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OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

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Memorandum

SUBJECT: Formation of Bromate Ion from Application of Dihalodialkylhydantoin Sanitizers (BCDMH and DBDMH) into Swimming Pools and Associated Cancer Risks for Swimmers. DP Barcode 324327.

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Attached is an assessment of the risks associated with the formation of bromate ion in swimming pools sanitized with dihalodialkylhydantoin, specifically BCDMH [1-Bromo-3-chloro-5,5-dimethylhydantoin] and DBDMH [1,3-Dibromo-5,5-dimethylhydantoin].

EXECUTIVE SUMMARY

This memorandum assesses the potential cancer risks for swimmers exposed to bromate ion as a result of application of BCDMH and DBDMH as swimming pool sanitizers. The formation of bromate ion, a known human carcinogen, has been reported to the EPA for dihalodialkylhydantoin applications when used to sanitize swimming pools. Given the labeled uses of dihalodialkylhydantoin, the formation of bromate ion occurs when the products are used in the presence of UV light and oxidizers (i.e., outdoor swimming pools). Pool water concentrations of bromate ion in outdoor swimming pools were submitted by the ACC Brominated Biocides Panel as well as by Arch Chemicals, Inc. ACC (2005) also provided data on the formation of bromate ion in indoor pools.

Cancer risk estimates for swimmers in outdoor pools sanitized by BCDMH and DBDMH are provided in this memorandum. Two data submissions indicate bromate ion concentrations from 0.56 ppm up to 2.25 ppm for applications of BCDMH and/or DBDMH in outdoor pools and 0.14 ppm for indoor pools. EPA has presented a range of cancer risk estimates associated with incidental ingestion of pool water at various concentrations of bromate ion. The cancer risk estimates represented by applications following the label directions (i.e., ACC 2005) in outdoor pools range from 1.3E-4 to 8.6E-5. The indoor pool cancer risk estimates are ~2E-5. Regulatory conclusions are out of the scope of this document.

1.0 INTRODUCTION

1.1 Purpose

The Antimicrobials Division (AD) received a 6(a)2 submission indicating potential risks associated with the use of bromine-based sanitizers and HOBr/Br⁻ i.e., BCDMH and DBDMH (Arch 2005). The swimming pools in the Arch submission associated with high levels of bromate ion were taken from pools treated with an exaggerated sodium bromide application. In addition, AD received data on bromate ion formation in outdoor swimming pools that were treated, according to the submission letter, under “*realistic*” pool use conditions and “*treated according to label directions*” for BCDMH (ACC 2005). AD has provided cancer risk estimates based on the bromate ion concentrations from both data submissions.

1.2 Chemical Identification

Three chemicals are considered in this document: bromate ion, BCDMH, and DBDMH. Table 1 presents the chemical identification information for the three chemicals.

	Bromate ^a	BCDMH	DBDMH
OPP Chemical Code	013908	006315	006317
CAS Number	7789-38-0 ^a	16079-88-2	77-48-5
Molecular Formula	NaBrO ₃	C ₅ H ₆ BrClN ₂ O ₂	C ₅ H ₆ Br ₂ N ₂ O ₂

^a The source of bromate is sodium bromate salt, and hence the chemical identifiers for sodium bromate are provided.

1.3 Physical/Chemical Properties

The physical and chemical properties of bromate, BCDMH, and DBDMH are provided in Table 2. The BCDMH and DBDMH applied to swimming pool will result in swimmers being exposed to bromate ion in outdoor uses.

Table 2. Physical/Chemical Properties of Sodium Bromate, BCDMH, and DBDMH			
Property	Sodium Bromate	BCDMH	DBDMH
Molecular Weight (g/mol)	150.89	241.49	285.93
Melting Point (° C)	314.4	139	196.5
Boiling Point (° C)	718	356	368.5
Physical State	Solid powder	Solid powder	Solid powder
Vapor Pressure (mm Hg)	4.19×10^{-18}	6.6×10^{-6}	3.1×10^{-7}
Solubility (water, g/L)	364	8.3	60.7
Log K _{ow}	-7.17	-0.94	-2.25
Henry's Law Constant (atm-m ³ /mol)	8.319×10^{-25}	2.5×10^{-6}	1.96×10^{-14}

EPI Suite Version 3.11, USEPA, 2003.
USEPA 2005a.

