significant results were seen when the analysis was isolated to those subjects with the highest THM exposures (greater than 40 ppb) and limited to those subjects with neural tube defects in which there were no other malformations (odds ratio 2.1; 95% confidence interval 1.1–4.0). Neither HAAs or haloacetonitriles (HANs) showed a clear relationship to neural tube defects but monitoring data on these DBPs were more limited than for THMs. Nitrates were not observed to be associated with neural tube defects. Certain chlorinated solvent contaminants were also studied but occurrence levels were too low to assess any relationship to neural tube defects. This study is available in the docket for this NODA. Although EPA has not completed its review of the study, the Agency is proceeding on the premise that this study will add to the weight-of-evidence concerning the potential adverse reproductive health effects from DBPs, but will not by itself provide sufficient evidence for further regulatory actions.

Two studies looked at early term miscarriage risk factors. The first of these studies (Waller *et al.*, 1998) examined the potential association between early term miscarriage and exposure to THMs. The second study (Swan *et al.*, 1998) examined the potential association between early term miscarriage and tap water consumption. Both studies used the same group of pregnant women (5,144) living in three areas of California. They were recruited from the Santa Clara area, the Fontana area in southern California, or the Walnut Creek area. The women were all members of the Kaiser Permanente Medical Care Program and were offered a chance to participate in the study when they called to arrange their first prenatal visit. In the Waller *et al.* (1998) study, additional water quality information from the women's drinking water utilities were obtained so that THM levels could be determined. The Swan *et al.* (1998) study provided no quantitative measurements of THMs (or DBPs), and thus, provided no additional information on the risk from chlorination byproducts. Because of this, only the Waller *et al.* (1998) study is summarized below.

In the Waller *et al.* (1998) study, utilities that served the women in this study were identified. Utilities' provided THM measurements taken during the time period participants were pregnant. The TTHM level in a participant's home tap water was estimated by averaging water distribution system TTHM measurements taken during a

participants first three months of pregnancy. This "first trimester TTHM level" was combined with self reported tap water consumption to create a TTHM exposure level. Exposure levels of the individual THMs (e.g., chloroform, bromoform, etc.) were estimated in the same manner. Actual THM levels in the home tap water were not measured.

Women with high TTHM exposure in home tap water (drinking five or more glasses per day of cold home tap water containing at least 75 ug per liter of TTHM) had an early term miscarriage rate of 15.7%, compared with a rate of 9.5% among women with low TTHM exposure (drinking less than 5 glasses per day of cold home tap water or drinking any amount of tap water containing less than 75 ug per liter of TTHM). An adjusted odds ratio for early term miscarriage of 1.8 (95% confidence interval 1.1–3.0) was determined.

When the four individual trihalomethanes were studied, only high bromodichloromethane (BDCM) exposure, defined as drinking five or more glasses per day of cold home tap water containing  $\geq 18$  ug/L bromodichloromethane, was associated with early term miscarriage. An adjusted odds ratio for early term miscarriage of 3.0 (95% confidence interval 1.4–6.6) was determined.

### 3. Summary of Key Observations

The Waller *et al.* (1998) study reports that consumption of tapwater containing high concentrations of THMs, particularly BDCM, is associated with an increased risk of early term miscarriage. EPA believes that while this study does not prove that exposure to THMs causes early term miscarriages, it does provide important new information that needs to be pursued and that the study adds to the weight-of-evidence which suggests that exposure to DBPs may have an adverse effect on humans.

EPA has an epidemiology and toxicology research program that is examining the relationship between DBPs and adverse reproductive and developmental effects. In addition to conducting scientifically appropriate follow-up studies to see if the observed association in the Waller *et al.* (1998) study can be replicated elsewhere, EPA will be working with the California Department of Health Services to improve estimates of exposure to DBPs in the existing study population. A more complete DBP exposure data base is being developed by asking water utilities in the study area to provide additional information, including levels of other types of DBPs (e.g., haloacetic



acids). These efforts will help further assess the significance of the Waller *et al.* (1998) study, associated concerns, and how further follow-up work can best be implemented. EPA will collaborate with the Centers for Disease Control and Prevention (CDC) in a series of studies to evaluate if there is an association between exposure to DBPs in drinking water and birth defects. The Agency is also involved in a collaborative testing program with the National Toxicology Program (NTP) under which several individual DBPs have been selected for reproductive and developmental screening tests. Finally, EPA is conducting several toxicology studies on DBPs other endpoints of concern including examining the potential effects of BDCM on male reproductive endpoints. This information will be used in developing the Stage 2 DBP rule. In the meantime, the Agency plans to proceed with the 1994 D/DBP proposal for tightening the control for DBPs.

#### 4. Requests for Comments

EPA is not considering any changes to the recommended regulatory approach contained in the 1994 proposal, and discussed further in the 1997 NODA, based on the new reproductive epidemiology studies discussed above. Nonetheless, EPA requests comments on the findings from the Klotz, *et al.* (1998) and Waller *et al.* (1998) study and EPA's conclusions regarding the studies.

### III. Significant New Toxicological Information for the Stage 1 Disinfectants and Disinfection Byproducts

The 1997 NODA reviewed new toxicological information that became available for several of the DBPs after the 1994 proposal (USEPA, 1997a and b). In that Notice, it was pointed out that several forthcoming reports were not available in time for consideration during the 1997 FACA process. Reports now available include a two-generation reproductive rat study of sodium chlorite sponsored by the Chemical Manufacturer Association (CMA, 1996); an EPA two-year cancer rodent study of bromate (DeAngelo *et al.*, 1998); and the *International Life Sciences Institute* (ILSI) expert panel report of chloroform and dichloroacetic acid (ILSI, 1997). These reports are discussed below, as well as EPA's analyses and conclusions based on this new information.

#### A. Chlorite and Chlorine Dioxide

The 1994 proposal included an MCLG of 0.08 mg/L and an MCL of 1.0 mg/L for chlorite. The proposed MCLG was based on an RfD of 3 mg/kg/d estimated

from a lowest-observed-adverse-effect-level (LOAEL) for neurodevelopmental effects identified in a rat study by Mobley *et al.* (1990). This determination was based on a weight of evidence evaluation of all the available data at that time (USEPA, 1994a). An uncertainty factor of 1000 was used to account for inter- and intra-species differences in response to toxicity (a factor of 100) and a factor of 10 for use of a LOAEL. The EPA proposed rule also included an MRDLG of 0.3 mg/L and an MRDL of 0.8 mg/L for chlorine dioxide. The proposed MRDLG was based on a RfD of 3 mg/kg/d estimated from a no-observed-adverse-effect-level (NOAEL) for developmental neurotoxicity identified from a rat study (Orme *et al.*, 1985; see USEPA, 1994a). This determination was based on a weight of evidence evaluation of all the available data at that time (USEPA, 1994a). An uncertainty factor of 300 was applied that was composed of a factor of 100 to account for inter- and intra-species differences in response to toxicity and a factor of 3 for lack of a two-generation reproductive study necessary to evaluate potential toxicity associated with lifetime exposure. To fill this important data gap, the Chemical Manufacturers Associations (CMA) agreed to conduct a two-generation reproductive study in rats. Sodium chlorite was used as the test compound. It should be noted that data on chlorite are relevant to assessing the risks of chlorine dioxide because chlorine dioxide rapidly disassociates to chlorite (and chloride) (USEPA, 1998b). Therefore, the new CMA two-generation reproductive chlorite study will be considered in assessing the risks for both chlorite and chlorine dioxide.

