Final Report

Monitoring Strategies for Chemicals of Emerging Concern (CECs) in Recycled Water

Recommendations of a Science Advisory Panel

Panel Members

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Acknowledgments

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Executive Summary

California presently recycles approximately 650,000 acre-feet of water per year, but has identified the potential to reuse an additional 1.5 million acre-feet in the future. To encourage expanded reuse in a state that is experiencing water shortages, the California State Water Resources Control Board (SWRCB) adopted a Recycled Water Policy in February 2009 intended to provide permitting clarity for recycled water projects. One challenge in developing that policy was how to address new classes of chemicals, such as pharmaceuticals, current use pesticides, and industrial chemicals, collectively referred to as chemicals of emerging concern (CECs). Many CECs are potentially present in recycled water, but the detection of many of these chemicals is so recent that robust methods for their quantification and toxicological data for interpreting potential human or ecosystem health effects are unavailable.

Recognizing that consideration of CEC effects on human health and aquatic life is a rapidly evolving field, and that regulatory requirements need to be based on best available science, the SWRCB included a provision in the Recycled Water Policy to establish a Science Advisory Panel. The Panel's primary charge is to provide guidance for developing monitoring programs that assess potential CEC threats from various water recycling practices, including indirect potable reuse via surface spreading; indirect potable reuse via subsurface injection into a drinking water aquifer; and urban landscape irrigation.

The Panel was formed in May 2009 and includes six national experts in the fields of chemistry, biochemistry, toxicology, epidemiology, risk assessment and engineering, with more than 100 years of combined experience investigating CEC issues. The Panel held four in-person meetings and numerous conference calls over the last year. The meetings included the opportunity for stakeholder input in clarifying their charge, exchange of information, dialog with the Panel and consideration of public comments on the draft report. This report provides the results from the Panel's deliberations, including four products intended to assist the State in refining its recycled water policy.

Product #1: A conceptual framework for determining which CECs to monitor

Given that thousands of chemicals are potentially present in recycled water and that information about those chemicals is rapidly evolving, the Panel recommends that the State rely on a transparent, science-based framework to guide prioritization of which CECs should be included in recycled water monitoring programs both now and in the future as additional data become available. Figure ES1 describes the Panel's recommended framework, which includes four steps:

1. Compile environmental concentrations (e.g., measured environmental concentration or MEC) of CECs in the source water for reuse projects;
2. Develop a monitor triggering level (MTL) for each of these compounds (or groups thereof) based on toxicological relevance;
3. Compare the environmental concentration (e.g., MEC) to the MTL. CECs with a MEC/MTL ratio greater than "1" should be prioritized for monitoring. Compounds

with a ratio less than "1" should only be considered if they represent viable treatment process performance indicators; and,

4. Screen the priority list to ensure that a commercially-available robust analytical method is available for that compound.

This part of the framework is focused on CECs for which there are concentration data from recycled source water and toxicological information. The framework also includes a provision for prioritizing chemicals for which such information is presently unavailable and which are referred to in the framework as *"unknown unknowns"*. For these chemicals, the framework focuses on the prediction of environmental concentrations and the use of bioanalytical and chemical screening methods to identify chemicals for which there is the greatest urgency in developing MEC and MTL data for further assessment. The Panel understands that a chemical-by-chemical approach for prioritization of CECs is difficult because of limited resources and the growing number of CECs being identified. The Panel recognizes that bioanalytical methods will likely be the best way to accomplish this task. Although the USEPA have developed high-throughput bioanalytical screens for chemical testing, a prioritization framework for the evaluation of water using bioanalytical methods is not available at this point in time. However, the Panel encourages this topic to be a focus of research and development and future review meetings by an independent advisory panel (suggested for 2013) as more information becomes available.

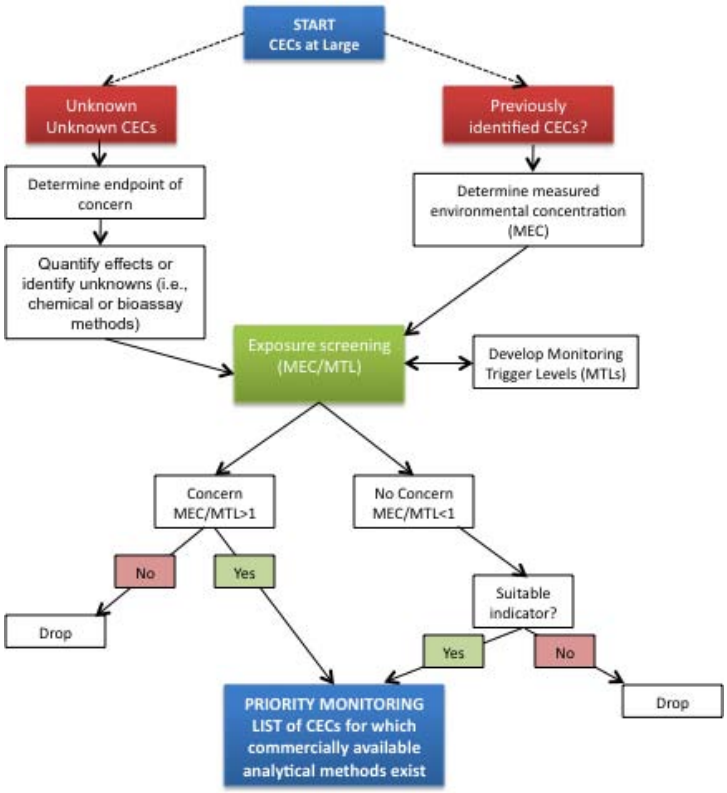

Figure ES1. Conceptual framework to prioritize CECs for inclusion in recycled water monitoring programs.

In addition to defining an approach to select CECs to monitor based on their potential to pose a health risk, the Panel also defined an approach to identify indicator compounds for assessing treatment performance. Most reuse projects employ multiple treatment processes with a demonstrated ability to remove contaminants, but the treatment processes need a monitoring program designed to protect against system performance failures. The Panel's

recommended approach for monitoring removal of CECs during treatment is to use a combination of surrogate parameters and CEC indicator compounds tailored to monitor the removal efficiency of individual unit processes. An indicator compound is an individual CEC that represents certain physicochemical and biodegradable characteristics of a family of trace organic constituents. The indicator compounds are relevant to fate and transport of broader classes of chemicals and provide a conservative assessment of removal during treatment. A surrogate parameter is a quantifiable change of a bulk parameter that can measure the performance of individual unit processes (often in real-time) or operations in removing trace organic compounds and/or assuring disinfection.

Product #2: Application of the framework to identify a list of chemicals that should be monitored presently

To assist the State in short-term program implementation, the Panel compiled available California MEC data and derived initial MTLs from drinking water benchmarks to apply its recommended screening approach and identify the chemicals that should be prioritized for present CEC monitoring. In applying the framework, the Panel made a number of conservative assumptions (e.g., MECs reported to the Panel are indeed representative for the entire state, analytical method used to quantify are accurate, etc.) to maximize the number of candidate chemicals that are toxicologically relevant.

For groundwater recharge projects, four indicator compounds were prioritized based on their toxicological relevance: N-nitrosodimethylamine, 17beta-estradiol, caffeine, and triclosan. In addition, four additional CECs (N,N-Diethyl-meta-toluamide (DEET), gemfibrozil, iopromide and sucralose) were identified for surface spreading and direct injection operations as viable performance indicator compounds along with certain surrogate parameters (e.g., ammonia, dissolved organic carbon, conductivity), which differ by the type of reuse practice. The Panel also recommended method reporting levels (MRLs) that were compound specific and that ranged from 1 to 100 ng/L for these CECs. For monitoring programs to assess CEC threats for urban irrigation reuse, none of the chemicals for which measurement methods and exposure data are available exceeded the threshold for monitoring priority. This is largely attributable to higher MTLs because of reduced water ingestion in a landscape irrigation setting compared to drinking water. For irrigation applications, the Panel recommends monitoring emphasis be placed on use of surrogate parameters that can demonstrate that the treatment processes employed are effective in removing CECs.

The Panel emphasizes that all compounds listed above represent an initial list based on the limited data that are presently available and on a number of qualifying assumptions discussed in the report. The Panel believes it is critical to emphasize that if a measured or predicted concentration of a CEC at the point of monitoring (POM) exceeds its respective MTL, the finding does not indicate a public health risk exists. The MTLs and their application in the Panel's proposed framework are developed to be conservative and used only for the purpose of prioritizing CECs for monitoring. The Panel's proposed MEC/MTL ratios should not be used to make predictions about risk.

While the priority list of CECs represents a conservative screening of "CECs at large", the information available for such screening is growing rapidly and the Panel urges the State to reapply this prioritization process on at least a triennial basis. In order to fill data gaps for CECs with limited or no information on MECs in California, the Panel suggests that the State initially conduct a more thorough review of CECs likely to occur in recycled water using MEC and predicted environmental concentration (PEC) data from the peer-reviewed literature and occurrence studies outside California. Those CECs that exhibit MEC/MTL ratios above "1" could be placed on a secondary monitoring list that is measured less frequently to confirm either presence or absence of these CECs in recycled water in California. In addition, this secondary monitoring list could be populated by CECs that exhibit a relatively low MTL (less than 500 ng/L) based on the Panel's initial screening of various toxicological data bases. Results of these efforts, along with the monitoring data collected as part of the Panel's recommended program, can provide the basis for revising the proposed initial monitoring list during the next, and each, triennial review.

Product #3: A sampling design and approach for interpreting results from CEC monitoring programs

The Panel recommends a phased, performance-based approach for implementing CEC recycled water monitoring programs and a multi-tiered framework for interpreting the resulting data. Use of multiple tiers allows for a flexible, adaptable response to increase or decrease the information requirements from the monitoring program based on the initial results, providing a cost-effective means for incremental information gathering. The report also contains specific performance-based recommendations regarding strict sampling and analytical measurement quality assurance guidelines that are required at each phase.

The first phase involves screening that would be initiated at project start-up and continue through the early years of project operation. Recommended monitoring frequency during this first phase would be quarterly at project start-up decreasing to twice annually for more mature operational phases. If a specific CEC consistently exhibits low occurrence, the Panel recommends deleting the CEC from further monitoring provided that production data do not suggest a significant increase in use. If CECs exceed thresholds identified in the report, the Panel recommends moving to a second phase of enhanced monitoring to confirm the presence and frequency of such CEC(s). The third phase, should concentrations continue to be high, would require initiation of source identification and/or toxicology studies. The final phase would involve engineering removal studies and/or modification of plant operation if found to be warranted by the results of the third phase.

While the Panel provides recommended thresholds for each of these phases, conservative values were selected because of limited MEC data and constraints on the time the Panel had to review toxicological information. The Panel also understands that differences in recycled water quality and facility operations will occur by region and that investigation of chronic exceedances will need to be tailored on a regional or case-by-case basis. Moreover, the Panel recognizes that these monitoring recommendations are appropriate for investigative purposes and should not be construed as directly applicable for determination of regulatory compliance.

Product #4: Priorities for future improvements in monitoring and interpretation of CEC data

The science of CEC investigation is still in its early stages and the State can undertake several activities that will greatly improve both monitoring and data interpretation for recycled water management. The Panel provides a number of such recommendations, including: 1) Develop and validate more and better analytical methods to measure CECs in recycled water; 2) Encourage development of bioanalytical screening techniques that allow better identification of the "unknown unknown" chemicals; and 3) Develop a process to predict likely environmental concentrations of CECs based on production, use and environmental fate, as a means for prioritizing chemicals on which to focus method development and toxicological investigation. These investigations should be conducted with guidance and review by a Science Advisory Panel.

In addition to these research recommendations, the Panel recommends that the State develop a process to rapidly compile, summarize, and evaluate monitoring data as they become available. The Panel further recommends that the State establish an independent review panel, such as this one, that can provide periodic review of the proposed selection approach, reuse practices, and environmental concentrations of ongoing CEC monitoring efforts, particularly as data from the monitoring programs recommended here become available.

Table of Contents

Acknowledgments i

Executive Summary ii

List of Tables x

List of Figures xi

Acronyms xii

1.0 Introduction 1

1.1 Background 1

1.2. The Science Advisory Panel 1

1.3 Charge to the Science Advisory Panel 2

1.4 Organization of the Report 3

1.5 Reuse Practices and Pathways to Exposure to CECs 3

1.5.1 Surface Spreading Operations 4

1.5.2 Subsurface Injection Operations 5

1.5.3 Landscape Irrigation 6

2.0 Regulatory Paradigm to Protect US and California Drinking Water 7

2.1 Defining the Universe of CECs Relevant to Water Recycling in California 7

2.2 USEPA's Candidate Contaminant List 3 8

2.3 Federal Regulatory Monitoring Requirements 11

2.4 California Specific Regulations of Drinking Water and Water Reuse 15

3.0 Water Reuse Practices in California, Assurance of Plant Performance, and Current Monitoring Requirements 19

3.1 Introduction 19

3.2 Current Levels of Water Recycling and Future Resource Demands 19

3.3 Current Water Recycling Regulations, Criteria and Policy 20

3.4 Key Criteria Governing Planned Indirect Potable Reuse Projects 23

3.5 Recycled Water - Case Examples 25

4.0 Toxicological Relevance of CECs in Recycled Water to Human Health 27

4.1 Introduction 27

4.2 Screening Process to Assess Toxicological Relevance of CECs 27
4.3 Derivation of Monitoring Trigger Levels 33
4.3.1 Initial Monitoring Trigger Levels 34
4.4 What are the appropriate constituents to be monitored? 35

5.0 Measured Environmental Concentrations of CECs in Recycled Water in California 37

5.1 Introduction 37
5.2 Occurrence of CECs in Recycled Water in California 37
5.3 Recommendations to Gather Additional MEC Data for CECs in California 41

6.0 Screening Unknown CECs in Recycled Water to Assess Exposure 44

6.1 Introduction 44
6.2 Bioanalytical Screening Tools 45
6.3.1 Strengths 47
6.3.2 Weaknesses 47
6.4 Quantifying Unknown Known CECs in Recycled Water 49

7.0 Prerequisites for Monitoring CECs in Recycled Water 51

7.1 Background and Analytical Components for Monitoring CECs in Recycled Water 51
7.2 Sample Collection/Preservation 51
7.2.1 Sample Collection 51
7.2.2 Preservation 52
7.2.3 Residual Oxidant Quenching 53
7.3 Instrumental Analysis 53
7.3.1 GC-MS 53
7.3.2 LC-MS 54
7.3.3 GC-MS vs. LC-MS 54
7.3.4 Isotope Dilution LC-MS 55
7.3.5 Quality Assurance/Quality Control Measures 55
7.3.6 Method Detection Limits 55
7.4 Requirements for CEC Monitoring 56
7.5 Monitoring for CECs using Commercially Available Methods 56
7.5.1 Availability of Commercial Laboratories for CEC Analyses 56
7.6 Selection/Establishment of Appropriate Method Reporting Limits 57

8.0 Monitoring Program for CECs in Water Reuse Leading to Urban Irrigation and Drinking Water Augmentation....59

8.1 The Proposed Prioritization Scheme for CECs in Recycled Water....59

8.2 Application of the CEC Prioritization Scheme to Identify Chemicals that should be Monitored at the Present Time....61

8.3 Indicator Compounds and Surrogate Parameters for Treatment Performance Assessment....65

8.4 Monitoring Program and Suggested Response(s) for Indirect Potable Reuse Projects....68

8.4.1 Guidance on Start-up and Baseline CEC Monitoring Programs for Groundwater Recharge Projects....68

8.4.2 Response to Monitoring Results....70

8.4.3 Review/Update of Monitoring and Response Plans....71

8.5 Monitoring for Additional CECs with Insufficient MECs....72

9.0 Recommendations....74

References....76

Appendix A - Biographies of Panel Members.... A - 1

Appendix B - Ecotoxicology Assessment....B - 1

Appendix C - Antibiotic Resistant Bacteria and Antimicrobials of Concern in Recycled and Drinking Water....C - 1

Appendix D - Federal Paradigm for Regulating CECs in Drinking Water.... D - 1

Appendix E - Summary of California Water Recycling Regulations and Additional Discussion of California Department of Health Groundwater Recharge Reuse Regulations....E - 1

