Overview: Quaternary Ammonium Compounds as Potential Designated Chemicals

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Office of Environmental Health Hazard Assessment

Presentation to the Scientific Guidance Panel

March 4, 2020

OEHHA

BIOMONITORING CALIFORNIA

SGP actions on quaternary ammonium compounds (QACs)

- March 2019: Panel requested preliminary screening of QACs
- July 2019: Preliminary screening reviewed by SGP
  - Panel recommended that OEHHA prepare a potential designated chemical document on QACs

Designated chemicals

- Entire pool of chemicals that can be considered for biomonitoring by the Program
- Chemicals are designated based on:
  - Inclusion in CDC's National Reports on Human Exposure to Environmental Chemicals program
  - Recommendations by the Scientific Guidance Panel (SGP) for Biomonitoring California

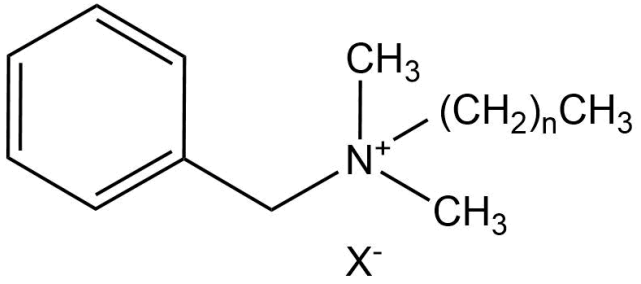
Background: Criteria for recommending designated chemicals

- ***Exposure or potential exposure*** to the public or specific subgroups
- The ***known or suspected health effects*** resulting from some level of exposure based on peer reviewed scientific studies
- The ***need to assess the efficacy of public health actions*** to reduce exposure to a chemical
- The ***availability of a biomonitoring analytical method*** with adequate accuracy, precision, sensitivity, specificity, and speed
- The ***availability of adequate biospecimen samples***
- The ***incremental analytical cost*** to perform the biomonitoring analysis for the chemical

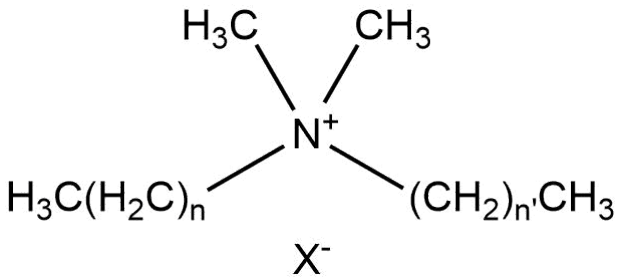
Presentation outline

- Description of QACs as a class
- Exposure potential
- Possible health concerns
- Potential to biomonitor
  - Information on absorption and excretion
  - Selected chemical properties and environmental fate
  - Available biomonitoring data/methods
  - Analytical considerations
- Public health importance

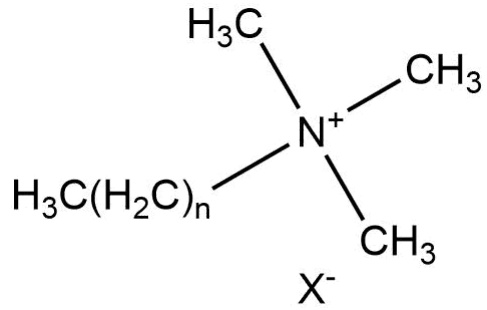
Chemical structures of selected QACs



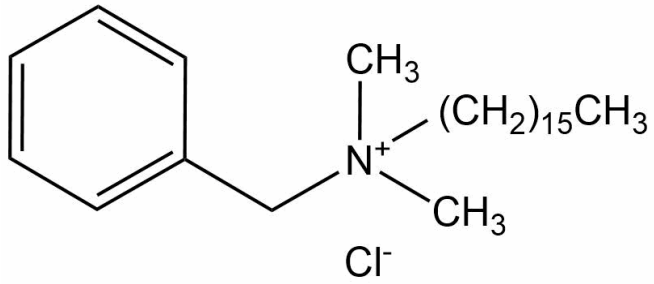
Benzylalkyldimethyl ammonium compounds (BACs)