2.0 USE INFORMATION

Formulations containing dihalodialkylhydantoin products are available as tablets/briquettes, powder, and granules. Concentrations of registered products range from 8.6% to 99.4%. Table 3 provides a listing of the dihalodialkylhydantoin products used in swimming pools. This listing is based on the comments received in the hydantoin Reregistration Eligibility Decision (RED) document and it differs slightly from the listing in EPA's OPPIN system. Because this memorandum is not a review of the labels per se, rather a response to the two data submissions, the accuracy of the label review is deferred to the hydantoin RED document.

Uses	Formulation	EPA Reg. No.
Swimming Pools	Tablet / Briquette	3377-72 5185-420 7616-66 1729-132 7124-104 6836-116, -118, -314, -317 66397-2, -3 57787-24 8622-41 67262-23
	Powder	6836-211, -316
	Granular	6836-250, -251, -315 5185-490 3377-61

Note: This listing is based on comments received for the hydantoin RED. The listing conflicts with the EPA OPPIN system. Resolution of the differences in product classification is deferred to the RED.

3.0 SUMMARY OF TOXICITY CONCERNS RELATING TO EXPOSURES

There are circumstances where applications of BCDMH and DBDMH form bromate ion. Bromate is a known human carcinogen. The cancer slope factor selected for bromate is listed in Table 4.

Exposure Scenario	Cancer Slope Factor	LOC for Risk Assessment	Study and Toxicological Endpoints
Bromate Cancer Slope Factor	0.7 (mg/kg/day) ⁻¹	For general population 1E-6	USEPA 2001, Kurokawa et al 1986a, Kurokawa et al 1986b, and DeAngelo 1998

4.0 RESIDENTIAL AND PUBLIC ACCESS PREMISES

4.1 Residential Exposure/Risk Pathway

Residential uses of dihalodialkylhydantoin products include use in swimming pools and hot tubs/spas. There are postapplication exposures associated with these uses. This memorandum provides risk estimates for the dihalodialkylhydantoin products that may generate bromate ion in swimming pools.

4.2 Formation of Bromate Ion In Outdoor Swimming Pools

The potential for bromate ion formation in outdoor swimming pools occurs in the presence of UV light and oxidizers (Dionex, 1995). EPA received a 6(a)2 submission that indicated concentrations of bromate in outdoor swimming pools when applying BCDMH and DBDMH activated with $\text{Ca}(\text{OCl})_2$ to produce hypobromous acid (HOBr/OBr^-) (Arch 2005). In response to the data developed by Arch Chemicals, Inc., the ACC Brominated Biocides Panel submitted additional data on bromate ion concentrations in outdoor/indoor pools treated with BCDMH. EPA is not concerned at this time with spas because incidental ingestion is expected to be negligible.

The bromate ion pool water concentrations used in this assessment are based on information provided in both of the data submissions (Arch 2005 and ACC 2005). The data collected by the ACC Brominated Biocides Panel were summarized in a letter submitted to EPA. These data are summarized in Table 5. EPA has not received the actual study report with specifics of the study (e.g., sampling/analysis methods).

Table 5. Bromate Ion Conc in Pool Water after Application of BCDMH (ACC 2005).

Pool Type and Location	Number of Samples	Bromate ion (ppm)
Outdoor -- Residential	75	0.56 ± 0.62
Outdoor -- Commercial	51	0.90 ± 0.62
Indoor -- Commercial	17	0.14 ± 0.16

The Arch (2005) bromate ion pool water concentrations submitted in the 6(a)2 are summarized in Table 6. For a complete review of the individual pool treatments see Arch (2005). Sampling and analysis methods were not reported. The application of sodium bromide at 25 ppm and in some pools DMH at 300 ppm do not appear to be label directed applications and may have resulted in the higher concentrations of bromate ion compared to that reported by ACC (2005).

