0.08 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 (EPA, 1994d). An uncertainty factor of 1000 was used to account for inter-and intra-species differences in response to toxicity (a factor of 100) and to account for use of a LOAEL (a factor of 10).

The 1994 proposal included an MRDLG of 0.3 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; EPA, 1994d). This determination was based on a weight of evidence evaluation of all available health data at that time (EPA, 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 CMA sponsored a two-generation reproductive study in rats (CMA, 1996).

As described in more detail in the 1998 NODA (EPA, 1998a), EPA reviewed the CMA study and completed an external peer review of the study (EPA, 1997d). In addition, EPA reassessed the noncancer health risk for chlorite and chlorine dioxide considering the new CMA study (EPA, 1998d). This reassessment was also peer reviewed (EPA, 1998d). Based on this reassessment, EPA requested comment in the 1998 NODA (EPA, 1998a) on 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 which reinforced the concern for neurodevelopmental effects associated with short-term exposures.

EPA 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 the NOAEL are summarized in EPA (1998d) and included the CMA study as well as previous reports on developmental neurotoxicity and other adverse health effects (EPA, 1998d). EPA continues to believe, as stated in the 1998 NODA (EPA, 1998a), that the RfD for chlorite should be 0.03 mg/kg/d (NOAEL of 3 mg/kg/d with an uncertainty factor of 100) and that a MCLG of 0.8 mg/L is appropriate. EPA has concluded that the RfD for chlorine dioxide should be 0.03 mg/L (NOAEL of 3 mg/kg/d with an uncertainty factor of 100) and that a MRDLG of 0.8 mg/L is appropriate.

c. Summary of Comments. EPA received numerous comments on the 1994 proposal (EPA, 1994a) and 1998 NODA (EPA, 1998a). The major comment from the 1994 proposal was that reliance on the Mobley et al. (1990) study for the MCLG for chlorite and the Orme et al. (1985) study for chlorine dioxide were inappropriate and that the results from the CMA study must be evaluated before any conclusions on the MCLG for chlorite or chlorine dioxide could be drawn. In relation to the 1998 NODA, several commenters supported changing the MCLG for chlorite and MRDLG for chlorine dioxide while others were concerned that the science did not warrant a change in these values. The major comments submitted against raising the MCLG and MRDLG focused on several issues. First, one commenter argued that the 1000-fold uncertainty factor used for chlorite in the proposal should remain in place because the CMA study used to reduce the uncertainty factor was flawed. Second, several commenters indicated that the LOAEL should be set at the lowest dose level (35 ppm) because certain effects at the lowest dose tested may have been missed. Finally, some commenters argued that an additional safety factor should be included to protect children and drinking water consumption relative to the body weight of children should be used instead of the default assumption of 2 L per day and 70 kg adult body weight.

EPA agrees with commenters on the 1994 proposal that the results from the CMA should be factored into any final decision on the MCLG for chlorite and chlorine dioxide. As explained in more detail in the 1998 DBP NODA (EPA, 1998a), EPA considered the findings from the CMA study along with other available data to reach its conclusions regarding the MCLG and MRDLG for chlorite and chlorine dioxide.

EPA disagrees with the commenter who suggested that the 1000-fold uncertainty factor for chlorite should remain because the CMA study was flawed. The study design for the neurodevelopmental component of the CMA study was in accordance with EPA's testing guidelines at the time the study was initiated. EPA had previously reviewed the study protocol for the CMA neurotoxicity component and had approved the approach. While EPA initially had some questions regarding the design of the neurodevelopmental component of the study (Moser, 1997), subsequent information submitted by the CMA provided clarification on certain aspects of the study design (CMA, 1998). EPA agrees that even with the clarifications that there are some limitations with the neurodevelopmental component of the CMA study. EPA believes that the neuropathology components of the CMA study were adequate. The functional operation battery had some shortcomings in that forelimb and hindlimb grip strength and foot splay were not evaluated. EPA believes the results from the motor activity component of the CMA study were difficult to interpret because of the high variability in controls. However, in its evaluation of the MCLG for chlorite and chlorine dioxide, EPA did not rely solely on the CMA study, but used a weight-of-evidence approach that included consideration of several studies. Thus, the shortcomings of one study are offset by the weight from other studies. EPA believes that the CMA study contributes to the weight-of the-evidence. The studies by Orme et al. (1985), Mobley et al. (1990), and CMA (1996) support a NOAEL of 3 mg/kg/d based on neurodevelopmental effects (e.g., decreased exploratory, locomotor behavior, decreased brain weight). Furthermore, the CMA study was reviewed by outside scientists as well as by EPA scientists. EPA's re-assessment for chlorite and chlorine dioxide presented in the 1998 March NODA was reviewed internally and externally in accordance with EPA peer-review policy. The three outside experts who reviewed the Agency's assessment agreed with the NOAEL of 3 mg/kg/day and the derived RfD.

