

Disinfectant/DBP	Screening <sup>1</sup>	Developmental <sup>2</sup>	Two-generation <sup>3</sup> reproductive
Chloroacetonitrile .....	✓	.....	
Dichloroacetonitrile .....	✓	✓	
Trichloroacetonitrile .....	✓	✓	
Bromoacetonitrile .....	✓	✓	
Dibromoacetonitrile .....	✓	.....	
Tribromoacetonitrile .....	.....	.....	
Bromochloroacetonitrile .....	✓	✓	
Propanal .....	✓	✓	
1,1 Dichloropropanone .....	✓	.....	
Hexachloropropanone .....	✓	.....	
Dichloromethane .....	✓	.....	
MX .....	✓	✓	
Bromate .....	✓	.....	
Chlorite .....	✓	✓	✓

✓ denotes the availability of at least one study in the following categories.

<sup>1</sup> Screening studies are for hazard identification. These types of studies include the following: whole embryo culture, NTP 35-day screening studies, Chernoff-Kavlock and its modified version, and short-term male reproductive toxicity screen.

<sup>2</sup> Developmental studies are used for dose-response determinations.

<sup>3</sup> Two-generation reproductive studies are multi-generation reproductive toxicity studies used for dose-response determinations.

Tyl concluded that, “The screening studies, performed for a number of DBPs, are ‘adequate’ and ‘sufficient’ only to detect potent reproductive/

developmental toxicants for hazard identification.” Tyl further confirms that the database identifies certain DBPs with potential reproductive or

developmental effects (Table III–2) and these are discussed further in the next section.

TABLE III–2.—POTENTIAL HAZARDS OF DBPs FOR REPRODUCTIVE AND DEVELOPMENTAL EFFECTS (ADAPTED FROM TYL, 2000)

Type of hazard	Disinfection byproducts
Developmental defects .....	TCAA, DCAA, MCAA and chlorite.
Whole litter resorption .....	Chloroform, bromoform, BDCM, DBCM, DCAA, TCAA, DCAN, and TCAN.
Fetotoxicity (reduced fetal body weights, increased variations) .....	Chloroform, BDCM, DBCM, DCAA, TCAA, DCAN, TCAN, DBAN, BCAN, MCAN.
Male reproductive effects (spermatotoxic) .....	DCAA, DBAA, BDCM.

a. *Developmental defects.* Tyl noted that adverse developmental effects that were reported from whole embryo culture tests on the developing heart, neural tube, eye, pharyngeal arch, and somites tended to be associated with haloacetic acids tested at high doses (Hunter *et al.* 1996; Saillenfait *et al.* 1995, Smith *et al.* 1989). Cardiovascular effects were also observed in vivo for TCAA and DCAA from developmental segment II toxicity studies at high doses (Smith *et al.* 1988, 1990).

b. *Whole litter resorption.* Whole litter resorption, likened to miscarriage or spontaneous abortion by Tyl 2000, was also observed at high doses in vivo for a range of DBPs as indicated in Table III–2 (Murray *et al.* 1979, Balster and Borzelleca, 1982, Narotsky *et al.* 1992; 1997 a, b; Bielmeier *et al.* 2001; Smith *et al.* 1990; Smith *et al.* 1988). Tyl noted that similar effects were observed in several epidemiology studies.

c. *Fetal toxicity.* Fetal toxic effects such as reduced fetal body weights and increased variation were observed at high doses in vivo for a range of DBPs (e.g., chloroform, BDCM, DBCM, DCAA,

TCAA, DCAN, TCAN, DBAN, BCAN) (Thompson *et al.* 1974; Schwetz *et al.* 1974; Murray *et al.* 1979; Ruddick *et al.* 1983; Narotsky *et al.* 1992, Balster and Borzelleca, 1982; Smith *et al.* 1990). Again, Tyl noted a similarity in effects observed in epidemiology studies.

d. *Male reproductive effects.* Animal toxicology studies report increased risks of adverse effects on the male reproductive system from high doses of haloacetic acids and other DBPs that have not been studied in human epidemiology studies. Male reproductive effects (e.g., inhibited spermiation, reduced epididymus, sperm number and motility, increased abnormal sperm, testicular damage and inhibited in vitro fertilization) were reported for DCAA, DBAA, TCAA and BDCM (Toth *et al.* 1992, Linder *et al.* 1997a, b; Linder *et al.* 1994a, b; Cosby and Dukelow 1992). Dr. Tyl noted that the adverse effects observed in the male reproductive toxicity screening studies (Toth *et al.* 1992; Linder *et al.* 1994a, b; 1997a, b) are confounded by a short dosing regimen and administration of test doses to only adult males.

From her review of the comprehensive animal toxicology database on reproductive and developmental health effects from DBP exposure, Dr. Tyl concludes that “some DBPs have an intrinsic capacity to do harm, specifically to the developing conceptus and the male (and possibly the female) reproductive system”. She concludes that “there is hazard to development from the haloacetic acids (TCAA, DCAA, MCAA) and acetate; to development from chloroform, bromoform, BDCM, DBCM, DCAA, TCAA, DCAN, and TCAN expressed as full litter resorption (which most likely indicates maternal endocrine/uterine effects); and fetotoxicity for chloroform, BDCM, DBCM, DCAA, TCAA, DCAN, TCAN, DBAN, BCAN, CAN, acetaldehyde, and possibly formaldehyde. Reproductive hazard exists for DCAA, DBAA, and possibly formaldehyde in males and for TCE and possibly formaldehyde in females.”