Since the 1994 proposal, CMA has completed the two-generation reproductive rat study (CMA, 1996). EPA has reviewed the CMA study and has completed an external peer review of the study (EPA, 1997c). In addition, EPA has reassessed the noncancer health risk for chlorite and chlorine dioxide considering the new CMA study (USEPA, 1998b). This reassessment has been peer reviewed (USEPA, 1998b). Based on this reassessment, EPA is considering changing the proposed MCLG for chlorite from 0.08 mg/L to 0.8 mg/L based on the NOAEL identified from the new CMA study. Since data on chlorite are considered relevant to chlorine dioxide risks and the two generation reproduction data gap has been filled, EPA is also considering changing the proposed MRDLG for chlorine dioxide from 0.3 mg/L to 0.8

mg/L. The basis for these changes are discussed below.

#### 1. 1997 CMA Two-Generation Reproduction Rat Study

The CMA two-generation reproductive rat study was designed to evaluate the effects of chlorite (sodium salt) on reproduction and pre- and post-natal development when administered orally via drinking water for two successive generations (CMA, 1996). Developmental neurotoxicity, hematological, and clinical effects were also evaluated in this study.

Sodium chlorite was administered at 0, 35, 70, and 300 ppm in drinking water to male and female Sprague Dawley rats (F<sub>0</sub> generation) for ten weeks prior to mating. Dosing continued during the mating period, pregnancy and lactation. Reproduction, fertility, clinical signs, and histopathology were evaluated in F<sub>0</sub> and F<sub>1</sub> (offspring from the first generation of mating) males and females. F<sub>1</sub> and F<sub>2</sub> (offspring from the second generation of mating) pups were evaluated for growth and development, clinical signs, and histopathology. In addition, F<sub>1</sub> animals from each dose group were assessed for neurotoxicity (e.g., neurohistopathology, motor activity, learning ability and memory retention, functional observations, auditory startle response). Limited neurotoxicological evaluations were conducted on F<sub>2</sub> pups.

The CMA report concluded that there were no treatment related effects at any dose level for systemic, reproductive/developmental, and developmental neurological end points. The report indicates that there were small statistically significant decreases in the maximum response to auditory startle response in the F<sub>1</sub> animals at the mid and high dose (70 and 300 ppm); this neurological effect was not considered to be toxicologically significant. A reduction in pup weight and decreased body weight gain through lactation in the F<sub>1</sub> and F<sub>2</sub> animals and a decrease in body weight gain in the F<sub>2</sub> males at 300 ppm were noted. Decreases in liver weight in F<sub>0</sub> and F<sub>1</sub> animals, as well as reductions in red blood cell indices in F<sub>1</sub> animals at 300 ppm and 70 ppm were noted. Minor hematological effects were found in F<sub>1</sub> females at 35 ppm. CMA concluded that the effects noted above were not clinically or toxicologically significant. A NOAEL of 300 ppm was identified in the CMA report for reproductive toxicity and for developmental neurotoxic effects, and a NOAEL of 70 ppm for hematological effects. EPA disagrees with the CMA conclusions regarding the NOAEL of 300 ppm for the reproductive and

developmental neurological effects for this study as discussed below.

## 2. External Peer Review of the CMA Study

EPA has evaluated the CMA 2-generation reproductive study and concluded that the study design was consistent with EPA testing guidelines (USEPA, 1992). Additionally, an expert peer review of the CMA study was conducted and indicated that the study design and analyses were adequate (USEPA, 1997c). Although the study design was considered adequate and consistent with EPA guidelines, the peer review pointed out some limitations in the study (USEPA, 1997c). For example, developmental neurotoxicity evaluations were conducted after exposure ended at weaning. This is consistent with EPA testing guidelines and should potentially detect effects on the developing central nervous system. Nevertheless, the opportunity to detect neurological effects due to continuous or lifetime exposure may be reduced. The peer review generally questioned the CMA conclusions regarding the NOAELs for this study and indicated that the NOAEL should be lower than

300 ppm. The majority of peer reviews recommended that the NOAEL for reproductive/developmental toxicity be reduced to 70 ppm given the treatment related effects found at 300 ppm, and that the NOAEL for neurotoxicity be reduced to 35 ppm based on significant changes in the maximum responses in startle amplitude and absolute brain weight at 70 and 300 ppm. The reviewers indicated that a NOAEL was not observed for hematological effects and noted that the CMA conclusion for selecting the 70 ppm NOAEL for the hematology variables needs to be explained further.

## 3. MCLG for Chlorite: EPA's Reassessment of the Noncancer Risk

EPA has determined that the NOAEL for chlorite should be 35 ppm (3 mg/kg/d chlorite ion, rounded) based on a weight of evidence approach. The data considered to support this NOAEL are summarized in USEPA (1998b) and included the CMA study as well as previous reports on developmental neurotoxicity (USEPA, 1998b). The NOAEL of 35 ppm (3 mg/kg/d chlorite ion) is based on the following effects observed in the CMA study at 70 and

300 ppm chlorite: Decreases in absolute brain and liver weight, and lowered auditory startle amplitude. Decreases in pup weight were found at the 300 ppm and thus a NOAEL of 70 ppm for reproductive effects is considered appropriate (USEPA, 1998b). Although 70 ppm appears to be the NOAEL for hemolytic effects, the NOAEL and LOAEL are difficult to discern for this endpoint given that minor changes were reported at 70 and 35 ppm. EPA considers the basis of the NOAELs to be consistent with EPA risk assessment guidelines (USEPA, 1991, 1998i, 1996a). Furthermore, a NOAEL of 35 ppm is supported by effects (particularly neurodevelopmental effects) found in previously conducted studies of chlorite and chlorine dioxide (USEPA, 1998b).

An RfD of 0.03 mg/kg/d is estimated using a NOAEL of 3 mg/kg/d and an uncertainty factor of 100 to account for inter- and intra-species differences. The revised MCLG for chlorite is calculated to be 0.8 mg/L by assuming an adult tap water consumption of 2 L per day for a 70 kg adult and using a relative source contribution of 80% (because most exposure to chlorite is likely to come from drinking water):

$$\text{MCLG for chlorite} = \frac{0.03 \text{ mg/kg/d} \times 70 \text{ kg} \times 0.8}{2 \text{ L/day}} = 0.84 \text{ mg/L}$$

MCLG for chlorite = 0.8 mg/L (Rounded)

Therefore, EPA is considering an increase in the proposed MCLG for chlorite from 0.08 mg/L to 0.8 mg/L. A more detailed discussion of this assessment is included in the docket for this Notice (USEPA, 1998b).

## 4. MRDLG for Chlorine Dioxide: EPA's Reassessment of the Noncancer Risk

EPA believes that data on chlorite are relevant to assessing the risk of chlorine dioxide because chlorine dioxide rapidly disassociates to chlorite (and

chloride) (USEPA, 1998b). Therefore, the findings from the 1997 CMA two-generation reproductive study on sodium chlorite should be considered in a weight of evidence approach for establishing the MRDLG for chlorine dioxide. Based on all the available data, including the CMA study, a dose of 3 mg/kg/d remains as the NOAEL for chlorine dioxide (USEPA, 1998b). The MRDLG for chlorine dioxide is increased 3 fold from the 1994 proposal since the CMA 1997 study was a two-

generation reproduction study. Using a NOAEL of 3 mg/kg/d and applying an uncertainty factor of 100 to account for inter- and intra-species differences in response to toxicity, the revised MRDLG for chlorine dioxide is calculated to be 0.8 mg/L. This MRDLG takes into account an adult tap water consumption of 2 L per day for a 70 kg adult and applies a relative source contribution of 80% (because most exposure to chlorine dioxide is likely to come from drinking water):

$$\text{MRDLG for Chlorine dioxide} = \frac{0.03 \text{ mg/kg/d} \times 70 \text{ kg} \times 0.8}{2 \text{ L/day}} = 0.84 \text{ mg/L}$$

MRDLG for Chlorine dioxide = 0.8 mg/L (Rounded)

EPA is considering revising the MRDLG for chlorine dioxide from 0.3 mg/L to 0.8 mg/L. A more detailed discussion of this assessment can be found in the docket for this Notice (USEPA, 1998b).