Table 6. Bromate Ion Conc in Pool Water after Application of BCDMH/DBDMH/NaBr (Arch 2005).

Pool Number	Chemical	Bromate ion (ppm)
1	DBDMH	1.7
2	DBDMH	4
3	Sodium bromide (activated)	125 (est. by Arch from regression)
4	DBDMH	0.7
5	DBDMH	1.6
6	BCDMH	4
7	BCDMH	3
8	Sodium bromide (activated)	15 (est. by Arch from regression)
9	BCDMH	1.2
10	BCDMH	0.8
Average	DBDMH	2.0
Average	BCDMH	2.25

Average	DBDMH + BCDMH	2.13
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Note: Pools were initially treated with 25 ppm NaBr (250 ppm for NaBr treated pools). Some pools (#4, 5, 9, and 10) also initially treated with 300 ppm DMH.

4.3 Exposure Route and Input Parameters for Swimming

EPA's concern for bromate ion is based on the oral route of exposure. The dermal exposure route is not of concern because the bromate ion will not penetrate the skin (i.e., low permeability constant (Kp)). The inhalation route of exposure is also expected to be negligible due to the very low vapor pressure of bromate (estimated $\sim 10^{-18}$ mm Hg). Oral exposure from incidental ingestion occurs while swimming but is expected to be negligible while sitting in a spa/hot tub (i.e., head is above water line). Therefore, the cancer risk assessment for bromate is limited to incidental oral exposure to swimmers in swimming pools.

The SWIMODEL 3.0 was developed by EPA as a screening tool to conduct exposure assessments of pesticides found in swimming pools (Versar, 2003). The SWIMODEL uses screening exposure assessment equations to calculate the high end exposure for swimmers expressed as a mass-based intake value (mg/event). The model focuses on potential chemical intakes only and does not account for metabolism or excretion. Detailed information and the downloadable executable file are available at <http://www.epa.gov/oppad001/swimodel.htm>. Although, the actual model was not used in this assessment, the same equations as provided in the SWIMODEL User's Manual (version 3.0) were used in a spreadsheet format to estimate postapplication incidental oral exposures to bromate ion when applying sodium bromide to outdoor swimming pools.

The input parameters for ingestion exposure while swimming are presented in Table 7. Exposure time and frequency for non-competitive swimmers are based on the summary statistics from the National Human Activity Pattern Survey (NHAPS) (USEPA, 1996) whereas competitive swimmer exposure time and frequency data are based on the Agency's review of the American Chemistry Council (ACC) study (ACC, 2002).

Table 7. Parameters for Swimming Ingestion Exposure						
Age	Adult		Child 7-10 yrs		Child 11-14 yrs	
Type of Swimmer	Comp.	Non-Comp.	Comp.	Non-Comp.	Comp.	Non-Comp.
Cw (mg/L)	6.0	6.0	6.0	6.0	6.0	6.0
IgR (L/hr)	0.0125	0.0125	0.05	0.05	0.025	0.05
ET(hr/day)	3	mean=0.93	1	mean=1.47	2	mean=1.37
		90 th %=2		90 th %=3		90 th %=2.6
EF (events/year)	238	88	65	102	189	82
BW(kg)	70	70	30	30	48	48

Where: Cw is chemical concentration in pool water, IgR is ingestion rate of pool water, ET is exposure time, EF is exposure frequency, and BW is body weight.