Appendix F - Recycled Water: Case Examples.... F - 1

Appendix G - Concept of Reliability.... G - 1

Appendix H - Current Pretreatment Regulatory Authority for Source Control.... H- 1

Appendix I - Overview and Summary of Key Studies of Toxicological Relevance of Reused Water....I - 1

Appendix J - Summary of Drinking Water Benchmarks for CECs....J - 1

Appendix K - 90th Percentile MEC of CECs in Secondary/Tertiary Treated Effluents in California....K -1

Appendix L - Assays currently Available Requiring Limited QA/QC Development.... L - 1

Appendix M - Prerequisites for Monitoring CECs in Recycled Water....M - 1

List of Tables

Table 2.1. Contaminants regulated in California, but not by USEPA. 16

Table 2.2. California Unregulated Contaminant Monitoring Requirements for Drinking Water. 16

Table 2.3. California notification substances and levels. 17

Table 3.1 .Summary of CDPH Water Recycling Treatment Requirements. 21

Table 3.2. Summary of CDPH Draft Groundwater Recharge Regulations (DRAFT August 5, 2008). 22

Table 3.3. General summary of wastewater treatment processes/operations. 25

Table 3.4. General summary of water reuse application and wastewater treatment 26

Table 5.1. 90th percentile MECs of CCL3 CECs in recycled water. 39

Table 5.2. 90th percentile MECs of non-CCL3 CECs in recycled water. 39

Table 5.3. CCL3 CECs with MTLs of less than 500 ng/L and no MECs in Recycled Water in California.. 41

Table 6.1. Commercially available EDSP Tier I Bioassays with adequate quality assurance guidelines. 46

Table 7.1. Recommended MRLs for health and performance based indicator CECs. 58

Table 8.1. Exposure screening for CCL3 and non-CCL3 CECs in recycled water. 64

Table 8.2. Health-based and performance-based indicator CECs and performance surrogates 66

Table 8.3. Application of surrogate/indicator framework to an overall treatment train. 67

Table 8.4. Suggested CECs with limited MEC for additional monitoring. 73

List of Figures

Figure ES1. Conceptual framework to prioritize CECs in recycled water monitoring programs. iii

Figure 1.1. Conceptual model of surface spreading reuse operations in California..... 4

Figure 1.2. Conceptual model of subsurface spreading reuse operations in California 5

Figure 1.3. Conceptual model of reuse operations for landscape irrigation in California using recycled water meeting Title 22 requirements. 6

Figure 2.1. Classes of CECs potentially present in recycled water to be considered for monitoring programs in California. 7

Figure 2.2. The CCL3 process 9

Figure 2.3. Initial process for selecting the CCL3 Universe. 10

Figure 3.1. Types of recycled water use in California as a percentage of annual Use, 2009 20

Figure 4.1. Conceptual exposure screening of CEC regarding relevance in recycled water. 28

Figure 4.2. Final decision tree for PNEC determining scheme for new and emerging contaminants.....30

Figure 5.1. Statistical assessment of CCL3 CECs and non-CCL3 CECs (e.g., ibuprofen). 38

Figure 6.1. Screening approach for unknown unknown CECs in recycled water.....44

Figure 6.2. Correlation between chemically estimated EEQs and bioassay EEQs. 46

Figure 6.3. Estimating PECs for unknown known CECs. 49

Figure 8.1. Conceptual CEC prioritization scheme. 59

Acronyms

ADIs	Allowable Daily Intakes
AOP	Advanced Oxidation Processes
APCI	Atmospheric Pressure Chemical Ionization
APPI	Atmospheric Pressure Photoionization
BOD	Biochemical Oxygen Demand
CCL3	USEPA Candidate Contaminant List 3
CCR	California Code of Regulations
CDPH	California Department of Public Health
CECs	Chemicals of Emerging Concern
CI	Chemical Ionization
COD	Chemical Oxygen Demand
CWC	California Water Code
DBPs	Disinfection By-products
DDT	Dichlorodiphenyltrichloroethane
DEET	N,N-Diethyl-meta-Toluamide
DPH	Department of Public Health
DWP	Drinking Water Program
DWR	Department of Water Resources
E2	17β-estradiol
EDCs	Endocrine Disrupting Compounds
EDSP	Endocrine Disruptor Screening Program
EDSTAC	Endocrine Disruptor Screening and Testing Advisory Committee
EE2	17α-ethinyl estradiol
EEQ	Estradiol Equivalent
EI	Electron Ionization
ESI	Electrospray Ionization
GC-MS	Gas Chromatography-Mass Spectrometry
HE	Health Effects
LC-MS	Liquid Chromatography-Mass Spectrometry
LOAEL	Lowest Observed Adverse Effect Level

Acronyms Continued

MCLGs	Maximum Contaminant Level Goals
MCLs	Maximum Contaminant Levels
MECs	Measured Environmental Concentrations
MDL	Method Detection Limit
MRDLGs	Maximum Residual Disinfectant Level Goals
MRDLs	Maximum Residual Disinfectant Levels
MRL	Method Reporting Limit
MS	Mass Spectrometry
MTLs	Monitoring Trigger Levels
NAS	National Academy of Sciences
NCOD	National Contaminant Occurrence Database
NDMA	N-nitrosodimethylamine
NDWAC	National Drinking Water Advisory Council
NIEHS/NTP	National Institute of Environmental Health Sciences/National Toxicology Program
NOAEL	No Observed Adverse Effect Level
NPDWR	National Primary Drinking Water Regulation
NRC	National Research Council
OEHHA	Office of Environmental Health Hazard Assessment
P	Proportion
PAHs	Polycylic Aromatic Hydrocarbons
PCBs	Polychlorinated Biphenyls
PCCL	Preliminary Candidate Contaminant List
PECs	Predicted Environmental Concentrations
PFCs	Perfluorinated Compounds
PFOA	Perfluorooctanoic Acid
PFOS	Perfluorooctanoic Sulfonate
POE	Point of Exposure
POM	Point of Monitoring
PPCPs	Pharmaceuticals and Personal Care Products

Acronyms Continued

QA/QC	Quality Assurance/Quality Control
RO	Reverse Osmosis
RSC	Relative Source Contribution
RWQCBs	Regional Water Quality Control Boards
SAB	Science Advisory Board
SAT	Soil-Aquifer Treatment
SETAC	Society of Environmental Toxicology and Chemistry
SOT	Society of Toxicology
SPE	Solid Phase Extraction
SDWA	Safe Drinking Water Act
SWRCB	State Water Resources Control Board
TEQ	Toxic Equivalent
TIE	Toxicity Identification Evaluation
TN	Total Nitrogen
TNI	The National Environmental Laboratory Accreditation Conference Institute
TOC	Total Organic Carbon
TOX	Total Organic Halides
TTC	Threshold of Toxicological Concern
UCM	Unregulated Contaminant Monitoring
UCMR	Unregulated Contaminant Monitoring Regulation
UF	Uncertainty Factor
URCIS	Unregulated Contaminant Monitoring Information System
US	United States
USEPA	United States Environmental Protection Agency
WHO	World Health Organization
YES	Yeast Estrogen Screening

1.0 Introduction

1.1 Background

Recycled water is becoming an increasingly important part of California's water supply. California presently recycles approximately 650,000 acre-feet of water per year, an amount that has doubled in the last twenty years (WateReuse, 2010). Future reuse potential in the State is estimated to be an additional 1.4 to 1.6 million acre-feet per year by 2030.

To encourage expanded reuse in a state that is experiencing water shortage, the California State Water Resources Control Board (SWRCB) adopted in February 2009 an updated Recycled Water Policy (adopted under Resolution No. 2009-0011) intended to provide permitting clarity while ensuring protection of water quality. The Policy states that local water and wastewater entities, together with stakeholders, will fund locally driven and collaborative processes to develop salt/nutrient management plans for each groundwater basin /sub-basin in California. In addition, the Policy and supporting information provide further definition and clarification to the collaborative roles of the SWRCB, the California Department of Public Health (CDPH), the Regional Water Quality Control Boards (RWQCB), and the California Department of Water Resources (DWR).

One challenge in developing that policy was how to address new classes of chemicals, such as pharmaceuticals and personal care products (PPCPs), currently used pesticides, and industrial chemicals, collectively referred to as chemicals of emerging concern (CECs). This diverse group of relatively unmonitored chemicals has been found to occur at trace levels in wastewater discharges, ambient receiving waters, and drinking water supplies, but many of them are so new that standardized measurement methods and toxicological data for interpreting their potential human or ecosystem health effects are unavailable. This lack of basic information and technology to efficiently measure CECs hampers the State's ability to assess their potential risks and develop regulatory protocols. For many of these chemicals, even information about product-specific applications is unavailable, making it difficult to ascertain the probability of exposure and the potential to impact beneficial uses of water resources in California.

1.2. The Science Advisory Panel

Recognizing that consideration of CEC effects on human health and aquatic life is a rapidly evolving field and that regulatory requirements need to be based on best available science, the SWRCB included a provision in the Recycled Water Policy to establish a Science Advisory Panel that would provide guidance in developing monitoring programs that assess the potential health threat of CECs from various water recycling practices. The Panel was formed in May 2009 and included six national experts in the fields of chemistry, biochemistry, toxicology, epidemiology, risk assessment, and engineering. These experts have more than 100 years of combined experience investigating CEC issues. A brief biography of each panel member is provided in Appendix A:

- Dr. Paul Anderson, ARCADIS and Boston University

- Dr. Nancy Denslow, University of Florida
- Dr. Jörg E. Drewes, Colorado School of Mines (*Chair*)
- Dr. Adam Olivieri, EOA, Inc.
- Dr. Daniel Schlenk, University of California-Riverside
- Dr. Shane Snyder, Total Environment Solutions, Inc.

The Panel held four in-person meetings and numerous conference calls. The meetings included the opportunity for stakeholder input in clarifying their charge, exchange of information, dialog with the Panel and consideration of public comments on the draft report. This report provides the results from the Panel's deliberations.

1.3 Charge to the Science Advisory Panel

The Panel was provided with five specific charge questions (see accompanying box), but was generally asked to review the occurrence, relevance, and quantification of CECs in recycled water in the State of California with the goal to provide recommendations for development of a monitoring program of CECs in recycled water. The Panel was asked to focus on three reuse practices in which CECs may represent a potential threat to human and aquatic health:

1) Indirect potable reuse via surface spreading of recycled water;
2) Indirect potable reuse via subsurface injection of recycled water into a potable aquifer; and
3) Urban landscape irrigation with recycled water.

Charge to the Science Advisory Panel

- *What are the appropriate constituents to be monitored, including analytical methods and method detection limits?*
- *What is the known toxicological information for the above constituents?*
- *Would the above lists of constituents change based on level of treatment and use? If so, how?*
- *What are possible indicators that represent suites of CECs?*
- *What levels of CECs should trigger enhanced monitoring of CECs in recycled water, groundwater, and/or surface waters?*

The Panel chose to focus its recommendations on toxicological relevance of CECs to human health because most water reuse practices have limited impact on ecological receptors (see Appendix B for a more detailed discussion). Other reuse practices that could result in discharge of recycled water to surface water, estuaries, and the ocean were also not addressed by the Panel. However, the SWRCB, in collaboration with the Packard Foundation, established another Science Advisory Panel in January 2010 that was charged to address CEC discharge to the ocean and potential effects of exposure of humans and ocean life to CECs from this practice. The report issued by the ocean discharge panel is forthcoming in the spring of 2011.

In considering the charge, the Panel defined CECs to represent personal care products, pharmaceuticals including antibiotics and antimicrobials; industrial, agricultural, and household chemicals; natural hormones; food additives (e.g., phytoestrogens, caffeine, sweeteners);

transformation products, inorganic constituents (e.g., boron, chlorate, gadolinium); and nanomaterials. The Panel also chose not to consider the occurrence of waterborne microbial pathogens or their acquisition of antibiotic resistance. Given the multiple barrier concept and water treatment process redundancy requirements in place, the Panel believes that the potential public health risk associated with exposure to pathogens in recycled water used for landscape irrigation or groundwater recharge[1] is very small. However, the Panel acknowledges that some uncertainties exist regarding the occurrence of emerging waterborne microbial pathogens and encourages additional research into their fate in water reuse systems.

The Panel did provide a cursory review of antibiotic resistance in relation to water reuse practices (see Appendix C) and realized that the issue was complex and that a thorough treatment required more resources than the Panel had access to. Nevertheless based on the cursory review the Panel conducted, antibiotic resistance does not appear to be an issue with the water reuse practices considered, but the Panel also recommends that a more appropriate panel (e.g., Centers for Disease Control and Prevention) complete a more thorough review and validate the Panel's preliminary conclusions.

1.4 Organization of the Report

This report contains 9 sections and 13 appendices. The remainder of this section describes the potential exposure scenarios for each of the three reuse practices the Panel was asked to consider. Sections 2 through 4 provide background material on the regulatory framework for CECs, the water reuse practices in California, and a review of toxicological relevance of CECs. Sections 5 through 7 describe the California relevant information needed to develop a recommended monitoring program. Section 8 describes the Panels' proposed framework for selecting CECs for monitoring programs, and Section 9 summarizes the Panel's recommendations.

1.5 Reuse Practices and Pathways to Exposure to CECs

To illustrate potential pathways of exposure of CECs to humans and aquatic life for the three reuse practices the Panel was asked to consider, the key treatment elements of each application, the points of monitoring (POMs) from a regulatory standpoint, and potential points of exposure (POEs) to humans and aquatic life are illustrated in Figures 1.1 to 1.3.

Groundwater recharge to augment drinking water supplies is currently practiced in several reuse projects in California. These projects apply recycled water either via surface spreading or subsurface injection. Surface spreading operations utilize recycled water with a quality equal to that resulting from tertiary treatment that then is applied to infiltration or recharge basins. Subsequently, this water is subjected to soil-aquifer treatment (SAT) resulting in additional

[1] Multiple barriers for the groundwater recharge projects include source control and consideration of the treatment processes at the water recycling plant, attenuation during groundwater recharge including detention time, dilution, and die-off, and various potable water treatment processes associated with the production of finished potable water.

improvements of water quality in the subsurface. During recharge, recycled water is subject to dilution with native groundwater and other recharged water sources, such as stormwater and imported surface water. Subsurface injection projects require more advanced treatment prior to injection and also take advantage of dilution with native groundwater and recharged water from other sources. For groundwater recharge projects in California, the recharged water is required to remain in the subsurface for a minimum of six months prior to extraction. Following extraction, the water is disinfected and may also receive other forms of post-treatment prior to entering distribution systems for drinking water supply.

1.5.1 Surface Spreading Operations

For surface spreading operations, the Panel recommends monitoring for CECs in the recycled water applied to a spreading basin and in the mound of the uppermost groundwater or a lysimeter in the vadose zone (Figure 1.1). This monitoring regime will confirm the presence of CECs and allow an assessment of the efficiency of SAT. Considering the ubiquitous occurrence of many CECs, it is noteworthy that CECs in recharged groundwater can also be introduced through other sources such as natural recharge from surface run-off or blending with native groundwater that is impacted by CECs.

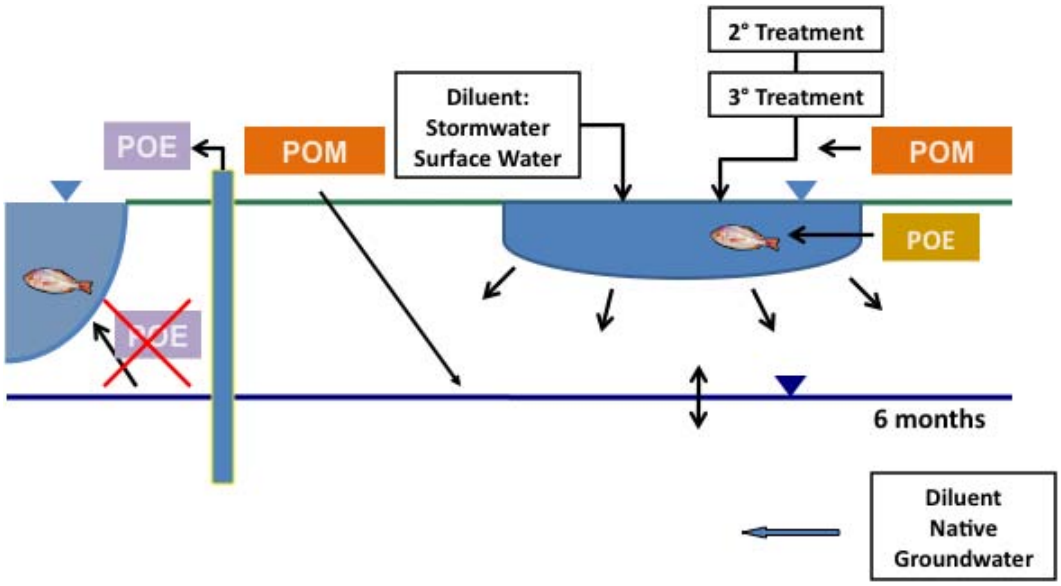

Figure 1.1. Conceptual model of surface spreading reuse operations in California (recycled water contribution <50% at point of extraction).

