JOHNS HOPKINS BLOOMBERG SCHOOL of PUBLIC HEALTH

Antimicrobial Pesticides as Pollutants

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Johns Hopkins University
Center for Water and Health

Beyond Pesticides, 25th National Pesticide Forum, Chicago, IL

June 2, 2007

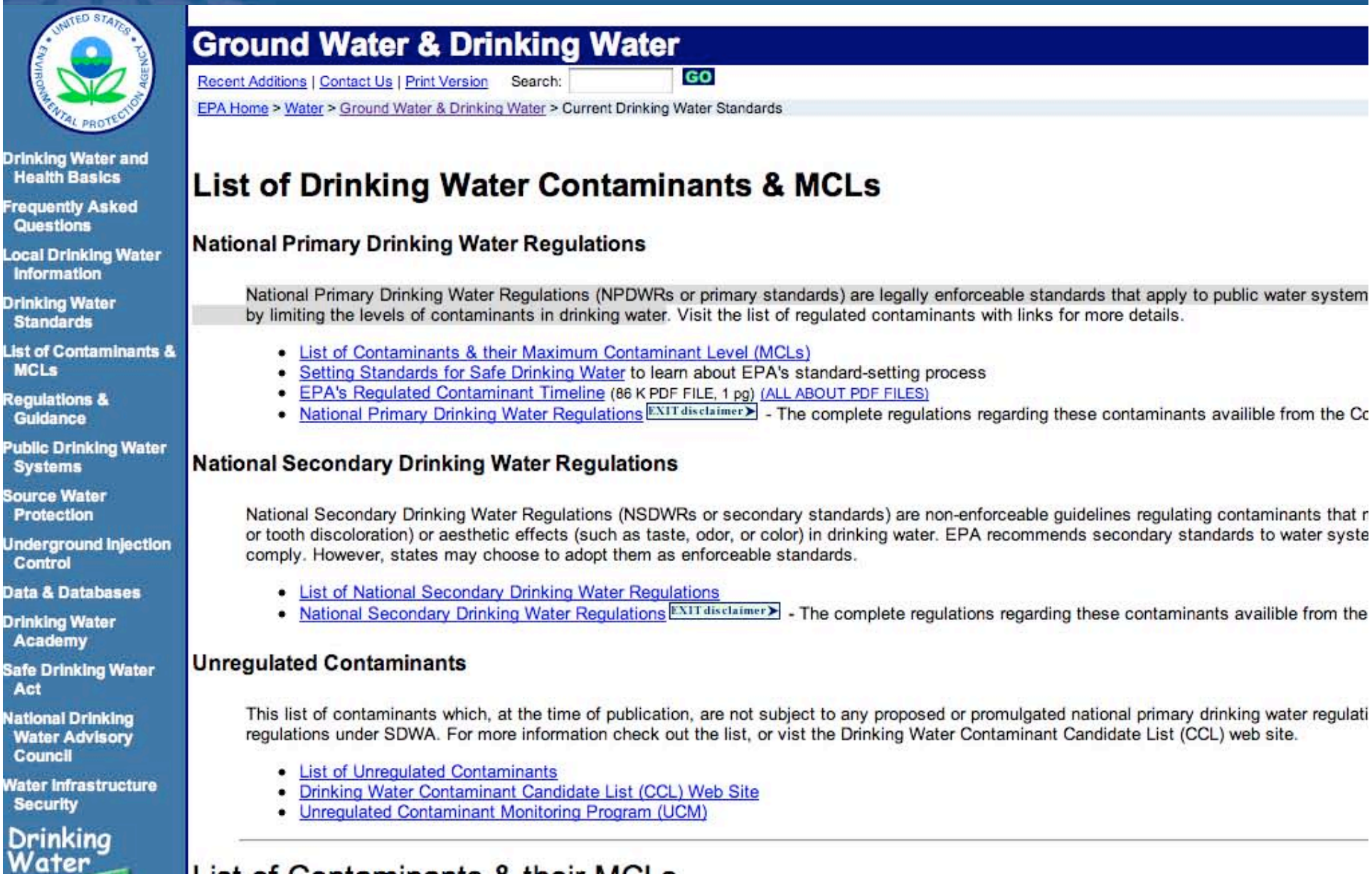
Overview

1. **Emerging pollutants**
   - Opportunities for learning from past mistakes

2. **Antimicrobials & wastewater treatment**
   - A case study of incompatibility

3. **Antimicrobials in agriculture**
   - An unintended destination of antimicrobials in consumer products

Safe Drinking Water Act (SDWA)



Ground Water & Drinking Water

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EPA Home > Water > Ground Water & Drinking Water > Current Drinking Water Standards

- Drinking Water and Health Basics
- Frequently Asked Questions
- Local Drinking Water Information
- Drinking Water Standards
- List of Contaminants & MCLs
- Regulations & Guidance
- Public Drinking Water Systems
- Source Water Protection
- Underground Injection Control
- Data & Databases
- Drinking Water Academy
- Safe Drinking Water Act
- National Drinking Water Advisory Council
- Water Infrastructure Security

Drinking Water

List of Drinking Water Contaminants & MCLs

National Primary Drinking Water Regulations

National Primary Drinking Water Regulations (NPDWRs or primary standards) are legally enforceable standards that apply to public water system by limiting the levels of contaminants in drinking water. Visit the list of regulated contaminants with links for more details.

- List of Contaminants & their Maximum Contaminant Level (MCLs)
- Setting Standards for Safe Drinking Water to learn about EPA's standard-setting process
- EPA's Regulated Contaminant Timeline (86 K PDF FILE, 1 pg) (ALL ABOUT PDF FILES)
- National Primary Drinking Water Regulations EXIT disclaimer - The complete regulations regarding these contaminants availible from the Cc

National Secondary Drinking Water Regulations

National Secondary Drinking Water Regulations (NSDWRs or secondary standards) are non-enforceable guidelines regulating contaminants that r or tooth discoloration) or aesthetic effects (such as taste, odor, or color) in drinking water. EPA recommends secondary standards to water syste comply. However, states may choose to adopt them as enforceable standards.

- List of National Secondary Drinking Water Regulations
- National Secondary Drinking Water Regulations EXIT disclaimer - The complete regulations regarding these contaminants availible from the

Unregulated Contaminants

This list of contaminants which, at the time of publication, are not subject to any proposed or promulgated national primary drinking water regulati regulations under SDWA. For more information check out the list, or vist the Drinking Water Contaminant Candidate List (CCL) web site.

- List of Unregulated Contaminants
- Drinking Water Contaminant Candidate List (CCL) Web Site
- Unregulated Contaminant Monitoring Program (UCM)

List of Contaminants & their MCLs

Primary Chemical Contaminants in SDWA

- Chemicals (~80 total)
  - Inorganic compounds (16)
    - Radionuclides (4 types/groups)
    - Elements (14)
  - **Organic compounds (~53)**
    - Non-halogenated compounds (12)
    - Halogenated compounds (~41)
    - Chlorinated compounds (40)
    - Pesticides (~24)

⇒ **75% of regulated organic drinking water contaminants are chlorinated organics**

⇒ **45% are pesticides**

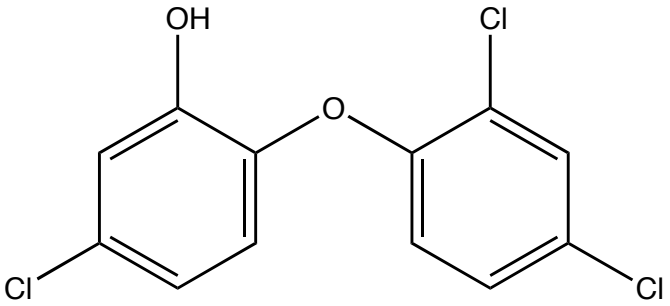
Lessons (To Be) Learned

- **Produce and use** chemicals that:
  - have natural counterpart or origin
  - degrade rapidly
  - have a good safety record

