

and colon cancer. The Stage 1 DBPR (USEPA 1998c) includes additional discussion of colon cancer risks associated with DBP exposure.

c. *New rectal cancer studies.* The evidence for an association between DBPs and rectal cancer is stronger than for colon cancer. Yang *et al.* (1998) and Hildesheim *et al.* (1998) both found associations between chlorinated drinking water exposure and rectal cancer, and the associations had a similar magnitude in both sexes. Hildesheim *et al.* also found an association in both sexes with lifetime average THM concentration. The consistency of the dose-response trends, the consistency between sexes, and the apparent control of important potential confounders in this study all support the observed associations.

d. *Other cancers.* Two new human epidemiology studies support the possibility of an association between DBPs and kidney cancer. Yang *et al.* (1998) found a positive association for both males and females between consumption of chlorinated drinking water and kidney cancer. Koivusalo *et al.* (1998) found a small, statistically significant, exposure-related excess risk for kidney cancer for males. The association for females was not significant in the Koivusalo *et al.* 1998 study. The current database for this endpoint of cancer, however, is insufficient to conclude an association.

Cantor *et al.* (1999) studied brain cancer, focusing on gliomas. None of the exposure variables were related to brain cancer among females, but males showed a statistically significant, monotonically increasing risk associated with duration of exposure to chlorinated surface water. This study suggests a possible association between chlorination byproducts and gliomas; however, the evidence from this study is not strong enough to support a conclusion of a causal association.

Infante-Rivard *et al.* (2001) conducted a population-based case-control study in Quebec Province, Canada, to examine possible associations between

childhood acute lymphoblastic leukemia and THMs. There were no associations with leukemia for any of the exposure indices for total THM, or specific THMs. Therefore, the study does not provide evidence of an association between any of the exposure variables and childhood leukemia.

3. Review of the Cancer Epidemiology Literature (WHO 2000)

The International Programme on Chemical Safety (IPCS) report on disinfectants and disinfection byproducts (WHO 2000) concludes that results of analytical epidemiological cancer studies are insufficient to support a causal relationship for bladder, colon, rectal, or any other cancer and chlorinated drinking water or THMs. The report notes that there is better evidence for an association between exposure to chlorinated surface water and bladder cancer than for other types of cancer. The WHO also concludes that based on the large number of people exposed to chlorinated drinking water, there is a need to address this potential health concern.

E. Cancer and Other Toxicology

Few new cancer toxicology studies have been completed since the Stage 1 DBPR was finalized in December 1998. The information provided in the following sections adds to the toxicology database and provides additional support for the Stage 2 DBPR to control DBP peaks (e.g., high TTHM and HAA5 levels) throughout distribution systems, but does not change the quantitative assessment of the MCLGs.

1. EPA Criteria Documents

To date, EPA has established lifetime cancer risk levels for four DBPs (bromoform, bromodichloromethane, bromate, and dichloroacetic acid) classified as "probable" carcinogens, as promulgated in the Stage 1 DBPR and reported in the Integrated Risk Information System (IRIS). Although researchers have continued to assess the

cancer risks of DBPs, there has been little change in the overall DBP carcinogenicity database since the Stage 1 DBPR.

The most significant new publication since the Stage 1 DBPR was a study of DCAA tumorigenicity in mice by DeAngelo *et al.* (1999). The Agency has used the data from this study to revise the slope factor for DCAA and a drinking water 10^{-6} lifetime cancer risk concentration. The slope factor is a measure of the potency of a carcinogen while the 10^{-6} lifetime cancer risk concentration provides an estimate of the concentration of a contaminant in drinking water that is associated with an estimated excess lifetime cancer risk of one in a million (Table III-3).

Another significant advancement beyond the Stage 1 DBPR was the evaluation of the chloroform tumorigenicity data on the basis of its nonlinear mode of action following the draft 1999 proposed Guidelines for Carcinogen Risk Assessment (USEPA 1999a). The new chloroform assessment became available on IRIS (2001) in October, 2001 (see section V for a more detailed discussion).

The Criteria Documents for bromoform, bromodichloromethane, dibromochloromethane, and dichloroacetic acid that support the Stage 2 proposal include cancer slope factors and 10^{-6} lifetime cancer risk concentrations that have been modified from their Stage 1 values in order to reflect the methodology proposed in the 1996/1999 draft cancer guidelines (USEPA 1999a) (Table III-3). These include the values based on the Maximum Likelihood Estimate of the dose producing effects in 10 percent of the animals (ED_{10}) and from the lower 95 percent confidence bound on that value (LED_{10}). Except for dibromochloromethane, which is classified as a possible human carcinogen, the DBPs in Table III-3 (and bromate as noted previously) are classified as probable human carcinogens.

TABLE III-3.—QUANTIFICATION OF CANCER RISK

Disinfection byproduct	Risk factors from LED_{10}		Risk factors from ED_{10}	
	Slope factor (mg/kg/day) $^{-1}$	10^{-6} Risk concentration (mg/L)	Slope factor (mg/kg/day) $^{-1}$	10^{-6} Risk concentration (mg/L)
Bromodichloromethane	0.034	0.001	0.022	0.002
Bromoform	0.0045	0.008	0.0034	0.01
Dibromochloromethane	0.04	0.0009	0.017	0.002
Dichloroacetic Acid	0.048	0.0007	0.014	0.003