For the practice of surface spreading, the Panel discussed potential POEs for remaining CECs related to human health and identified an extraction or pumping well downstream of the spreading operation as the most important pathway for potential exposure. Due to the depth of groundwater where surface spreading is practiced, recycled water used in groundwater recharge operations usually does not ex-filtrate into lakes, reservoirs, or streams located downstream of a recharge facility. Thus, the Panel felt that the potential exposure of humans or aquatic life to CECs in recharged recycled water in surface water sources downstream of the

recharge basins is considered negligible (Figure 1.1). Surface spreading operations are usually subject to wet/dry cycles involving periodic drying of a recharge basin. This mode of operation does not provide a habitat for establishment of perennial fish populations. Thus, the Panel felt that both the exposure of aquatic life, such as fish, to CECs in spreading basins during a wet cycle, as well as human exposure to CECs through consumption of fish from spreading basins, is assumed to be negligible.

1.5.2 Subsurface Injection Operations

For direct injection into a potable aquifer projects using highly treated recycled water, the POM is the recycled water after above-ground advanced treatment prior to injection into an aquifer (Figure 1.2). Considering the isolation of recycled water from direct contact after injection into the subsurface, the Panel concluded that any potential exposure to humans by remaining CECs in recycled water is limited to water extracted from the pumping well downstream of a recharge facility.

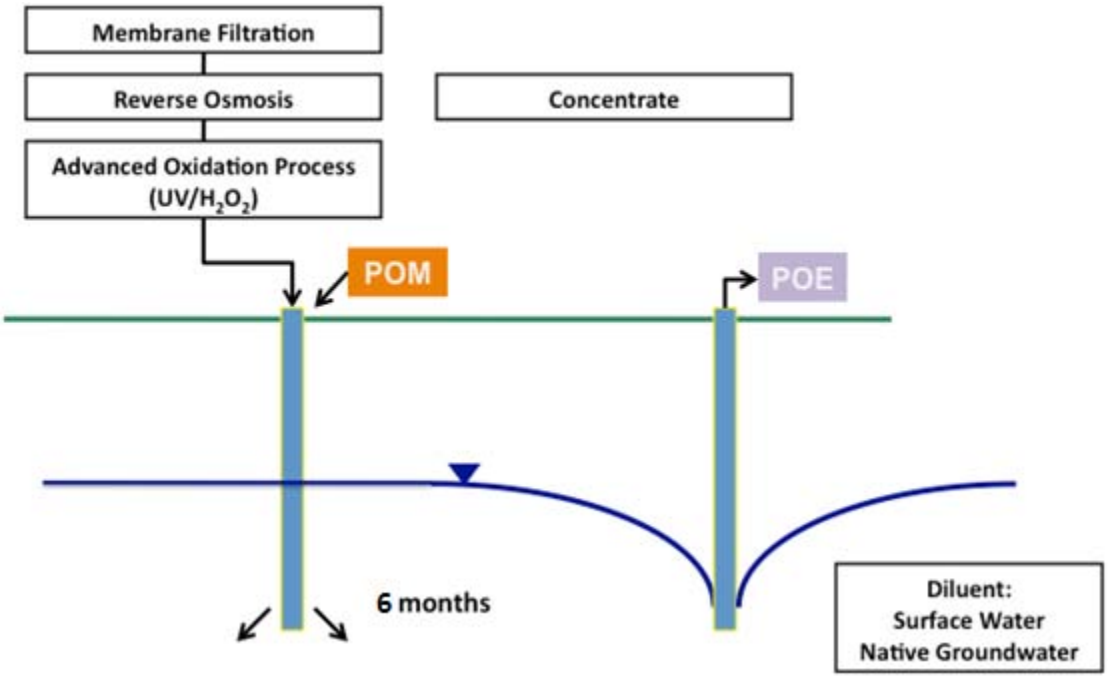

Figure 1.2. Conceptual model of subsurface spreading reuse operations in California (recycled water contribution >50% at point of extraction).

In California, direct injection projects require treatment of recycled water using reverse osmosis (RO) followed by - in some cases – advanced oxidation processes (AOP). Reverse osmosis is a physical separation process generating a concentrate that contains all chemicals that are rejected by the RO membrane. CECs are concentrated in this brine stream and where ocean discharge or discharge to surface water is practiced, aquatic life can be exposed to CECs at the point or in the vicinity of the discharge. Potential exposure pathways to CECs from this practice were not addressed by this Panel but will be evaluated by another Science Advisory

Panel that was specifically charged to address CEC discharge to the ocean and potential exposure to human health and ocean life from this practice.

1.5.3 Landscape Irrigation

Landscape irrigation is the most commonly practiced form of reuse in the State of California. Recycled water used for these applications requires either secondary or tertiary treatment (as specified in California's Title 22 regulation) depending on restricted or unrestricted access of areas irrigated with recycled water (Figure 1.3). Numeric water quality permit effluent requirements generally have to be met once the finished recycled water completes the final stage of treatment.

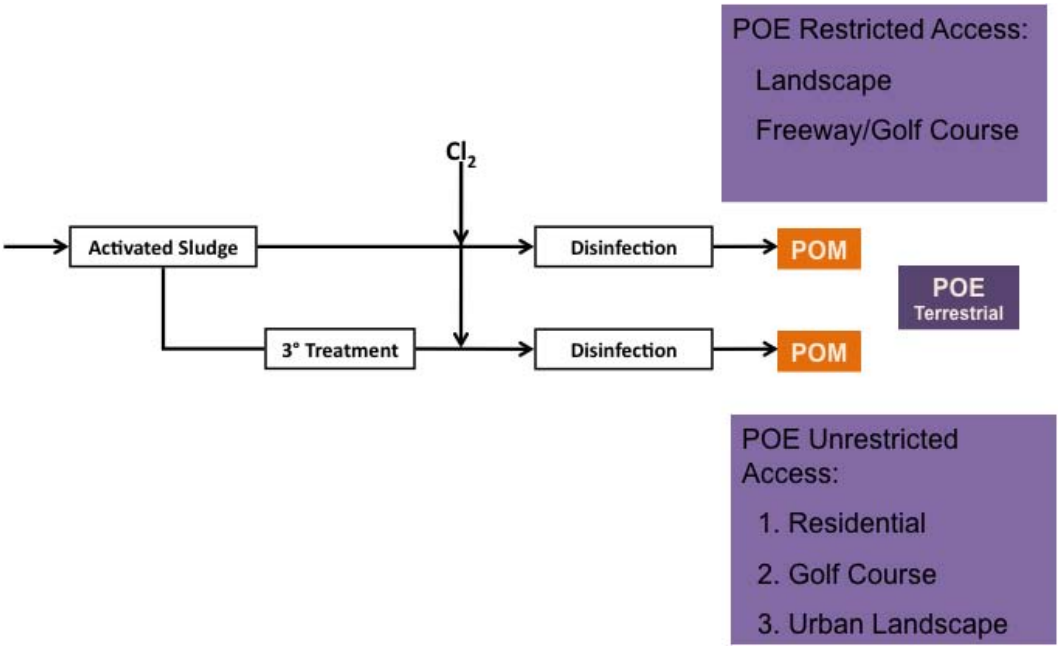

Figure 1.3. Conceptual model of reuse operations for landscape irrigation in California using recycled water meeting Title 22 requirements.

State Water Resources Control Board requirements also address water quality objectives in receiving waters (i.e., surface and ground waters). In addition, both restricted and unrestricted landscape irrigation applications are subject to specific permit requirements (i.e., best management practices) that minimize any unintentional discharge, ponding, flooding of recycled water, and subsequent public exposure. Thus, the Panel concluded that exposure of aquatic life to any CECs remaining in recycled water used for landscape irrigation is considered negligible and unintentional public exposure is minimized. Exposure to terrestrial wildlife from CECs might occur in the topsoil or root zone that usually is exposed recycled water. While human exposure to CECs can occur through incidental contact with and accidental consumption of recycled water from sprinkler heads, faucets, or hydrants, it does not warrant a monitoring program for CECs to protect public health.

2.0 Regulatory Paradigm to Protect US and California Drinking Water

2.1 Defining the Universe of CECs Relevant to Water Recycling in California

After reviewing the federal regulatory approach to identify potential contaminants in drinking water as well as California's approach to include additional contaminants in monitoring efforts in drinking and recycled water, the Panel concluded that it is important to develop a sound and transparent process that can guide in the prioritization of CECs to be included in monitoring programs of recycled water applications within the State. In order to be all encompassing, the Panel considered CECs at large as a starting point for its deliberation and agreed that the United States Environmental Protection Agency (USEPA) Candidate Contaminant List 3 (CCL3) selection process represents a transparent and comprehensive approach that provides a very good basis for identifying CECs that are relevant and potentially present in recycled water and not already regulated at the federal or state level. However, as noted previously, the Panel also recognizes that even CCL3 is not likely inclusive of a diversity of monitoring data that has been collected in the State of California for various CECs.

The Panel acknowledged that recycled water quality is subject to ongoing monitoring requirements and although recycled water has been extensively researched in the past, it has the potential to contain compounds that have yet to be identified and quantified using laboratory analytical methods (Figure 2.1). These compounds can be described as "unknown unknowns" representing chemicals, which presence in recycled water is unknown and no analytical methods currently exist for their detection. Some of these compounds might pose a potential threat to human health and the environment.

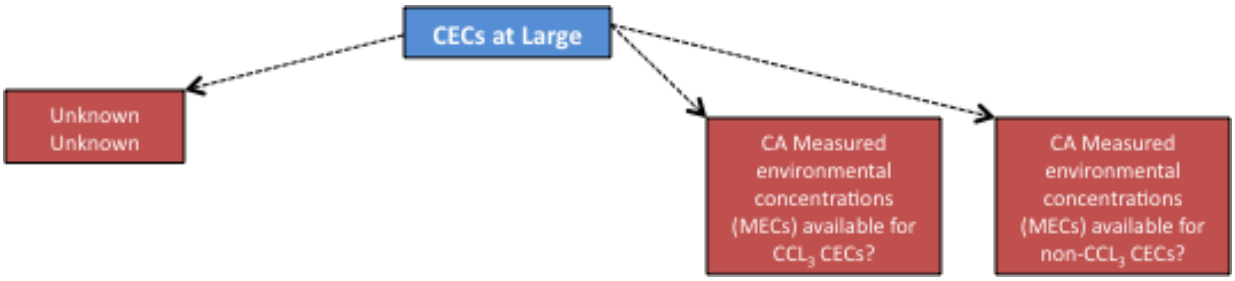

Figure 2.1. Classes of CECs potentially present in recycled water to be considered for monitoring programs in California.

Recycled water also contains chemicals that have been previously identified, analytical methods exist for their detection, and measured environmental concentrations (MECs) are available in California recycled water (these compounds can be described as "known knowns"). These CECs are either listed on the CCL3 ("CCL3 CECs") or do not appear on CCL3 ("non-CCL3 CECs").

Other compounds, such as transformation products, are known to occur in recycled water but the concentrations at which they occur have not yet been quantified. These compounds can be described as "unknown knowns" and, although MECs in recycled water are not currently

available in California, predicted environmental concentrations (PECs) could be developed for such compounds if use and other information are available.

The Panel concluded that any proposed monitoring strategy for CECs needs to address the different categories of compounds present or potentially present in recycled water as well as their relevance to public and environmental health. The Panel's approach to identify the public health relevance of CECs in recycled water is described in Section 4 of this report. MECs of CECs in California are presented in Section 5. Bioanalytical methods that may be useful for a better characterization of "unknown unknowns" are discussed in Section 6.

2.2 USEPA's Candidate Contaminant List 3

To protect public health, the United States (US) Government has a long and rich history in developing regulations for contaminants in drinking water. The process has evolved over several decades and the key elements that are most germain to this effort were instituted as a result of the Safe Drinking Water Act (SDWA) of 1974, and more specifically, can be found in the identification of currently non-regulated contaminants on the USEPA Candidate Contaminant List (CCL). The process to develop the current list, CCL3, was far more systematic and objective than the more subjective selection of contaminants used for its predecessors, CCL1 and CCL2. The CCL3 selection process utilized the expert opinions provided by National Academy of Sciences (NAS)/National Research Council (NRC) Panels as well as the National Drinking Water Advisory Council (NDWAC) and Science Advisory Board (SAB). This multi-step process includes three key elements:

- Identification of a broad universe of potential biological chemical and chemical contaminants (CCL Universe);
- Application of screening criteria based on potential occurrence and human health relevance (preliminary CCL or PCCL); and,
- Selection of priority contaminants based on more detailed occurrence and health effect data as well as expert judgment, public comment, and external advisory committees (draft and final CCL).

A draft of the CCL3 was released in February 2008 and the final CCL3 was published in October 2009 (Appendix D, Table D-1). The general process utilized in the development of the CCL3 is shown schematically in Figure 2.2. The CCL3 Universe is to encompass a wide array of potential water contaminants, both chemical and microbial. The Universe includes not only compounds known or anticipated to occur in water supplies, but also releases to the environment and production volume. Additionally, the Universe is to include contaminants with demonstrated or adverse health effects, regardless of occurrence data. Due to the wide array of potential data, the USEPA chose to follow the advice of the NDWAC, in relying primarily on easily accessible databases for the information that would be used to generate the CCL3 Universe. The accessibility became a highly limiting factor, as any database to be used must be electronically accessible and free of charge. The EPA initially identified some 284 potential databases on which they could rely for populating the CCL3 Universe

(http://www.epa.gov/safewater/ccl/pdfs/ccl3_docs/CCL3_Chemicals_Universe_08-31-09_508_v3.pdf); however, these databases were culled based on relevance, completeness, redundancy, and retrievability (Appendix D, Figure D-1). Of the 284 databases initially identified, 142 were eliminated due to relevance, 12 eliminated due to completeness, 26 eliminated due to redundancy, and 64 eliminated due to retrievability. In terms of relevance, several databases were found to contain only descriptive data such as used for pesticide labeling or nomenclature that is not related to occurrence or toxicity and these were not utilized. Completeness was gauged based on minimum documentation and quality requirements, such as: contact information, description of data elements, information on how data were obtained, and whether or not data were peer-reviewed. Redundancy was assessed to avoid duplication and when redundant data was found, the more comprehensive database was utilized. Retrievability was a major limitation for database inclusion; databases that provided information in tabular format that could be extracted and formatted were used while databases providing information in text format were generally not considered. However, databases with simple lists in text format that could be easily imported were sometimes used. Due to transparency concerns, databases that were available only by subscription (fees) or were proprietary were not utilized. Ultimately, only 40 databases were utilized (Appendix D, Table D-2). The limitations on the databases that were screened are likely the greatest hindrances in utilizing the CCL3 for prioritization of CECs in reuse systems. While some databases are clearly relevant, much of the data published in peer-reviewed literature and various reports would not have been considered in the CCL3 Universe. Without question, monitoring data from water agencies/utilities in California would not likely have been included among the databases evaluated, which is a major limitation of relying solely on the CCL3 as a priority list for CECs of interest to California.