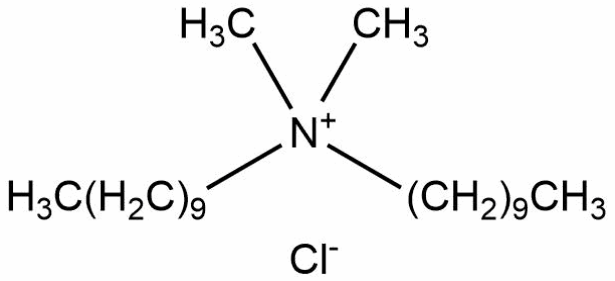
Dialkyldimethyl ammonium compounds (DADMACs)



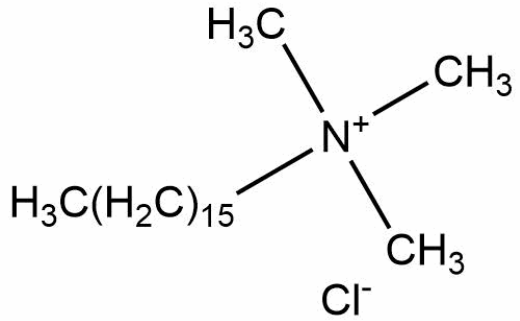
Alkyltrimethyl ammonium compounds (ATMACs)