4.3.3 Cancer Risks

The potential cancer risks resulting from incidental oral exposure of bromate ion in outdoor swimming pools treated with dihalodialkylhydantoins are estimated from the following two equations:

$$(1) \quad LADD = Cw \times IgR \times ET \times EF \times ED / BW \times AT \times 365 \text{ d/yr}$$

where:

LADD = Lifetime average daily dose (mg/kg/day);
 Cw = Chemical concentration in pool water (mg/L);
 IgR = Ingestion rate of pool water (L/hour);
 ET = Exposure time, mean (hours/day);
 EF = Exposure frequency (events/year);
 ED = Exposure duration (years);
 BW = Body weight; and
 AT = Averaging time (70 year lifetime).

$$(2) \quad \text{Cancer Risk} = LADD \text{ (mg/kg/day)} \times \text{Cancer Slope Factor of } 0.7 \text{ (mg/kg/day)}^{-1}$$

In addition to estimating the LADD, EPA's new *Cancer Assessment Guidelines and Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens* recommend that additional safety factors for various age groups are warranted for mutagens (USEPA 2005d and 2005e). Bromate is a mutagen, as noted in the following IRIS discussion (the reader is referred to IRIS, <http://www.epa.gov/iris/subst/1002.htm>, for a listing of the primary citations noted below):

"The genotoxicity of bromate has been evaluated in a variety of in vitro and in vivo systems. It has tested positive in the Salmonella typhimurium assay in the presence of metabolic activation and in an in vitro test for chromosomal aberrations that uses Chinese hamster fibroblasts (Ishidate et al., 1984). Dose-dependent increases in the number of aberrant metaphase cells were observed following single oral doses of potassium bromate to Long-Evans rats (Fuji et al., 1988). Bromate caused significant increases in the number of micronuclei following either i.p. injection (Hayashi et al., 1988; Awogi et al., 1992) or gavage dose (Hayashi et al., 1989; Nakajima et al., 1989) in mice. Also, i.p. injection of bromate in F344 rats resulted in significantly increased micronuclei in reticulocytes (Sai et al., 1992a). Bromate was cytotoxic, increased the frequency of cells with micronuclei, increased the number of chromosome aberrations, and increased DNA migration in a series of assays that used V79 Chinese hamster cells (Speit et al., 1999). Furthermore, potassium bromate clearly induced gene mutations at the HPRT locus of V79 Chinese hamster cells (Speit et al., 1999)."

The additional safety factors or age-dependent adjustment factors (ADAFs) recommended in the EPA guidance are reported in Table 8.

Table 8. Age-dependent Adjustment Factors (ADAFs).

Age Group	Safety Factor or Age-Dependent Adjustment Factor (ADAF)
0 to 2 years olds	10x
2 to 16 year olds	3x
16 to 70 year olds	1x

To estimate potential cancer risk, the safety factors have been applied to the risk estimates for each of the specific age groups (e.g., 0 to 2 year olds LADD mg/kg/day x CSF x 10). Cancer risks for the 5 age groups are then summed to estimate the potential lifetime cancer risk.

The estimated LADDs and potential cancer risks for competitive and non competitive swimmers using the age-dependent adjustment factors (ADAF or safety factor) are presented in Table 9 for ACC (2005) and Table 10 for Arch (2005). The cancer risks are presented for various age groups with the total risk representing a "lifetime" of swimming.

Based on these assumptions, the cancer risks estimated from the water concentrations in the ACC (2005) submission range from 1.3E-4 to 8.6E-5 for swimmers in outdoor pools and ~2E-5 for indoor pools. The cancer risks estimated from the water concentrations in the Arch (2005) submission range from 3.5E-4 to 2.9E-4 for swimmers in outdoor pools. The non competitive swimmer risks are slightly higher than the competitive swimmer risks, but nearly equivalent.

Table 9. ACC (2005) Submitted Bromate Ion Water Concentrations for BCDMH Applications and Cancer Risks for Swimmers.