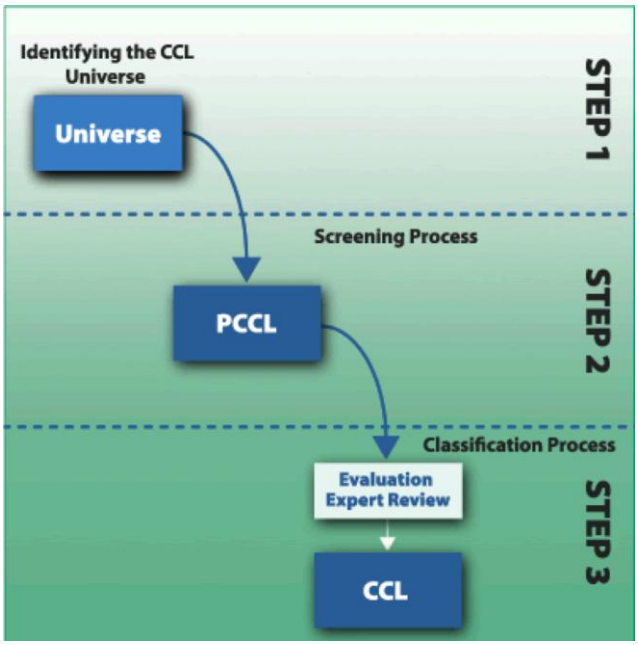

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Figure 2.2. The CCL3 process (from http://www.epa.gov/safewater/ccl/ccl3_processflowdiagram_docs.html).

From the 40 databases screened, nearly 26,000 substances were identified. Therefore, USEPA developed a pre-Universe selection process to evaluate those compounds that were most suitable for inclusion in the Universe (Figure 2.3). The initial process essentially determined whether or not a contaminant had health effects (HE) and occurrence data. If only HE data were available, these contaminants would be screened to determine if the

contaminant was toxicologically relevant (see section of PCCL process regarding relevance). Chemicals for which only occurrence data were available were sequentially evaluated for finished or ambient source water data, release data, or production of over 1 billion pounds/year (Appendix D, Table D-4).

This pre-Universe selection process identified 7,720 chemicals, which went on to the final selection process (Appendix D, Figure D-4). The final selection process first evaluated whether or not primary drinking water standards already existed, which eliminated 1,009 chemicals (mostly radionuclides and compounds with multiple isomers, such as polychlorinated biphenyls (PCBs). Four-hundred thirty substances that are considered mixtures, such as petroleum products and resin acids, were eliminated from further consideration. Also, substances that are not "chemically defined" (such as wood dust and surgical implants) were eliminated. Lastly, two substances were removed because they are considered biological and would not be considered within the chemical Universe. The USEPA also considered 174 contaminants that were nominated through the public input process and 132 of those nominated were already considered. The remaining nominations were evaluated through the same criteria as all other chemicals for consideration of the CCL3 Universe. Once the draft CCL3 was released in February 2008, the USEPA subsequently received 177 comments. From these comments, 30 additional contaminants were added to the Universe.

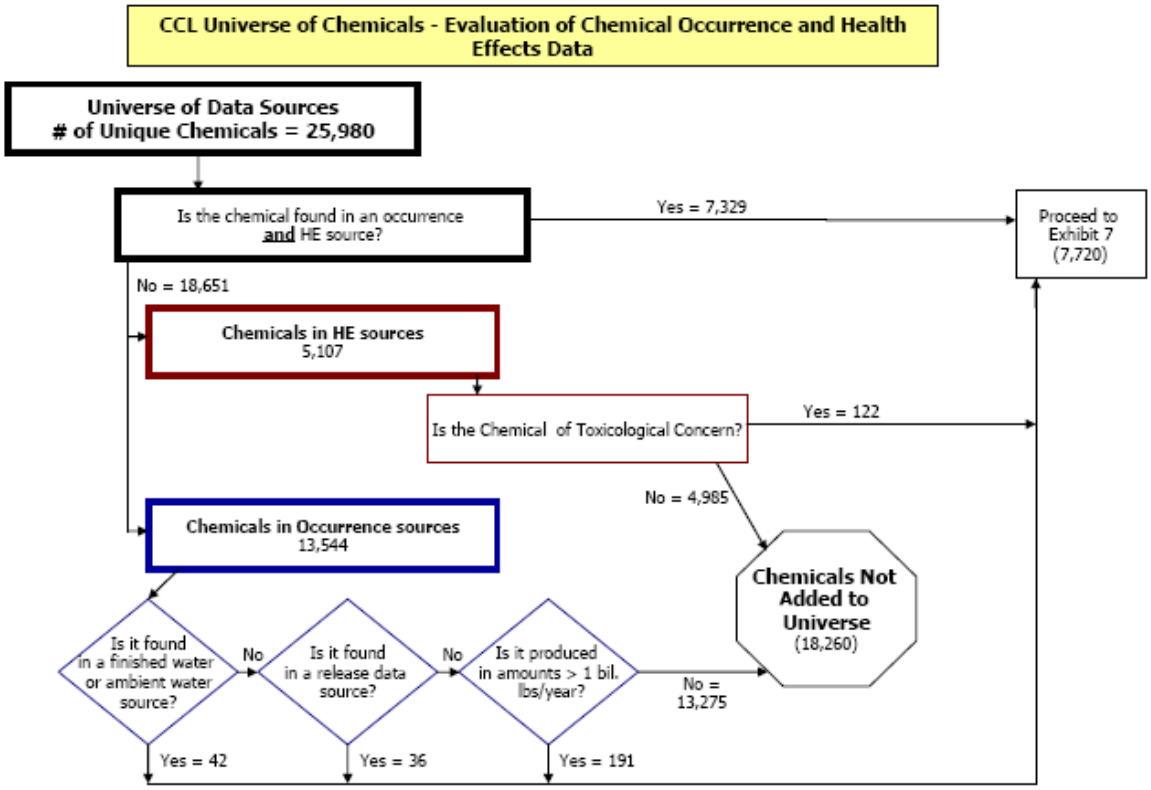


Figure 2.3. Initial process for selecting the CCL3 Universe.

2.3 Federal Regulatory Monitoring Requirements

To monitor the list of regulated contaminants, individual water systems submit samples of their water for laboratory testing to verify that the water they provide to the public meets all federal and state standards. The frequency and location of sampling varies among systems and by contaminant but is based on a Standard Monitoring Framework established by the USEPA to provide a uniform structure for monitoring requirements for current and subsequent drinking water regulations. This framework consists of a nine-year compliance cycle, which is divided into three three-year compliance periods. Monitoring requirements vary depending on the contaminant group, whether the water system uses ground water or surface water, and on the number of people served.

In addition, states may grant monitoring waivers in certain situations and for certain contaminants after the required initial monitoring period. As a state gains a better understanding of the contamination sources that may affect the quality of a drinking water supply, it can tailor the monitoring requirements for the system. The SDWA, therefore, provides that a state may allow a waiver if the state has an approved source water assessment program and has completed a source water assessment for that system. The SDWA further requires USEPA to issue guidance for states to use in meeting these source water assessment requirements and directs USEPA to issue the source water assessment guidance at the same time as these alternative monitoring guidelines.

For a state to issue a waiver in the form of alternative monitoring guidelines, it must ensure that the public health will be protected from drinking water contamination, and waivers must address contaminants individually. Furthermore, the public water system must show the state that the contaminant is not present in the drinking water supply or, if it is present, that it is reliably and consistently below its maximum contaminant level (MCL). The guidelines further require that if a contaminant is detected at levels at or above its MCL or if its concentration is no longer reliably or consistently below the MCL, the system must either demonstrate that the contaminant source has been removed or that other action has been taken to eliminate the contamination or test for the detected contaminant according to the applicable National Primary Drinking Water Regulation (NPDWR). The following boxes provide illustrative examples for both select regulated and unregulated contaminants.

Bromate

Amendments to the SDWA in 1996 required the USEPA to develop rules to balance the risks between microbial pathogens and disinfection byproducts (DBPs). This was done to strengthen protection against microbial contaminants, especially Cryptosporidium, and at the same time reduce potential health risks of DBPs. The Stage 1 Disinfectants and Disinfection Byproducts Rule, announced in December 1998, was among the first of a set of rules under the 1996 SDWA Amendments. The rule established maximum residual disinfectant level goals (MRDLGs) and maximum residual disinfectant levels (MRDLs) for three chemical disinfectants—chlorine, chloramine and chlorine dioxide. It also established maximum contaminant level goals (MCLGs) and MCLs for total trihalomethanes, haloacetic acids, chlorite and bromate.

Under this rule, all drinking water treatment plants that use ozone during the treatment process are required to test for bromate on a monthly basis. Compliance is based on the annual average of bromate concentration in the finished water, which must not exceed the MCL of 10 µg/L.

Perchlorate

The EPA uses the Unregulated Contaminant Monitoring (UCM) program to collect data for contaminants suspected to be present in drinking water, but that do not have health-based standards set under the SDWA. The first cycle of the UCM rule (UCMR1), covering the period 2001–2005, was published in the Federal Register September 17, 1999 for a list of contaminants that included perchlorate.

UCMR1 established a tiered monitoring approach based on the availability of analytical methods for each contaminant and the size of the utility. All large drinking water utilities (>10,000 persons served) and a randomly selected group of small utilities (<10,000 persons served) were required to monitor perchlorate. Surface water systems were monitored quarterly during a one-year period and ground water systems were monitored twice in a one-year period. One of these quarterly or semiannual sampling events was required to occur in the most vulnerable period of May through July, or an alternate vulnerable period designated by the State, to ensure monitoring of potentially higher perchlorate concentrations. The monitoring results from these systems were used to estimate national occurrence of perchlorate.

N-nitrosodimethylamine **(NDMA)**

The UCMR supporting the second cycle of monitoring (UCMR2) was signed on December 20, 2006. UCMR2 requires monitoring a select group of contaminants during 2008–2010, including NDMA. Similar to UCMR1, UCMR2 uses a tiered monitoring approach based on the availability of analytical methods for each contaminant and the size of the utility. NDMA was placed on the screening survey list, for which monitoring requires analytical method technologies not commonly used by drinking water laboratories.

All drinking water utilities serving more than 100,000 people, 320 representative utilities serving 10,001-100,000 people, and 480 representative utilities serving less than 10,001 people are required to monitor for NDMA during a 12-month period between January 2008 and December 2010. For systems using groundwater, monitoring must occur twice in a consecutive 12-month period and sample events must occur 5 to 7 months apart. For systems using surface water or groundwater under the direct influence of surface water, monitoring must occur in four consecutive quarters, with sampling events occurring three months apart. Therefore, a system could conduct monitoring in either: (1) January, April, July, October; (2) February, May, August, November; or (3) March, June, September, December.

Atrazine

Atrazine is defined as a synthetic organic chemical in 40 CFR 141.61(c). Therefore, monitoring and the potential for a waiver are determined as follows (per 141.24(h); note that some sections have been removed for brevity):

(1) Groundwater systems shall take a minimum of one sample at every entry point to the distribution system, which is representative of each well after treatment (hereafter called a sampling point). Each sample must be taken at the same sampling point unless conditions make another sampling point more representative of each source or treatment plant;

(2) Surface water systems shall take a minimum of one sample at points in the distribution system that are representative of each source or at each entry point to the distribution system after treatment. Each sample must be taken at the same sampling point unless conditions make another sampling point more representative of each source or treatment plant;

(3) If the system draws water from more than one source and the sources are combined before distribution, the system must sample at an entry point to the distribution system during periods of normal operating conditions (i.e., when water representative of all sources is being used);

Atrazine (Continued)

(4) Monitoring frequency:

(i) Each community and non-transient non-community water system shall take four consecutive quarterly samples for each contaminant listed in § 141.61(c) during each compliance period beginning with the initial compliance period.

(ii) Systems serving more than 3,300 persons which do not detect a contaminant in the initial compliance period may reduce the sampling frequency to a minimum of two quarterly samples in one year during each repeat compliance period.

(iii) Systems serving less than or equal to 3,300 persons which do not detect a contaminant in the initial compliance period may reduce the sampling frequency to a minimum of one sample during each repeat compliance period.

(5) Each community and non-transient water system may apply to the State for a waiver from the requirement of paragraph (h)(4) of this section. A system must reapply for a waiver for each compliance period; and

(6) A State may grant a waiver after evaluating the following factor(s):

Knowledge of previous use (including transport, storage, or disposal) of the contaminant within the watershed or zone of influence of the system. If a determination by the State reveals no previous use of the contaminant within the watershed or zone of influence, a waiver may be granted. If previous use of the contaminant is unknown or it has been used previously, then the following factors shall be used to determine whether a waiver is granted.

(i) Previous analytical results;

(ii) The proximity of the system to a potential point or non-point source of contamination. Point sources include spills and leaks of chemicals at or near a water treatment facility or at manufacturing, distribution, or storage facilities, or from hazardous and municipal waste landfills and other waste handling or treatment facilities. Nonpoint sources include the use of pesticides to control insect and weed pests on agricultural areas, forest lands, home and gardens, and other land application uses;

(iii) The environmental persistence and transport of the pesticide or PCBs;

(iv) How well the water source is protected against contamination due to such factors as depth of the well and the type of soil and the integrity of the well casing.

(7) If an organic contaminant listed in § 141.61(c) is detected (as defined by paragraph (h)(18) of this section) in any sample, then:

(i) Each system must monitor quarterly at each sampling point which resulted in a detection.

(ii) The State may decrease the quarterly monitoring requirement specified in paragraph (h)(7)(i) of this section provided it has determined that the system is reliably and consistently below the maximum contaminant level. In no case shall the State make this determination unless a groundwater system takes a minimum of two quarterly samples and a surface water system takes a minimum of four quarterly samples.

(iii) After the State determines the system is reliably and consistently below the maximum contaminant level the State may allow the system to monitor annually. Systems which monitor annually must monitor during the quarter that previously yielded the highest analytical result.

(iv) Systems which have 3 consecutive annual samples with no detection of a contaminant may apply to the State for a waiver as specified in paragraph (h)(6) of this section.

(v) If monitoring results in detection of one or more of certain related contaminants (aldicarb, aldicarb sulfone, aldicarb sulfoxide and heptachlor, heptachlor epoxide), then subsequent monitoring shall analyze for all related contaminants.

Atrazine (Continued)

(7) If an organic contaminant listed in § 141.61(c) is detected (as defined by paragraph (h)(18) of this section) in any sample, then:

(i) Each system must monitor quarterly at each sampling point which resulted in detection.

(ii) The State may decrease the quarterly monitoring requirement specified in paragraph (h)(7)(i) of this section provided it has determined that the system is reliably and consistently below the maximum contaminant level. In no case shall the State make this determination unless a groundwater system takes a minimum of two quarterly samples and a surface water system takes a minimum of four quarterly samples.

(iii) After the State determines the system is reliably and consistently below the maximum contaminant level the State may allow the system to monitor annually. Systems which monitor annually must monitor during the quarter that previously yielded the highest analytical result.

(iv) Systems which have three consecutive annual samples with no detection of a contaminant may apply to the State for a waiver as specified in paragraph (h)(6) of this section.

(v) If monitoring results in detection of one or more of certain related contaminants (aldicarb, aldicarb sulfone, aldicarb sulfoxide and heptachlor, heptachlor epoxide), then subsequent monitoring shall analyze for all related contaminants.

(8) Systems which violate the requirements of § 141.61(c) as determined by paragraph (h)(11) of this section must monitor quarterly. After a minimum of four quarterly samples show the system is in compliance and the State determines the system is reliably and consistently below the MCL, as specified in paragraph (h)(11) of this section, the system shall monitor at the frequency specified in paragraph (h)(7)(iii) of this section.

(9) The State may require a confirmation sample for positive or negative results. If a confirmation sample is required by the State, the result must be averaged with the first sampling result and the average used for the compliance determination as specified by paragraph (h)(11) of this section. States have discretion to delete results of obvious sampling errors from this calculation.

(10) The State may reduce the total number of samples a system must analyze by allowing the use of compositing. Composite samples from a maximum of five sampling points are allowed, provided that the detection limit of the method used for analysis is less than one-fifth of the MCL. Compositing of samples must be done in the laboratory and analyzed within 14 days of sample collection.

(i) If the concentration in the composite sample detects one or more contaminants listed in § 141.61(c), then a follow-up sample must be taken within 14 days at each sampling point included in the composite, and be analyzed for that contaminant.

(ii) If duplicates of the original sample taken from each sampling point used in the composite sample are available, the system may use these instead of resampling. The duplicates must be analyzed and the results reported to the State within 14 days after completion of the composite analysis or before the holding time for the initial sample is exceeded whichever is sooner.