Benzylhexadecyldimethyl ammonium chloride

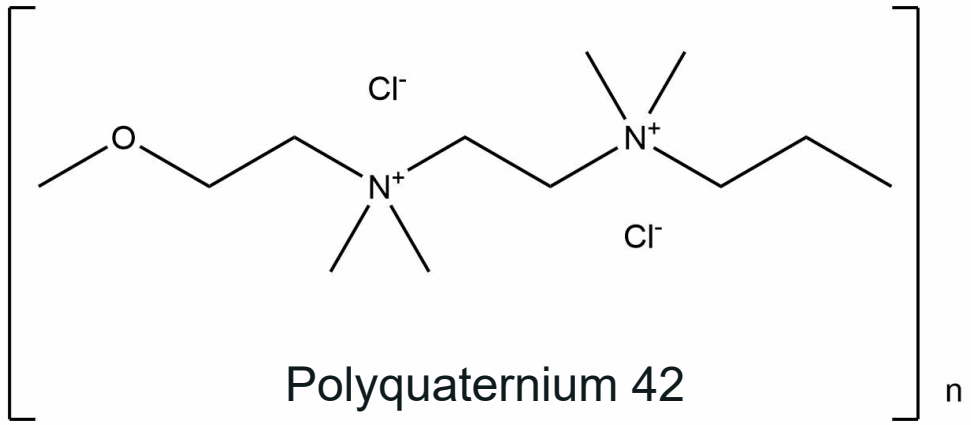


Didecyldimethyl ammonium chloride

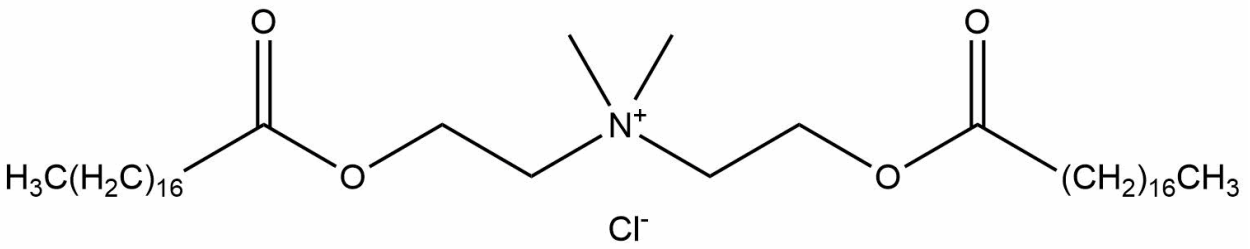


Hexadecyltrimethyl ammonium chloride

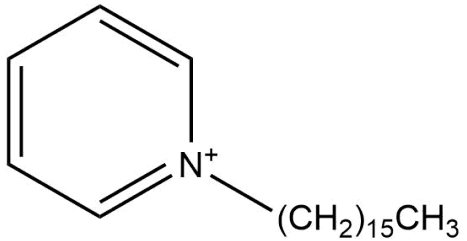
Chemical structures of selected QACs (cont.)



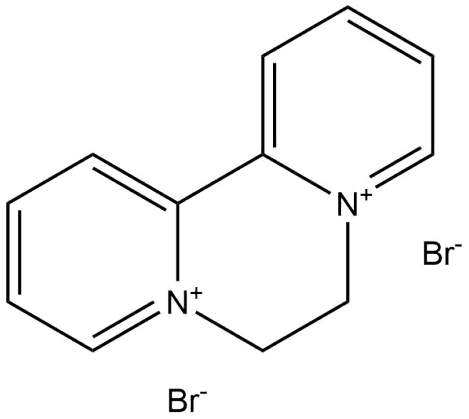
Polyquaternium 42



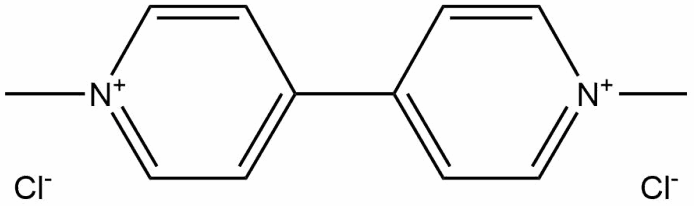
Esterquat 1



Cetylpyridinium chloride



Diquat dibromide



Paraquat dichloride

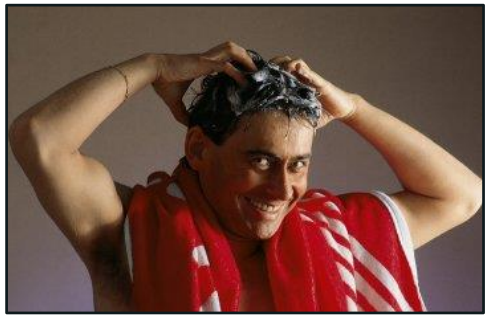
Volume of use for QACs reviewed

- National aggregate production volume
  - Located 20 QACs with >100K pounds produced/imported in 2015
  - Of these, 11 were high production chemicals (>1M pounds)
- California data for QACs identified as registered pesticides, including those used as antimicrobials
  - About half had sales >100K pounds in 2018
  - Several had sales >1M pounds in 2018
  - Agricultural application of paraquat dichloride >1M pounds (rank #23) in 2017

Chemical functions include:

- Antimicrobial
- Preservative
- Antistatic
- Softening
- Surfactant
- Corrosion inhibitor

QACs are used in a variety of products and applications



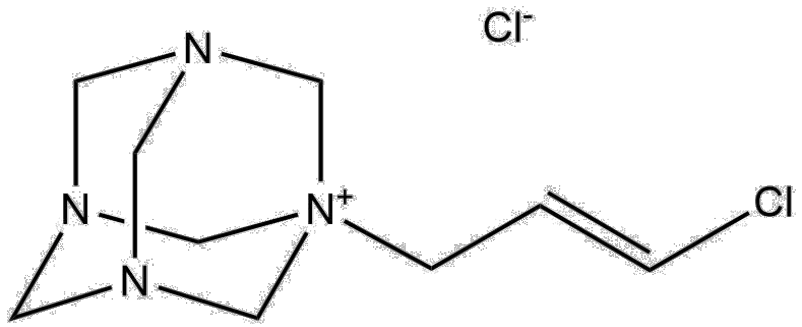
Environmental detections

- Detected in:
  - Sediment
  - Sludge
  - Wastewater treatment plant (WWTP) influent and effluent
- Other detections:
  - Indoor house dust samples collected in Germany
  - Air samples from a US hospital
  - Fish sampled from Nordic countries – mostly cod, some perch