Parameters	Residential Outdoor		Commercial Outdoor		Commercial Indoor	
	Competitive	Noncomp	Competitive	Noncomp	Competitive	Noncomp
$LADD = Cw \times IgR \times ET \times EF \times ED / BW \times AT \times 365 \text{ d/yr}$	0.56	0.56	0.9	0.9	0.14	0.14
Concentration of ai in pool water (mg/L)	na	0.05	na	0.05	na	0.05
Ingestion Rate of pool water (L/hr)	na	0.05	na	0.05	na	0.05
child 0-2 yr	0.05	0.05	0.05	0.05	0.05	0.05
child 3-6 yr	0.025	0.05	0.025	0.05	0.025	0.05
child 7-10 yr	0.0125	0.025	0.0125	0.025	0.0125	0.025
child 11-15 yr						
adult 16+						
Exposure Time (hr/day)						
ET						
child 0-2 yr	na	0.8	na	0.8	na	0.8
child 3-6 yr	na	1.44	na	1.44	na	1.44
child 7-10 yr	1	1.47	1	1.47	1	1.47
child 11-15 yr	1.65	1.4	1.65	1.4	1.65	1.4
adult 16+	1.83	0.97	1.83	0.97	1.83	0.97
Exposure Frequency (days/yr)						
EF						
child 0-2 yr	na	64	na	64	na	64
child 3-6 yr	na	106	na	106	na	106
child 7-10 yr	65	102	65	102	65	102
child 11-15 yr	189	82	189	82	189	82
adult 16+	238	87	238	87	238	87
Exposure Duration (yr)						
ED						
child 0-2 yr	na	2	na	2	na	2
child 3-6 yr	na	4	na	4	na	4
child 7-10 yr	4	4	4	4	4	4
child 11-15 yr	5	5	5	5	5	5
adult 16+	22	30	22	30	22	30
Averaging Time (yr)	70	70	70	70	70	70
Body weight (kg)						
BW						
child 0-2 yr	na	10	na	10	na	10

	na	19	na	19	na	19	na	19
child 3-6 yr	na	19	na	19	na	19	na	19
child 7-10 yr	30	30	30	30	30	30	30	30
child 11-15 yr	50	50	50	50	50	50	50	50
adult 16+	70	70	70	70	70	70	70	70
Child 0-2yrs dose (mg/kg/day)	na	0.000011	na	0.000018	na	0.000018	na	0.000003
Child 3-6yrs dose (mg/kg/day)	na	0.000035	na	0.000057	na	0.000057	na	0.000009
Child 7-10yrs dose (mg/kg/day)	0.0000095	0.000022	0.0000153	0.000035	0.000024	0.000035	0.000024	0.000005
Child 11-15 yrs dose (mg/kg/day)	0.000017	0.000013	0.000027	0.000020	0.000004	0.000020	0.000004	0.000003
Adult 16+ dose (mg/kg/day)	0.000038	0.000020	0.000060	0.000032	0.000009	0.000032	0.000009	0.000005
Cancer slope factor (mg/kg/day) ⁻¹								
0-2 ADAF	0.7							
2-16 ADAF	10							
16-70 ADAF	3							
Child 0-2yrs risk	na	7.9E-05	na	1.3E-04	na	1.3E-04	na	2.0E-05
Child 3-6yrs risk	na	7.4E-05	na	1.2E-04	na	1.2E-04	na	1.8E-05
Child 7-10yrs risk	2.0E-05	4.6E-05	3.2E-05	7.4E-05	5.0E-06	7.4E-05	5.0E-06	1.2E-05
Child 11-15 yrs risk	3.6E-05	2.6E-05	5.8E-05	4.2E-05	9.0E-06	4.2E-05	9.0E-06	6.6E-06
Adult 16+ risk	2.6E-05	1.4E-05	4.2E-05	2.2E-05	6.6E-06	2.2E-05	6.6E-06	3.5E-06
Total risk	8.2E-05	8.6E-05	1.3E-04	1.4E-04	2.1E-05	1.4E-04	2.1E-05	2.2E-05

a Age groups are based on the SWIMODEL and the cancer assessment guidelines.

b Safety factor (SF) values are based on the recommendations in the cancer assessment guidelines. The SFs are used in the calculation of the cancer risk estimates. The SFs are not included in the calculation/presentation of the LADD.

c Lifetime average daily dose (LADD) (mg/kg/day) = LADD = Cw x IgR x ET x EF x ED / BW x AT x 365 d/yr.