(iii) If the population served by the system is >3,300 persons, then compositing may only be permitted by the State at sampling points within a single system. In systems serving ≤3,300 persons, the State may permit compositing among different systems provided the 5-sample limit is maintained.

(15) The State may increase the required monitoring frequency, where necessary, to detect variations within the system (e.g., fluctuations in concentration due to seasonal use, changes in water source).

(16) Each public water system shall monitor at the time designated by the State within each compliance period.

In order to assess the occurrence of contaminants suspected to impact drinking water, the USEPA established an UCM program. The initial UCM round took place between 1988 and 1993, when 62 contaminants were monitored in 40 states. The resulting data became part of the Unregulated Contaminant Monitoring Information System (URCIS). The second round of UCM occurred between 1993 and 1997 and included data from 35 states of 48 (then) unregulated contaminants. In 1996, the SDWA was amended and the UCM program was significantly revised and a new Unregulated Contaminant Monitoring Regulation (UCMR) established. Contaminants detected under the UCMR must be reported to customers in a Consumer Confidence Report issued by the system and reviewed by the state. The EPA is required to review and update the UCMR every five years. The first UCMR (UCMR1) was issued in September 1999 and the second UCMR (UCMR2) was issued in January 2007. UCMR data are entered into the National Contaminant Occurrence Database (NCOD). The UCMR3 is currently in development and will likely include steroid hormones, organic perfluorinated compounds (PFCs), and other CECs. While the UCMR is generally based on the CCL, this is not always the case. The primary exception involves compounds included within an analytical method. For instance, even though perfluorooctanoic acid (PFOA) and perfluorooctanoic sulfonate (PFOS) are the only PFCs specifically included in the CCL3, it is expected that the UCMR PFC list will include other PFCs that are simultaneously monitored using USEPA method 537. Therefore, while the UCMR generally follows the CCL, it often contains other compounds that are simultaneously measured using the methods employed.

2.4 California Specific Regulations of Drinking Water and Water Reuse

Under USEPA granted primacy, the state of California has the authority to uphold the provisions of the Safe Drinking Water Act and to enforce all related federal standards. While the state is not permitted (without special exemption) to relax the drinking water standards of the Safe Drinking Water Act, the state may develop and enforce additional and/or more stringent requirements. The State of California has a long-standing history of developing rigorous standards beyond the requirements of the USEPA. The CDPH enforces both the federal and state drinking water regulations through the drinking water program (DWP) within the Division of Drinking Water and Environmental Management. Field operations branches are responsible for water regulation enforcement and work with the USEPA, the SWRCB, the Regional Water Quality Control Boards (RWQCBs), and other interested parties to achieve regulatory goals. A monitoring and evaluation unit exists under the technical programs branch, which collects results from analytical laboratories and reports subsequent drinking water quality data that meets the USEPA's data reporting requirements. The contaminants with enforceable standards in California are generally comparable to those mandated by the USEPA, albeit at times California regulations are more stringent. However, there are several contaminants regulated by the State of California for which no federal standard currently exists (Table 2.1). Considering the charge of this Panel, these chemicals were not considered CECs since they are already regulated in the State of California.

California administers a state unregulated contaminant monitoring rule program (Table 2.2), which requires routine monitoring and reporting. The State of California also has established a series of notification levels for 29 unregulated contaminants (Table 2.3).

Interestingly, besides notification compounds that are also listed in the California UCMRs, these contaminants are not part of mandated monitoring programs, nor is reporting to the public mandated, but it is recommended. Notification levels are established by the State using health-based criteria described in detail at http://www.cdph.ca.gov/certlic/drinkingwater/Documents/Notificationlevels/NotificationLevels.pdf. Thus, contaminants listed in Tables 2.2 and 2.3 were considered CECs.

Table 2.1. Contaminants regulated in California, but not by USEPA.

Contaminant	CA MCL (mg/L)
1,1-Dichloroethane	0.005
1,3-Dichloropropene	0.0005
Methyl-tert-butyl ether (MTBE)	0.013
1,1,2,2-Tetrachloroethane	0.001
Trichlorofluoromethane	0.15
1,1,2-Trichloro-1,2,2-trifluoroethane	1.2
Bentazon	0.018
Molinate	0.02
Thiobencarb	0.07
Perchlorate	0.006

Table 2.2. California Unregulated Contaminant Monitoring Requirements for Drinking Water.

Contaminant	Detection Limit for Reporting (µg/L)
Boron	100
Chromium-6	1
Dichlorodifluoromethane	0.5
Ethyl tertiary butyl ether	3
Tertiary amyl methyl ether	3
Tertiary butyl alcohol	2
1,2,3-Trichloropropane	0.005
Vanadium	3

Table 2.3. California notification substances and levels.

	Compound	Notification Level (mg/L)
1	Boron	1
2	n-Butylbenzene	0.26
3	sec-Butylbenzene	0.26
4	tert-Butylbenzene	0.26
5	Carbon disulfide	0.16
6	Chlorate	0.8
7	2-Chlorotoluene	0.14
8	4-Chlorotoluene	0.14
9	Dichlorodifluoromethane (Freon 12)	1
10	1,4-Dioxane	0.003
11	Ethylene glycol	14
12	Formaldehyde	0.1
13	HMX	0.35
14	Isopropylbenzene	0.77
15	Manganese	0.5
16	Methyl isobutyl ketone (MIBK)	0.12
17	Naphthalene	0.017
18	N-Nitrosodiethyamine (NDEA)	0.00001
19	N-Nitrosodimethylamine (NDMA)	0.00001
20	N-Nitrosodi-n-propylamine (NDPA)	0.00001
21	Propachlor	0.09
22	n-Propylbenzene	0.26
23	RDX	0.0003
24	Tertiary butyl alcohol (TBA)	0.012
25	1,2,3-Trichloropropane (1,2,3-TCP)	0.000005
26	1,2,4-Trimethylbenzene	0.33
27	1,3,5-Trimethylbenzene	0.33
28	2,4,6-Trinitrotoluene (TNT)	0.001
29	Vanadium	0.05

As discussed in Section 3, draft regulations have been established for groundwater recharge with recycled water. These draft regulations require that monitoring for all primary and secondary MCLs take place as well as testing for total nitrogen (TN) and total organic carbon (TOC). Additionally, the draft groundwater recharge regulations suggest quarterly monitoring for priority toxic pollutants listed in the State of California's Water Quality Standards, chemicals with State notification levels (Table 2.3), and additional constituent monitoring as specified by the State. The requirements for additional constituent monitoring are provided in Endnote 4 and 5 of the draft regulations. Endnote 5 suggests that indicators of wastewater be monitored, which may include unregulated compounds, such as pharmaceuticals, endocrine disruptors, personal care products, and *"other indicators of the presence of municipal wastewater as specified by CDPH".* (http://www.cdph.ca.gov/HealthInfo/environhealth/water/Pages/Waterrecycling.aspx).

3.0 Water Reuse Practices in California, Assurance of Plant Performance, and Current Monitoring Requirements

3.1 Introduction

Water reclamation, recycling, and reuse are integral components of water resource planning and management. In the past, the driving motivation for water reuse was to supplement scarce resources and to provide a means of avoiding effluent disposal into surface waters. With increased water demand brought on by continued drought and increasing population, recycled wastewater is now considered an important water resource. Non-potable and potable use of recycled water can enable communities to maximize and extend the use of limited water resources.

Utilization of appropriately treated wastewater as alternative and/or supplemental water sources to increase the supply of high quality water for potable uses includes applications such as:

- Landscape irrigation (e.g., parks, golf courses, residential);
- Agricultural irrigation (e.g., crops, commercial);
- Industrial uses (e.g., cooling towers, construction);
- Urban non-potable (e.g., toilet flushing, fire fighting);
- Potable water uses (e.g., blending in reservoirs, blending in groundwater, direct use); and
- Recreational/environmental uses (e.g., lakes, marshes, stream flow augmentation).

The purpose of this section is to provide a summary of the following key items. A more detailed discussion can be found in Appendices E (CDPH Draft Groundwater Recharge Regulations), F (Recycled Water Case Examples), G (Concept of Reliability), and H (Pretreatment Regulatory Authority for Source Control).

3.2 Current Levels of Water Recycling and Future Resource Demands

For nearly a century, recycled water has been used intentionally as a non-potable water supply source in California. The implementation of reclamation projects has increased significantly even in the face of regulatory, economic, and social constraints. In 1989, reuse of municipal wastewater in California was estimated at 325,000 acre-feet per year[2]. In 2002 the SWRCB conducted a comprehensive statewide survey of municipal facilities that focused on documenting the current levels of non-potable reuse of treated municipal wastewater. The results of the 2002 survey indicated that, as of the end of 2001, approximately 525,000 acre-feet per year of recycled water was used in California. More recent SWRCB data indicate that

[2]One acre-foot is equivalent to approximately 325,851 gallons of water.

during 2009 approximately 646,100 acre-feet per year of recycled water was used (WateReuse, 2010). A summary of the statewide survey is shown in Figure 3.1 suggesting that the top three reuses are for agricultural uses (37%), landscape irrigation (18%), and groundwater recharge and seawater intrusion barrier uses (27%). At the present time, estimates indicate that about 8 to 10 percent of municipal wastewater is recycled in planned reuse projects. Estimates regarding future reuse indicate that California has the potential to recycle an additional 1.4 to 1.6 million acre-feet per year of water by the year 2030 (WateReuse, 2010).

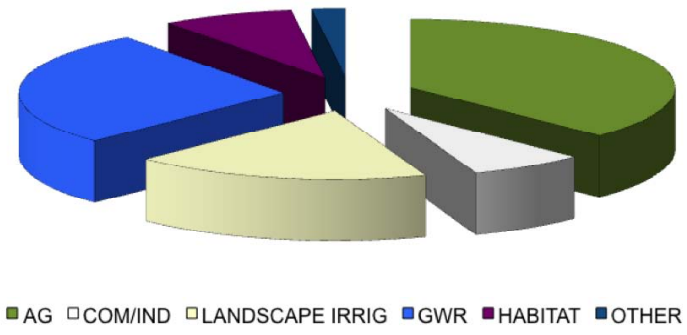


Figure 3.1 Types of recycled water use in California as a percentage of annual use, 2009 (Source: WateReuse, 2010).

3.3 Current Water Recycling Regulations, Criteria and Policy

Recycled wastewater in California is mainly regulated by three state agencies: the Department of Public Health (DPH), the SWRCB, and the nine RWQCB. The SWRCB and the RWQCBs have the primary responsibility for the protection and enhancement of the waters of the State. The SWRCB also has the primary responsibility for administering water rights. The DPH has the authority and responsibility to establish public health criteria for wastewater reclamation, including groundwater recharge, and reviews all proposals and plans for such projects throughout the state. Local health agencies and water districts can develop policies and programs, which are more stringent than those specified by the DPH.

State statutes and regulations pertaining to the use of recycled water in California can be found in the California Water Code (CWC), California Code of Regulations (CCR), and California Health and Safety Code. Water quality control plans (basin plans) may also contain the recycled water use policy of individual RWQCB. The DPH Wastewater Reclamation Criteria governing various uses other than indirect potable reuse are contained in Title 22, Division 4 of the CCR. A summary of the Title 22 criteria is presented in Table 3.1.

Table 3.1 .Summary of California Department of Public Health Water Recycling Treatment Requirements.

Purpose of Use	Treatment Requirement
Orchards and Vineyards (no contact with edible crops), Nonfood bearing Trees, Fodder or Fiber Crops, Seed Crops (not eaten by humans), Food Crops (with additional pathogen treatment for crop), and Flushing Sanitary Sewers	Undisinfected Secondary[a]
Cemeteries, Freeway Landscaping, Gold Courses (restricted access), Ornamental Nursery stock, Sod farms, Pasture (milk animals), Non-edible vegetation (controlled access), Commercial/Industrial cooling towers (with drift reduction), Landscape impoundments (no decorative fountains), Industrial boiler feed, Soil compaction, Mixing concrete, Dust control (roads), Cleaning roads, Nonstructural fire fighting	Disinfected Secondary, 23 MPN/100 mL[b]
Food crops (edible portion above ground – no contact), Restricted recreational impoundments	Disinfected Secondary, 2.2 MPN/100 mL[c]
Food crops, Parks and playgrounds, School yards, Residential landscaping, Golf courses (unrestricted), Commercial/Industrial cooling towers (mist devices), Unrestricted recreational impoundments (with specific pathogen monitoring), Flushing toilet and urinals, Structural fire fighting, Decorative fountains, Artificial snow making, Commercial car washes, Groundwater recharge (with additional treatment – see CDPH draft groundwater regulations)	Disinfected Tertiary[d]

a Undisinfected secondary treatment: means oxidized wastewater (Oxidized wastewater: wastewater in which the organic matter has been stabilized, is non-putrescible, and contains dissolved oxygen.)

b Disinfected secondary – 23 recycled water: oxidized and disinfected so that the median concentration of total coliform bacteria does not exceed a most probable number of 23 per 100 mL and the MPN does not exceed 240 per 100 mL in more than one sample in any 30 day period.

c Disinfected secondary – 2.2 recycled water: oxidized and disinfected so that the median concentration of total coliform bacteria does not exceed a most probable number of 2.2 per 100 mL and the MPN does not exceed 23 per 100 mL in more than one sample in any 30 day period.

d Disinfected tertiary recycled water: means a filtered and disinfected wastewater that meets a CT (product of total chlorine residual and modal contact time measured at the same point) value of not less than 450 mg-min. per L at all times with a modal contact time of 90 min. (based on peak dry weather design flow) or provides a 5 log removal/reduction of MS2 F-specific phage or polio virus or similar virus).

Filtered wastewater: an oxidized, coagulated, clarified wastewater which has been passed through natural undisturbed soils of filter media, such as sand or diatomaceous earth, so that the turbidity, as determined by an approved laboratory method, does not exceed 5 turbidity units more than 5 percent of the time during any 24-hour period, an average of 2 NTU during a 24-hour period, and does not exceed a 10 NTU at any time; in addition, the filter may not exceed 5 gals per min per square foot (traveling bridge automatic backwash filters cannot exceed 2 gals per min).

(Source: Summary adapted from California Code of Regulations, Title 22, Division 4, Division of Environmental Health.)

A summary of the August 2008 CDPH draft groundwater Recharge Reuse Regulations is presented in Table 3.2. The draft recharge regulations address the supplementing of groundwater through surface or subsurface application of treated municipal wastewater prior to eventual extraction via drinking water wells for potable use. The proposed California criteria for groundwater recharge reflect a cautious approach toward potential short- and long-term health concerns. The recently adopted State Water Board Recycled Water Policy and supporting information provide further definition and clarification to the collaborative roles of the SWRCB, the CDPH, and the RWQCBs as they relate to permitting and monitoring water recycling projects. The Policy and supporting documentation clearly and appropriately envision that the RWQCBs rely on the DPH's expertise for establishing permit conditions (e.g., monitoring conditions) needed to protect human health. A more detailed discussion of the key California regulations (both current and draft), criteria, and policy that impact reuse projects is provided in Appendix E.

To protect public drinking water supplies, the CDPH also has regulations to prevent cross connections between recycled water systems and potable water systems. Local health departments and the CDPH have enforcement authority over these cross connection prevention regulations. The California Building Standards Commission sets plumbing standards for use of recycled water in buildings and industries.

Table 3.2. Summary of CDPH Draft Groundwater Recharge Regulations (DRAFT August 5, 2008).

Contaminant	Reuse Applications	
	Surface Spreading	**Direct Injection**
Pathogenic microorganisms[1]	Disinfected secondary and filtered recycled water	Disinfected secondary and filtered recycled water
Secondary treatment Filtration Disinfection	Oxidized ≤2 NTU ≤5-log virus inactivation, ≤ 2.2 total coliform per 100 mL	Same
Retention time underground	Min. 6 months	Same
Control nitrogen compounds	Three options – e.g., Option1 = TN ≤ 5 mg/L as N in reuse water	Same
Regulated contaminants	Me*et al*l drinking water MCLs	Same
Recycled Water Contribution RWC) Initial Operation	20 to ≤50% depends on % RO and AOP treatment and NDMA and 1,4-dioxane reduction	≤50% plus all RW treated with RO and AOP treatment and NDMA and 1,4-dioxane reduction
Max RWC	Up to 100% (see note 2) plus TOC performance over 20 weeks meets $TOC_{max} \leq 0.5$ mg/L / $RWC_{proposed}$ (may be increased with DPH approval)	Up to 100% (see note 2) plus TOC performance over 20 weeks meets $TOC_{max} \leq 0.5$ mg/L / $RWC_{proposed}$ (may be increased with DPH approval)

Table 3.2. Continued

Contaminant	Reuse Applications	
	Surface Spreading	**Direct Injection**
Diluent Water	Implement monitoring program, quality < to primary MCLs, meet nitrogen controls, determine volume for credit	Same
Downgradient Monitoring	One location at least 3 months prior to domestic supply Additional points including each aquifer	Same
Source Control and Outreach	Industrial monitoring and investigation	Same
Unregulated Contaminants	Data collection for pharmaceuticals, endocrine disruptors and other indicators	Data collection for pharmaceuticals, endocrine disruptors and other indicators

Notes:

[1]-See Title 22 requiremenst for disinfected filtered (section 60301.320) and tertiary (section 60302.230) recycled water.