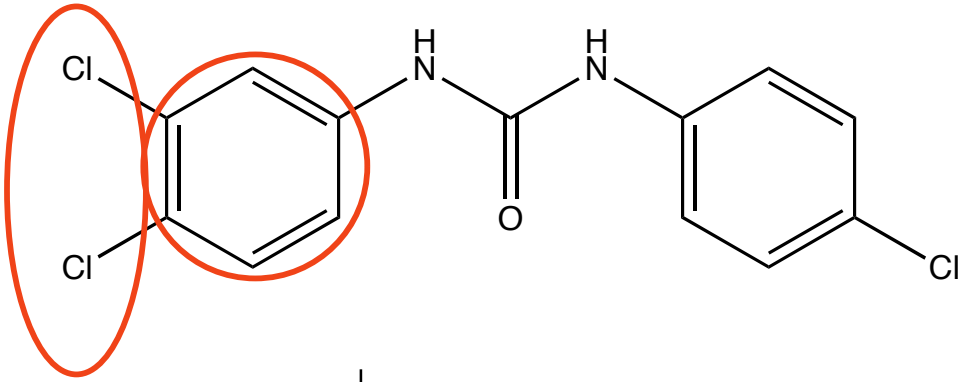
- **Avoid** chemicals that are
  - halogenated (Cl, Br, F substituents)
  - rare in nature / have random structure / mixtures
  - structurally related to chemicals of concern

A case study of incompatibility:
Antimicrobials & wastewater treatment

Triclosan (TCS)



Triclocarban (TCC)



Property	Triclosan	Triclocarban
Year Introduced	1964	1957
Log K_{OW} (at 25ºC, pH 7)	4.8	4.9

For each molecule in water, there are ~10^5 in octanol (fat)

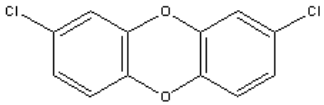
>1500 New Antimicrobial Products Since the Year 2000

- Production is increasing
- Benefits have been called into question (FDA, 2005)
- New risks are emerging

Image: Beyond Pesticides

Known / Potential Environmental and Human Health Risks of Triclosan

Degradates
(including chloroform)

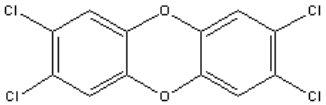


✓

Persistent
Environmental
Contaminant
✓

Cross-resistance
to Antibiotics
✓

Impurities



✓

Triclosan

Bioaccumulation
✓

Acts as Carcinogen,
Mutagen or
Teratogen?
(No, at least not directly)

Endocrine Disruption
✓

Antimicrobials: Endocrine Disruption in Frogs

Aquatic Toxicology 80 (2006) 217–227

AQUATIC TOXICOLOGY

www.elsevier.com/locate/aquatox

The bactericidal agent triclosan modulates thyroid hormone-associated gene expression and disrupts postembryonic anuran development

Nik Veldhoen [a], Rachel C. Skirrow [b], Heather Osachoff [b], Heidi Wigmore [b], David J. Clapson [a], Mark P. Gunderson [a], Graham Van Aggelen [b], Caren C. Helbing [a,*]

[a] *Department of Biochemistry and Microbiology, P.O. Box 3055, Stn. CSC, University of Victoria, Victoria, British Columbia V8W 3P6, Canada*
[b] *Pacific Environmental Science Centre, 2645 Dollarton Highway, North Vancouver, British Columbia V7H 1V2, Canada*

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Cell assay: concentrations of as low as 30 ng/L
alter thyroid hormone receptor mRNA expression

Antimicrobials: Unintended Modes of Action in Mussels

ELSEVIER

Available online at www.sciencedirect.com
ScienceDirect

Comparative Biochemistry and Physiology, Part C 145 (2007) 464–472

CBP

www.elsevier.com/locate/cbpc

Effects of Triclosan on *Mytilus galloprovincialis* hemocyte function and digestive gland enzyme activities: Possible modes of action on non target organisms

Laura Canesi [a,*], Caterina Ciacci [b], Lucia Cecilia Lorusso [b], Michele Betti [b], Gabriella Gallo [a], Giulio Pojana [c], Antonio Marcomini [c]

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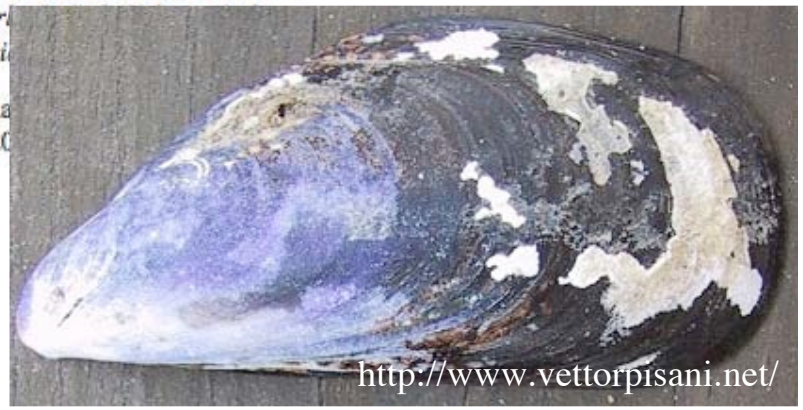
[b] *Istituto di Scienze Fisiologiche, Università "Carl*
[c] *Università Ca' Foscari di Venezi*

Received 9 November 2006; received in revised form 29 Janua
Available online 9 February 20



Antimicrobials: Endocrine Disruption in Rats

http://www.ealing.gov.uk/

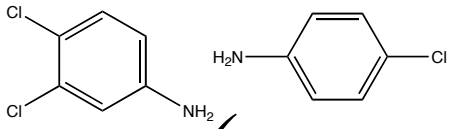
Short-Term *in Vivo* Exposure to the Water Contaminant Triclosan: Evidence for Disruption of Thyroxine

Kevin M. Crofton[1], Katie B. Paul[2], Michael J. DeVito[3] and Joan M. Hedge[1]

[1] Neurotoxicology Division and [3]Experimental Toxicology Division,
National Health and Environmental Effects Research Laboratory,
Office of Research and Development, U.S. EPA, Research Triangle Park, NC;
[2]Curriculum in Toxicology, University of North Carolina, Chapel Hill, NC.

Known / Potential Environmental and Human Health Risks of Triclocarban

Degradates



✓

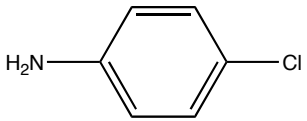
Persistent Environmental Contaminant

✓

Cross-resistance to Antibiotics

?

Impurities



? ✓

Triclocarban

Bioaccumulation

?