## 5. External Peer Review of EPA's Reassessment

Three external experts have reviewed the EPA reassessment for chlorite and

chlorine dioxide (see USEPA, 1998b). Two of the three reviewers generally agreed with EPA conclusions regarding the identified NOAEL of 35 ppm for neurodevelopmental toxicity. The other reviewer indicated that the developmental neurological results from the CMA study were transient, too inconsistent, and equivocal to identify a NOAEL. EPA believes that although

different responses were found for startle response (as indicated by measures of amplitude, latency, and habituation), this is not unexpected given that these measures examine different aspects of the nervous system, and thus can be differentially affected. Although no neuropathology was observed in the CMA study, neurofunctional (or neurochemical)

changes such as startle responses can indicate potential neurotoxicity without neuropathological effects. Furthermore, transient effects are considered an important indicator of neurotoxicity as indicated in EPA guidelines (USEPA, 1998i). EPA maintains that the NOAEL is 35 ppm (3 mg/kg/d) from the CMA chlorite study based on neurodevelopmental effects as well as changes in brain and liver weight. This conclusion is supported by previous studies on chlorite and chlorine dioxide (USEPA, 1998b). Other comments raised by the peer reviewers concerning improved clarity and completeness of the assessment were considered by EPA in revising the assessment document on chlorite and chlorine dioxide.

#### 6. Summary of Key Observations

EPA continues to believe that chlorite and chlorine dioxide may have an adverse effect on the public health. EPA identified a NOAEL of 35 ppm for chlorite based on neurodevelopmental effects from the 1997 CMA two-generation reproductive study, which is supported by previous studies on chlorite and chlorine dioxide. In addition, EPA identified a NOAEL of 70 ppm for reproductive/developmental effects and hemolytic effects. EPA considers this study relevant to assessing the risk to chlorine dioxide. Based on the EPA reassessment, EPA is considering adjusting the MCLG for chlorite from 0.08 mg/L to 0.8 mg/L. Because data on chlorite are considered relevant to chlorine dioxide risks, EPA is considering adjusting the MRDLG for chlorine dioxide from 0.3 mg/L to 0.8 mg/L. The MRDL for chlorine dioxide would remain at 0.8 mg/L. The MCL for chlorite would remain at 1.0 mg/L because as noted in the 1994 proposal, 1.0 mg/L for chlorite is the lowest level achievable by typical systems using chlorine dioxide and taking into consideration the monitoring requirements to determine compliance. In addition, given the margin of safety that is factored into the estimation of the MCLG, EPA believes that 1.0 mg/L will be protective of public health. It should be noted that the MCLG and MRDLG presented for chlorite and chlorine dioxide are considered to be protective of susceptible groups, including children given that the RfD is based on a NOAEL derived from developmental testing, which includes a two-generation reproductive study. A two-generation reproductive study evaluates the effects of chemicals on the entire developmental and reproductive life of the organism. Additionally, current methods for developing RfDs are designed to be protective for sensitive

populations. In the case of chlorite and chlorine dioxide a factor of 10 was used to account for variability between the average human response and the response of more sensitive individuals.

#### 7. Requests for Comments

Based on the recent two-generation reproductive rat study for chlorite (CMA, 1996), EPA is considering revising the MCLG for chlorite from 0.08 mg/L to 0.8 mg/L and the MRDLG for chlorine dioxide from 0.3 mg/L to 0.8 mg/L. EPA requests comments on these possible changes in the MCLGs and on EPA's assessment of the CMA report.

#### B. Trihalomethanes

The 1994 proposed rule included an MCL for TTHM of 0.08 mg/L. MCLGs of zero for chloroform, BDCM and bromoform were based on sufficient evidence of carcinogenicity in animals. The MCLG of 0.06 mg/L for dibromochloromethane (DBCM) was based on observed liver toxicity from a subchronic study and limited animal evidence for carcinogenicity. As stated in the 1997 NODA, several new studies have been published on bromoform, BDCM, and chloroform since the 1994 proposal. The 1997 NODA concluded that the new studies on THMs contribute to the weight-of-evidence conclusions reached in the 1994 proposed rule, and that the new studies are not anticipated to change the proposed MCLGs for BDCM, DBCM, and bromoform. Since the 1997 NODA, the EPA has evaluated the significance of an ILSI panel report on the cancer risk assessment for chloroform. EPA has conducted a reassessment of chloroform (USEPA, 1998c), considering the ILSI report. The EPA reassessment of chloroform has been peer reviewed (USEPA, 1998c). Based on EPA's reassessment, the Agency is considering changing the proposed MCLG for chloroform from zero to 0.3 mg/L.

#### 1. 1997 International Life Sciences Institute Expert Panel Conclusions for Chloroform

In 1996, EPA co-sponsored an ILSI project in which an expert panel was convened and charged with the following objectives: (i) Review the available database relevant to the carcinogenicity of chloroform and DCA, excluding exposure and epidemiology data; (ii) consider how end points related to the mode of carcinogenic action can be applied in the hazard and dose-response assessment; (iii) use guidance provided by the 1996 EPA Proposed Guidelines for Carcinogen Assessment to develop recommendations for appropriate

approaches for risk assessment; and (iv) provide a critique of the risk assessment process and comment on issues encountered in applying the proposed EPA Guidelines (ILSI, 1997). The panel was made up of 10 expert scientists from academia, industry, government, and the private sector. It should be emphasized that the ILSI report does not represent a risk assessment, per se, for chloroform (or DCA) but, rather, provides recommendations on how to proceed with a risk assessment for these two chemicals.

To facilitate an understanding of the ILSI panel recommendations for the dose-response characterization of chloroform, the EPA 1996 Proposed Guidelines for Carcinogen Risk Assessment must be briefly described. For a more detail discussion of these guidelines, refer to USEPA (1996b).

The EPA 1996 Proposed Guidelines for Carcinogen Risk Assessment describes a two-step process to quantifying cancer risk (USEPA, 1996b). The first step involves modeling response data in the empirical range of observation to derive a point of departure. The second step is to extrapolate from this point of departure to lower levels that are within the range of human exposure. A standard point of departure was proposed as the lower 95% confidence limit on a dose associated with 10% extra risk (LED<sub>10</sub>). Based on comments from the public and the EPA's Science Advisory Board, the central or maximum likelihood estimate (i.e., ED<sub>10</sub>) is also being considered as a point of departure. Once the point of departure is identified, a straight-line extrapolation to the origin (i.e., zero dose, zero extra risk) is conducted as the linear default approach. The linear default approach would be considered for chemicals in which the mode of carcinogenic action understanding is consistent with low dose linearity or as a science policy choice for those chemicals for which the mode of action is not understood.