[2] Increasing RWC requires meeting a number of criteria. For example, a health effects study must be conducted including and exposure assessment, review of available epidemiology studies, and evaluation of individual and cumulative effects of regulated contaminants.

BOD = biochemical oxygen demand; NA = not applicable; NTU = nephelometric turbidity unit; RWC = the percent recycled water contribution in groundwater extracted by drinking-water wells; SAT = soil aquifer treatment; TOC = total organic carbon.

3.4 Key Criteria Governing Planned Indirect Potable Reuse Projects

In May 1993, a California Potable Reuse Committee was formed by the DPH and the California Department of Water Resources to look into the feasibility and safety of potable reuse of recycled water following advanced treatment. The members concluded that planned indirect potable reuse of advanced treated recycled water using surface water reservoirs is feasible if six specific criteria were addressed (see Appendix E).

In addition, in 1998, the National Research Council (NRC) evaluated the issue of potable reuse and provided specific recommendations to consider in both evaluating and governing such uses (NRC, 1998). Although the NRC recommendations are not specifically part of the California water reclamation and reuse laws, regulations and/or guidance, their recommendations are relevant to the specific questions being addressed by this Panel. In addition, the recommendations of the NRC are consistent with and expand the recommendations contained in the 1996 California surface water augmentation framework document (see Appendix E).

The 1998 NRC report recommended that water agencies considering potable reuse fully evaluate the potential public health impacts from the microbial pathogens and chemical contaminants found or likely to be found in treated wastewater through special microbiological, chemical, toxicological, and epidemiological studies, monitoring programs, risk

assessments, and system reliability assessments. In addition, the 1998 NRC report also provided some specific recommendations regarding reliability and quality assurance.

The NRC recommendations (NRC, 1998) combined with current practices and recommended criteria established in the State of California, as summarized below, should be carefully considered for evaluating and managing potable reuse projects:

1. Utilize the Best Available Technology in advanced wastewater treatment;
2. Utilize multiple, independent barriers, especially using robust barriers for the removal of microbiological contaminants[3];
3. Employ quantitative reliability assessments to monitor and assess performance and reliability (i.e., both process control and final water quality monitoring and assessment as well as assessment of mechanical reliability);
4. Avoid "short-circuiting" in environmental buffers including the maintenance of appropriate retention times within the environmental buffers as well as the maintenance of water quality in the environmental buffer (i.e., groundwater and/or reservoir(s));
5. Provide for alternative means for disposing of the production water that does not meet required standards;
6. Develop and implement a well coordinated public health surveillance systems to document and possibly provide early warning of any adverse health events associated with the ingestion of recycled water;
7. Implement an effective source control program;
8. Operators of water reclamation facilities should receive training and certification regarding the principles of operation of advanced treatment processes, the pathogenic organisms likely to be found in wastewaters, and the relative effectiveness of the various treatment processes in reducing contaminants concentrations;
9. Utilize an independent monitoring oversight authority to provide a third-party review of operational, regulatory, and environmental issues associated with the indirect potable project;
10. Institute formal channels of coordination between water reclamation agencies, regulatory agencies, and agencies responsible for public water systems; and
11. Establish a CEC monitoring program that incorporates use of indicators and surrogates to represent CECs.

[3] See Sakaji *et al*. (Sakaji, 1998) and Olivieri *et al*. (Olivieri, 1999) for additional detail and discussion.

3.5 Recycled Water - Case Examples

In California, a typically arid and semi-arid region of the United States, groundwater recharge and irrigation are major reuse options to a) replenish existing groundwater resources, b) to protect groundwater resources via salt water intrusion barriers and c) to augment and replace potable water currently used for agricultural and irrigation practices. Summaries were prepared for two of the oldest and largest groundwater recharge projects in the nation (Appendix F):

- Orange County Water District - Groundwater Replenishment via direct injection and surface spreading; and
- Montebello Forebay Groundwater Recharge Project via surface spreading.

In addition, summaries were provided for two of the many ongoing landscape irrigation projects (i.e., City of Sunnyvale and City of San Jose); summaries are presented in Appendix F. The summaries briefly cover how the projects address many of the above key factors and identify how to locate additional information. A summary of the basic treatment processes/ operations typically utilized for wastewater treatment is provided in Table 3.3 and a summary of those processes used for groundwater recharge reuse projects and for landscape irrigation projects is provided in Table 3.4.

Table 3.3. General summary of wastewater treatment processes/operations. (Adapted from Asano *et al.* 2006).

Treatment Level	Description
Preliminary	Removal of wastewater constituents, such as rags, sticks, grit etc., that may cause operational problems
Primary	Partial removal of suspended solids and organics
Advanced primary	Enhanced removal of suspended solids and organic matter (via chemical addition and filtration)
Secondary	Removal of biodegradable organic matter (in solution or suspension) and suspended solids
Secondary with nutrient removal	Secondary treatment with additional processes designed specifically to remove nutrients such as nitrogen and phosphorous
Tertiary	Removal of residual suspended solids through use of granular/surface filtration and/or membranes
Advanced	Removal of total dissolved solids and trace constituents (nutrient removal may be included as well) with membranes and advanced oxidation processes
Disinfection	Removal/destruction of microbial pathogens

Table 3.4. General summary of water reuse application and wastewater treatment processes/operations.

Water Reuse Application	Treatment Level
Groundwater Recharge – Surface Water Spreading	Preliminary, primary, secondary (sometimes advanced secondary), nutrient removal, tertiary, disinfection
Groundwater Recharge – Direct Injection	Preliminary, primary, secondary (sometimes advanced secondary), nutrient removal, tertiary, advanced, and disinfection
Landscape Irrigation – Restricted	Preliminary, primary, secondary (sometimes advanced secondary), disinfection
Landscape Irrigation - Unrestricted	Preliminary, primary, secondary (sometimes advanced secondary), tertiary, disinfection

In summary, all of the above key potable reuse project elements (see Section 3.4), except for the items noted below, appear to be adequately addressed as part of current State regulations and guidance.

- (#3) Employ quantitative reliability assessments to monitor and assess performance and reliability (i.e., both process control and final water quality monitoring and assessment as well as assessment of mechanical reliability);
- (#6) Develop and implement a well coordinated public health surveillance systems to document and possibly provide early warning of any adverse health events associated with the ingestion of recycled water;
- (#9) Utilize an independent monitoring oversight authority to provide a third-party review of operational, regulatory, and environmental issues associated with the project; and
- (#11) Establish a CEC monitoring program that incorporates use of indicators and/or surrogates to represent suites of CECs.

Further, based on the preliminary review of two major indirect reuse projects, the above key elements appear to be required and implemented for indirect potable reuse. Additional information on key elements that are not currently being adequately addressed (numbers 3, 6, 9 and 11 above) is provided in Appendices G and H.

4.0 Toxicological Relevance of CECs in Recycled Water to Human Health

4.1 Introduction

The purpose of this section is to introduce the Panel's process for determining the toxicological relevance of CECs in recycled water with respect to human health.

To evaluate the known toxicological information for CECs regarding human health, the Panel reviewed results of many of the key studies conducted over the past 40 years on the toxicological relevance to humans of CECs in recycled water. Those studies include epidemiological studies examining effects in humans directly, studies in which laboratory animals have been exposed to recycled water, bio-analytical studies, and risk assessments that predict the potential effects to humans of individual CECs in recycled water (see summary in Appendix I). While almost all of these studies report the absence of adverse effects from recycled water use, the epidemiological studies are, in the Panel's view, particularly important. The earliest studies were conducted in the 1970's and 1980's with a focus on the potential effects of disinfection byproducts produced following disinfection of drinking water with chlorine. Some of those early studies report an increase in bladder and rectal cancers possibly associated with chlorination byproducts (see summary in Sloss, 1996). More recent studies of recycled water find, essentially, no adverse health outcomes in populations using recycled water (see summary in Appendix I). Though epidemiologic studies, like any study, can have limitations, in particular the influence of confounding factors such as uncertainty about the exact amount of exposure to recycled water (NRC, 1998) or whether long term exposure to CECs over generations can affect human health through as yet unknown (e.g., epigenetic) mechanisms, the fact that different research groups have investigated different populations over the course of several decades, and reported similar results, is important. The epidemiologic studies are particularly important, as are laboratory animal and bio-analytical studies, because they look at exposure to the entire mixture of chemicals that may be present in recycled water. That mixture includes chemicals, both naturally occurring and man-made, that have not been identified yet, as well as the interactions between those that have been previously identified. In summary, the Panel views the predominantly negative findings of the combined epidemiological studies, laboratory rodent studies, bio-analytical screening studies and risk assessments as several concordant lines of evidence that appropriately treated recycled water represents a safe source of water to supplement potable drinking water supplies.

4.2 Screening Process to Assess Toxicological Relevance of CECs

The predominantly negative findings described above do not preclude the need to monitor recycled water to assure its continued safety. One reason for monitoring is the potential presence of newly developed compounds that were not being manufactured at the time the above mentioned epidemiological studies were conducted. As described in Section 2 of this report, CECs to be considered in monitoring programs can be selected for a variety of reasons, only one of which is the potential to pose a risk to human health (i.e., toxicological relevance).

To identify CECs that have the greatest potential to be of toxicological relevance to human health, the Panel developed a screening process.

In principle, the screening process is simple: MECs or PECs of CECs at the POM for a particular water reuse scenario are compared to monitoring trigger levels (MTLs) developed for that particular water reuse scenario. This process is referred to as the "Exposure Screening MEC/MTL" (Figure 4.1). If the concentration of a CEC is less than the MTL, then that CEC is assumed to have little or no potential to pose an unacceptable potential risk to human health and does not need to be included in a CEC monitoring program, at least with respect to its toxicological relevance (such a CEC would fall into the "No Concern" box following the "Exposure Screening" flowchart, Figure 4.1). Note that such CECs may yet be included in a monitoring program because they may be relevant as indicator compounds (see the "Suitable Indicator" portion of the flowchart). If the concentration of a CEC is equal to or greater than the MTL, then the CEC should be considered for inclusion in a monitoring program (such a CEC would fall into the "Concern" box following the "Exposure Screening" flowchart). The Panel believes it is important to stress that exceedance of a MTL by a measured or predicted concentration at the POM does not mean that the CEC poses a health risk to humans. The comparison to MTLs should be conducted at the POM, not the point of exposure. As discussed in Section 5, CEC concentrations at the point of exposure are likely to be many fold lower than they are at the POM.

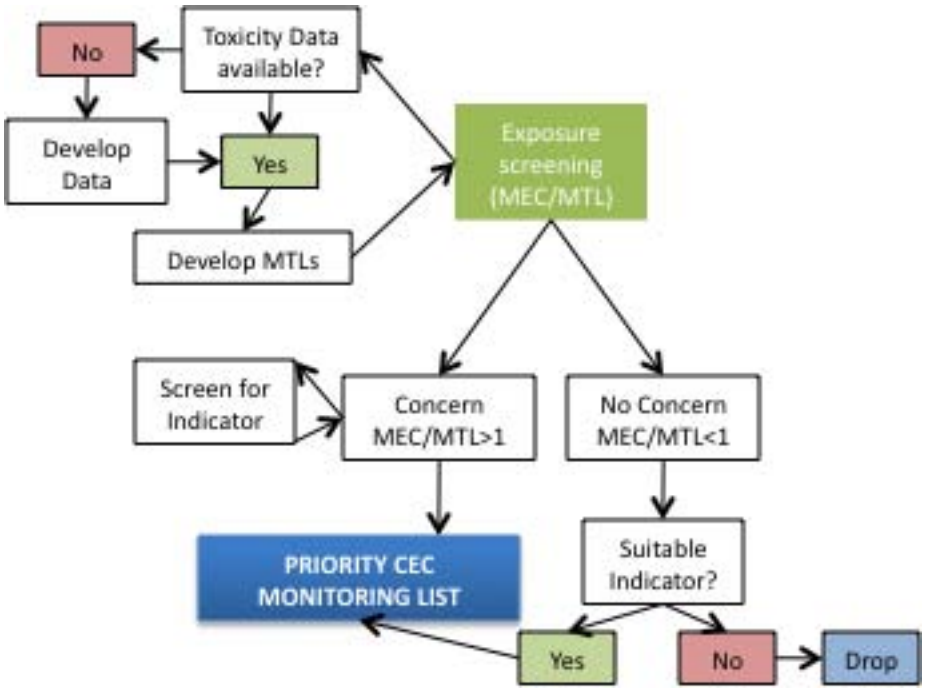


Figure 4.1. Conceptual exposure screening of CEC regarding relevance in recycled water.

Central to the screening process is the development of MTLs for each water reuse scenario. It is important to note that the process the Panel has recommended should not be viewed as a process to establish drinking water or surface water criteria for CECs, though such a process may bear substantial similarity to the MTL process. Regulatory agencies already have policies and procedures in place to develop such criteria. The chemical and toxicological properties of compounds currently viewed as CECs are not unique compared to substances already considered by the State for regulatory purposes and thus CECs are amenable to the typical criteria development process. When regulatory agencies determine that a drinking or surface water criterion is required for a compound viewed as a CEC, it is the Panel's view that already established policies and procedures should be followed (see discussion in Section 2).

In recommending an approach to develop MTLs, an overriding goal for the Panel was that the MTLs be sufficiently low (i.e., conservative) such that a compound which has the potential to pose a human health concern can be identified and included as a potential CEC for monitoring. The Panel could have recommended that California simply using drinking water benchmarks (e.g., either drinking water standards, criteria or screening levels) already derived by various regulatory agencies and peer-reviewed publications to establish MTLs (see Appendix J for such a compilation). However, the Panel felt reliance upon existing benchmarks assembled from a variety of sources had at least two important drawbacks that must be kept in mind when developing MTLs.

First, it leads to the establishment of MTLs derived using different assumptions, which, in turn, means that neither the Panel nor anyone using such MTLs understands how conservative each one is; at least not without reviewing the details of the derivation of each of the drinking water benchmarks upon which the MTLs are based. The protectiveness of a benchmark will depend upon the information and methods used to derive it. For example, selecting the lowest of two benchmarks without a detailed review of their derivation precludes the user from understanding the basis and protectiveness of each benchmark. The lower of the two benchmarks may be based upon new toxicological information not available to the authors who derived the higher benchmark. Alternatively, both groups of authors may have used the same toxicity information but differed in their application of uncertainty factors for various reasons. While having a set of benchmarks that vary in their level of protectiveness is not inherently unacceptable, the Panel sees value to having MTLs that have a common level of protectiveness because they are derived using a common set of exposure and toxicity assumptions.

The second drawback of using existing drinking water benchmarks to establish MTLs is that such benchmarks are only available for CECs that we know about today. A substance that is not known today, but is "discovered" or predicted to be in recycled water in the future (referred to as a "known unknown" in the flowchart in Figure 2.1), would not likely have a literature-based benchmark. For such a compound, a monitoring program would not have a drinking water benchmark to which to compare a measured concentration and, thus, the MEC or PEC of the compound could not be compared to an MTL.