Acts as Carcinogen, Mutagen or Teratogen

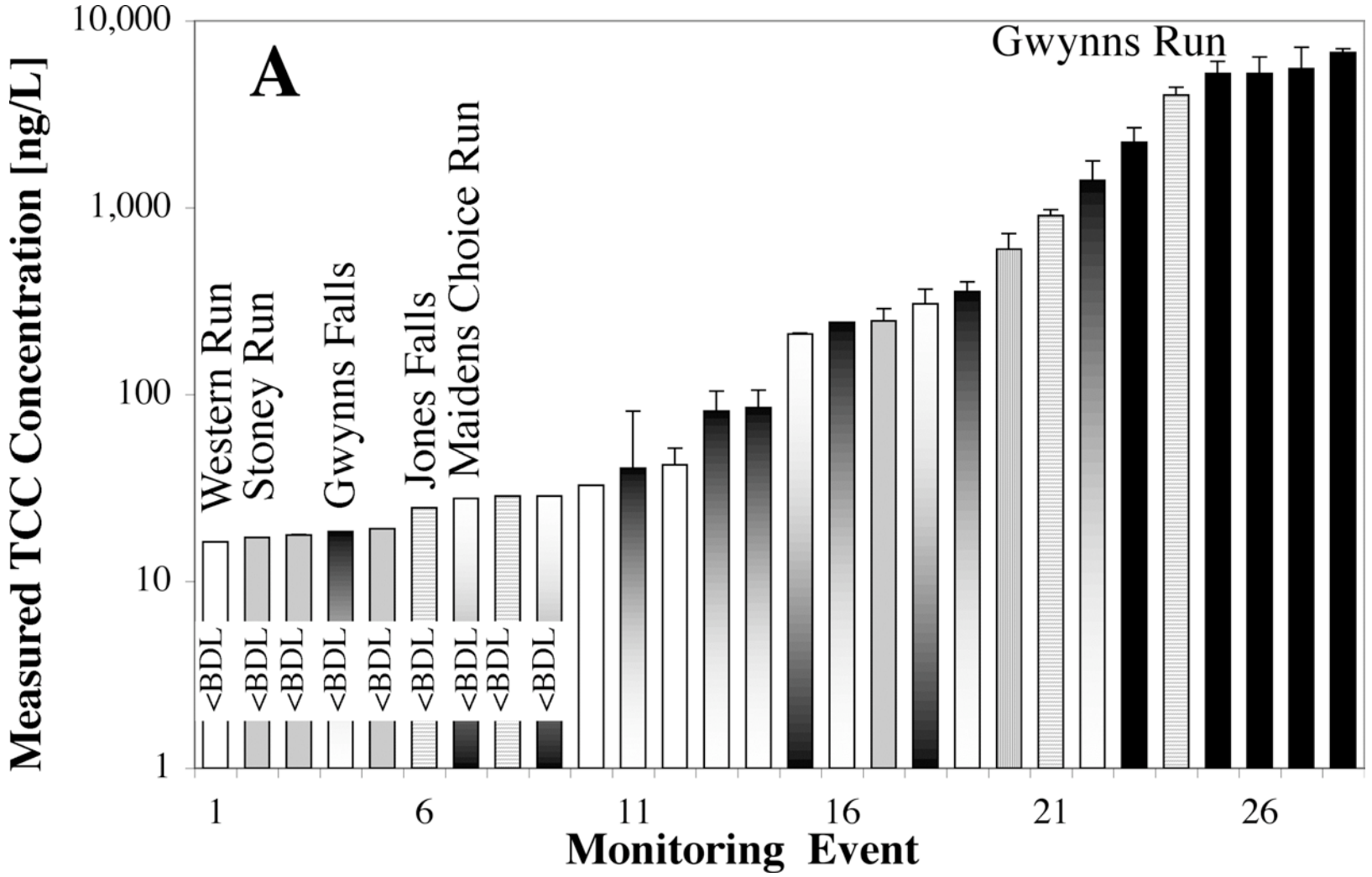
?

(Plausible Connection)

Endocrine Disruption

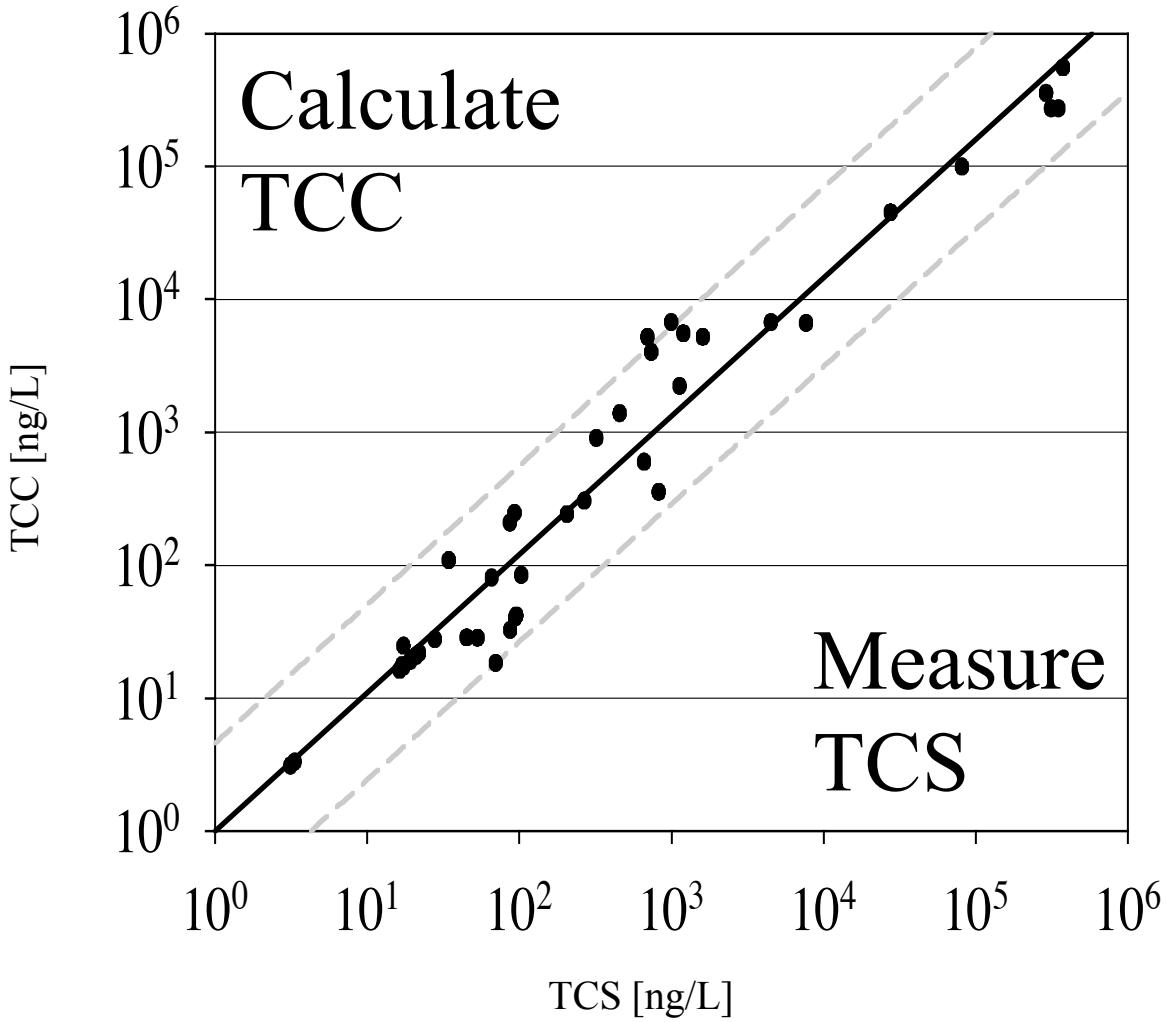
?