Finally, EPA disagrees that an additional safety factor should be applied to provide additional protection for children or that drinking water consumption relative to the body weight of children should be used in developing the MCLG. 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. In addition, the important exposure is that of the pregnant and lactating female and the nursing pup. The 2 liter per day water consumption and the 70 kg body weight assumptions are viewed as adequately protective of all groups.

Based on a review of all the data and public comments, EPA believes that the MCLG for chlorite should be 0.8 mg/L and the MRDLG for chlorine dioxide should be 0.8 mg/L. EPA believes the MCLG and MRDLG are consistent with the discussions during the regulatory negotiations which recognized the need for an acceptable two-generation reproductive study prior to reducing the uncertainty factors for chlorite and chlorine dioxide. EPA believes the CMA provided an acceptable two-generation study with which to reduce the uncertainty factors. In addition, EPA believes potential health concerns in the proposal with having a MCLG for chlorite significantly below the MCL are no longer relevant because the MCL for chlorite in today's rule will remain at 1.0 mg/L while the MCLG has been revised to 0.8 mg/L. Given the margin of safety that is factored into the estimation of the MCLG of 0.8 mg/L, EPA believes that the MCL of 1.0 mg/L will be protective of public health of all groups, including fetuses and children.

The MCLG for chlorite is based on an RfD of 0.03 mg/kg/d using a NOAEL of 3 mg/kg/d and an uncertainty factor of 100 to account for inter- and intra-species differences. The 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 ingestion of drinking water—EPA,1998u). A more detailed discussion of this assessment is included in the public docket for this rule (EPA, 1998d).

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

$$\text{MCLG for chlorite} = 0.8\ \text{mg/L (Rounded)}$$

For chlorine dioxide the MCLG is based on 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 ingestion of drinking water—EPA, 1998u). A more detailed discussion of this assessment is included in the public docket for this rule (EPA, 1998d).

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

$$\text{MRDLG for chlorine dioxide} = 0.8\ \text{mg/L (Rounded)}$$

8. MCLG for Bromate

a. Today's Rule. The final MCLG for bromate is zero. The zero MCLG is based on a weight-of-evidence evaluation of both the cancer and noncancer effects which indicates there is sufficient laboratory animal data to conclude that bromate is a probable (likely under the 1996 proposed cancer guidelines) human carcinogen. EPA believes the data are insufficient at this time to determine the mode of carcinogenic action for bromate, and therefore a low dose linear extrapolation approach is used to estimate lifetime cancer risk as a default.

b. Background and Analysis. The 1994 proposed rule included a MCLG of zero for bromate based on a determination that bromate was a probable human carcinogen. This determination was based on results from a two species rodent bioassay by Kurokawa et al. (1986a and 1986b) that found kidney tumors in rats. Since the 1994 proposed rule, EPA has completed and analyzed a new chronic cancer study in male rats and mice for potassium bromate (DeAngelo et al., 1998). EPA reassessed the cancer risk associated with bromate exposure (EPA, 1998e), had this reassessment peer reviewed (EPA, 1998e), and presented its findings in the March 1998 NODA (EPA, 1998a). The new rodent cancer study by DeAngelo et al. (1998) contributes to the weight of the evidence for the potential human carcinogenicity of potassium bromate and confirms the study by Kurokawa et al. (1986 a,b).

c. Summary of Comments. Several commenters supported the zero MCLG for bromate. Others believed the MCLG of zero was not justified because there is evidence of a carcinogenic threshold. This evidence indicates that bromate causes DNA damage indirectly via lipid peroxidation, which generates oxygen radicals which in turn induce DNA damage. Other commenters argued that even if there is no carcinogenic threshold, EPA has overstated the potency of bromate by using the linearized multistage model and should instead use the Gaylor-Kodell model.

In response, EPA disagrees with commenters who believed that the zero MCLG was inappropriate. At this time, under the principles of both the 1986 EPA Guidelines for Carcinogen Risk Assessment (EPA, 1986) and the draft 1996 EPA Proposed Guidelines for Carcinogen Risk Assessment (EPA, 1996b) weight-of-evidence approach, bromate is considered to be a probable or likely human carcinogen. This weight of evidence conclusion of potential human carcinogenicity 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 in vitro genotoxicity assays. Furthermore, EPA believes there is insufficient evidence at this time to draw conclusions regarding the mode of carcinogenic action for bromate. EPA acknowledges there are studies available showing that bromate may generate oxygen radicals which increase lipid peroxidation and damage DNA. However, no data are available that link this proposed mechanism to tumor induction. Thus, EPA believes that while there are studies which provide some evidence to support the commenters' claims, these studies are insufficient at this time to establish