The EPA 1996 Proposed Guidelines for Carcinogen Risk Assessment are different from the 1986 guidelines approach that applied the linearized multi-stage model (LMS) to extrapolate low dose risk. The LMS approach under the 1986 guidelines was the only default for low dose extrapolation. Under the 1996 proposed guidelines both linear and nonlinear default approaches are available. The nonlinear approach applies a margin of exposure (MoE) analysis rather than estimating the probability of effects at low doses. In order to use the nonlinear default, the agent's mode of action in causing tumors must be reasonably understood.

The MoE analysis is used to compare the point of departure with the human exposure levels of interest (i.e., MoE = point of departure divided by the environmental exposure of interest). The key objective of the MoE analysis is to describe for the risk manager how rapidly responses may decline with dose. A shallow slope suggests less risk reduction at decreasing exposure than does a steep one. Information on factors such as the nature of response being used for the point of departure (i.e., tumor data or a more sensitive precursor response) and biopersistence of the agent are important considerations in the MoE analysis. A numerical default factor of no less than 10-fold each may be used to account for human variability and for interspecies differences in sensitivity when humans may be more sensitive than animals.

The ILSI expert panel considered a wide range of information on chloroform including rodent tumor data, metabolism/toxicokinetic information, cytotoxicity, genotoxicity, and cell proliferation data. Based on its analysis of the data, the panel concluded that the weight of evidence for the mode of action understanding indicated that chloroform was not acting through a direct DNA reactive mechanism. The evidence suggested, instead, that exposure to chloroform resulted in recurrent or sustained toxicity as a consequence of oxidative generation of highly tissue reactive and toxic metabolites (i.e., phosgene and hydrochloric acid (HCl)), which in turn would lead to regenerative cell proliferation. Oxidative metabolism was considered by the panel to be the predominant pathway of metabolism for chloroform. This mode of action was considered to be the key influence of chloroform on the carcinogenic process. The ILSI report noted that the weight-of-evidence for the mode of action was stronger for the mouse kidney and liver responses and more limited, but still supportive, for the rat kidney tumor responses.

The panel viewed chloroform as a likely carcinogen to humans above a certain dose range, but considered it unlikely to be carcinogenic below a certain dose range. The panel indicated that "This mechanism is expected to involve a dose-response relationship which is nonlinear and probably exhibits an exposure threshold." The panel, therefore, recommended the nonlinear default or margin of exposure approach as the appropriate one for quantifying the cancer risk associated with exposure to chloroform.

## 2. MCLG for Chloroform: EPA's Reassessment of the Cancer Risk

In the 1994 proposed rule, EPA classified chloroform under the 1986 EPA Guidelines for Carcinogen Risk Assessment as a Group B2, probable human carcinogen. This classification was based on sufficient evidence of carcinogenicity in animals. Kidney tumor data in male Osborne-Mendel rats reported by Jorgenson *et al.* (1985) was used to estimate the carcinogenic risk. An MCLG of zero was proposed. Because the mode of carcinogenic action was not understood at that time, EPA used the linearized multistage model and derived an upper bound carcinogenicity potency factor for chloroform of  $6 \times 10^{-3}$  mg/kg/d. The lifetime cancer risk levels of  $10^{-6}$ ,  $10^{-5}$ , and  $10^{-4}$  were determined to be associated with concentrations of chloroform in drinking water of 6, 60, and 600  $\mu$ g/L.

Since the 1994 rule, several new studies have provided insight into the mode of carcinogenic action for chloroform. EPA has reassessed the cancer risk associated with chloroform exposure (USEPA, 1998c) by considering the new information, as well as the 1997 ILSI panel report. This reassessment used the principles of the 1996 EPA Proposed Guidelines for Carcinogen Risk Assessment (USEPA, 1996b), which are considered scientifically consistent with the Agency's 1986 guidelines (USEPA, 1986). Based on the current evidence for the mode of action by which chloroform may cause tumorigenesis, EPA has concluded that a nonlinear approach is more appropriate for extrapolating low dose cancer risk rather than the low dose linear approach used in the 1994 proposed rule. Because tissue toxicity is key to chloroform's mode of action, EPA has also considered noncancer toxicities in determining the basis for the MCLG. After evaluating both cancer risk and noncancer toxicities as the basis for the MCLG, EPA concluded that the RfD for hepatotoxicity should be used. Hepatotoxicity, thus, serves as the basis for the MCLG given that this is the primary effect of chloroform and the more sensitive endpoint. Therefore, EPA is considering changing the proposed MCLG for chloroform from zero to 0.3 mg/L based on the RfD for hepatotoxicity. The basis for these conclusions are discussed below.

*a. Weight of the Evidence and Understanding of Mode of Carcinogenic Action.* EPA has fully considered the 1997 ILSI report and the new science that has emerged on chloroform since the 1994 proposed rule. Based on this

new information, EPA considers chloroform to be a likely human carcinogen by all routes of exposure (USEPA, 1998c). Chloroform's carcinogenic potential is indicated by animal tumor evidence (liver tumors in mice and renal tumors in both mice and rats) from inhalation and oral exposures, as well as metabolism, toxicity, mutagenicity and cellular proliferation data that contribute to an understanding of mode of carcinogenic action. Although the precise mechanism of chloroform carcinogenicity is not established, EPA agrees with the ILSI panel that a DNA reactive mutagenic mechanism is not likely to be the predominant influence of chloroform on the carcinogenic process. EPA believes that there is a reasonable scientific basis to support a mode of carcinogenic action involving cytotoxicity produced by the oxidative generation of highly reactive metabolites, phosgene and HCl, followed by regenerative cell proliferation as the predominant influence of chloroform on the carcinogenic process (USEPA, 1998c). EPA, therefore, agrees with the ILSI report that the chloroform dose-response should be considered nonlinear.

A recent article by Melnick *et al.* (1998) was published after the 1997 ILSI panel report and concludes that cytotoxicity and regenerative hyperplasia alone are not sufficient to explain the liver carcinogenesis in female B6C3F1 mice exposed to trihalomethanes, including chloroform. Although this article raises some interesting issues, EPA views the results for chloroform supportive of the role that toxicity and compensatory proliferation may play in chloroform carcinogenicity because statistically significant increases ( $p < 0.05$ ) in hepatotoxicity and cell proliferation are found for chloroform in this study.

*b. Dose-Response Assessment.* EPA has used several different approaches for estimating the MCLG for chloroform: the LED<sub>10</sub> for tumor response; the ED<sub>10</sub> for tumor response; and the RfD for hepatotoxicity. Each of these approaches are described below. EPA believes the RfD based on hepatotoxicity serves as the most appropriate basis for the MCLG for the reasons discussed below.

EPA has presented the linear and nonlinear default approaches to estimating the cancer risk associated with drinking water exposure to chloroform (USEPA, 1998c). EPA considered the linear default approach because of remaining uncertainties associated with the understanding of chloroform's mode of carcinogenic action: for example, lack of data on

cytotoxicity and cell proliferation responses in Osborne-Mendel rats, lack of mutagenicity data on chloroform metabolites, and the lack of comparative metabolic data between humans and rodents. Although these data deficiencies raise some uncertainty about how chloroform may influence tumor development at low doses, EPA views the linear dose-response extrapolation approach as overly conservative in estimating low-dose risk.

EPA concludes that the nonlinear default or margin of exposure approach is the preferred approach to quantifying the cancer risk associated with chloroform exposure because the evidence is stronger for a nonlinear mode of carcinogenic action. The tumor kidney response data in Osborne-Mendel rats from Jorgenson *et al.* (1985) are used as the basis for the point of departure (i.e., LED<sub>10</sub> and ED<sub>10</sub>) because a relevant route of human exposure (i.e., drinking water) and multiple doses of chloroform (i.e., 5 doses including zero) were used in this study (USEPA, 1998c). The animal data were adjusted to equivalent human doses using body weight raised to the 3/4 power as the interspecies scaling factor, as proposed in the 1996 EPA Proposed Guidelines for Carcinogen Risk Assessment. The ED<sub>10</sub> and LED<sub>10</sub> were estimated to be 37 and 23 mg/kg/d, respectively.