Triclocarban Contamination in Baltimore Streams



Halden & Paull, ES&T 38(18):4849-4855 (2004)

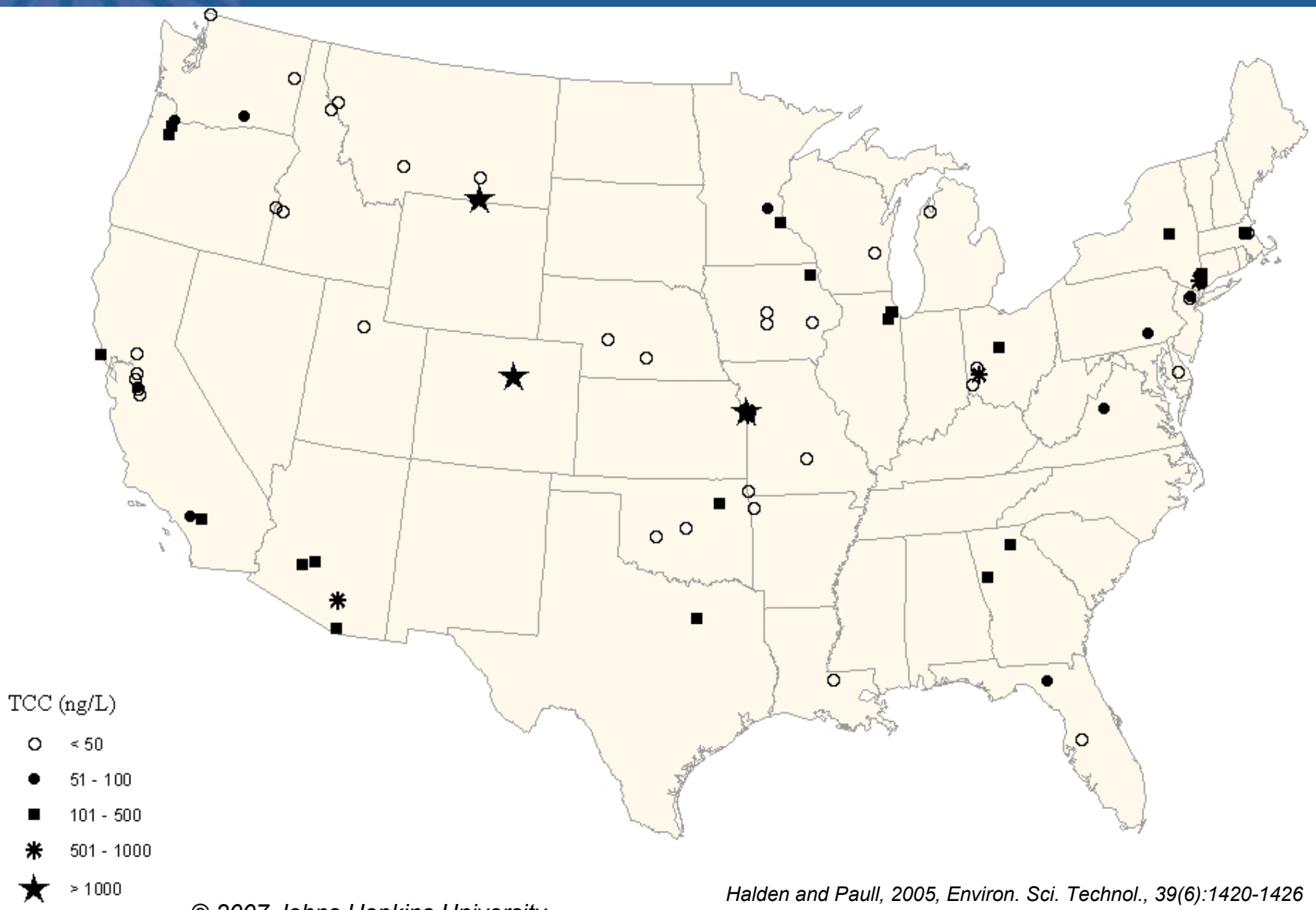
Co-Occurrence of TCC and TCS in MD Streams



$R^2 = 0.988$

Halden and Paull, 2005, Environ. Sci. Technol., 39(6):1420-1426

Predictions for 85 Streams Across the U.S.



Halden and Paull, 2005, Environ. Sci. Technol., 39(6):1420-1426

Predicted Nationwide Contamination Was Confirmed Experimentally

	Model	Experimental	
		Upstream	Downstream
Number of samples	85	18	18
Detection Frequency	60%	56%	100%
Mean [ng/L]	213	12±15	84 ±109

(Sapkota et al., Environmental Research 2007)

Antimicrobials Defy Wastewater Treatment

Environ. Sci. Technol. **2006**, *40*, 3634−3639

Partitioning, Persistence, and Accumulation in Digested Sludge of the Topical Antiseptic Triclocarban during Wastewater Treatment

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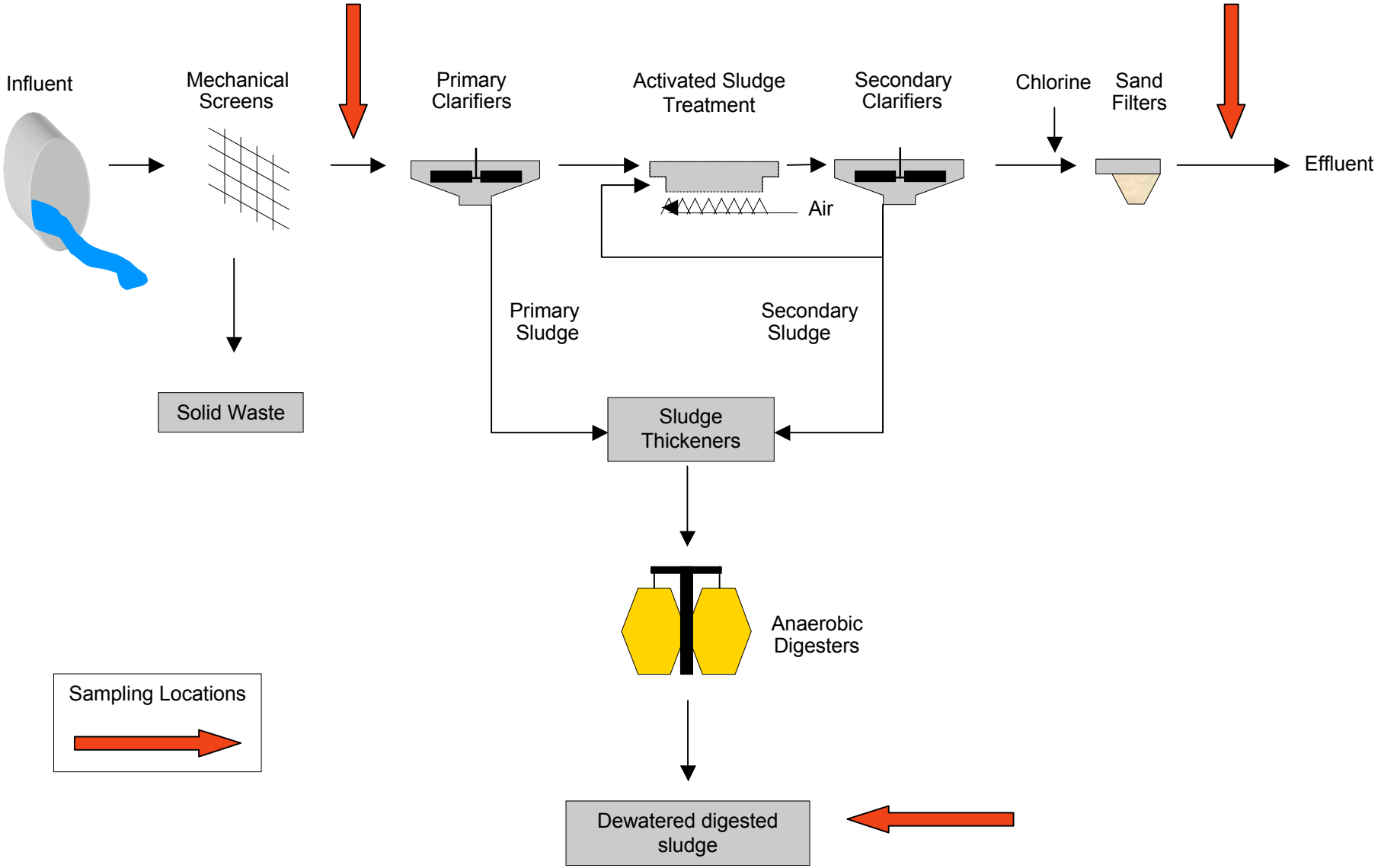
attention has been focused on PPCPs passing through conventional wastewater treatment plants (WWTPs) and becoming detectable in effluent-receiving streams (*3*), few studies have explored the partitioning of compounds into municipal wastewater residuals and their subsequent fate during sludge treatment (*1*, *4*, *5*). This lack of information is due in part to the difficulty of accurately detecting and quantifying PPCPs in the challenging analytical matrix of municipal sludge. Previously, our laboratory employed isotope dilution gradient liquid chromatography with electrospray ionization mass spectrometry (*6*) to perform a preliminary analysis of the behavior of PPCPs in a large activated sludge WWTP (*5*). Following development of a more selective method using triple quadrupole tandem mass spectrometry (*7*), this novel tool was applied to conduct a mass balance for a specific PPCP whose environmental fate has long been neglected (*4*).