In lieu of recommending use of already established drinking water benchmarks from several sources, the Panel reviewed the recent literature on CECs to determine whether anyone had published a relatively simple process that could be used to derive screening level allowable daily intakes (ADIs) that could then be employed to establish MTLs that have a common derivation and a consistent and transparent level of protectiveness. In the course of that review the Panel identified a process to derive screening level acceptable daily intakes (ADIs) for a variety of CECs in recycled water presented in *"Identifying Hormonally Active Compounds, Pharmaceuticals, and Personal Care Product Ingredients of Health Concern from Potential Presence in Water Intended for Indirect Potable Reuse"* (Snyder *et al*. 2010). Snyder *et al*. (2010) developed a common process based upon a simple decision tree, readily available information for each compound, and a common set of assumptions to establish a screening level ADI (Figure 4.2). The process of deriving an MTL is presented in the boxes in the flowchart to the left of the Exposure Screening box (Figure 4.1). In that process the flowchart asks whether toxicity data to develop an ADI are available, and if they are, the process described below is followed to develop a MTL[4].

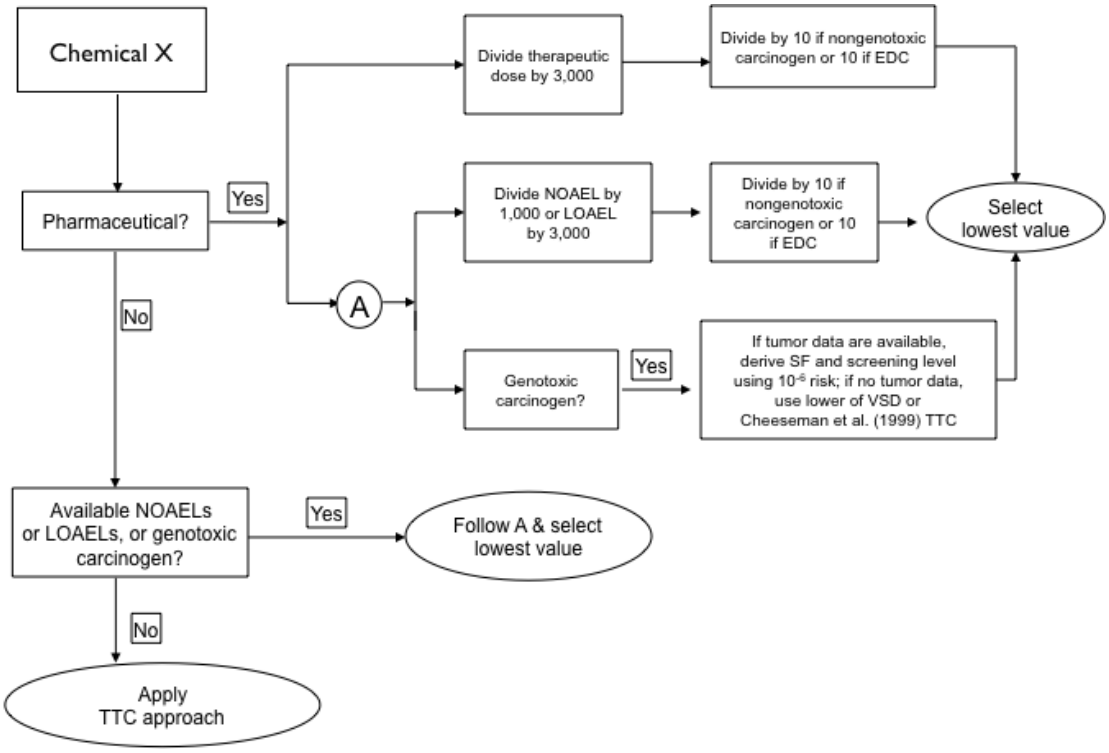


Figure 4.2 .Final Decision Tree for PNEC Determining Scheme for New and Emerging Contaminants (adopted from Snyder *et al*. 2010).

[4] The Panel wishes to point out that if the State of California, or another agency that the State of California recognizes as having the expertise to develop ADIs, has developed an ADI for a potential CEC, then the Panel recommends that the ADI developed by the State should be used to establish an MTL in lieu of the process described in Snyder *et al*. (2010).

A critical consideration in the Panel's decision to recommend this approach in the derivation of screening level ADIs was the involvement of a large number of potential stakeholders and experts in the development of the screening benchmark derivation process described in Snyder *et al*. (2010) and what the Panel viewed as a comprehensive review of available screening benchmark derivation methods undertaken by the authors and stakeholders involved in Snyder *et al*. (2010).

The overall goal of Snyder *et al*. (2010) was to review methodologies for developing screening level human health risk-based criteria for CECs potentially present in recycled water. Snyder *et al*. (2010) identified several methodologies that could be used to develop screening level benchmarks for protection of public health. From those methodologies, the authors, in conjunction with outside experts devised a simple, conservative approach for the development of health risk-based guidelines for CECs *"that selects the lowest calculated level (i.e., most protective of human health) from several possible risk assessment schemes"*. The Panel emphasized that application of the decision tree in the development of screening values should be performed in consultation with appropriate experts in toxicology and risk assessment. A summary of the proposed approach is excerpted from the Executive Summary of Snyder *et al*. (2010) below:

1) If the chemical is a pharmaceutical, select the lowest value from among comparison values derived using the following processes:
    a) Divide the therapeutic dose (on a milligram per kilogram body weight basis, based upon range of doses and age groups for which the chemical is prescribed) by a default uncertainty factor (UF) of 3,000; divide by an additional UF of 10 if the compound is either a non-genotoxic carcinogen or an endocrine disrupting compounds (EDC).
    b) Divide the literature-based no observed adverse effect level (NOAEL) by a default UF of 1,000 or the lowest observed adverse effect level (LOAEL) by a default UF of 3,000; divide by an additional UF of 10 if the compound is either a non-genotoxic carcinogen or an EDC.
    c) If the compound is a genotoxic carcinogen and tumor incidence data are available, develop a slope factor and establish a comparison value assuming a *de minimis* cancer risk of 1 in 1,000,000.
    d) If the compound is a genotoxic carcinogen and no tumor incidence data are available, use the lower of the virtually safe dose derived using the method of Gaylor and Gold (1998) or the threshold of toxicological concern (TTC).
2) If the chemical is not a pharmaceutical and either a literature-based NOAEL or LOAEL can be identified or the chemical is a genotoxic carcinogen, set guidelines based on toxicological data following (b), (c), and (d), above.
3) If the chemical is not a pharmaceutical but does not have either a literature-based NOAEL or LOAEL or there is no evidence it is a genotoxic carcinogen, derive a screening level based on the TTC.

The Panel appreciates that the process described in Snyder *et al*. (2010) is meant for derivation of screening level human health risk-based criteria for CECs present in drinking water. Though not specifically derived for application as MTLs, the Panel believes the conservative nature of the toxicity benchmarks using the process described in Snyder *et al*. (2010), will result in trigger levels that are sufficiently conservative to be used as MTLs for the protection of human health. Though the Snyder *et al*. (2010) process was developed for PPCPs, and endocrine disrupting compounds, the Panel believes the process can be applied to most any CEC for calculating an MTL. Users of the MTLs derived using the Snyder *et al*. (2010) process should note that MTLs so derived did not consider protection of ecological receptors.

The authors of Snyder at al. (2010) also *"recommended that if the risk assessor/ toxicologist notes a "flag" suggesting the potential for unique toxicity (e.g., evidence from toxicity studies suggests the compound is a frank teratogen at the lowest dose, or the compound is a chemotherapy agent), then the compound should be subject to a full compound-specific risk analysis rather than using the rapid screening approach presented here".* In developing MTLs for the initial list of candidate CECs to be monitored, the Panel came across another situation in which the screening level ADIs derived using the Snyder *et al*. (2010) decision tree likely need additional careful consideration before being used to derive MTLs. The specific example is the screening ADI value to use for 17β-estradiol (E2); E2 has been extensively studied, and its potential effects are well understood. Several expert scientific bodies and regulatory agencies have conducted reviews of available toxicity information (see text box below). Some of those agencies have selected an ADI that is about 2000-fold higher than the screening level ADI determined using the decision tree presented in Snyder *et al*. (2010) (see text box below).

Toxicity of 17β-estradiol (E2)

Various expert bodies have recognized that E2 is a potential carcinogen (WHO 2000 (Toxicological Evaluation of Certain Veterinary Drug Residues in Food. WHO Food Additive Series: 43. Estradiol-17 β , Progesterone, and Testosterone. Geneva:World Health Organization, International Programmeon Chemical Safety. available: http://www.inchem.org/documents/jecfa/jecmono/v43jec01.htm); EPA in the CCL dossiers.) Sufficient data are available to derive a cancer slope factor (SF) of 39 $(mg/kg\text{-}day)^{-1}$ (CA OEHHA, 1992 as cited in Snyder *et al*. (2010)). Based on the carcinogenic potential of E2 and the availability of the SF, the Snyder *et al*. (2010) decision tree would lead to the establishment of a screening level ADI of 0.000026 μg/kg-day assuming an allowable excess lifetime cancer risk of one in one million ($1x10^{-6}$). This screening level ADI is nearly 2000 times lower than the ADI of 0.05 μg/kg-day recommended by Australia (Australian-guideline, 2008), the only regulatory body that has proposed a drinking water guideline for E2 (see Appendix J summarizing drinking water levels identified by the Panel). The Australia drinking water guideline is based upon the WHO ADI, which is derived through the application of a total uncertainty factor of 100 to a NOAEL of 0.3 mg/day derived from studies of changes in several hormone-dependent parameters in postmenopausal women. Given the WHO's review of the extensive toxicity and epidemiological data available for E2 and decision to base the ADI for E2 on a non-cancer endpoint, the Expert Panel believes the WHO ADI is just as valid as the ADI that can be derived using the CA OEHHA slope factor and a $1x10^{-6}$ excess lifetime cancer risk level. Indeed, given that the mechanism by which tumors were induced in the rodent study, upon which cancer slope factor is based, has no equivalent in humans, the WHO ADI may have greater validity than the ADI based upon the results of the rodent cancer bioassay. The decision of which ADI to use for compounds like E2 is one of science policy and needs to consider previous precedent as well as new precedent such a decision establishes. For example, if the ADI based upon the CA OEHHA slope factor is accepted and used to establish MTLs, it likely means that many common dietary items that contain naturally occurring E2 and other steroid estrogens (e.g., dairy products and various meats) pose a potentially unacceptable cancer risk. If WHO's ADI is used, consumption of many common dietary items would not pose an unacceptable risk.

The Expert Panel was not prepared to conduct a detailed review of the toxicity of E2 (or any other CECs) for the purpose of developing an initial list of CECs to monitor. The Panel believes that as part of developing a final monitoring list of CECs to protect public health, substantial discrepancies between screening level ADIs should be carefully examined and understood before a final ADI is selected for the derivation of a MTL.

4.3 Derivation of Monitoring Trigger Levels

Two unique sets of MTLs need to be developed, corresponding to the differing degree of exposure to recycled water this is assumed to be associated with the two water reuse practices described in Section 1. To translate the screening level ADIs derived using the decision tree presented in Snyder *et al*. (2010) into MTLs for potable water use (as opposed to landscape irrigation), the Panel adopted the common approach of assuming that an adult female (the Panel recommends using USEPA's default bodyweight of 60 kilograms for an adult female) consumes 2 liters of water per day for her entire life. Thus, the screening level ADI is multiplied by 60 kg and divided by 2 liters/person-day (Equation 4.1) to derive the potable water use MTL. The Panel also believes that it is appropriate to incorporate a relative source contribution (RSC) in the derivation of MTLs, though the value of the RSC should depend upon the particular CEC. For CECs where drinking water is assumed to be the dominant exposure pathway for the general public, an RSC of 1.0 is appropriate (e.g., human use pharmaceuticals, disinfection byproducts). While CECs with many potential environmental sources other than drinking water (e.g., most pesticides) should employ an RSC of less than 1.0. Given the Panel's resource and time constraints, it did not feel it was in a position to recommend specific RSCs for specific classes of CECs, but recommends that the next Panel review the development of RSCs and recommend values to use in the development of MTLs.

$$\text{Monitoring Trigger Level} = \frac{\text{Screening Level ADI} \times 60\text{ kg} \times \text{RSC}}{2\text{ L/day}} \qquad \text{(Eq. 4.1)}$$

To derive the MTLs for landscape irrigation, the Panel recommends using the same assumptions as used to derive MTLs for potable use, with the exception of the water ingestion rate. Few quantitative data were available to rigorously characterize the potential incidental ingestion rate of water for the landscape irrigation scenario. The Panel started by reviewing information compiled by USEPA on incidental water ingestion while swimming (USEPA 2009a) as a possible source to develop an estimate of the amount of water consumed in the landscape irrigation scenario. The Panel felt that in most cases, measured amounts of water ingested incidentally while swimming would be substantially greater than the amounts of water that might be ingested from landscape irrigation. USEPA reports that children ingest more water while swimming than adults (mean and upper 95% ingestion rates of 37 and 49 mL/hour for children and 16 and 20 mL/hour for adults). The Panel also reviewed studies reporting on the proportion of daily drinking water intake due to park irrigation (Cooper & Olivieri, 1998; Sakaji *et al.* 1998; Ottoson & Stenstrom, 2003). These studies form a better basis from which to estimate incidental irrigation exposures than studies of swimming exposures. Based upon these

studies, the Panel selected a high-end incidental ingestion fraction of 1% of total daily water intake being comprised of intake from landscape irrigation. Given that total daily intake is assumed to be 2 liters per day for the derivation of potable use MTLs, the intake for landscape irrigation was assumed to be 0.02 liters, or 20 milliliters per day. Thus, the expected ingestion of water associated with landscape irrigation is 100-fold lower than that assumed for potable water use. As this is the only difference between the two sets of MTLs for the two reuse practices, the landscape irrigation MTLs are 100 times greater than the MTLs for potable reuse.

4.3.1 Initial Monitoring Trigger Levels

The Panel believes that MTLs derived following the process described above, will be consistent, protective of public health, and when compared to representative MECs or PECs, will lead to the identification of CECs that should be included in a monitoring program based upon their toxicological relevance to humans. The Panel also recognizes that full implementation of its recommended process (including derivation of MTLs) will require more resources than were available to the Panel. For example, review of available toxicity information for each CEC and the use of that information in the flow chart presented in Snyder *et al*. (2010) (see Figure 4.2), could take significant effort and toxicological expertise and judgment. The Panel had the required expertise and judgment, but simply did not have the time and resources at its disposal to conduct such a review. That being said, the Panel did want to develop an understanding of whether its recommended framework of comparing measured (or predicted) environmental concentrations to MTLs to identify CECs to include in a monitoring program was workable. The Panel also felt it was within their charge to provide regulators with initial MTLs so that monitoring could be readily implemented.

To conduct such an evaluation, the Panel derived initial MTLs based upon drinking water benchmarks available from seven different sources (see Appendix J). These sources include drinking water benchmarks developed by three regulatory agencies (USEPA, CDPH, Australian Environmental Protection and Heritage Council), two papers recently published in scientific journals (Schwab *et al*. 2005, Schriks *et al*. 2009), and two peer-reviewed research reports focusing on the development of benchmarks for CECs (Snyder *et al*. 2008a, Cotruvo *et al*. 2010). The key assumptions each of the sources used to derive drinking water benchmarks are described in Appendix J.

When information from these seven sources is combined, drinking water benchmarks are presented for 418 compounds that might be classified as CECs. The majority of CECs have only a single benchmark (i.e., only one of the sources presents a benchmark for that CEC) that could be used as the MTL. However, several CECs, often the pharmaceuticals, have multiple benchmarks. For some CECs, those benchmarks are similar (e.g., codeine, ethinyl estradiol, di-n-butyl phthalate) while for others, the benchmarks can be quite disparate (e.g., ibuprofen, DDE, DEET, triclosan).

The drinking water benchmark selected as the basis for the initial MTLs for each compound is highlighted (in pink) in Appendix J. As described in Appendix J footnotes, the benchmarks are derived by combining assumptions about the toxicity of a CEC and potential exposure to the CEC via consumption of drinking water. The assumptions about the potential toxicity of a

particular CEC and how the ADI for that particular CEC was derived can vary between the sources of the benchmarks. Details of those differences are available from the sources. Summarizing the derivation of the allowable intake for each benchmark was beyond the scope of the Panel's charge.

