Roadmap for Interdisciplinary Research on Drinking Water Disinfection By-Products

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Office of Research & Development

What I will cover…

- Provide an overview
- Summarize important issues with drinking water DBPs
- Focus on emerging, unregulated DBPs
- Identify gaps and where we need to go next to solve this important problem

Richardson, Plewa, Wagner, Schoeny, and DeMarini. Occurrence, genotoxicity, and carcinogenicity of regulated and emerging disinfection by-products in drinking water: A review and roadmap for research. *Mutation Research* **2007**, *636*, 178-242.

Drinking Water DBPs—What are the Issues?

Concern over possible human health risk:

- Epidemiologic studies: risk of bladder cancer; some cause cancer in laboratory animals
- Recent concerns about possible reproductive & developmental effects (from epi studies)

Goal: Comprehensively identify DBPs formed from different disinfectants, test for toxicity, understand their formation, minimize or eliminate in drinking water

Drinking Water DBPs: How are they formed?

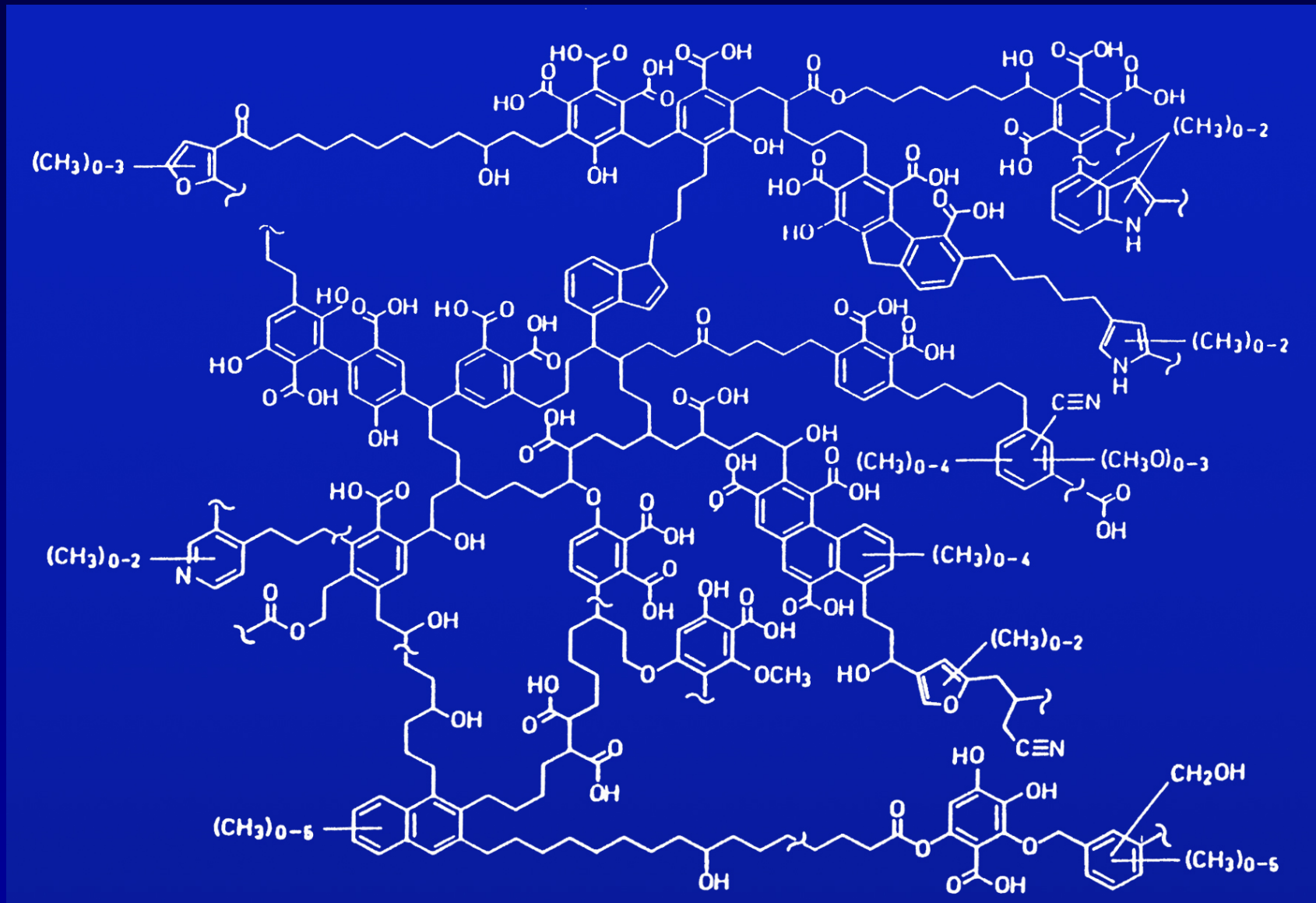

Fig. 12.7 Chemical network structure of humic acids according to Schulten and Schnitzer.[7] Reproduced by permission of Springer-Verlag.

DBPs discovered in 1974

1974 V. 23, Part 2 June

☆ Discovery of DBPs

FORMATION OF HALOFORMS DURING CHLORINATION OF NATURAL WATERS

By
J. J. ROOK
Rotterdam Waterworks

Investigations have shown that haloforms are produced during chlorination of humic substances in natural waters. In view of possible physiological effects it is suggested that some caution might be needed in applying chlorination to such waters.

1. INTRODUCTION

Gas chromatographic headspace gas analysis, described earlier by the author[1], has been applied to different types of surface waters for routine quality control of water treatment at the Berenplaat plant. Treatment comprises storage, superchlorination, combined activated carbon addition and coagulation, filtration, cascade aeration and postchlorination.

This analytical method, which detects low polar volatiles, such as the lower alkanes, freons, chlorinated solvents and substituted benzenes and toluenes, has shown effective removal of such micropollutants during the 3 weeks' storage of the river water, the reduction varying from 40% in winter to over 90% in summer.

Interpretation of the results has been confused by the appearance of additional peaks in the chromatograms of chlorinated water. These have been identified as being due to the formation of various haloforms by chloro-bromination of naturally occurring humic substances.

Headspace gas chromatography of a given surface water produces a "fingerprint" of peaks on the chromatogram that does not usually change very much over long periods. Identification of the peaks requires the use of a mass spectrometer, chromatographic retention times alone not being sufficiently characteristic. Mass spectrometry has confirmed, at least for river Rhine water, that the variety of volatile micropollutants does not vary much from year to year, but there are seasonal changes.

Comparison of headspace fingerprints of water before and after breakpoint chlorination indicated that the volatile micropollutants passed this treatment step in diminished concentrations. A less reassuring, and initially puzzling, observation was the appearance of four new peaks, which were clearly produced by chlorination (Fig. 1). Fortunately the concentrations of the four new impurities in the water were significantly reduced in subsequent purification by adsorption on to powdered activated carbon. Their concentrations were further reduced by volatilization while flowing through open channels, by filtration and finally by cascade aeration, the overall removal amounting to 60—70%.

This investigation sought to identify these by-products of chlorination and the cause of their formation. This meant tracing their origin in either impurities in chlorine or in the chlorination of precursor substances present in the water.

Jon Rook

oxidation or removal of NH_3-N is only partial rather than mplete.

ost treatment. It may be advantageous to follow breakpoint orination with dechlorination by carbon adsorption or by a sulfur compound. Carbon adsorbs any chloroorganics t may be produced during the breakpoint procedure. In the e of wastewater, this may solve any problems of toxicity to ; in the case of water treatment, it may improve taste-and- r characteristics of the treated water.

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CEMBER 1974 rel-66 (12)

The Occurrence of Organohalides in Chlorinated Drinking Waters

T.A. Bellar, J.J. Lichtenberg, and R.C. Kroner

The national media have reported that the chlorination of water during treatment is responsible for the formation of potentially harmful chlorinated organic materials—notably chloroform—in the nation's water supplies. The following report by three research scientists from the Natl. Envir. Res. Ctr. of EPA describes that agency's research concerning these organohalides. The report concludes that the number of organohalides formed during the chlorination process does not constitute any immediate threat to the public health or welfare, but that more research into possible long-term effects is warranted.

A contribution submitted to the JOURNAL on Nov. 7, 1974, by T.A. Bellar, J.J. Lichtenberg, and R.C. Kroner (Active Member, AWWA), all of the Natl. Envir. Res. Ctr., EPA, Cincinnati, Ohio.

In recent years there has been great speculation and concern about the effect of chlorination upon organic materials contained in natural waters and wastewaters. Considering the widespread use of chlorine in water- and sewage-treatment processes, household and commercial laundering, paper-pulp bleaching, and related processes, it is easy to postulate the possible inadvertent, widespread production of chlorinated organic materials. There are an infinite number of organic materials commonly contained in natural waters and wastewaters that may react with free chlorine. For the most part mechanisms for these reactions have not been studied because rapid and precise analytical methods capable of monitoring the reaction products have not been available. Kleopfer and Fairless,[1] Novak et al,[2] Friloux,[3,4] Grob,[5] and others[6] have reported the presence of organohalides in finished waters, but because of the nature of the studies made and the analytical methods used, no conclusions could be drawn as to the source of these compounds.

Recently the Methods Dev. and Qual. Assurance Lab. of the Natl. Envir. Res. Ctr. in Cincinnati has developed and reported on a procedure for isolating and measuring nanogram quantities of volatile and semi-volatile organic materials in wastewaters (see "Determining Volatile Organics at Microgram-Per-Litre Levels by Gas Chromatography" on

T.A. BELLAR ET AL 703

Tom Bellar

>600 DBPs Identified

Halogenated DBPs
- Halomethanes
- Haloacids
- Haloaldehydes
- Haloketones
- Halonitriles
- Haloamides
- Halonitromethanes
- Halofuranones (e.g., MX)
- Oxyhalides (e.g., bromate)
- Many others

Non-halogenated DBPs
- Nitrosamines
- Aldehydes
- Ketones
- Carboxylic acids
- Others