As part of the margin of exposure analysis, a 100 fold factor was applied to account for the variability and uncertainty associated with intra- and interspecies differences in the absence of data specific to chloroform. An additional factor of 10 was applied to account for the remaining uncertainties associated with the mode of

carcinogenic action understanding and the nature of the tumor dose response relationship being relatively shallow. EPA believes 1000 fold represents an adequate margin of exposure that addresses inter- and intra-species differences and uncertainties in the database. Other factors considered in determining the adequacy of the margin of exposure include the size of the human population exposed, duration and magnitude of human exposure, and persistence in the environment. Taking these factors into consideration, a MoE of 1000 is still regarded as adequate. Although a large population is chronically exposed to chlorinated drinking water, chloroform is not biopersistent and humans are exposed to relatively low levels of chloroform in the drinking water (generally under 100 µg/L), which are below exposures needed to induce a cytotoxic response. Furthermore, EPA believes that a MoE of 1000 is protective of susceptible groups, including children. The mode of action understanding for chloroform's cytotoxic and carcinogenic effects involves a generalized mechanism of toxicity that is seen consistently across different species. Furthermore, the activity of the enzyme (i.e., CYP2E1) involved in generating metabolites key to chloroform's mode of action is not greater in children than in adults, and probably less (USEPA, 1998c). Therefore, the ED<sub>10</sub> of 37 mg/kg-d and the LED<sub>10</sub> of 23 mg/kg-d is divided by a MoE of 1000 giving dose estimates of 0.037 and 0.023 mg/kg/d for carcinogenicity, respectively. These estimates would translate into MCLGs of 1.0 mg/L and 0.6 mg/L, respectively.

The underlying basis for chloroform's carcinogenic effects involve oxidative

generation of reactive and toxic metabolites (phosgene and HCl) and thus are related to its noncancer toxicities (e.g., liver or kidney toxicities). It is important, therefore, to consider noncancer outcomes in the risk assessment (USEPA, 1998c). The electrophilic metabolite phosgene would react with macromolecules such as phosphatidyl inositols or tyrosine kinases which in turn could potentially lead to interference with signal transduction pathways (i.e., chemical messages controlling cell division), thus, leading to carcinogenesis. Likewise, it is also plausible that phosgene reacts with cellular phospholipids, peptides, and proteins resulting in generalized tissue injury. Glutathione, free cysteine, histidine, methionine, and tyrosine are all potential reactants for electrophilic agents. Hepatotoxicity is the primary effect observed following chloroform exposure, and among tissues studied for chloroform-oxidative metabolism, the liver was found to be the most active (LSI, 1997). In the 1994 proposed rule, data from a chronic oral study in dogs (Heywood *et al.*, 1979) were used to derive the RfD of 0.01 mg/kg/d (USEPA, 1994a). This RfD is based on a LOAEL for hepatotoxicity and application of an uncertainty factor of 1000 (100 was used to account for inter- and intra-species differences and a factor of 10 for use of a LOAEL). The MCLG is calculated to be 0.3 mg/L by assuming an adult tap water consumption of 2 L of tap water per day for a 70 kg adult, and by applying a relative source contribution of 80% (EPA assumes most exposure is likely to come from drinking water):

$$\text{MCLG for Chloroform Based on RfD for Hepatotoxicity} = \frac{0.01 \text{ mg/kg/d} \times 70 \text{ kg} \times 0.8}{2 \text{ L/day}} = 0.3 \text{ mg/L (rounded)}$$

Therefore, 0.3 mg/L based on hepatotoxicity in dogs (USEPA, 1994a) is being considered as the MCLG because liver toxicity is a more sensitive effect of chloroform than the induction of tumors. Even if low dose linearity is assumed, as it was in the 1994 proposed rule, a MCLG of 0.3 mg/L would be equivalent to a  $5 \times 10^{-5}$  cancer risk level. EPA concludes that an MCLG based on protection against liver toxicity should be protective against carcinogenicity given that the putative mode of action understanding for chloroform involves cytotoxicity as a key event preceding tumor development. Therefore, the

recommended MCLG for chloroform is 0.3 mg/L. The assessment that forms the basis for this conclusion can be found in the docket for this Notice (USEPA, 1998c).

### 3. External Peer Review of EPA's Reassessment

Three external experts reviewed the EPA reassessment of chloroform (USEPA, 1998c). The peer review generally indicated that the nonlinear approach used for estimating the carcinogenic risk associated with exposure to chloroform was reasonable and appropriate and that the role of a direct DNA reactive mechanism

unlikely. Other comments concerning improved clarity and completeness of the assessment were considered by EPA in revising the chloroform assessment document.

### 4. Summary of Key Observations

Based on the available evidence, EPA concludes that a nonlinear approach should be considered for estimating the carcinogenic risk associated with lifetime exposure to chloroform via drinking water. It should be noted that the margin of exposure approach taken for chloroform carcinogenicity is consistent with conclusions reached in a recent report by the World Health

Organization for Chloroform (WHO, 1997). The 1994 proposed MCLG was zero for chloroform. EPA believes it should now be 0.3 mg/L given that hepatic injury is the primary effect following chloroform exposure, which is consistent with the mode of action understanding for chloroform. Thus, the RfD based on hepatotoxicity is considered a reasonable basis for the chloroform MCLG. EPA believes that the RfD used for chloroform is protective of sensitive groups, including children. Current methods for developing RfDs are designed to be protective for sensitive populations. In the case of chloroform a factor of 10 was used to account for variability between the average human response and the response of more sensitive individuals. Furthermore, the mode of action understanding for chloroform does not indicate a uniquely sensitive subgroup or an increased sensitivity in children.

EPA continues to conclude that exposure to chloroform may have an adverse effect on the public health. EPA also continues to believe the MCL of 0.080 mg/L for TTHMs is appropriate despite the increase in the MCLG for chloroform. EPA believes that the benefits of the 1994 proposed MCL of 0.080 mg/L for TTHMs will result in reduced exposure to chlorinated DBPs in general, not solely THMs. EPA considers this a reasonable assumption at this time given the uncertainties existing in the current health and exposure databases for DBPs in general. Moreover, the MCLGs for BDCM and bromoform remain at zero and thus, a TTHM MCL of 0.080 mg/L is appropriate to assure that levels of these two THMs are kept as low as possible. In addition, the MCL for TTHMs is used as an indicator for the potential occurrence of other DBPs in high pH waters. The MCL of 0.080 mg/L for TTHMs to control DBPs in high pH waters (in conjunction with the MCL of 0.060 mg/L for HAA5 to control DBPs in lower pH waters) and enhanced coagulation treatment technique remains a reasonable approach at this time for controlling chlorinated DBPs in general and protecting the public health. There is ongoing research being sponsored by the EPA, NTP, and the American Water Works Research Foundation to better characterize the health risks associated with DBPs.

#### 5. Requests for Comments

Based on the information presented above, EPA is considering revising the MCLG for chloroform from zero to 0.30 mg/L. EPA requests comments on this possible change in the MCLG and on EPA's cancer assessment for chloroform

based on the results from the ILSI report (1997) and new data.