Possible health concerns

- Dermal irritation
- Respiratory effects, including asthma
- Nervous system effects
- Reproductive and developmental effects
- Immunological effects
- Altered cellular function and effects on metabolism

Possible health concern: Dermal irritation example

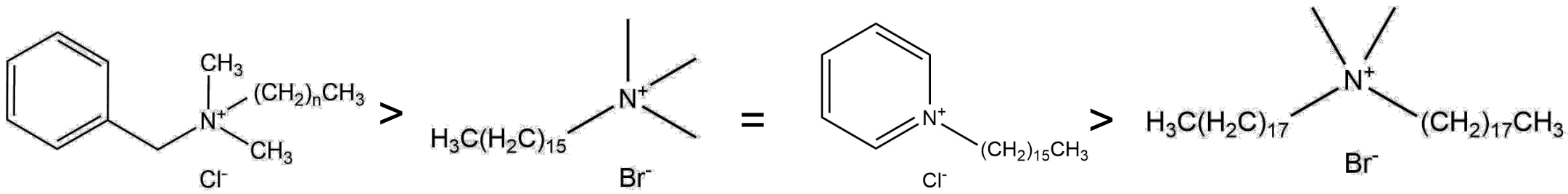


Quaternium 15

- Biocide, preservative, and surfactant
- Used in cosmetics and personal care products, and in cleaning products
- Formaldehyde releaser
- Allergic contact dermatitis

Possible health concern: Respiratory effects

- Some QACs identified by the Association of Occupational and Environmental Clinics (AOEC) as asthmagens
- Some epidemiologic studies and case reports linked QAC exposures with work-related asthma
- Reduced tidal volume with a concomitant increase in respiratory rate observed in mice after inhalation exposure to QACs (Larsen et al., 2012)



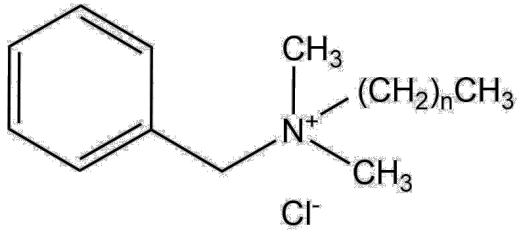
Benzalkonium chloride

Hexadecyltrimethyl ammonium bromide

Cetylpyridinium chloride

Dioctadecyldimethyl ammonium bromide

- Inhibition of mitochondrial respiration



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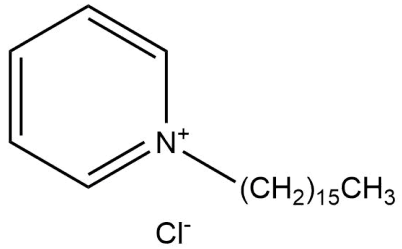
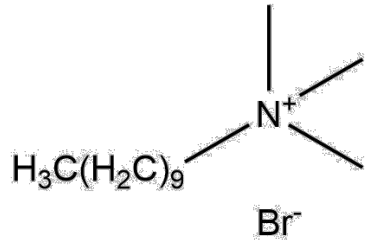