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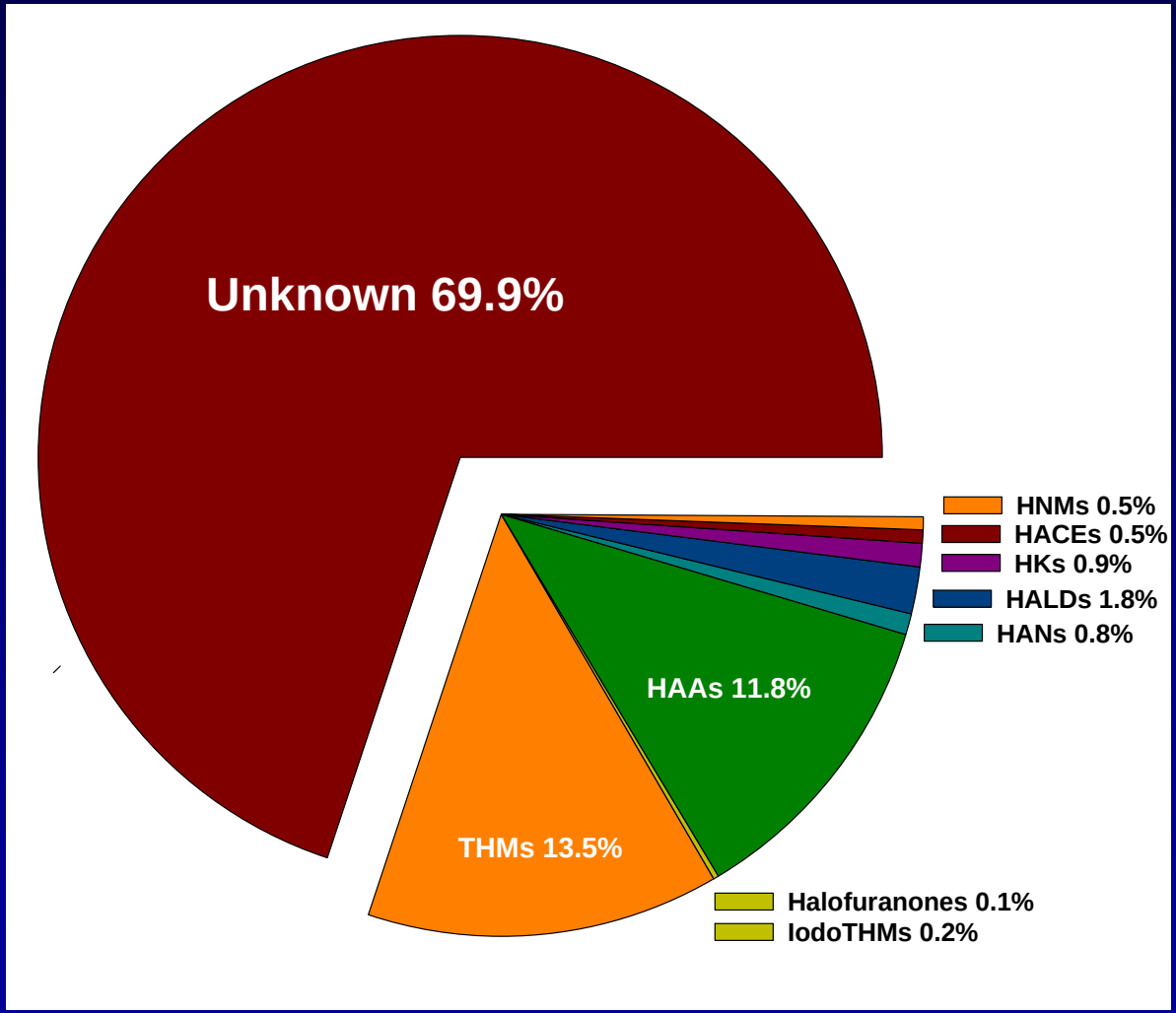
- Others

N-DBPs

But, more than 50% still not known….



Nationwide Occurrence Study, Krasner et al., *Environ. Sci. Technol*. **2006**, *40*, 7175-7185.

~50% of TOX >1000 Da: Khiari, et al., Proc. 1996 AWWA Water Quality Technology Conference

Only 11 DBPs Regulated in U.S.

DBP	MCL (µg/L)
Total THMs	80
5 Haloacetic acids	60
Bromate	10
Chlorite	1000

Little known about occurrence, toxicity of unregulated DBPs

Regulated DBPs do not cause bladder cancer in animals!

Only 11 DBPs Regulated in U.S.

DBP	MCL (µg/L)
Total THMs	80
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Bromate	10
Chlorite	1000

And, you will hear some odd things next from David DeMarini, such as…

- One regulated DBP never tested for cancer
- Two unregulated DBPs are carcinogens
- Many unregulated DBPs more genotoxic than regulated ones

Only 11 DBPs Regulated in U.S.

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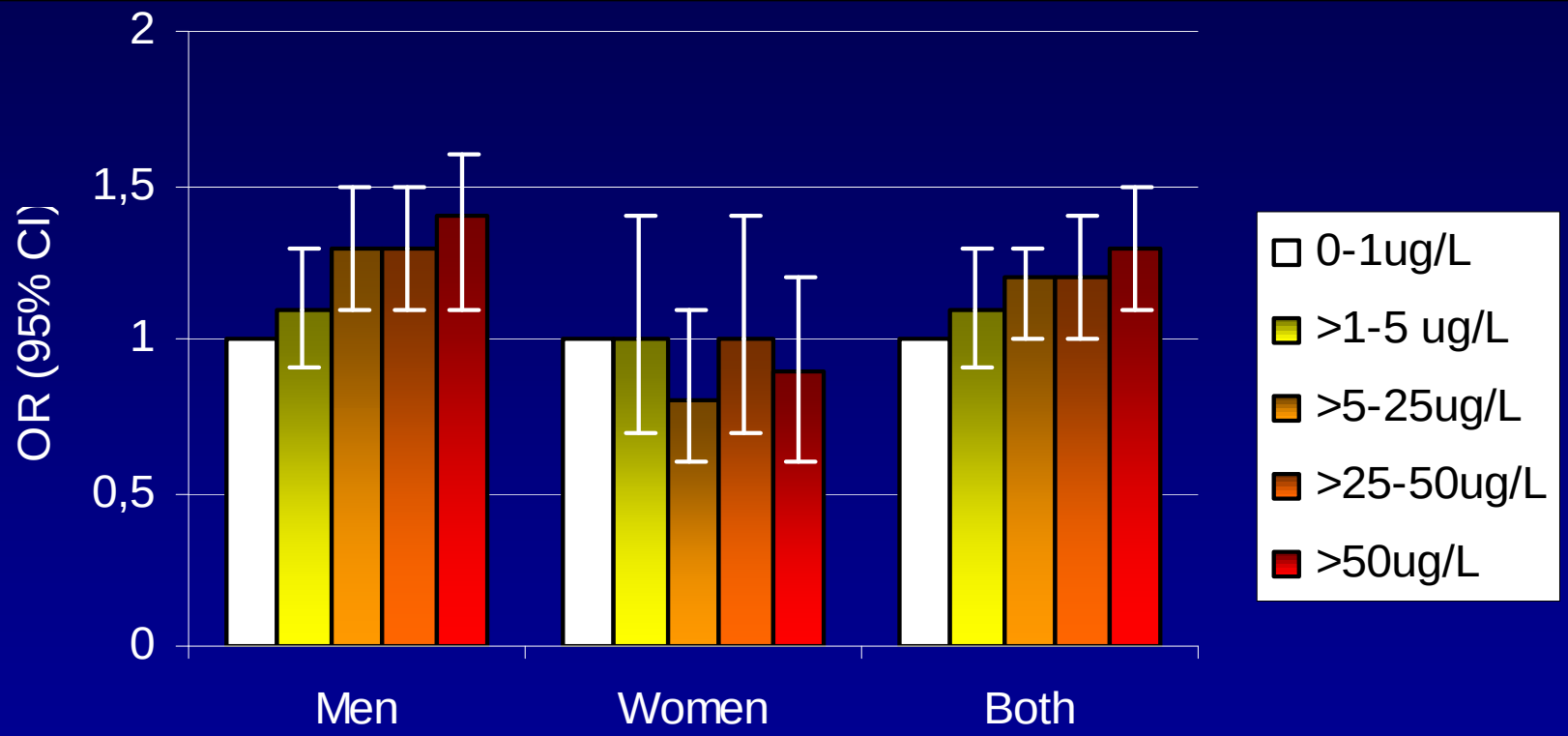
There are still many gaps to fill!!

Bladder cancer and drinking water: Pooled analysis



OR adjusted by (sex), study, age, smoking status, ever worked in high-risk occupations, heavy coffee consumption and total fluid intake

Villanueva et al., Epidemiology **2004**, *15*, 357-367.

Exposure routes

Inhalation

(shower, swimming pool, etc.)

Volatile DBP
e.g. THMs

Ingestion

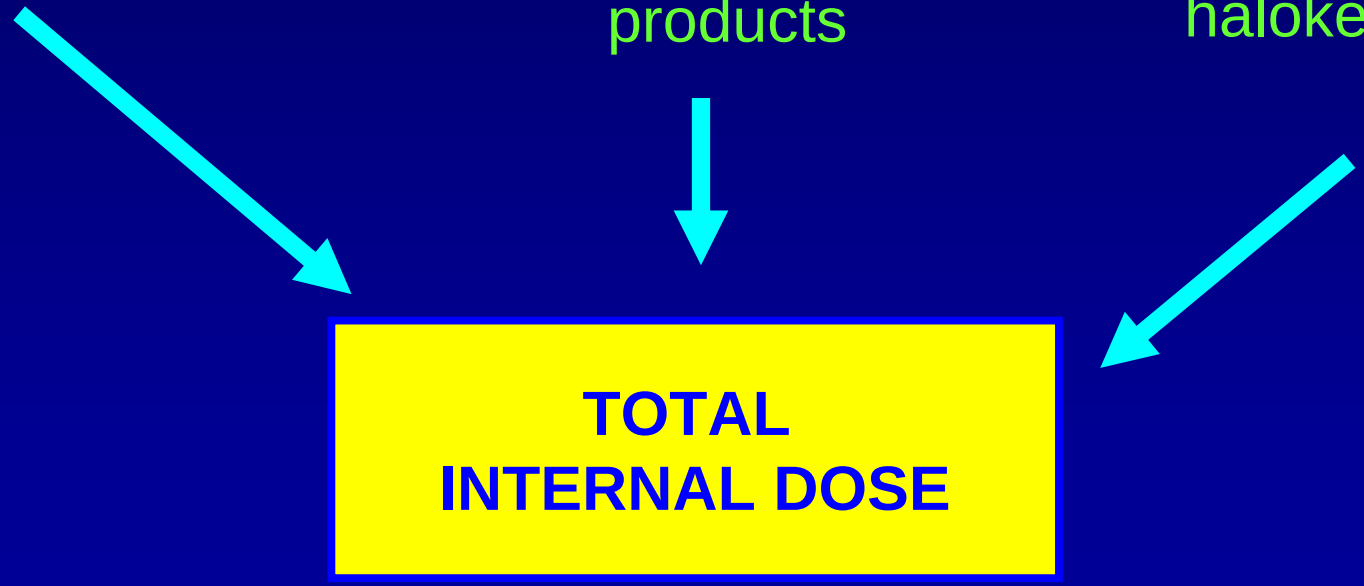
(water, coffee, tea, water-based food and beverages)

All disinfection by-products

Dermal absorption

(swimming pool, bath, etc.)

Permeable DBPs
e.g. THMs, haloketones, …



Slide courtesy of Manolis Kogevinas, Centre for Research in Environmental Epidemiology/IMIM, Barcelona

Route of exposure is important….

- Can get 2X exposure from 10 min shower compared to drinking 2L of tap water (inhalation)
- Some DBPs dermally absorbed
- Evidence of increased bladder cancer with swimming in indoor pools (inhalation, dermal): Villanueva et al., *Am. J. Epidemiol*. 2007, *165*, 148-156.