#### C. Haloacetic Acids

The 1994 proposed rule included an MCL of 0.060 mg/L for the haloacetic acids (five HAAs—monobromoacetic acid, dibromoacetic acid, monochloroacetic acid, dichloroacetic acid, and trichloroacetic acid). An MCLG of zero was proposed for dichloroacetic acid (DCA) based on sufficient evidence of carcinogenicity in animals, and an MCLG of 0.3 mg/L for trichloroacetic acid (TCA) was based on developmental toxicity and possible carcinogenicity. As pointed out in the 1997 NODA, several toxicological studies have been identified for the haloacetic acids since the 1994 proposal (also see USEPA, 1997b).

Since the 1997 NODA, the EPA has evaluated the significance of the 1997 ILSI panel report on the cancer assessment for DCA. EPA has conducted a reassessment of DCA (USEPA, 1998e) using the principles of the EPA 1996 Guidelines for Carcinogen Risk Assessment (USEPA, 1996b), which are considered scientifically consistent with the Agency's 1986 guidelines (USEPA, 1986). This reassessment has been peer reviewed (USEPA, 1998e). Based on the scope of the ILSI report, EPA's own assessment and comments from peer reviewers, the Agency believes that the MCLG for DCA should remain as proposed at zero. This conclusion is discussed in more detail below.

#### 1. 1997 International Life Sciences Institute Expert Panel Conclusions for Dichloroacetic Acid (DCA)

ILSI convened an expert panel in 1996 (ILSI, 1997) to explore the application of the USEPA's 1996 Proposed Guidelines for Carcinogen Risk Assessment (USEPA, 1996a) to the available data on the potential carcinogenicity of chloroform and dichloroacetic acid (as described under the chloroform section). The panel considered data on DCA which included chronic rodent bioassay data and information on mutagenicity, tissue toxicity, toxicokinetics, and other mode of action information.

The ILSI panel concluded that the tumor dose-response (liver tumors only) observed in rats and mice was nonlinear (ILSI, 1997). The panel noted that the liver was the only tissue consistently examined for histopathology. It further concluded that all the experimental doses that produced tumors in mice also produce hepatotoxicity (i.e., most doses used exceeded the maximally tolerated dose). Although the mode of carcinogenic action for DCA was

unclear, the ILSI panel concluded that DCA does not directly interact with DNA. It speculated that the hepatocarcinogenicity was related to hepatotoxicity, cell proliferation, and inhibition of program cell death (apoptosis). The panel concluded that the potential human carcinogenicity of DCA "cannot be determined" given the lack of adequate rodent bioassay data, as well as human data. This conclusion is in contrast to the 1994 EPA proposal in which it was concluded that DCA was a Group B<sub>2</sub> probable human carcinogen. In its current reevaluation of DCA carcinogenicity, EPA disagrees with the panel's conclusion that the human carcinogenic potential of DCA can not be determined. EPA's more recent assessment of DCA data includes published information not available at the time of the ILSI panel assessment. Based on the current weight of the evidence EPA concludes that DCA is a likely human carcinogen as it did in the 1994 proposed rule for the reasons discussed below.

#### 2. MCLG for DCA: EPA's Reassessment of the Cancer Hazard

In the 1994 proposed rule, DCA was classified as a Group B<sub>2</sub>, probable human carcinogen in accordance with the 1986 EPA Guidelines for Carcinogen Risk Assessment (USEPA, 1986). The DCA categorization was based primarily on findings of liver tumors in rats and mice, which was regarded as "sufficient" evidence in animals. No lifetime risk calculation was conducted at that time; EPA proposed an MCLG of zero (USEPA, 1994a).

EPA has prepared a new hazard characterization regarding the potential carcinogenicity of DCA in humans (USEPA, 1998e). The objective of this report was to develop a weight-of-evidence characterization using the principles of the EPA's 1996 Proposed Guidelines for Carcinogen Risk Assessment (USEPA, 1996), as well as to consider the issues raised by the 1997 ILSI panel report. The EPA hazard characterization relies on information available in existing peer-reviewed source documents. Moreover, this hazard characterization considers published information not available to the ILSI panel (e.g., mutagenicity studies). This new characterization addresses issues important to interpretation of rodent cancer bioassay data, in particular, mechanistic information pertinent to the etiology of DCA-induced rodent liver tumors and their relevance to humans.

Based on the hepatocarcinogenic effects of DCA in both rats and mice in multiple studies, and mode of action

related effects (e.g., mutational spectra in oncogenes, elevated serum glucocorticoid levels, alterations in cell replication and death), EPA concludes that DCA should be considered as a "likely" cancer hazard to humans (USEPA, 1998e). This is similar to the 1994 view of a B2, probable human carcinogen, in the proposed rule.

DCA concentrations as low as 0.5 g/L have been observed to cause a tumor incidence in mice of about 80% and in rats of about 20% in a lifetime bioassays, as well as inducing multiple tumors per animal (USEPA, 1998e). Higher doses of DCA are associated with up to 100% tumor incidence and as many as four tumors per animal in a number of studies. Time-to-tumor development in mice is relatively short and decreases with increased dose. The ILSI panel concluded that doses of 1 g/L or greater in mice produced severe hepatotoxicity, and thus exceeded the MTD. They further indicated that there was marked hepatotoxicity at 0.5 g/L of DCA, (albeit not as severe as the higher doses). EPA agrees that there was hepatotoxicity at all the doses wherein there was a tumor response in mice. It should be noted that the MTD selected for the DeAngelo et al. (1991) mouse study was a dose that results in a 10% inhibition of body weight gain when compared to controls. This is within the limits designated in EPA guidelines (USEPA, 1998e). Furthermore, no hepatotoxicity was seen in the rat studies, where DCA induced liver tumors of approximately 20% at the lowest dose, 0.5g/L (USEPA, 1998e). It appears that the ILSI report did not give full consideration to the rat tumor results as part of the overall weight-of-evidence for potential human carcinogenicity. EPA agrees with the ILSI panel, that the rodent assay data are not complete for DCA; for example, full histopathology is lacking for both sexes in two rodent species. This deficiency results in uncertainty concerning the potential of DCA to be tumorigenic at lower doses and at tissue sites other than liver. Nevertheless, the finding of increased tumor incidences as well as multiplicity at DCA exposure levels (0.5 g/L) in both rats and mice where minimal hepatotoxicity and no compensatory replication was seen supports the belief that observed tumors are related to chemical treatment.

Although DCA has been found to be mutagenic and clastogenic, responses generally occur at relatively high exposure levels (USEPA, 1998e). EPA acknowledges that a mutagenic mechanism may not be as important influence of DCA on the carcinogenic process at lower exposure levels as it

might be at higher exposures. Evidence is still accumulating that suggests a mode of carcinogenic action for DCA through modification of cell signaling systems, with down-regulation of control mechanisms in normal cells giving a growth advantage to altered or initiated cells (USEPA, 1998e). The tumor findings in rodents and the mode of action information contributes to the weight-of-evidence concern for DCA (USEPA, 1998e; ILSI, 1997). EPA considers that a contribution of cytotoxicity and compensatory proliferation at high doses cannot be ruled out at this time; however, these effects were inconsistently observed in mice at lower exposure levels, and not at all in mice at 0.5 g/L, or in rats, at all exposure doses. Although the shape of the tumor dose responses are nonlinear, there is, however, an insufficient basis for understanding the possible mechanisms that might contribute to DCA tumorigenesis at low doses, as well as the shape of the dose response below the observable range of tumor responses.