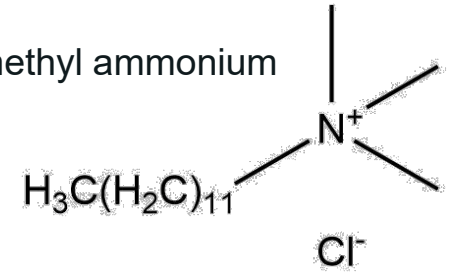
Cetylpyridinium chloride

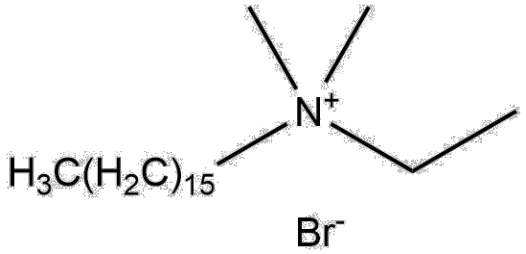


Decyltrimethyl ammonium bromide

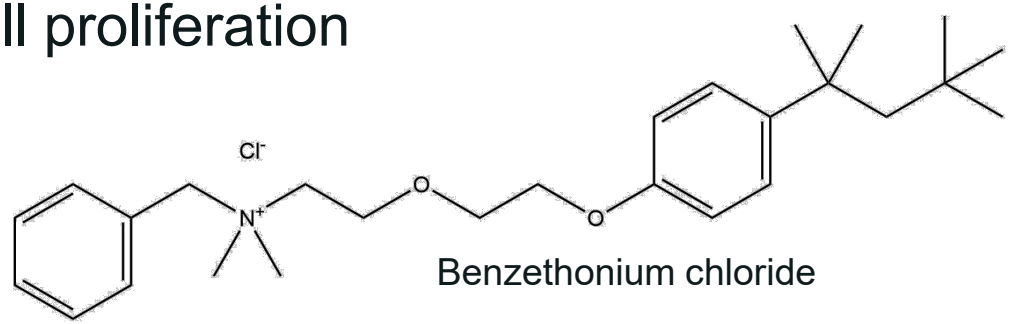
- Selected ToxCast/Tox21 results
  - Located 21 QACs active in >100 assays
  - Various effects at sub-cytotoxic concentrations noted, including altered gene expression and cell proliferation

Dodecyltrimethyl ammonium chloride





Ethylhexadecyldimethyl ammonium bromide



Benzethonium chloride

Information on absorption and excretion

- Absorption rates for selected QACs located
  - Reported dermal rates range from <1-8.3%
  - Reported oral rates range from 10-88%
- Excretion
  - Majority of dose administered in animal studies excreted as parent QAC in feces
  - Limited information located on metabolites excreted in urine