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Does this mean that bladder cancer is caused by volatile or dermally absorbed DBPs??

Does this mean we shouldn't worry about high MW DBPs?

Should we study rats taking showers?

Unlike other contaminants that may or may not be present in drinking water…

DBPs
are ubiquitous

But…

On the new proposed U.S. EPA Contaminant Candidate List (CCL-3) for drinking water (104 chemicals)

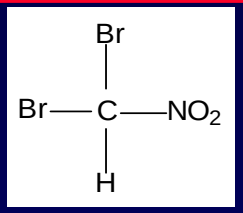
Only 10 of 104 chemicals are DBPs:
5 nitrosamines, formaldehyde, acetaldehyde, benzyl chloride, chlorate, bromochloromethane

And, 4 of these chosen for other reasons (industrial contaminants, etc.)

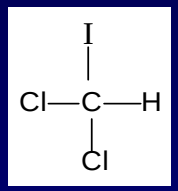
Many other DBPs far more prevalent than these, but they are not listed as priorities

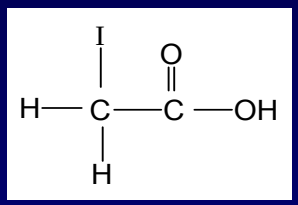
Emerging DBPs

- Halonitromethanes (up to 3 ppb; highly genotoxic); new *in vivo* effects; increased with preozonation
  Krasner, Weinberg, Richardson, et al., *ES&T* 2006, 40, 7175-7185.

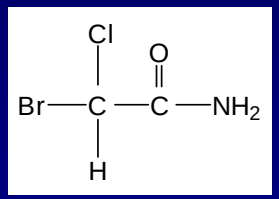


- Iodo-THMs and Iodo-Acids (iodo-THMs up to 15 ppb; iodo-acids up to 1.7 ppb; both classes highly cytotoxic or genotoxic); increased with chloramination
  Richardson et al., *ES&T* 2008, 42, 8330.

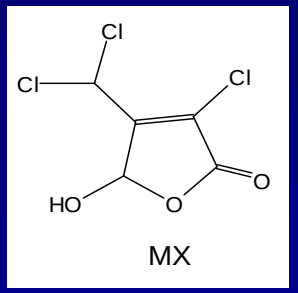




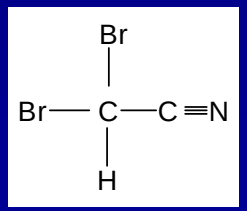
- Haloamides (up to 14 ppb; highly genotoxic) may be increased with chloramination



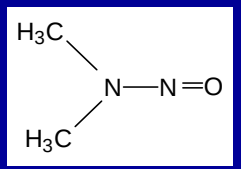
- Halofuranones (up to 2.4 ppb for total MX analogues; genotoxic, carcinogenic); chloramination can also form



- Haloacetonitriles (up to 41 ppb; ~10% of THM4; genotoxic, cytotoxic); may be increased with chloramination



- Nitrosamines (up to 180 ppt; probable human carcinogens) increased with chloramination



Emerging DBPs

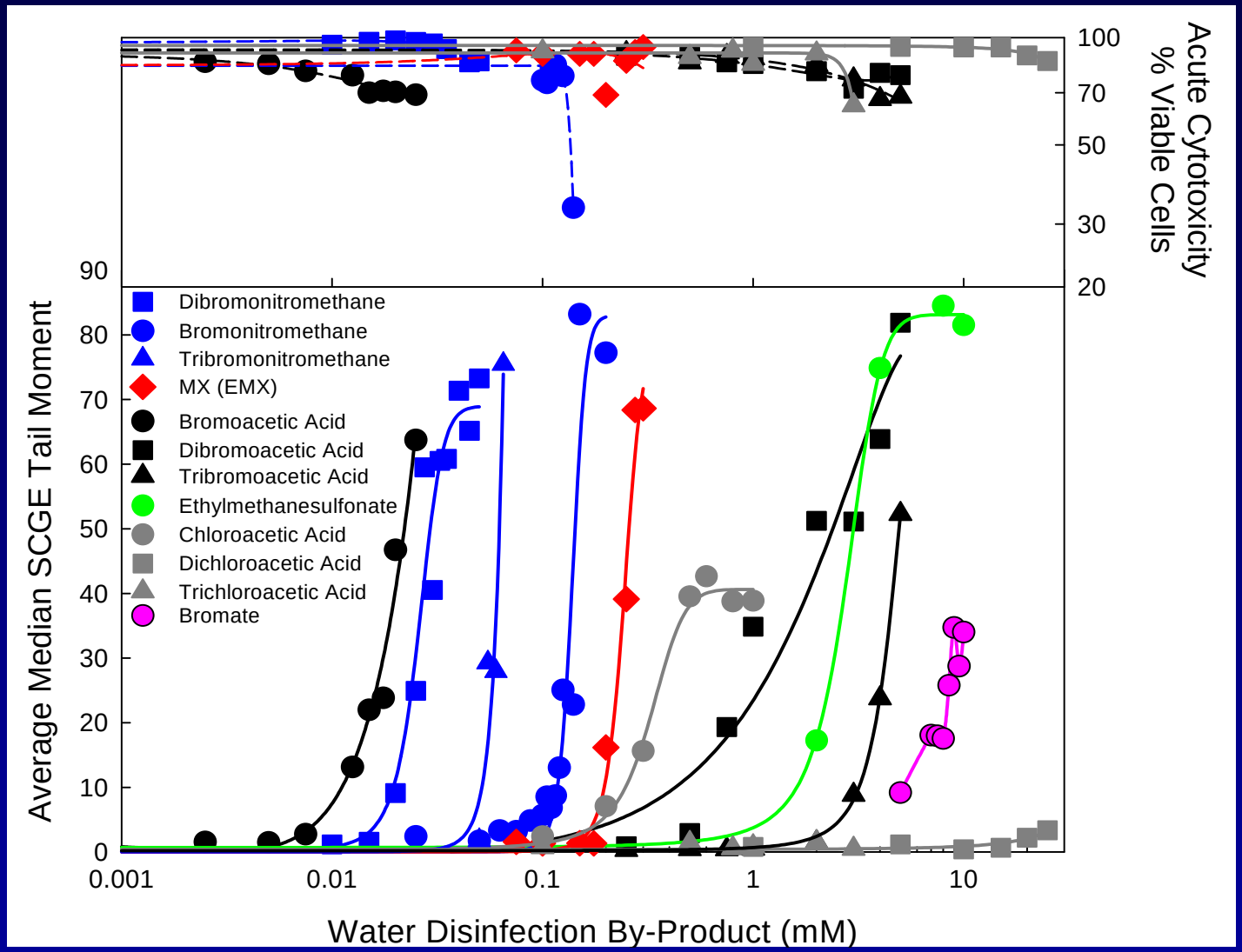
- EPA Method 521 for nitrosamines (GC/MS/MS); sub-ng/L detection
- Also an LC/MS/MS method for 9 nitrosamines:
  Zhao, Boyd, Hrudey, Li, *Environ. Sci. Technol*. 2006, 40 (24): 7636-7641.
- NDMA on draft CCL-3 and UCMR-2

Nationwide DBP Occurrence Study

- Prioritized >500 unregulated DBPs reported in literature (likely to cause cancer)
- Measured these in waters across U.S.
- Important findings:
  - New emerging DBPs identified (e.g., iodo-acids)
  - Alternative disinfectants increased formation of many priority DBPs
  - Many priority, unregulated DBPs found at significant levels

Krasner, Weinberg, Richardson, et al., *Environ. Sci. Technol*. 2006, 40, 7175-7185.

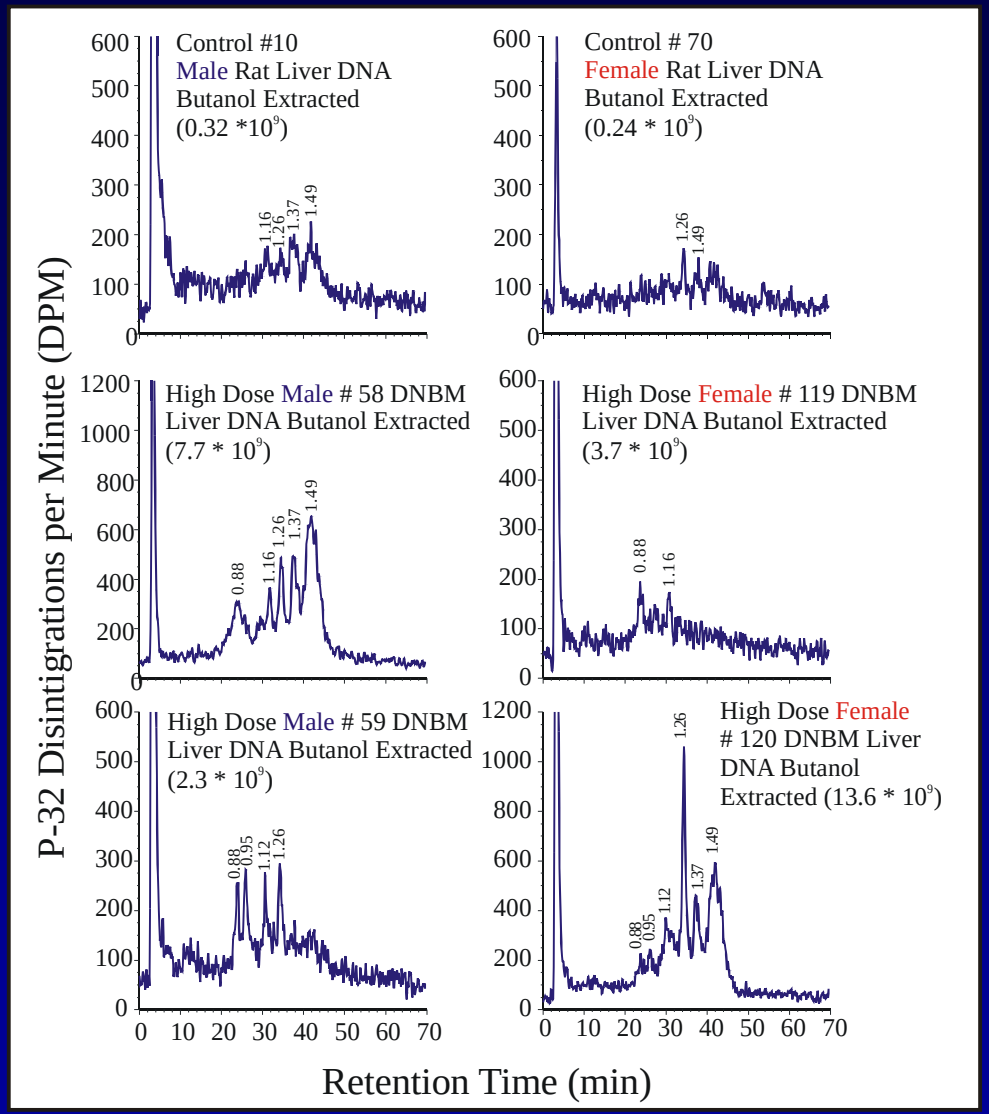
Halonitromethane Genotoxicity



Plewa et al., *ES&T* 2004, 38, 4713-4722.

