

classifying exposure on the basis of chlorination (yes/no) and amount of natural organic matter in the water. Statistically significant associations with exposure were found for risks of any birth defect, cardiac, respiratory, and urinary tract defects. For specific birth defects, a statistically significant association was found for a defect of the septum in the heart.

Windham *et al.*, 2003, assessed the relationship between exposure to THMs in drinking water and characteristics of the menstrual cycle among 403 women who provided daily urine samples for an average of 5.6 cycles. Women whose tap water had TTHM levels more than 0.060 mg/l had statistically significantly shorter menstrual cycles than women whose tap water had lower TTHMs. On average, the menstrual cycles of women with the higher levels of TTHMs were one day shorter than cycles of women with the lower levels (adjusted difference: -1.1 days, 95% confidence interval: -1.8 days to -0.4 days). This shortening occurred during the first half of the cycle, before ovulation (adjusted difference: -0.9 days; 95% confidence interval: -1.6 days to -0.2 days). There were no changes in bleed length or in the regularity of the cycles. Based on their study, Windham *et al.*, 2003, suggested that THM exposure may affect ovarian function, but since this is the first study to examine human menstrual cycle variation in relation to THM exposure, more research is needed to confirm the relationship. The public health implication of a small reduction in menstrual cycle length is not clear, but if THMs are related to disturbances in ovarian function, that might provide insight into the observed associations between THMs and a variety of adverse reproductive outcomes.

EPA's epidemiology research program continues to examine the relationship between exposure to DBPs and adverse developmental and reproductive effects.

The Agency is supporting several studies using improved study designs to provide better information for characterizing potential risks. Details on EPA's epidemiology research program can be found at <http://cfint.rtpnc.epa.gov/dwportal/cfm/dwMDBP.cfm>.

#### B. Reproductive and Developmental Toxicology

Several new reproductive and developmental toxicology studies have become available since the December 1998 Stage 1 DBPR. This discussion presents some conclusions derived from these studies and reports, including hazard identification, as well as implications for the Stage 2 DBPR.

EPA conducted a literature search of animal toxicology studies on chronic and subchronic DBP exposures associated with reproductive and developmental health effects, evaluated the current reproductive and developmental toxicological database for several individual DBPs, and assessed two independent reviews (Tyl 2000 and WHO 2000). As a result of these analyses, EPA has concluded that although the database is not strong enough to quantify risk, it is sufficient to support a hazard concern. This hazard concern supports the need to address potential reproductive and developmental health effects in the Stage 2 DBPR. The following section describes how this conclusion was reached.

#### 1. EPA Analysis and Research

Since the Stage 1 DBPR, EPA has continued to support reproductive and developmental toxicological research on various disinfection byproducts through extramural and intramural research programs. Information on EPA's toxicology programs can be found at <http://www.epa.gov/nheerl/>. These studies, along with data on several DBPs

published after the 1998 Stage 1 DBPR, are summarized in the updated children's health document, "Health Risks to Fetuses, Infants, and Children: A Review" (USEPA 2003a).

In addition to this compilation of data, EPA has also prepared individual health criteria documents that provide detailed summaries of the relevant new information, as well as an overall characterization of the human health risks from exposure to certain DBPs (USEPA 2003b-USEPA 2003h, USEPA 2003l). From these new evaluations, EPA has concluded that several new studies on individual byproducts contribute to the weight of evidence for an association between DBP exposure and adverse effects on the developing fetus and reproduction. These effects include fetal loss, cardiovascular effects, and male reproductive effects and are associated with bromodichloromethane (BDCM), dichloroacetic acid (DCAA), trichloroacetic acid (TCAA), bromochloroacetic acid (BCAA), and dibromoacetic acid (DBAA). The data from these new studies do not change the MCLGs that were established as a part of the Stage 1 DBPR.

#### 2. Tyl 2000

Tyl (2000) conducted a comprehensive review of the reproductive and developmental toxicology literature on DBPs representing over thirty-five studies. Adverse effects reported by these studies include developmental effects, whole litter resorption, reduced fetal body weights, and male reproductive effects (*e.g.*, inhibited spermiation, increased abnormal sperm). Many of these studies are categorized as high-dose, short-term screening studies that can be used to assess potential hazard (Table III-1), while the long term, two-generation reproduction studies could be an appropriate basis for quantitative risk assessment.

Disinfectant/DBP	Screening <sup>1</sup>	Developmental <sup>2</sup>	Two-generation <sup>3</sup> reproductive
Chlorine .....	.....	✓	
Chlorine Dioxide .....	✓	✓	
Chloramine .....	.....	✓	
Chloroform .....	✓	✓	✓
Bromoform .....	✓	✓	✓
Bromodichloromethane .....	✓	✓	in progress
Dibromochloromethane .....	✓	✓	
Monochloroacetic acid .....	✓	✓	
Dichloroacetic acid .....	✓	✓	
Trichloroacetic acid .....	✓	✓	
Monobromoacetic acid .....	✓	✓	
Dibromoacetic acid .....	✓	✓	in progress
Tribromoacetic acid .....	✓	.....	
Bromochloroacetic acid .....	✓	.....	in planning stage
Bromodichloroacetic acid .....	✓	.....	
Dibromochloroacetic acid .....	✓	.....	