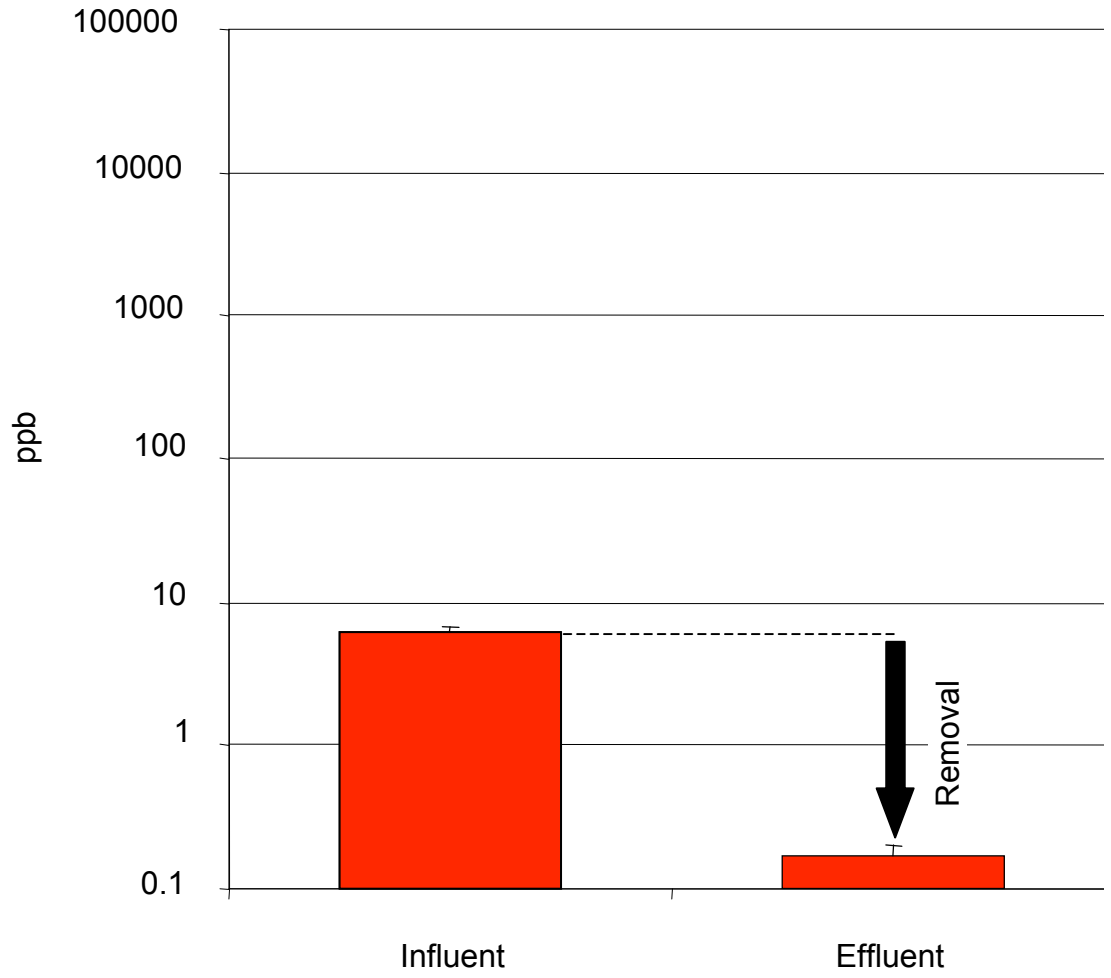
- Activated sludge WWTP
- 600 ML/D (180 MGD)
- Population served: 1.3 M