Halonitromethanes also genotoxic to Salmonella (DeMarini et al.)

Dibromonitromethane—DNA Adducts



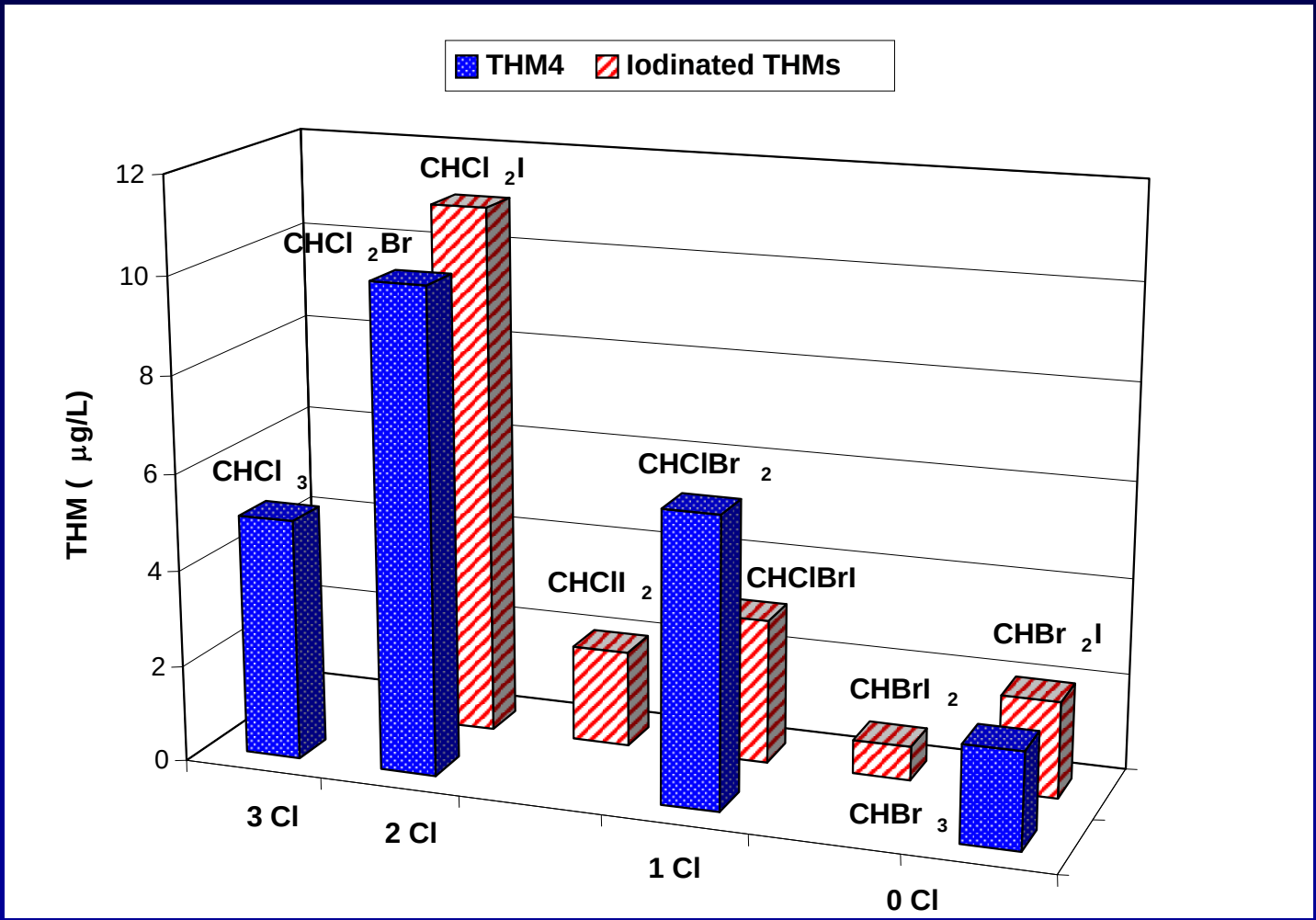
DBNM produces DNA adducts in the livers of rats after only 30 days of exposure

(in vivo, male and female rats)

Tony also now seeing effects in normal human colon cells

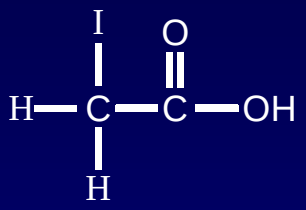
Data courtesy of Tony DeAngelo & Leon King, U.S. EPA, NHEERL, RTP, NC

Iodo-THMs

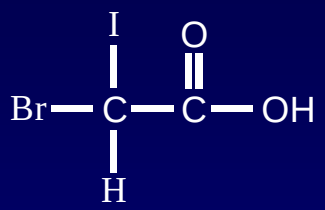


Krasner, Weinberg, Richardson, et al., *Environ. Sci. Technol*. 2006, 40, 7175-7185.

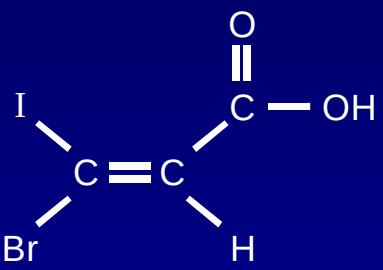
New Iodo-Acids



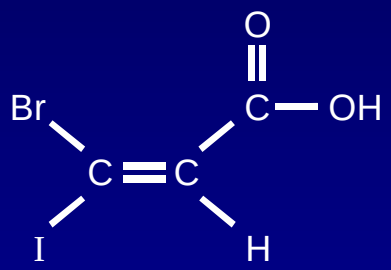
Iodoacetic acid



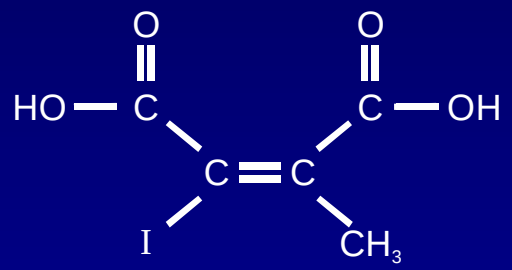
Bromoiodoacetic acid



(Z)-3-Bromo-3-iodopropenoic acid



(E)-3-Bromo-3-iodopropenoic acid



(E)-2-Iodo-3-methylbutenedioic acid

Initially discovered using GC/MS

Highly genotoxic

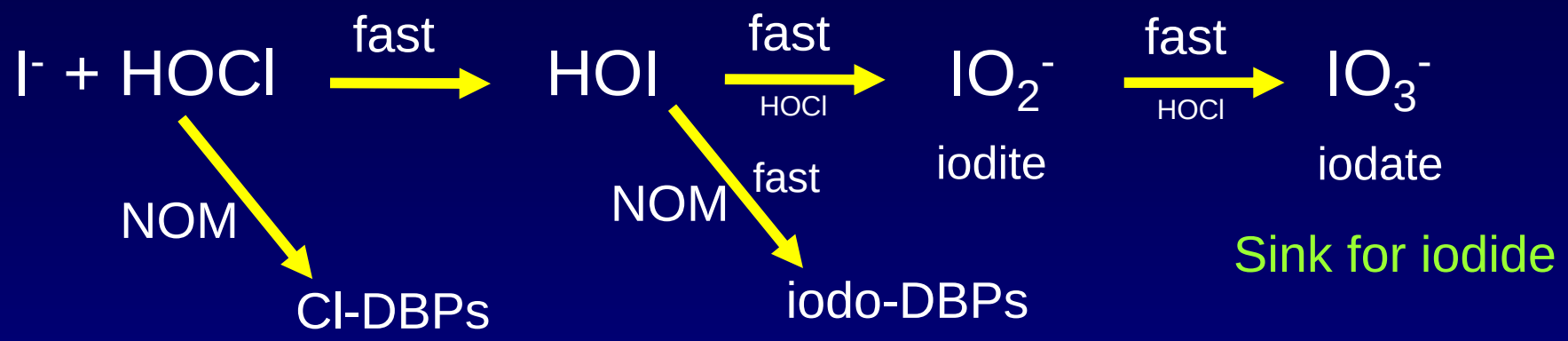
Increase in formation with NH_2Cl vs. Cl_2

Occurrence Study now completed (23 cities in U.S. & Canada)

Richardson et al., *Environ. Sci. Technol.* 2008, 42, 8330-8338.

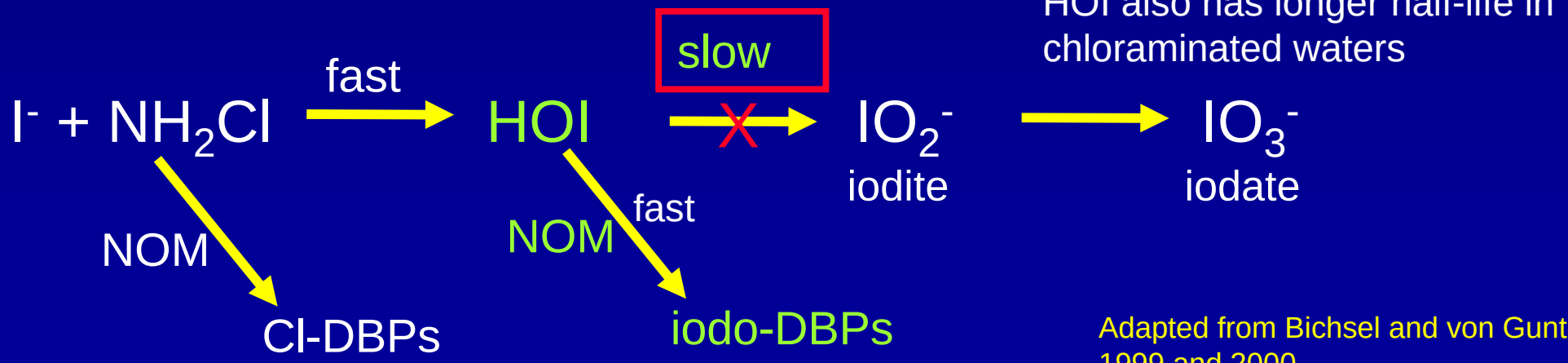
Iodo-DBPs Maximized with Chloramines

Chlorine:



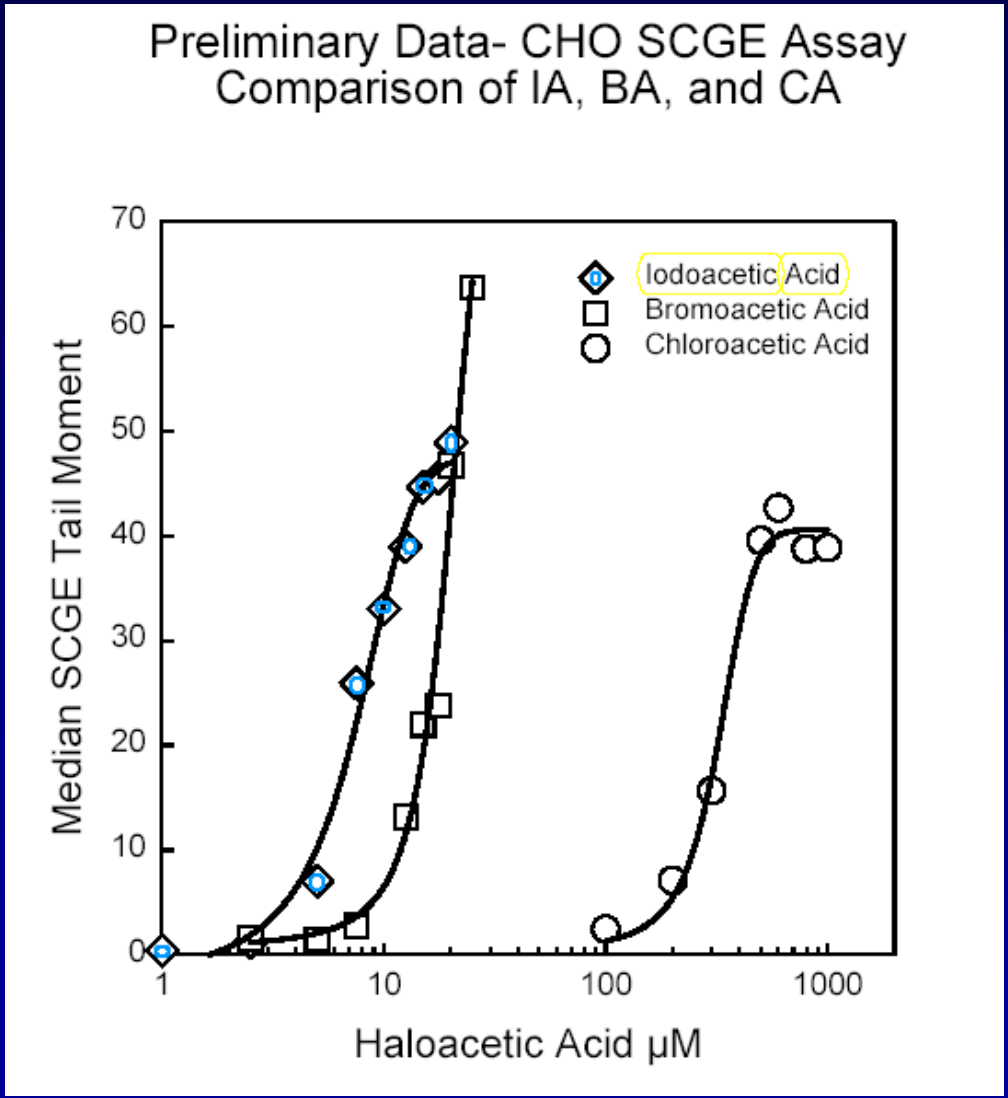
HOCl also competes for rxn with NOM, so much lower iodo-DBPs with chlorine

Chloramines:



Adapted from Bichsel and von Gunten, 1999 and 2000

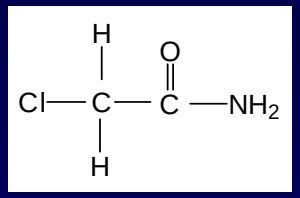
Genotoxicity of Iodoacetic acid



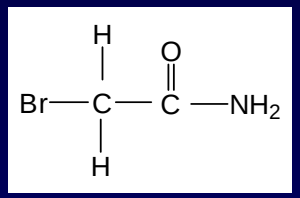
Plewa et al., *Environ. Sci. Technol*. 2004

IA also caused developmental effects in mouse embryos (Hunter et al., 1995)

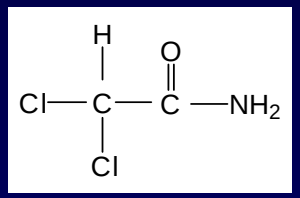
Haloamides



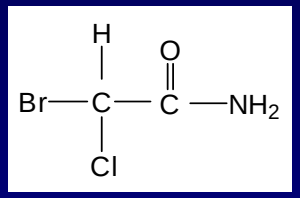
Chloroacetamide



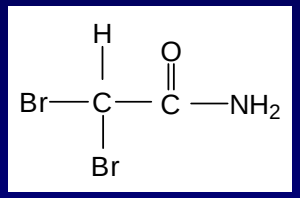
Bromoacetamide



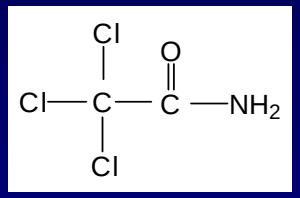
Dichloroacetamide



Bromochloroacetamide

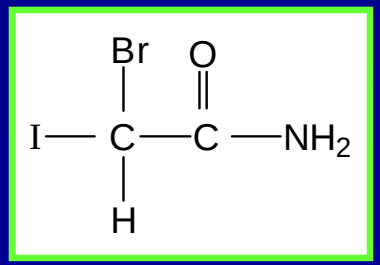


Dibromoacetamide



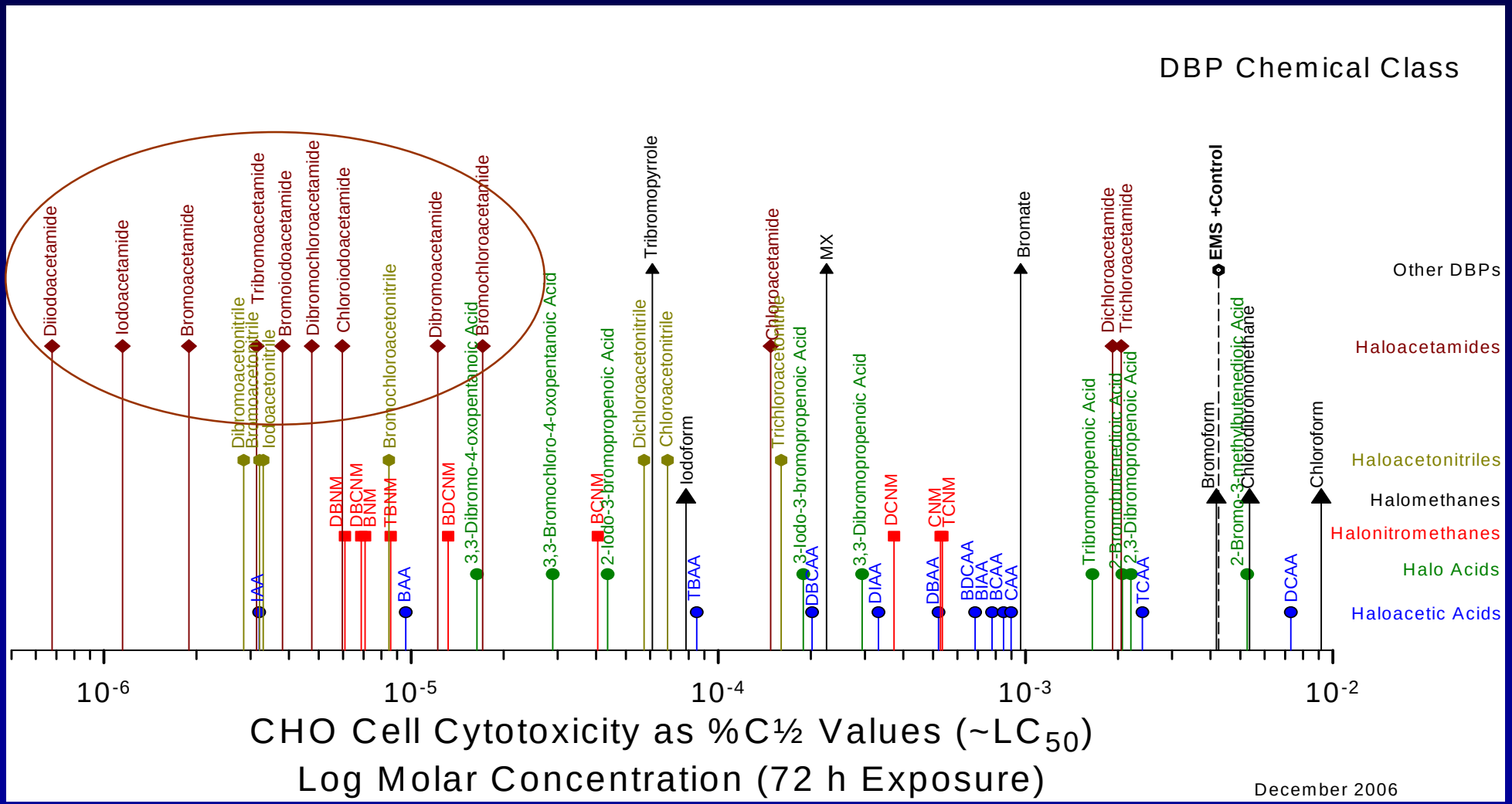
Trichloroacetamide

- New class of DBP recently identified
- Nationwide DBP Occurrence Study: up to 14 ug/L; NH_2Cl may increase their formation
- Highly genotoxic, cytotoxic
- New iodoamide DBP: Bromoiodoacetamide
  - Found in drinking water from 6 states