Where Cw=Chemical concentration in pool water (mg/L); IgR=Ingestion rate of pool water (L/hour);

ET=Exposure time (hours/day); EF=Exposure frequency (events/year); ED=Exposure duration (years);

BW=Body weight; and AT=Averaging time (70 year lifetime).

d Cancer Risk = LADD (mg/kg/day) x Cancer Slope Factor of 0.7 (mg/kg/day)⁻¹

Table 10. Arch (2005) Submitted Bromate Ion Water Conc for DBDMH and BCDMH Applications and Cancer Risks for Swimmers.

Postapplication Dose from Ingestion Parameters	DBDMH		BCDMH		DBDMH and BCDMH	
	Competitive	Noncomp	Competitive	Noncomp	Competitive	Noncomp
$LADD = Cw \times IgR \times ET \times EF \times ED / BW \times AT \times 365 \text{ d/yr}$						
Concentration of ai in pool water (mg/L)	2.00	2.00	2.25	2.25	2.13	2.13
Ingestion Rate of pool water (L/hr)						
child 0-2 yr	na	0.05	na	0.05	na	0.05
child 3-6 yr	na	0.05	na	0.05	na	0.05
child 7-10 yr	0.05	0.05	0.05	0.05	0.05	0.05
child 11-15 yr	0.025	0.05	0.025	0.05	0.025	0.05
adult 16+	0.0125	0.025	0.0125	0.025	0.0125	0.025
Exposure Time (hr/day)						
child 0-2 yr	na	0.8	na	0.8	na	0.8
child 3-6 yr	na	1.44	na	1.44	na	1.44
child 7-10 yr	1	1.47	1	1.47	1	1.47
child 11-15 yr	1.65	1.4	1.65	1.4	1.65	1.4
adult 16+	1.83	0.97	1.83	0.97	1.83	0.97
Exposure Frequency (days/yr)						
child 0-2 yr	na	64	na	64	na	64
child 3-6 yr	na	106	na	106	na	106
child 7-10 yr	65	102	65	102	65	102
child 11-15 yr	189	82	189	82	189	82
adult 16+	238	87	238	87	238	87
Exposure Duration (yr)						
child 0-2 yr	na	2	na	2	na	2
child 3-6 yr	na	4	na	4	na	4
child 7-10 yr	4	4	4	4	4	4
child 11-15 yr	5	5	5	5	5	5
adult 16+	22	30	22	30	22	30
Averaging Time (yr)	70	70	70	70	70	70
Body weight (kg)						
AT						
BW						

4.4 Data Limitations/Uncertainties

There are several data limitations and uncertainties associated with the postapplication cancer exposure/risk assessment. These uncertainties include:

- Calculation for the swimming pool scenarios rely on the use of SWIMODEL, a model which has the following limitations:
 - SWIMODEL focuses on potential chemical intakes only. It does not account for metabolism or excretion of the chemical of concern.
 - SWIMODEL does not predict or calculate chemical concentration values in exhaled air or blood. Therefore, biological monitoring results cannot be directly compared or related to SWIMODEL outputs.
 - SWIMODEL assumes 100% absorption of ingested chemical.
- Neither data submission (ACC 2005 and Arch 2005) provided details of the sampling and analysis methods. No QA/QC data were included in either submission. ACC (2005) indicated that the pools were treated as per label directions but specifics were not provided. Finally, the ACC (2005) submission did not provide the individual data points for the bromate ion concentrations.
- The pool treatments in the Arch (2005) submission appear to be based on exaggerated applications of sodium bromide which may account for the higher bromate ion concentration in those pools.

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