Process Diagram of Activated Sludge Wastewater Treatment Plant

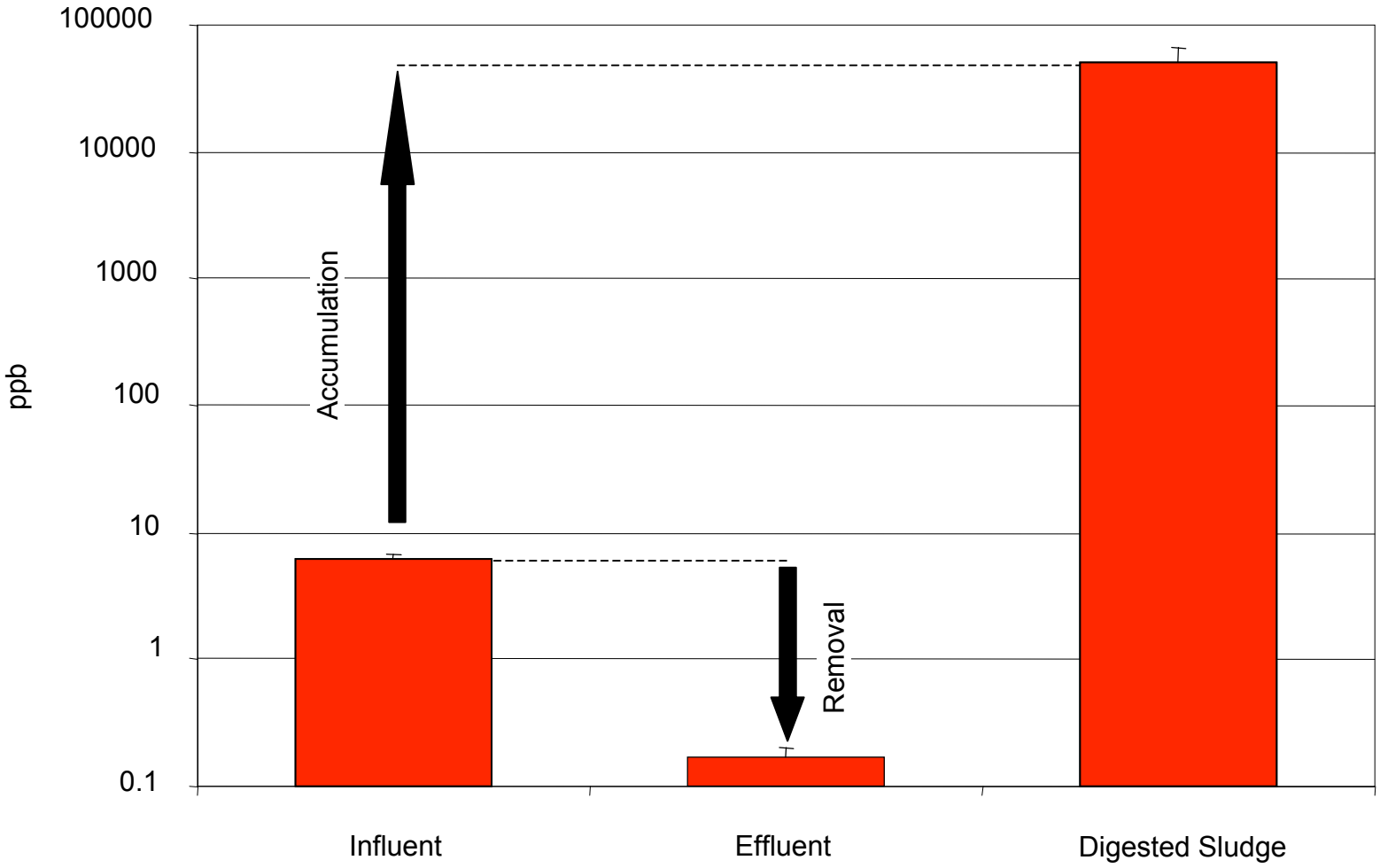


ES&T 40(11) 3634-39, (2006)

Triclocarban Is Removed From Wastewater

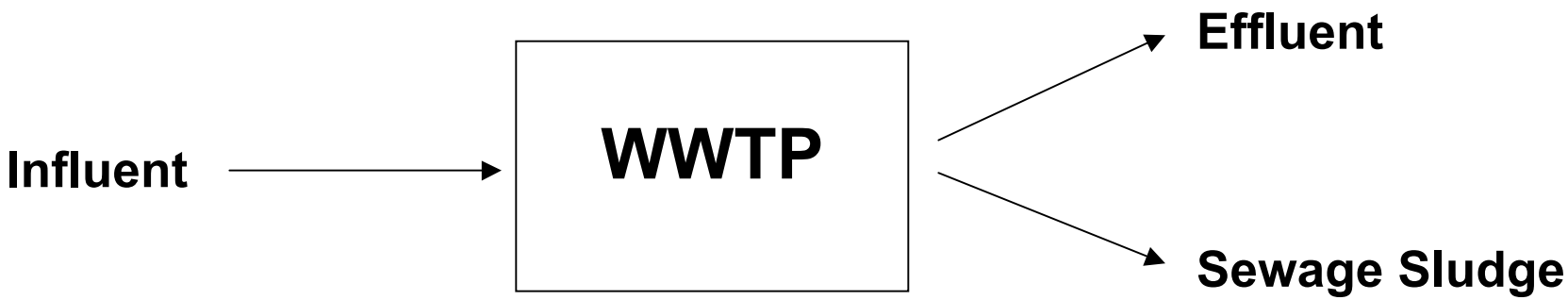


...Only to Accumulate in Sludge



ES&T 40(11) 3634-39, (2006)

Mass Balance Calculation



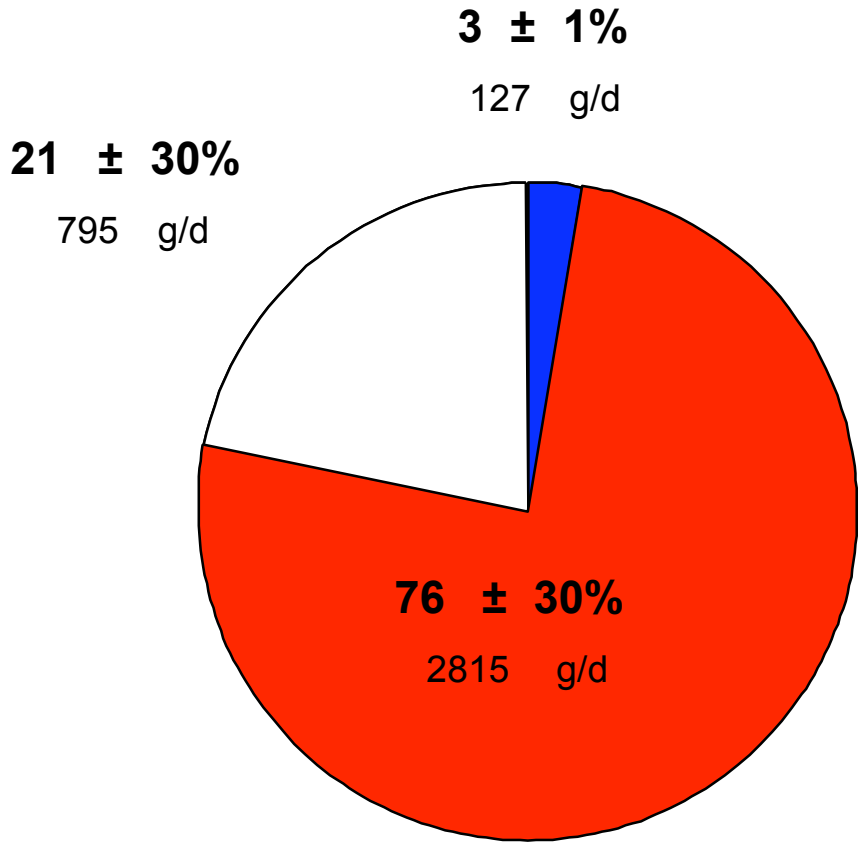
$$M_{trans} = \left(Q_{\inf} \times C_{\inf}\right) - \left(Q_{eff} \times C_{eff}\right) - \left(TS_{dig} \times Q_{dig} \times C_{dig}\right) - M_{vol}$$

M = Mass loading (kg/d)
Q = Flow rate (L/d)
C = Concentration (g/L)
TS = Total solids (%)

M_{vol} = negligible

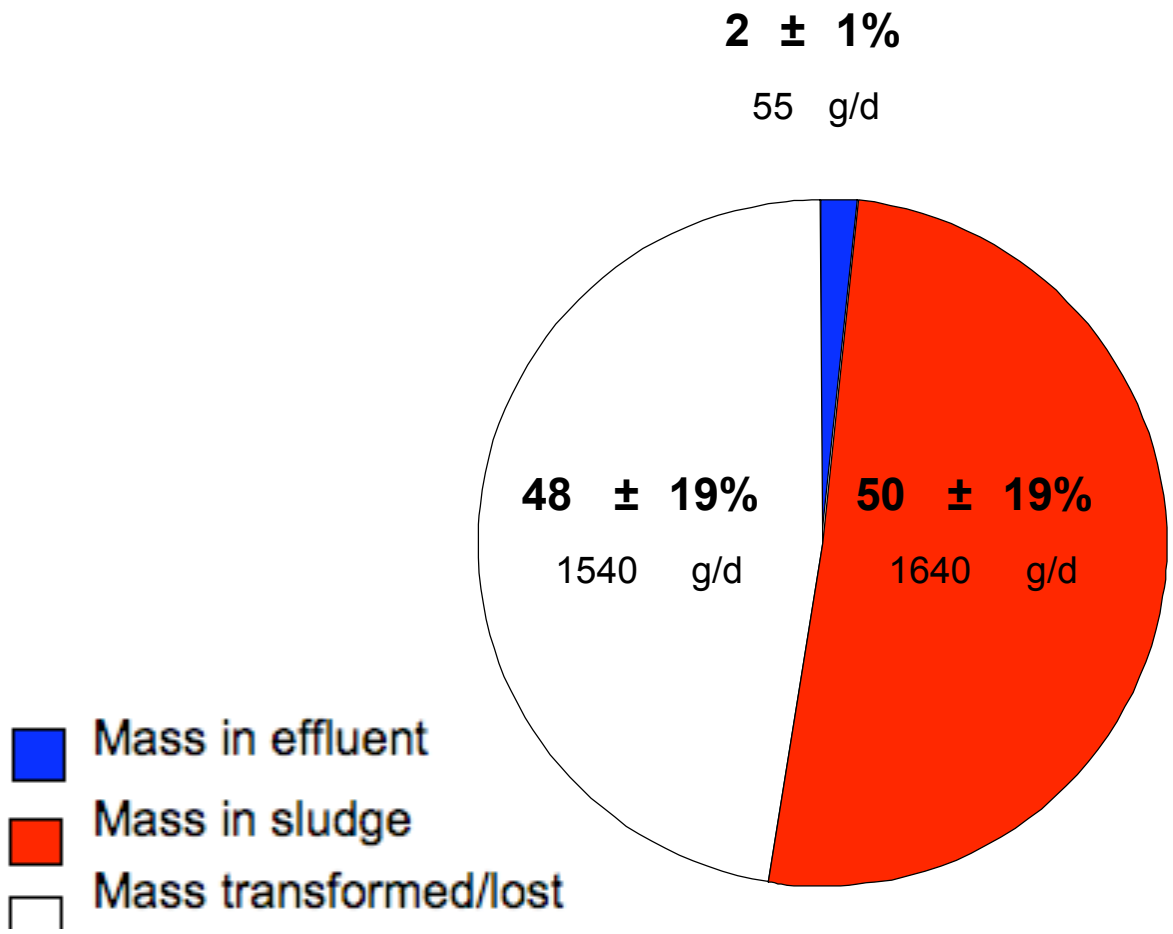
ES&T 40(11) 3634-39, (2006)