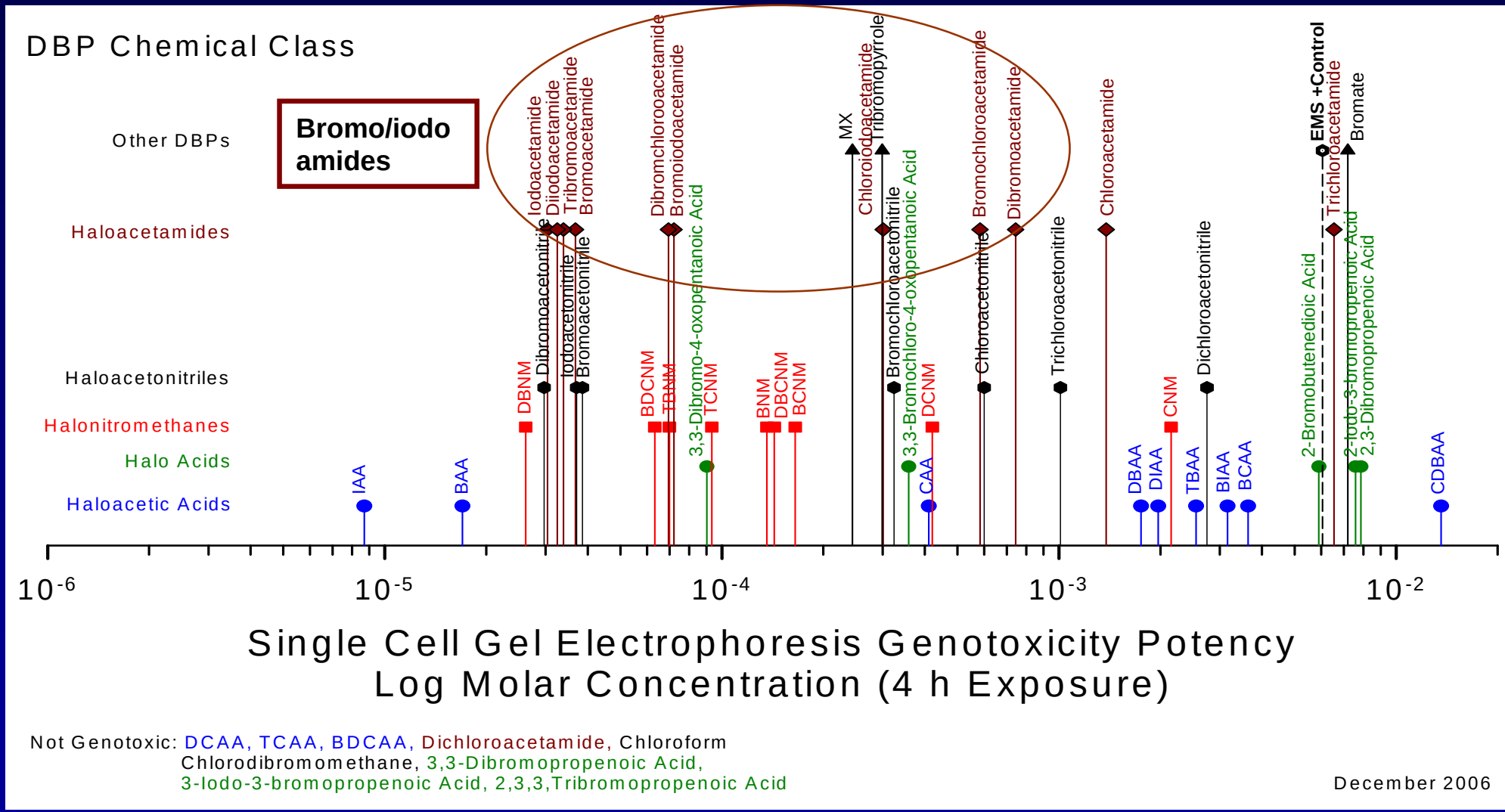
Plewa et al., *Environ. Sci. Technol*. 2008, 42, 955-961.

Haloamides--Cytotoxicity



Data courtesy of Michael Plewa, University of Illinois

Haloamides--Genotoxicity

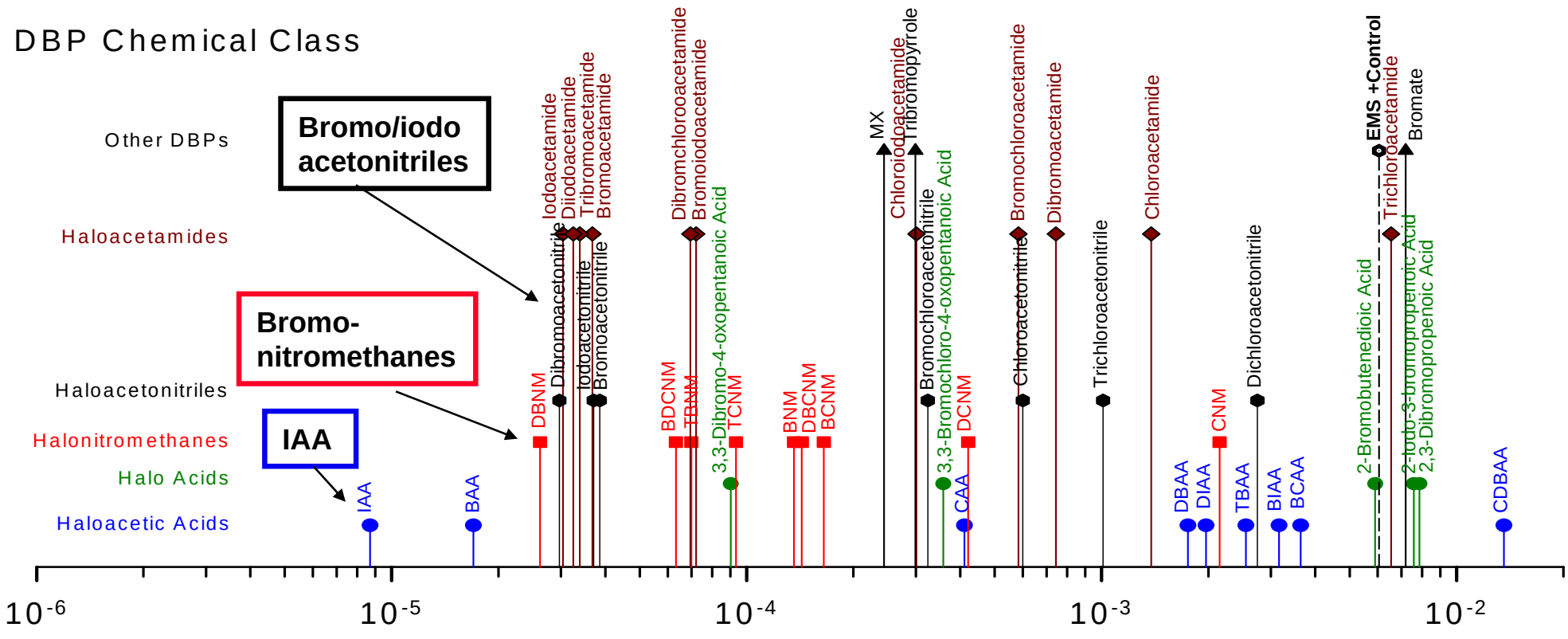


Not Genotoxic: DCAA, TCAA, BDCAA, Dichloroacetamide, Chloroform
Chlorodibromomethane, 3,3-Dibromopropenoic Acid,
3-Iodo-3-bromopropenoic Acid, 2,3,3,Tribromopropenoic Acid

December 2006

Data courtesy of Michael Plewa, University of Illinois

Genotoxicity of Other DBPs



Not Genotoxic: DCAA, TCAA, BDCAA, Dichloroacetamide, Chloroform
Chlorodibromomethane, 3,3-Dibromopropenoic Acid,
3-Iodo-3-bromopropenoic Acid, 2,3,3,Tribromopropenoic Acid

December 2006

Data courtesy of Michael Plewa, University of Illinois

But, all of this toxicity testing is for separate, individual DBPs…

DBPs
are really present as MIXTURES

>300 DBPs probably
present in glass of water

Four Lab Study

Integrated Disinfection By-products Mixtures Research: Toxicological and Chemical Evaluation of Alternative Disinfection Treatment Scenarios

A collaborative effort between:

NHEERL (National Health and Environmental Effects Research Laboratory), RTP

NERL (National Exposure Research Laboratory), Athens

NRMRL (National Risk Management Research Laboratory), Cincinnati

NCEA (National Center for Environmental Assessment), Cincinnati

Purpose:

To address concerns related to potential health effects from exposure to DBPs that cannot be addressed directly from toxicological studies of individual DBPs or simple DBP mixtures

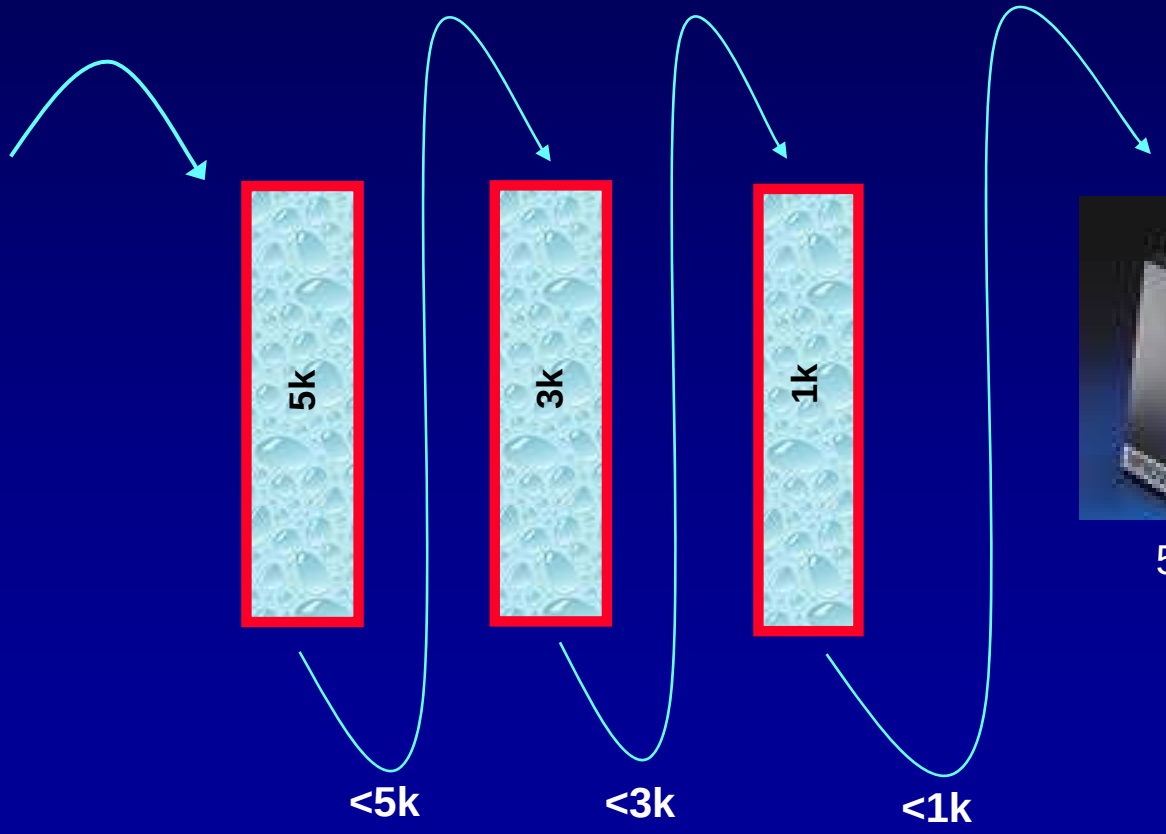
Sid Hunter will cover this study on Tuesday

What about >50% unidentified DBPs that are believed to be high molecular weight?