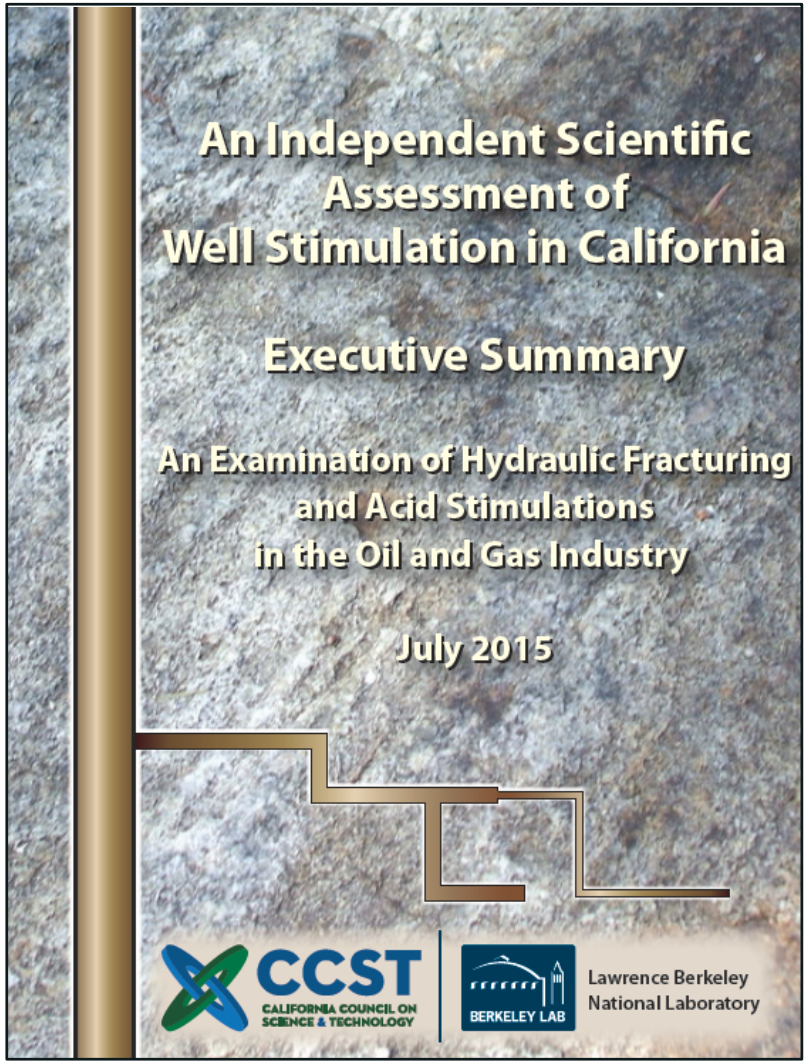
Selected chemical properties and environmental fate information

- Chemical properties
  - Water solubility varies by chain length
  - Limited information located on bioaccumulation/ bioconcentration
- Environmental fate
  - Strongly sorbed by soils and sewage-affected sediments
  - >70-90% removed in wastewater treatment
  - Biodegradation appears to be greatest for shorter-chain QACs under aerobic conditions

Potential to biomonitor

- Very little biomonitoring data located
- Methods papers
  - Spiked diquat dibromide and paraquat dichloride in human urine (Whitehead et al., 2010)
  - Determination of phosphatidylcholine-derived QACs in human plasma, serum, and urine (Steuer et al., 2016)
- Preliminary biomonitoring research in progress
- Method(s) development would be required to measure QACs in future Biomonitoring California studies