TCC Mass Balance for a Mid-Atlantic Plant



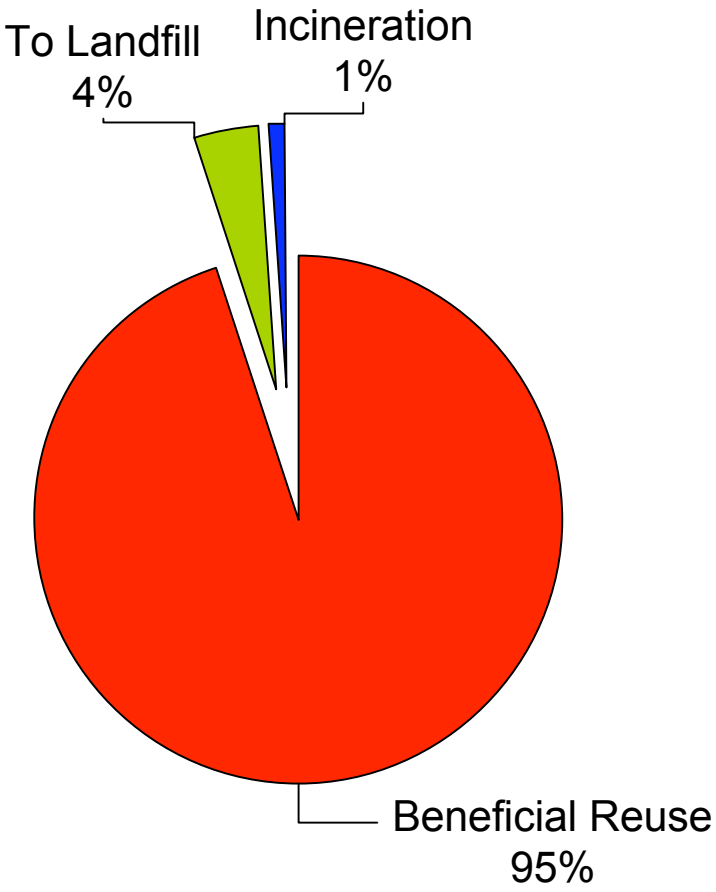
ES&T 40(11) 3634-39, (2006)

Triclosan Mass Balance for a Mid-Atlantic Plant



Heidler & Halden, 2007. Chemosphere, 66(2):362-369.

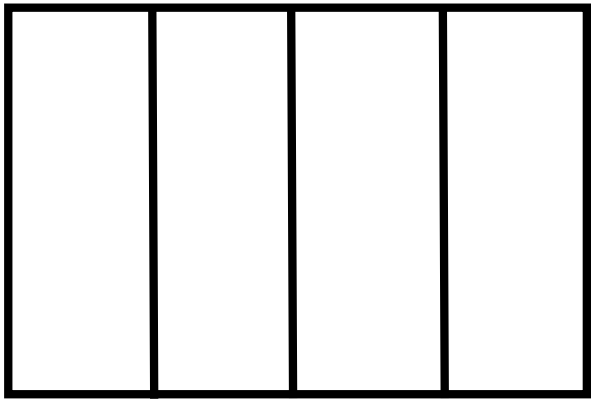
Fate of Sludge Produced at the WWT Plant



ES&T 40(11) 3634-39, (2006)

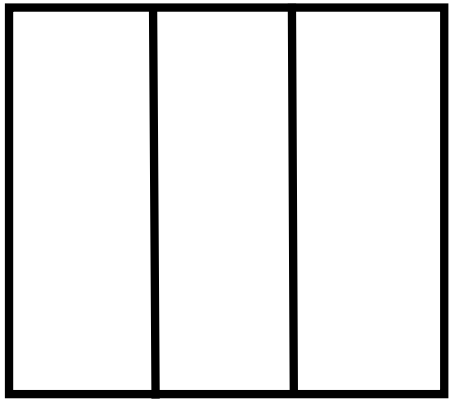
Unexpected Consequences of Consumer Behavior