Bioassay-Directed Research

Molecular size:

Ultrafiltration membrane device

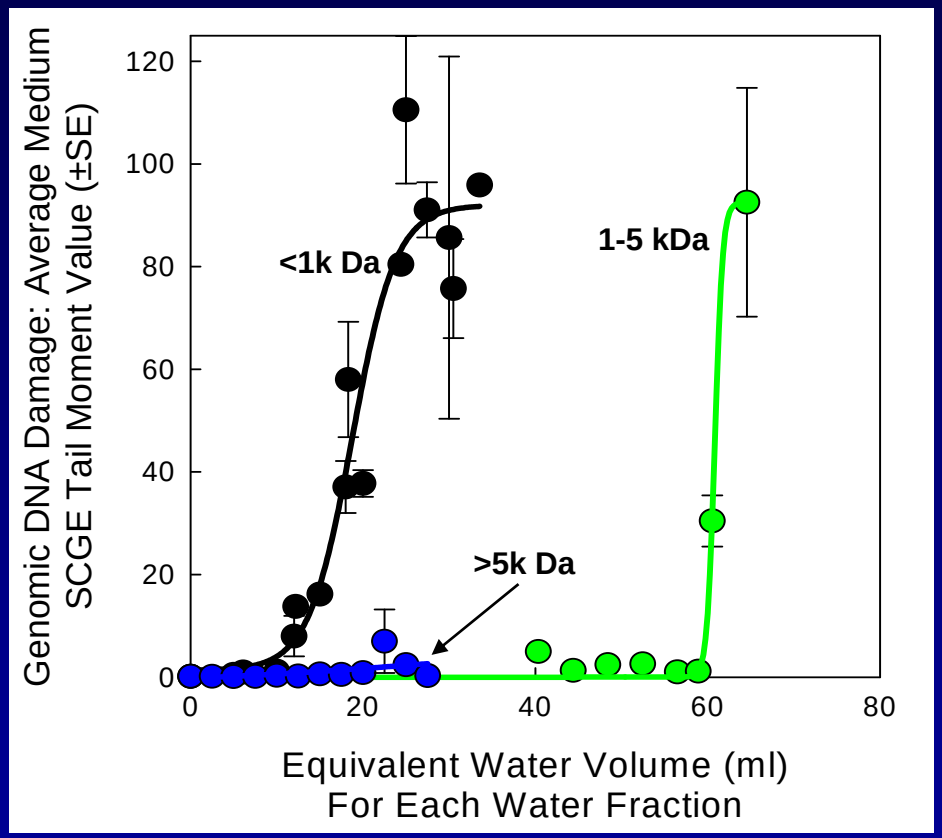


500 MW

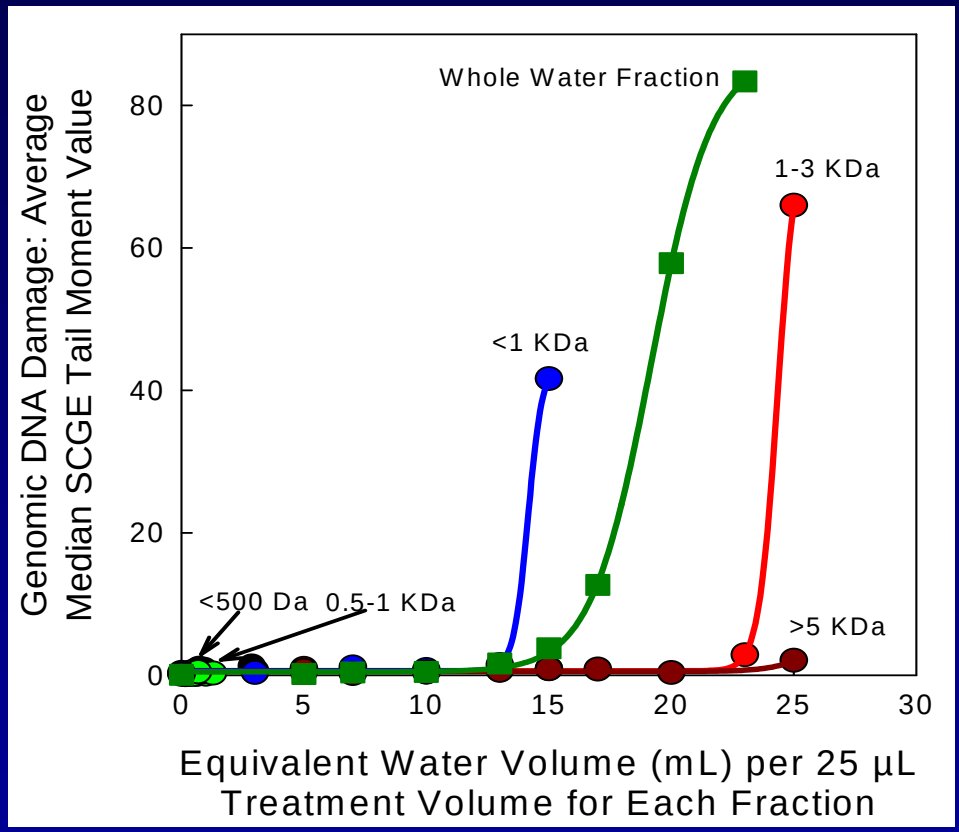
Fractions collected: >5kDa 3-5kDa 1-3kDa <1kDa 500-1kDa <500Da

MS and Toxicity Characterization of drinking water fractions

Genomic DNA Damage Analysis of Ultrafiltration Fractions



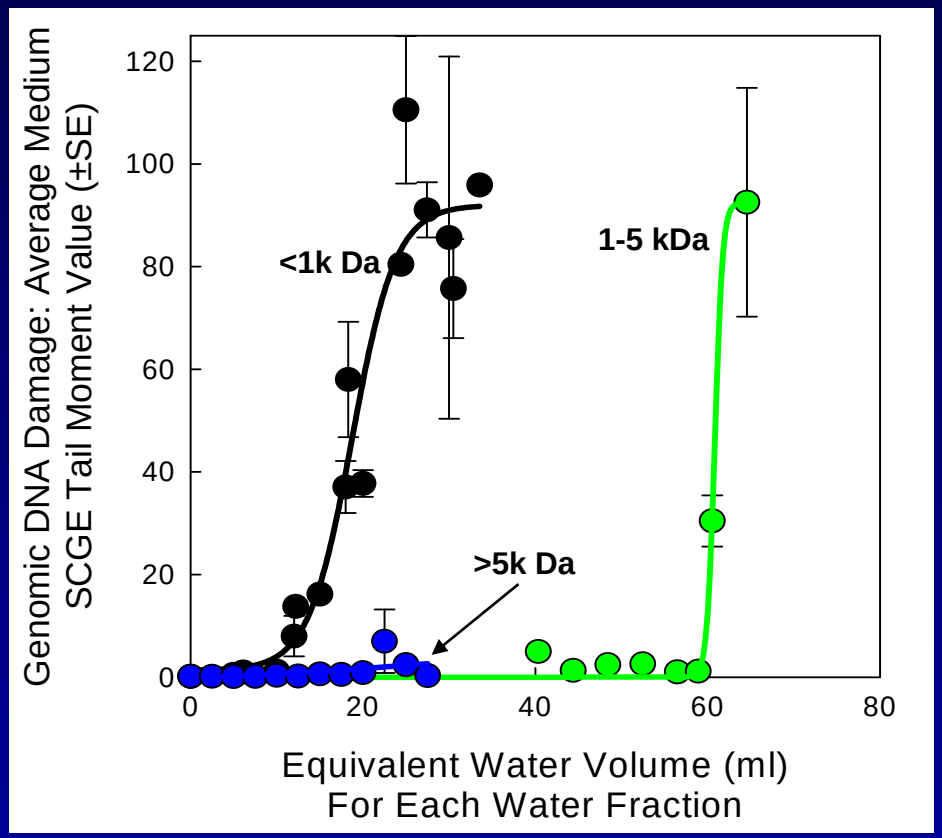
Plant 1 (Chloramination, high Br)

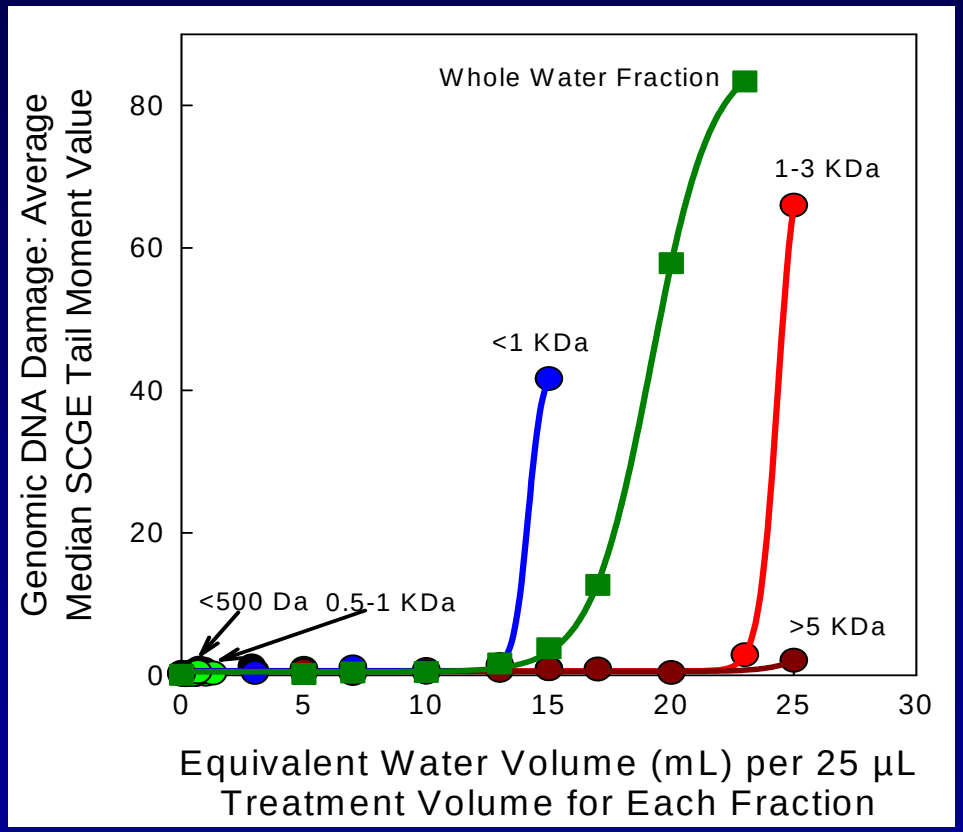


Plant 2 (Chlorination, low Br)

Corresponding raw waters not genotoxic

Genomic DNA Damage Analysis of Ultrafiltration Fractions





Does this mean that we don't need to worry about DBPs >5000 Da?