In summary, EPA considers the mode of action through which DCA induces liver tumors in both rats and mice to be unclear. As discussed above, EPA considers the overall weight of the evidence to support placing DCA in the "likely" group for human carcinogenicity potential. This hazard potential is indicated by tumor findings in mice and rats, and other mode of action data using the 1996 guideline weight-of-evidence process. The remaining uncertainties in the data base include incomplete bioassay studies for full histopathology and information on an understanding of DCA's mode of carcinogenic action. The likelihood of human hazard associated with low levels of DCA usually encountered in the environment or in drinking water is not understood. Although DCA tumor effects are associated with high doses used in the rodent bioassays, reasonable doubt exists that the mode of tumorigenesis is solely through mechanisms that are operative only at high doses. Therefore, as in the 1994 proposed rule, EPA believes that the MCLG for DCA should remain as zero to assure public health protection. NTP is implementing a new two year rodent bioassay that will include full histopathology at lower doses than those previously studied. Additionally, studies on the mode of carcinogenic action are being done by various investigators including the EPA health research laboratory.

### 3. External Peer Review of EPA's Reassessment

Three external experts reviewed the EPA reassessment of DCA (USEPA, 1998e). The review comments were generally favorable. There was a range of opinion on the issue of whether DCA should be considered a likely human cancer hazard. One reviewer agreed that the current data supported a human cancer concern for DCA, while another reviewer believed that it was premature to judge the human hazard potential. The third reviewer did not specifically agree or disagree with EPA's conclusion of "likely" human hazard. Other issues raised by the peer review concerned the dose response for DCA carcinogenicity. The peer review generally concluded on the one hand that the mode of action was incomplete to support a nonlinear approach, but on the other hand, the mutagenicity data did not support low dose linearity. One reviewer believed that the possibility of a low dose risk could not be dismissed. Other comments concerning improved clarity and completeness of the assessment were considered by EPA in revising the DCA assessment document.

### 4. Summary of Key Observations

EPA continues to believe that exposure to DCA may have an adverse effect on the public health. Based on the above discussion, EPA considers DCA to be a "likely" cancer hazard to humans. This conclusion is similar to the conclusion reached in the 1994 proposed rule that DCA was a probable human carcinogen (i.e., Group B<sub>2</sub> Carcinogen). EPA considers the DCA data inadequate for dose-response assessment, which was the view in the 1994 proposed rule. EPA, therefore, believes at this time that the MCLG should remain at zero to assure public health protection. The assessment that this conclusion is based on can be found in the docket for this Notice (USEPA, 1998e).

### 5. Requests for Comments

Based on the information presented above, EPA is considering maintaining the MCLG of zero for DCA. EPA requests comments on maintaining the zero MCLG for DCA and on EPA's cancer assessment for DCA in light of conclusions from the ILSI report (1997) and new data.

#### D. Bromate

The 1994 proposed rule included an MCL of 0.010 mg/L and an MCLG of zero for bromate. Since the 1994 proposed rule, EPA has completed and analyzed a new chronic cancer study in male rats and mice for bromate

(DeAngelo *et al.*, 1998). EPA has reassessed the cancer risk associated with bromate exposure and had this reassessment peer reviewed (USEPA, 1998d). Based on this reassessment, EPA believes that the MCLG for bromate should remain as zero.

#### 1. 1998 EPA Rodent Cancer Bioassay

In the cancer bioassay by DeAngelo *et al.* (1998), 78 male F344 rats were administered 0, 20, 100, 200, 400 mg/L potassium bromate (KBrO<sub>3</sub>) in the drinking water, and 78 male B6C3F1 mice were administered 0, 80, 400, 800 mg/L KBrO<sub>3</sub>. Exposure was continued through week 100. Although a slight increase in kidney tumors was observed in mice, there was not a dose-response trend. In rats, dose-dependent increases in tumors were found at several sites (kidney, testicular mesothelioma, and thyroid). This study confirms the findings of Kurokawa *et al.* (1986a and b) in which potassium bromate was found to be a multi-site carcinogen in rats.

#### 2. MCLG for Bromate: EPA's Reassessment of the Cancer Risk

In the 1994 proposal, EPA concluded that bromate was a probable human carcinogen (Group B2) under the 1986 EPA Guidelines for Carcinogen Risk Assessment weight of evidence classification approach. Combining the incidence of rat kidney tumors reported in two rodent studies by Kurokawa *et al.* (1986a), lifetime risks of 10<sup>-4</sup>, 10<sup>-5</sup>, and 10<sup>-6</sup> were determined to be associated with bromate concentrations in water at 5, 0.5, and 0.05 ug/L, respectively.

The new rodent cancer study by DeAngelo *et al.* (1998) contributes to the weight of the evidence for the potential human carcinogenicity of KBrO<sub>3</sub> and confirms the study by Kurokawa *et al.* (1986a, b). Under the principles of the 1996 EPA Proposed Guidelines for Carcinogen Risk Assessment weight of evidence approach, bromate is considered to be a likely human carcinogen. This weight of evidence conclusion is based on sufficient experimental findings that include the following: Tumors at multiple sites in rats; tumor responses in both sexes; and evidence for mutagenicity including point mutations and chromosomal aberrations *in vitro*. It has been suggested that bromate causes DNA damage indirectly via lipid peroxidation, which generates oxygen radicals which in turn induce DNA damage. There is insufficient evidence, however, to establish lipid peroxidation and free radical production as key events responsible for the induction of the multiple tumor responses seen in

the bromate rodent bioassays. The assumption of low dose linearity is considered to be a reasonable public health protective approach for extrapolating the potential risk for bromate because of limited data on its mode of action.

Cancer risk estimates were derived from the DeAngelo *et al.* (1998) study by applying the one stage Weibull model for the low dose linear extrapolation (EPA, 1998d). The Weibull model, which is a time-to-tumor model, was considered to be the preferred approach to account for the reduction in animals at risk that may be due to the decreased survival observed in the high dose group toward the end of the study. However, mortality did not compromise the results of this study (USEPA, 1998d). The animal doses were adjusted to equivalent human doses using body weight raised to the <sup>3</sup>/<sub>4</sub> power as the interspecies scaling factor as proposed in the 1996 EPA cancer guidelines (USEPA, 1996b). The incidence of kidney, thyroid, and mesotheliomas in rats were modeled separately and then the risk estimates were combined to represent the total potential risk to tumor induction. The upper bound cancer potency (q<sup>1\*</sup>) for bromate ion is estimated to be 0.7 per mg/kg/d (USEPA, 1998d). Assuming a daily water consumption of 2 liters for a 70 kg adult, lifetime risks of 10<sup>-4</sup>, 10<sup>-5</sup> and 10<sup>-6</sup> are associated with bromate concentrations in water of 5, 0.5 and 0.05 ug/L, respectively. This estimate of cancer risk from the DeAngelo *et al.* study is similar with the risk estimate derived from the Kurokawa *et al.* (1986a) study presented in the 1994 proposed rule. The cancer risk estimation presented for bromate is considered to be protective of susceptible groups, including exposures during childhood given that the low dose linear default approach was used as a public health conservative approach.

#### 3. External Peer Review of the EPA's Reassessment

Three external expert reviewers commented on the EPA assessment report for bromate (USEPA, 1998d). The reviewers generally agreed with the key conclusions in the document. The peer review indicated that it is a reasonable default to use the rat tumor data to estimate the potential human cancer risk. The peer review also indicated that the mode of carcinogenic action for bromate is not understood at this time, and thus it is reasonable to use a low dose linear extrapolation as a default. One reviewer indicated that it was not appropriate to combine tumor data from

different sites unless it is shown that similar mechanisms are involved. EPA modeled the three tumor sites separately to derive the cancer potencies, and thus did not assume a similar mode of action. The slope factors from the different tumor response were combined in order to express the total potential tumor risk of bromate. Other comments raised by the peer reviewers concerning improved clarity and completeness of the assessment were considered by EPA in revising this document.