Antibacterial bar soap used by consumers



4 Soap bars

"Active" ingredient (Triclocarban) applied onto soils

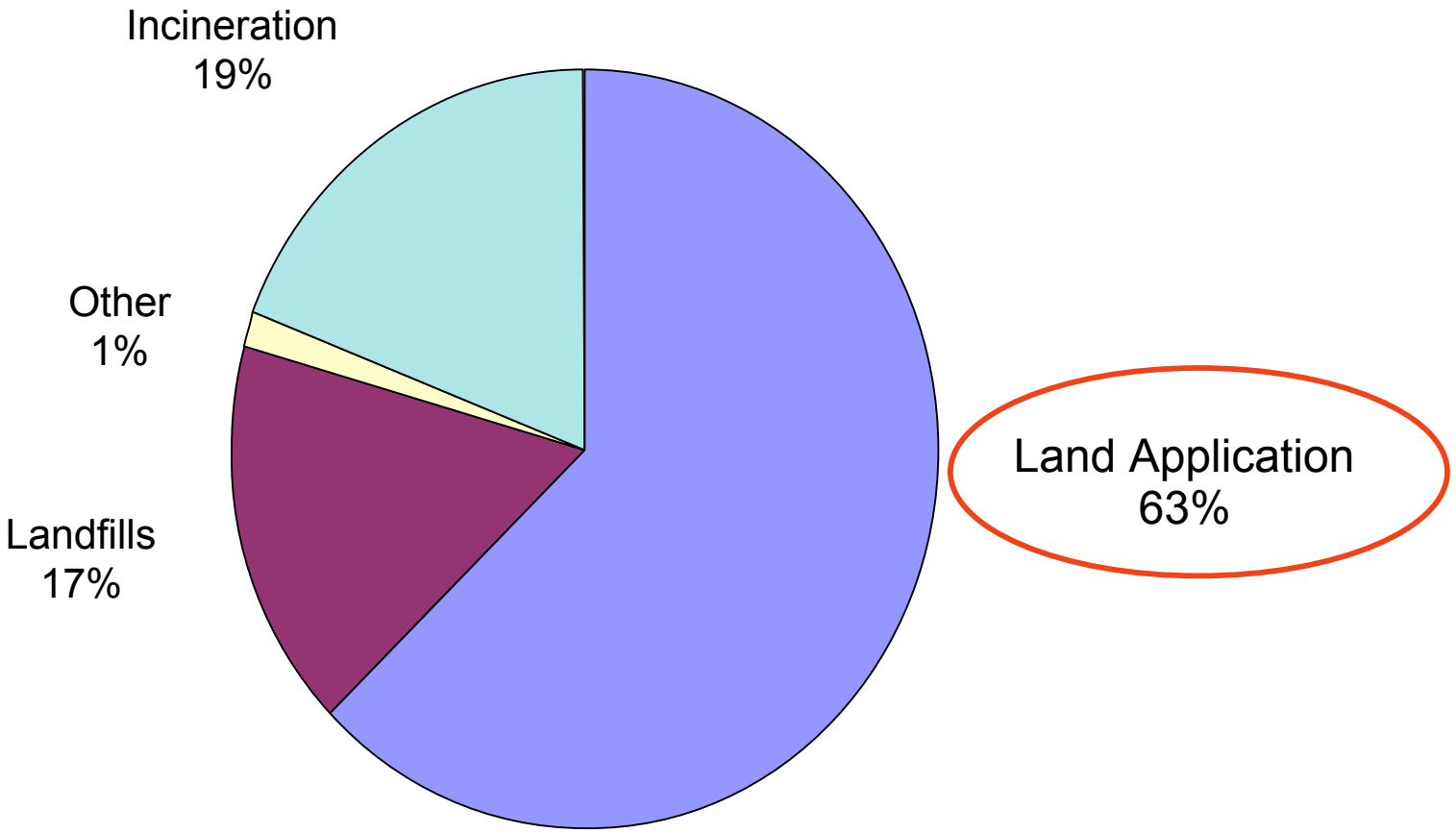


3 Soap bars

Environ. Sci. & Technol. 40(11) 3634-39, (2006)

Biosolids Recycling on a National Scale

12.5 Billion dry lb/yr (125,000 railroad cars) of sludge



Biosolids Applied to Land, National Research Council of the National Academies, 2002

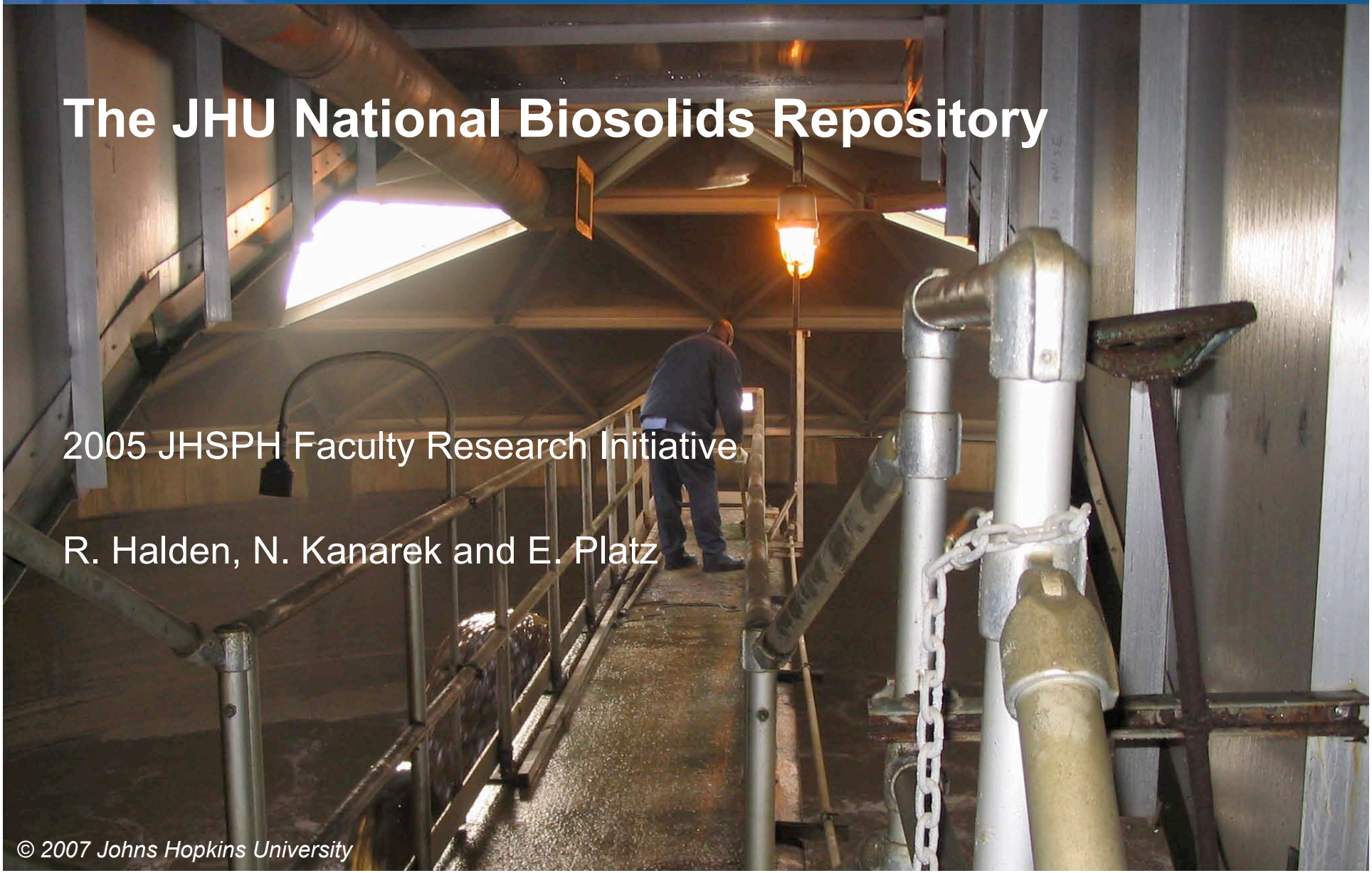
Agricultural Land as a Disposal Site for Antimicrobials

Preliminary estimate of mass of antimicrobial compounds deposited on U.S. soils based on 15 treatment plants

	TCS	TCC
Mass applied ± 95%CI (U.S. pounds/year)	135,000 ± 75,000	350,000 ± 113,000

Unpublished data; Heidler et al.

Sludge: a Repository of Recalcitrant Chemistry



The JHU National Biosolids Repository

2005 JHSPH Faculty Research Initiative

R. Halden, N. Kanarek and E. Platz

Lessons (To Be) Learned

- **View "waste" as a resource**
  - e.g., "wastewater" really is raw drinking water, keep pollutants out (metals, antimicrobials, etc.)

- **Control chemical inputs into the environment more tightly**
  - evidence of failure to learn from past mistakes

- **Pollution prevention is the fastest, most economical and most effective way of improving environmental and human health**
  - applies to pesticides, pharmaceuticals, personal care products, etc.

Will Persistent Antimicrobials Be Taken Off the Market?

Select concerns:

- no proven benefit for use in general household settings (FDA panel, 2005)
- production still increasing (>1 million pounds/yea)
- detectable in most U.S. surface waters
- toxic to aquatic biota at ng/L level (parts-per-trillion)
- promote cross-resistance to clinically important antibiotics
- environmentally persistent
- accumulate in algae
- endocrine disrupting properties
- occur in agricultural soils at ppm levels
- detectable in fish, house dust, adult & fetal blood and in
- 97% of U.S. breast milk samples

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- Guy Hollyday
- John Martin and Nick Frankos

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- JHU Center for a Livable Future
- JHU Faculty Research Initiative
- CDC