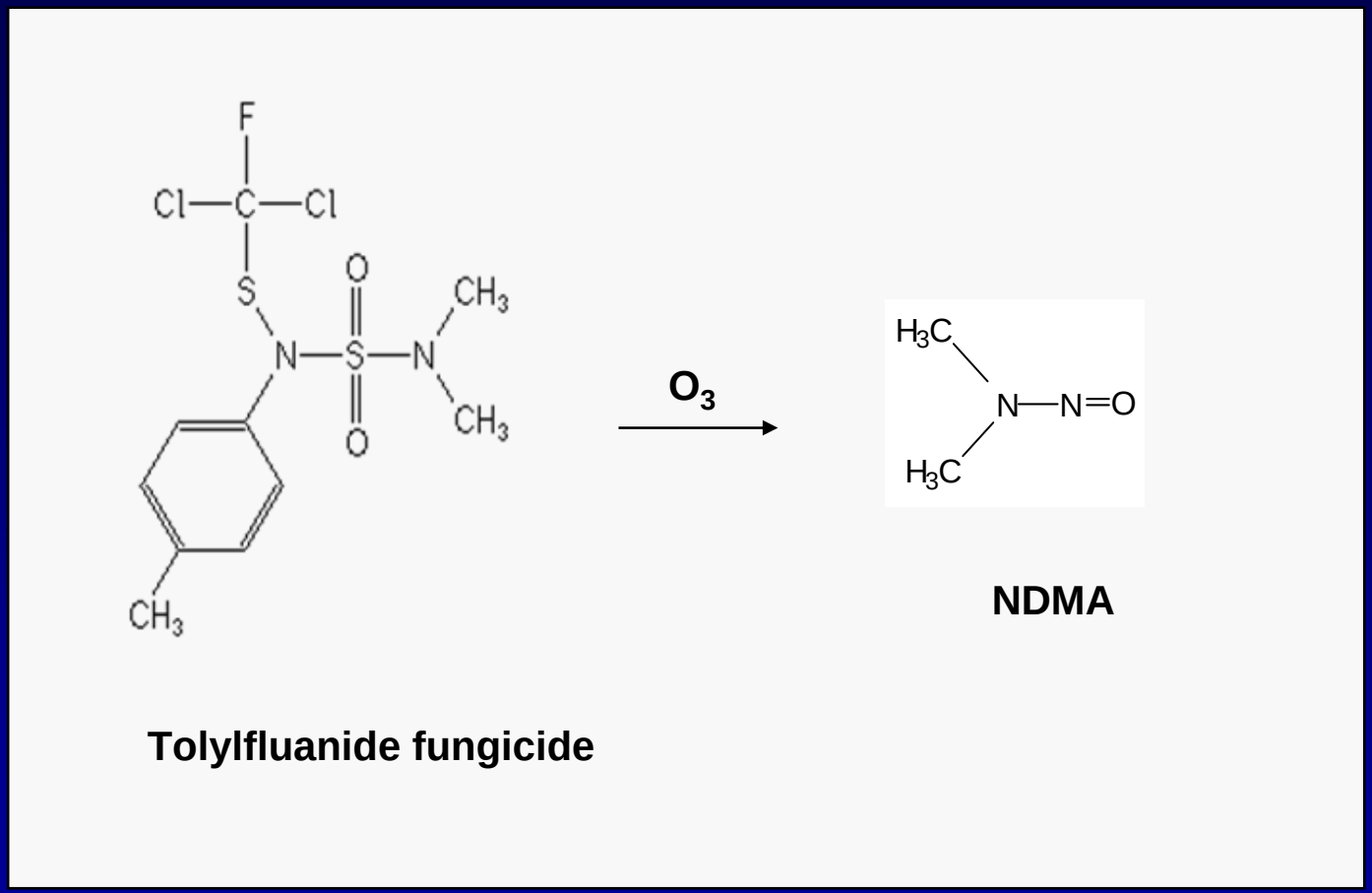
Does this mean our focus on lower molecular weight DBPs was good?

But, what about 1000-3000 Da fraction?

DBPs can also form from pollutants…

- Pesticides
- Pharmaceuticals
- Antibacterial agents
- Estrogens
- Textile dyes
- Pesticides
- Bisphenol A
- Parabens
- Alkylphenol ethoxylate surfactants
- Algal toxins

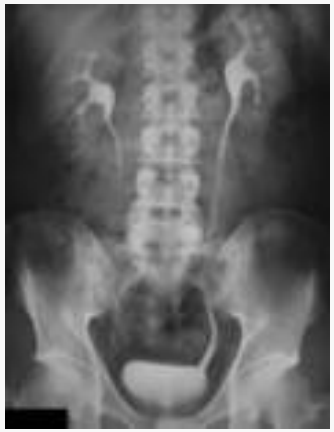
Formation of NDMA from a fungicide

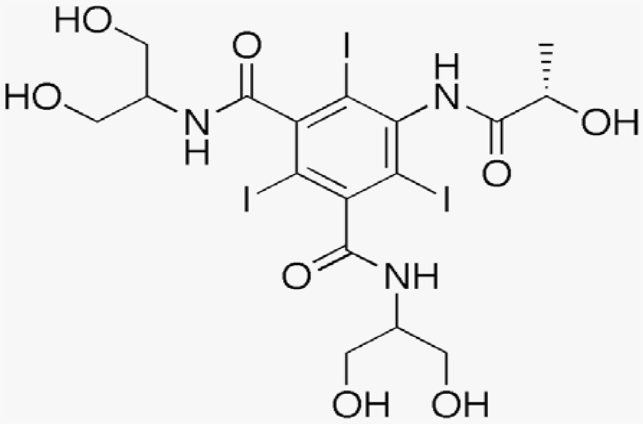


Schmidt and Brauch, *ES&T* 2008

Urs von Gunten also has new results indicating the catalytic effect of bromide on this reaction

Formation of iodo-DBPs from X-ray contrast media





Iopamidol

\+ NOM $\xrightarrow[NH_2Cl]{HOCl}$ Iodo-DBPs

Richardson, Duirk, Lindell, Cornelison, Ternes, presented at Micropol Conference, June 2009

Iodo-DBP Occurrence Study

	Iodide (µg/L)	Sum iodo-acids (µg/L)	Sum iodo-THMs (µg/L)
Plant 2	1.0	0.37	4.9
Plant 4	ND	0.10	1.2
Plant 11	1.5	0.21	2.3
Plant 15	ND	0.17	2.4

Detection limit = 0.13 µg/L

Richardson et al., *Environ. Sci. Technol.* 2008, 42, 8330-8338.

ICM in U.S. Drinking Water Sources (ng/L)

	Iopamidol	Iomeprol	Iopromide	Iohexol	Diatrizoate
Plant 1	11	ND	ND	ND	ND
Plant 2	510	ND	24	120	93
Plant 4	110	ND	6	49	ND
Plant 10	ND	ND	ND	ND	ND
Plant 11	100	ND	ND	85	ND
Plant 12	280	ND	ND	120	ND
Plant 13	ND	ND	ND	ND	ND
Plant 15	2700	ND	25	ND	ND
Plant 17	ND	ND	ND	ND	ND
Plant 19	ND	ND	ND	ND	ND

Courtesy of Thomas Ternes, Federal Institute of Hydrology, Germany
ICM measured using LC/ESI-MS/MS; DLs = 5-20 ng/L

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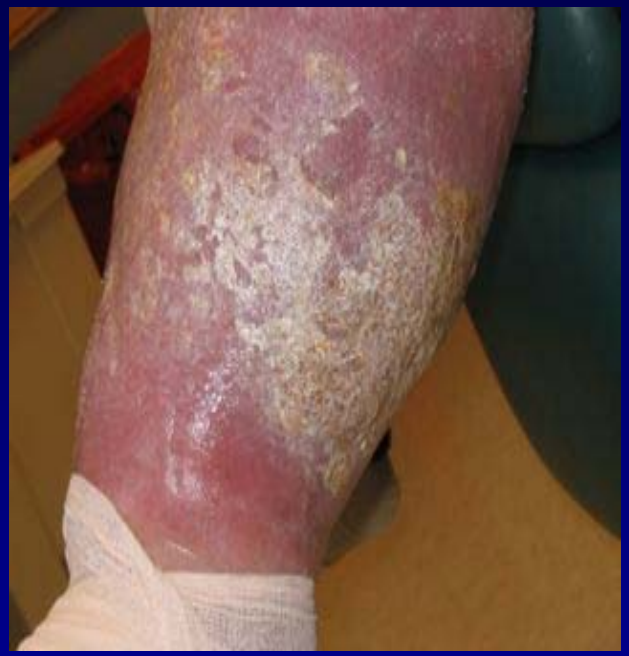
Courtesy of Thomas Ternes, Federal Institute of Hydrology, Germany
ICM measured using LC/ESI-MS/MS; DLs = 5-20 ng/L

Roadmap—Where do we go from here?

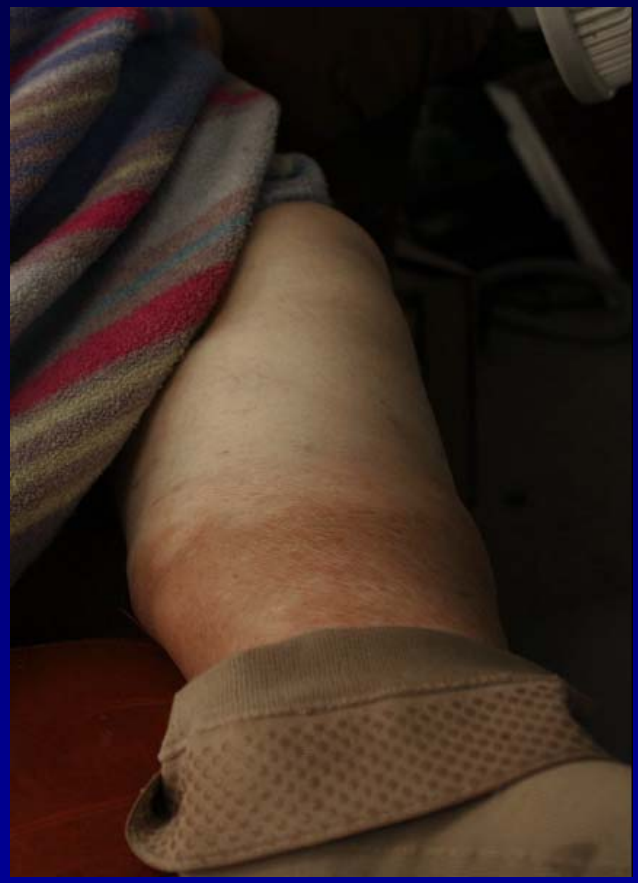
- Human health effects not solved yet—need more toxicity studies
- Studies on route of exposure
  Have we been looking at the wrong route of exposure?
- DBPs are present as complex mixtures—need toxicity studies addressing this
- What is in the unidentified fraction—anything of concern?
- What about ‘pollutant’ DBPs?
- What about DBPs from alternative disinfectants—do we know everything we need to know before plants switch?
- Chloramination? UV disinfection? Membrane disinfection?
- What about other respiratory/skin effects reported for chloraminated water? Need showering and dermal exposure studies

Serious skin rash issues….



“Before”

Showering with chloraminated water



“After”

Showering with chlorinated water at the YMCA in another town

Acknowledgments

Michael Plewa

Jane Ellen Simmons

Tony DeAngelo

David DeMarini

A few fabulous toxicologists who have helped push this field forward….

Also, Mike Narotsky, Sid Hunter, Rex Pegram, ….

In closing…

For the other chemists in the audience:

Ever wonder what happens when you have to scale things up for toxicity testing?

(*Especially* when working with Michael Plewa)

The Land of Extraordinarily Large Lab Equipment

Chris

Toxicity?
20 L → 1 mL

Steve

Cristal