Public health importance



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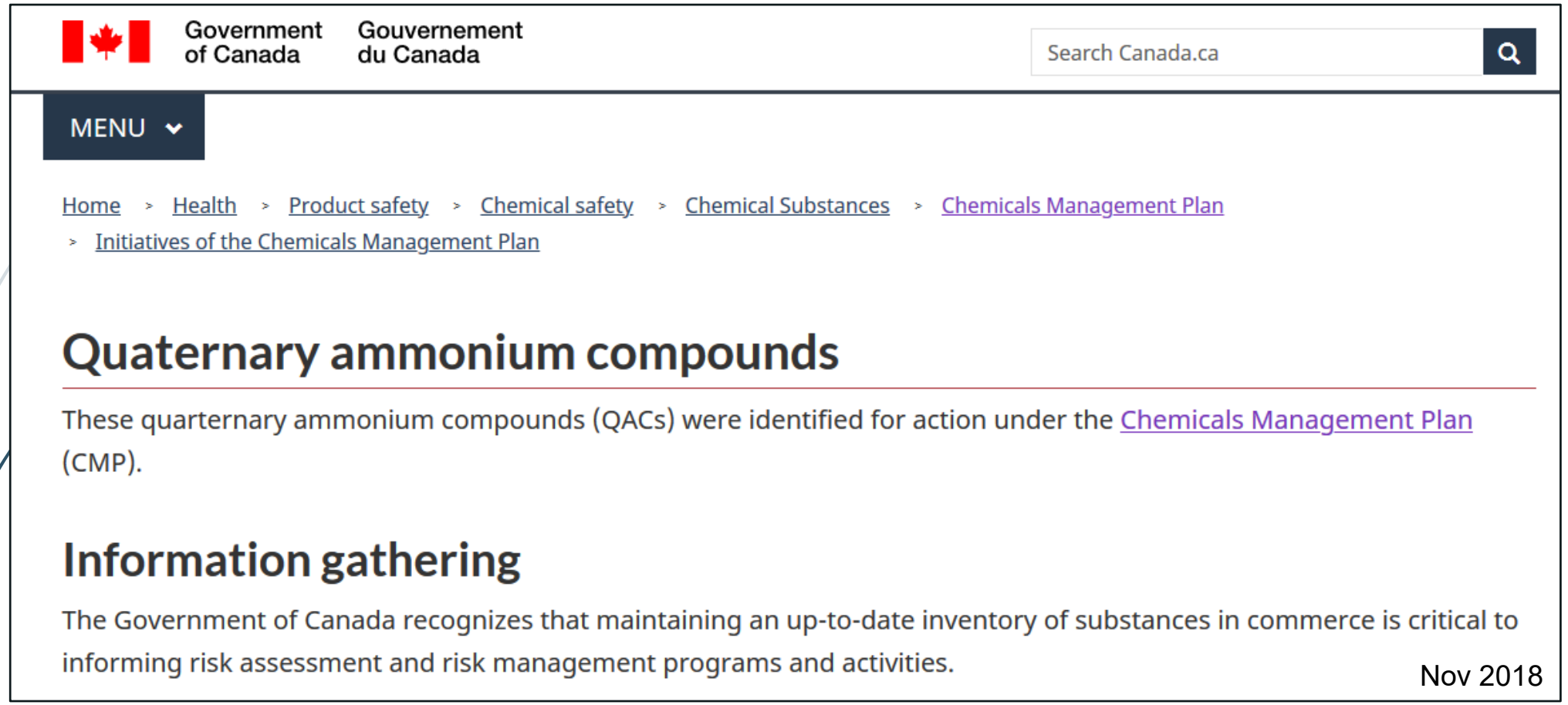

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Quaternary ammonium compounds

These quarternary ammonium compounds (QACs) were identified for action under the Chemicals Management Plan (CMP).

Information gathering

The Government of Canada recognizes that maintaining an up-to-date inventory of substances in commerce is critical to informing risk assessment and risk management programs and activities.

Nov 2018

Public health importance

State of the Science Review

Do we know how best to disinfect child care sites in the United States? A review of available disinfectant efficacy data and health risks of the major disinfectant classes

Stephanie M. Holm MD, MPH [a,b,c], Victoria Leonard RN, PhD [d], Timur Durrani MD, MPH [a,d,e], Mark D. Miller MD, MPH [a,d]

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[d] Western States Pediatric Environmental Health Specialty Unit–University of California San Francisco, San Francisco, CA
[e] California Poison Control System, San Francisco, CA

Jan 2019

Public health importance

Benzalkonium Chlorides: Uses, Regulatory Status, and Microbial Resistance

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[b]Department of Computer Science, University of California, Davis, Davis, California, USA
[c]Genome Center, University of California, Davis, Davis, California, USA

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July 2019

Public health importance

Identifying and Prioritizing Chemicals with Uncertain Burden of Exposure: Opportunities for Biomonitoring and Health-Related Research

Edo D. Pellizzari,[1] Tracey J. Woodruff,[2] Rebecca R. Boyles,[3] Kurunthachalam Kannan,[4] Paloma I. Beamer,[5] Jessie P. Buckley,[6] Aolin Wang,[2] Yeyi Zhu,[7,8] and Deborah H. Bennett[9] (Environmental influences on Child Health Outcomes)

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Dec 2019

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State of the Science Review

Benzalkonium Chlorides: Uses, Regulatory Status, and Microbial Resistance

Beatriz Merchel Piovesan Pereira,[a,b] Ilias Tagkopoulos[b,c]

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Questions?