#### 4. Summary of Key Observations

EPA continues to believe that exposure to bromate may have an adverse effect on the public health. The DeAngelo *et al.* (1998) study confirms the tumor findings reported in the study by Kurokawa *et al.* (1986a) and contributes to the weight of the carcinogenicity evidence for bromate. EPA believes that the an MCL of 0.010 mg/L and an MCLG of zero should remain for bromate as proposed in 1994. The assessment that this conclusion is based on can be found in the docket for this Notice (USEPA, 1998d).

#### 5. Requests for Comments

Based on the recent two-year cancer bioassay on bromate by DeAngelo *et al.* (1998), EPA is considering maintaining the MCLG of zero for bromate. EPA requests comments on maintaining the zero MCLG for bromate and on EPA's cancer assessment for bromate.

#### IV. Simultaneous Compliance Considerations: D/DBP Stage 1 Enhanced Coagulation Requirements and the Lead and Copper Rule

EPA received comment on the November 3, 1997 **Federal Register** Stage 1 D/DBP Notice of Data Availability that expressed concern regarding utilities' ability to comply with the Stage 1 D/DBP enhanced coagulation requirements and Lead and Copper Rule (LCR) requirements simultaneously. Commentors stated that enhanced coagulation will lower the pH and alkalinity of the water during treatment. They indicated concern that the lower pH and alkalinity levels may place utilities in noncompliance with the LCR by causing violations of optimal water quality control parameters and/or an exceedence of the lead or copper action levels. EPA is not aware of data that suggests that low pH and alkalinity levels cannot be adjusted upward following enhanced coagulation to meet LCR compliance requirements. However, as discussed below, the Agency solicits further comment and data on this issue.

The LCR separates public water systems into three categories: large



(>50,000), medium ( $\leq 50,000$  but  $> 3,300$ ) and small ( $< 3,300$ ). Small and medium systems that do not exceed the lead and copper action levels (90th percentile levels of 0.015 mg/L and 1.3 mg/L, respectively) during the required monitoring are deemed to have optimized corrosion control. These systems do not have to operate under optimal water quality control parameters. Optimal water quality control parameters consist of pH, alkalinity, calcium concentration, and phosphate and silicate corrosion inhibitors. They are designated by the State. Small and medium systems exceeding the action limits must operate under State specified optimal water quality parameters. Large systems must operate under optimal water quality parameters specified by the State unless the difference in lead levels between the source and tap water samples is less than the Practical Quantification Limit (PQL) of the prescribed method (0.005 mg/L).

Maintenance of each optimal water quality control parameter mentioned above (except for calcium concentration) is directly related to meeting specified pH and alkalinity levels at the entry point to the distribution system and in tap samples to establish LCR compliance. In treatment trains that EPA is aware of, utilities have the technological capability to raise the pH (by adding caustic—NaOH,  $\text{Ca}(\text{OH})_2$ ) and alkalinity (by adding  $\text{Na}_2\text{CO}_3$  or  $\text{NaHCO}_3$ ) of the water following enhanced coagulation and before it enters the distribution system. Although certain utilities may need to add chemical feed points to provide chemical adjustment, pH and alkalinity can be maintained at the values used prior to the implementation of enhanced coagulation. Systems that operate with pH and alkalinity optimal water quality control parameters should be able to meet the State-prescribed values by providing pH and alkalinity adjustment prior to entry to the distribution system. Systems that operate without pH and alkalinity optimal water quality control parameters can raise the pH and alkalinity to the levels they were at before enhanced coagulation by providing chemical adjustment prior to distribution system entry.

The goal of calcium carbonate stabilization is to precipitate a layer of  $\text{CaCO}_3$  scale on the pipe wall to protect it from corrosion. As the pH of a water decreases, the concentration of bicarbonate increases and the concentration of carbonate, which combines with calcium to form the desired  $\text{CaCO}_3$ , decreases. At the lower

pH used during enhanced coagulation, it will generally be more difficult to form calcium carbonate. However, post—coagulation pH adjustment will increase the pH and hence the concentration of carbonate available to form calcium carbonate scale. Systems that must meet a specific calcium concentration to remain in compliance with optimal water quality control parameters should not experience an increase in LCR violations due to the practice of enhanced coagulation provided the pH is adjusted prior to distribution system entry and the calcium level in the water prior to and after implementation of enhanced coagulation remains the same.

EPA recognizes that the inorganic composition of the water may change slightly due to enhanced coagulation. For example, small amounts of anions and compounds that can affect corrosion rates ( $\text{Cl}^-$ ,  $\text{SO}_4^{2-}$ ) may be removed or added to the water. The effect of these constituents is difficult to predict, but EPA believes they should be minimal for the great majority of systems due to the generally modest changes in the water's inorganic composition and because alkalinity and pH levels have a greater influence on corrosion rates. Increases in sulfate concentration due to increased alum addition during enhanced coagulation can actually lower the corrosion rates of lead pipe. EPA requests comment on whether changes in the inorganic matrix can be quantified to allow States to easily assess potential impacts to corrosion control.

EPA requests comment on how lowering the pH and alkalinity during enhanced coagulation may cause LCR compliance problems, given that both pH and alkalinity levels can be adjusted to meet optimal water quality parameters prior to entry to the distribution system. EPA also requests comment on whether decreasing the pH and alkalinity during enhanced coagulation, and then increasing it prior to distribution system entry, may increase exceedences of lead and copper action levels.

EPA is currently developing a simultaneous compliance guidance document working with stakeholders. The document will provide guidance to States and systems on maintaining compliance with other regulatory requirements (including the LCR) during and after the implementation of the Stage 1 D/DBP rule and the Interim Enhanced Surface Water Treatment Rule. EPA requests comment on what issues should be addressed in the guidance to mitigate concerns about simultaneous compliance with

enhanced coagulation and LCR requirements. Further, the Agency requests comment on whether the proposed enhanced coagulation requirements and the existing LCR provisions that allow adjustment of corrosion control plans are flexible enough to address simultaneous compliance issues. Is additional regulatory language necessary to address this issue, or is guidance sufficient to mitigate potential compliance problems?

## V. Compliance With Current Regulations

EPA reaffirms its commitment to the current Safe Drinking Water Act regulations, including those related to microbial pathogen control and disinfection. Each public water system must continue to comply with the current regulations while new microbial and D/DBP rules are being developed.

## VI. Conclusions

This Notice summarizes new health information received and analyzed for DBPs since the November 3, 1997 NODA and requests comments on several issues related to the simultaneous compliance with the Stage 1 D/DBP Rule and the Lead and Copper Rule. Based on this new information, EPA has developed several new documents. EPA is requesting comments on this new information and EPA's evaluation of the information included in the new documents. Based on an assessment of the new toxicology information, EPA believes the MCLs and MRDLs in the 1994 proposal, and confirmed in the 1997 FACA process, will not change. Based on the new information, EPA is considering increasing the proposed MCLG of zero for chloroform to 0.30 mg/L and the proposed MCLG for chlorite from 0.080 mg/L to 0.80 mg/L. EPA is also considering increasing the MRDLG for chlorine dioxide from 0.3 mg/L to 0.8 mg/L.

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