Just as assumptions about the potential toxicity of a CEC can vary between sources, so can assumptions about exposure. For example, some sources developed drinking water benchmarks based upon a child's bodyweight and assumed a lower total water consumption rate; however, on a per kilogram basis, a child's intake is actually greater than an adult's (Schwab *et al*. 2005) while the others were based on an adult's total intake. All sources assumed long-term daily consumption of drinking water. Some sources consistently adjusted the allowed exposure from drinking water to account for potential exposure from other pathways (e.g., diet) while other sources did not. This adjustment is referred to as the RSC in the US. The Australian guidelines refer to it as a proportion (P) from water (Australian-guideline, 2008). The decision to use or not use an RSC (or P) does not appear to be random. For example, Schwab *et al*. (2005) did not use an RSC because the only CECs they evaluated were pharmaceuticals. For people not taking a particular pharmaceutical for therapeutic use, drinking water exposure likely comprises the majority of such a person's daily exposure, so the need to account for exposure from other sources is compound-specific. In other words, the RSC can be set to 1.0 for pharmaceuticals. The Australian guidelines similarly use a P of 1.0 for human-use pharmaceuticals but use a P of 0.1 for other compounds, including pharmaceuticals with veterinary or agricultural applications (Australian-guideline, 2008).

Given the conservative nature of the initial MTL selection process followed by the Panel for the purposes of this report, the Panel believes the MTLs highlighted in Appendix J are health protective and appropriate for use in a CEC monitoring program. This report refers to those MTLs as "initial MTLs" to emphasize that they were derived using a process distinct from the one recommended by the Panel. A key part of the framework proposed by the Panel is periodic review of the MTLs and MECs/PECs used to identify indicator CECs to be included in a monitoring program. The Panel anticipates that as part of such future periodic reviews, the "initial MTLs" presented in this report will be updated following the Panel's recommended approach.

4.4 What are the appropriate constituents to be monitored?

Establishing MTLs is only half of the information required to determine whether a CEC needs to be included in a monitoring program. The other set of needed information is on predicted or MECs of the CEC in recycled water. CECs with concentrations that have been documented to be below MTLs would not need to be included in a monitoring program; CECs with concentrations above the MTL would be candidates to be included in or retained in a monitoring program.

Currently, baseline monitoring data exist for many CECs occurring in recycled water in California. These data can be compared to MTLs to determine whether to include them in a monitoring program. The Panel has summarized available data relevant to California in Section 5.

The Panel believes it is critical to emphasize that if measured or predicted concentrations of a CEC at the POM exceed respective MTLs, exceedences do not necessarily indicate the existence of public health risks. The MTLs and their application in the Panel's proposed framework are developed to be conservative and used only for the purpose of prioritizing CECs for monitoring. The Panel's proposed framework is not designed to develop estimates of potential risk from CECs in recycled water.

5.0 Measured Environmental Concentrations of CECs in Recycled Water in California

5.1 Introduction

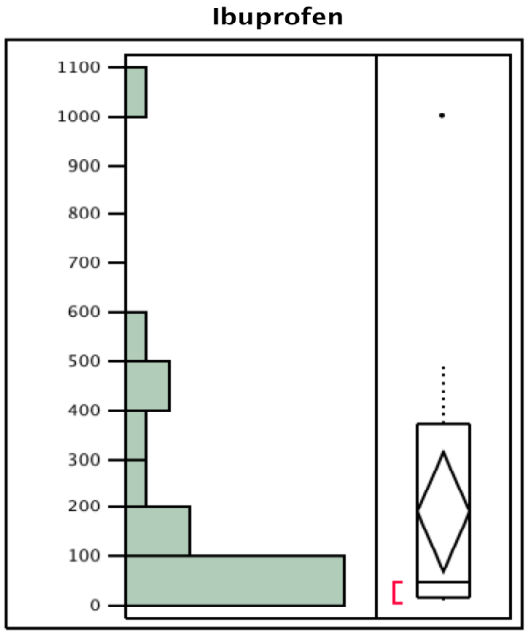
In order to compile MECs of CECs in recycled water in California, the Panel developed a survey that considered sampling locations, analytical methods used for their quantification, frequencies, and treatment processes for the water reuse practices of interest to the State Board. The survey was provided to stakeholders in California and CEC monitoring data were requested for the time period 2007 and 2009. The Panel received survey responses from water and wastewater utilities in California, the WateReuse Association of California, commercial laboratories, and research laboratories that were engaged in monitoring efforts for CECs in recycled water projects in California. The Panel screened these databases and summarized the occurrence of CECs in these reuse applications.

While the Panel acknowledged that these reuse practices engage conventional and advanced water treatment processes that result in very different water qualities, the Panel chose a conservative approach in comparing MECs to MTLs (see Section 4) for the exposure screening that was proposed to select indicator CECs for monitoring programs. This conservative measure considered a water quality that represents a secondary or tertiary treated effluent quality meeting California's Title 22 requirements for urban irrigation. These MECs were also chosen as a representative wastewater effluent quality for groundwater recharge practices using surface spreading or direct injection into a potable aquifer. The Panel acknowledged that the water quality for these groundwater recharge reuse practices both at the POM after travel through the vadose zone and the aquifer, as well as at the point of exposure, are likely to be many-fold lower. Nevertheless, the effect of additional water treatment on water quality was not considered in deriving MECs and the most conservative values were used in the prioritization. Given that no standardized methods were used to generate MEC data in the past, the Panel also recognizes that variability and false positive/negative issues likely confound the MECs considered for the development of the Panel's CEC priority list.

5.2 Occurrence of CECs in Recycled Water in California

MECs for CCL3 and non-CCL3 CECs (see Section 2) representing secondary or tertiary effluent qualities were compiled (representative of a Title 22 water quality as noted above) to represent the final MEC for the purposes of the reports analysis. The combined effluent qualities represent a conservative estimate of MECs for groundwater recharge projects since treatment credit is not including additional advanced water treatment processes, dilution in the aquifer, and/or incidental treatment in the soil-aquifer system. In addition, the combined secondary/tertiary effluent derived MEC represents a reasonable and conservative estimate for all landscape irrigation uses (restricted and non-restricted). Further, if CECs were reported as not detected, the method detection limit (MDL) was adopted as the lowest occurrence value, a conservative assumption. For each CEC various statistical parameters were determined as illustrated for ibuprofen in Figure 5.1. Distribution plots for all CECs are listed in Appendix K. For

the CCL3 and non-CCL3 CECs, the 90th percentile of each MEC was recorded. Table 5.1 summarizes the 90th percentile MECs of CCL3 CECs. The 90th percentiles of MECs for non-CCL3 CECs are summarized in Table 5.2. Of the chemicals considered by the Panel, MECs for eight CCL3 CECs were compiled. For the non-CCL3 CECs, 43 MECs were identified.



Quantiles

100.0%	maximum	1000
99.5%		1000
97.5%		1000
90.0%		500
75.0%	quartile	370
50.0%	median	50
25.0%	quartile	16
10.0%		10
2.5%		5.5
0.5%		5.5
0.0%	minimum	5.5

Moments

Mean	191.21053
Std Dev	253.12773
Std Err Mean	58.071484
Upper 95% Mean	313.21419
Lower 95% Mean	69.206866
N	19

Figure 5.1. Statistical assessment of CCL3 CECs and non-CCL3 CECs (e.g., ibuprofen).

Table 5.1. 90th percentile MECs of CCL3 CECs in recycled water.

CCL3 CECs	Occurrence in Recycled Water Secondary/Tertiary Treated (ng/L)	MTLs		MEC/MTL	
		Potable Reuse	Irrigation	Potable Reuse	Irrigation
17α-estradiol	1	3.5E+02	3.5E+03	0.00	0.00
17β-estradiol	8.4	9.0E-01	9.0E+00	9.33	0.93
Erythromycin	113	4.9E+03	4.9E+04	0.02	0.00
Estrone	73	3.5E+02	3.5E+03	0.21	0.02
Ethinyl estradiol	1	2.8E+02	2.8E+03	0.00	0.00
PFOA	28	1.1E+03	1.1E+04	0.03	0.00
PFOS	90	2.0E+02	2.0E+03	0.45	0.05
Nitrosodiethylamine (NDMA)	68	1.0E+01	1.0E+02	6.80	0.68

Table 5.2. 90th percentile MECs of non-CCL3 CECs in recycled water.

Non-CCL3 CECs	Occurrence in Recycled Water Secondary/Tertiary Treated (ng/L)	MTLs		MEC/MTL	
		Potable Reuse	Irrigation	Potable Reuse	Irrigation
4-Nonylphenol	161	500000	5000000	0.00	0.00
Atorvastatin	79	5000	50000	0.02	0.00
Diclofenac	230	1800	18000	0.13	0.01
Epitestosterone (cis-Testosterone)	10	N/A	N/A		
Ketoprofen	43	3500	35000	0.01	0.00
Metoprolol	246	25000	250000	0.01	0.00
o-hydroxy atorvastatin	10	N/A	N/A		
Propanolol	25	40000	400000		
Simvastatin hydroxyacid	25	N/A	N/A		
Sucralose	26390	N/A	N/A	0.02	0.00
Acetaminophen	550	350000	3500000	0.00	0.00
Bisphenol A	286	350000	3500000	0.00	0.00
Dilantin	217	N/A	N/A		
Tris (2-chloroethyl) phosphate (TCEP)	688	2500	25000	0.28	0.03

Table 5.2. Continued

Non-CCL3 CECs	Occurrence in Recycled Water Secondary/Tertiary Treated (ng/L)	MTLs		MEC/MTL	
		Potable Reuse	Irrigation	Potable Reuse	Irrigation
4-octylphenol	207	50000	500000	0.00	0.00
Atenolol	1780	70000	700000	0.03	0.00
Azithromycin	1200	3900	39000	0.31	0.03
Caffeine	900	350	3500	2.57	0.26
Carbamazepine	400	1000	10000	0.40	0.04
Ciprofloxacin	100	17000	170000	0.01	0.00
Clofibric acid	820	30000	300000	0.03	0.00
DEET	1520	2500	25000	0.61	0.06
Diethylstilbestrol	10	N/A	N/A		
Fluoxetine (Prozac)	31	10000	100000	0.00	0.00
Furosemide	38	N/A	N/A		
Gemfibrozil	3550	45000	450000	0.08	0.01
Ibuprofen	500	34000	340000	0.01	0.00
Iopromide	2174	750000	7500000	0.00	0.00
Meprobamate	430	260000	2600000	0.00	0.00
Methylisothio-cyanate	114	N/A	N/A		
Musk ketone	25	350000	3500000	0.00	0.00
Naproxen	851	220000	2200000	0.00	0.00
Primidone	264	N/A	N/A		
Progesterone	18	110000	1100000	0.00	0.00
Salicylic acid	110	29000	290000	0.00	0.00
Sulfamethoxazole	1400	35000	350000	0.04	0.00
TCDPP	296	1000000	10000000	0.00	0.00
TCPP	5920	N/A	N/A		
Testosterone (trans-Testosterone)	37	7000	70000	0.01	0.00
Triclocarban	223	N/A	N/A		
Triclosan	485	350	3500	1.39	0.14
Trimethoprim	112	61000	610000	0.00	0.00
Warfarin	16	2300	23000	0.01	0.00

5.3 Recommendations to Gather Additional MEC Data for CECs in California

As stated above, the MEC data considered by the Panel for CECs in California secondary and tertiary treated effluents were provided by various stakeholders in response to the occurrence survey the Panel distributed. It is important to note that the survey was unspecific regarding which CEC MECs were requested. Thus, the survey resulted in some data gaps regarding MEC data for all CCL3 CECs. For non-CCL3 CECs, MECs were reported for those CECs that were part of previously developed analytical methods and previous monitoring strategies for CECs in recycled water in California. Thus, the list of non-CCL3 CECs for which MECs were available does not represent the entire spectrum of non-CCL3 CECs potentially present in recycled water or the most important CECs based on production volume, use practice, or physicochemical properties suggesting a high likelihood of occurrence in recycled water.

In order to fill data gaps for CECs with limited or no information on MECs in California, the Panel suggests that the State conduct a more thorough review of CECs likely to occur in recycled water using MEC and PEC data from peer-reviewed literature and occurrence studies outside California. Those CECs that exhibit MEC/MTL ratios above "1" could be placed on a secondary monitoring list of CECs with low frequency of occurrence to confirm either presence or absence of these CECs in recycled water in California. In addition, this secondary monitoring list could be populated by CCL3 CECs that exhibit a relatively low MTL (less than 500 ng/L) based on the Panel's summary of available drinking water benchmarks. Table 5.3 lists CCL3 CECs with no MEC information for California and with initial MTLs of less than 500 ng/L. The Panel conducted a cursory review of production data and physicochemical properties and suggested a few CCL3 CECs that could be targeted through a secondary monitoring program to confirm their presence or absence in recycled water. Results of these efforts, along with the monitoring data collected as part of the Panel's recommended program, can provide the basis for revising the proposed initial monitoring list during the next, and each, triennial review.

Table 5.3. CCL3 CECs with MTLs of less than 500 ng/L and no MECs in Recycled Water in California. 90th percentile MECs in recycled water were not available for these CECs.

CCL3 CECs	MTLs Potable Reuse (ng/L)	Note	Recommend Gathering MEC Information	Available Analytical Method
1,2,3-Trichloropropane	5.0E+00	On Cal UCMR	Yes	Yes
1,3-Butadiene	1.0E+01	High production volume industrial chemical; rapid volatility from water; log Kow 1.99; main uptake via lungs in humans	No	No
3-Hydroxycarbofuran	4.2E+02	Pesticide; low likelihood to occur in recycled water at elevated concentrations	No	No
4,4'-Methylenedianiline	2.2E+01	Industrial chemical; only slightly soluble in water; low likelihood to occur in recycled water at elevated concentrations	No	No

Table 5.3. Continued

CCL3 CECs	MTLs Potable Reuse (ng/L)	Note	Recommend Gathering MEC Information	Available Analytical Method
Acetamide	5.0E+02	Industrial chemical; well water soluble; low likelihood to occur in recycled water at elevated concentrations	No	No
Alachlor OA	4.0E+02	Herbicide; low likelihood to occur in recycled water at elevated concentrations	No	No
Alpha.-Hexachlorocyclohexane	6.0E+00	Pesticide; log Kow 3.78; low likelihood to occur in recycled water at elevated concentrations	No	No
Benzyl chloride	2.0E+02	Not stable in activated sludge/wastewater	No	No
Cumene hydroperoxide	7.6E+01	very unstable in the environment; unlikely to persist during water reclamation	No	No
Dicrotophos	4.9E+02	Insecticide; low likelihood to occur in recycled water at elevated concentrations	No	No
Equilenin	3.5E+02	Steroid replacement drug; low likelihood to occur in recycled water at elevated concentrations	No	No
Equilin	3.5E+02	Steroid replacement drug; low likelihood to occur in recycled water at elevated concentrations	No	No
Estriol	3.5E+02	Steroid; occurrence in recycled water usually less than 5 ng/L	No	No
Ethylene oxide	1.1E+02	intermediate industrial chemical; unstable in the environment; low likelihood to occur in recycled water at elevated concentrations	No	No
Hydrazine	1.0E+01	Industrial chemical	Yes	Yes
Mestranol	2.8E+02	Synthetic estrogen; low likelihood to occur in recycled water at elevated concentrations	No	No
Nitroglycerin	2.9E+02	Industrial chemical; low likelihood to occur in recycled water at elevated concentrations	No	No
N-nitrosopyrrolidine (NPYR)	2.0E+01	Low likelihood to occur in recycled water at elevated concentrations	No	No
Norethindrone	4.0E+01	Contraceptive drug; low likelihood to occur in recycled water at elevated concentrations	No	No
o-Toluidine	1.9E+02	Herbicide; low likelihood to occur in recycled water at elevated concentrations	No	No
Oxirane, methyl-	2.3E+02	Industrial chemical; low likelihood to occur in recycled water at elevated concentrations	No	No
Oxydemeton-methyl	9.1E+02	Insecticide; low likelihood to occur in recycled water at elevated concentrations	No	No

Table 5.3. Continued

CCL3 CECs	MTLs Potable Reuse (ng/L)	Note	Recommend Gathering MEC Information	Available Analytical Method
Oxyfluorfen	4.8E+02	Herbicide; low likelihood to occur in recycled water at elevated concentrations	No	No
Profenofos	3.5E+02	Pesticide; low likelihood to occur in recycled water at elevated concentrations	No	No
Quinoline	1.0E+01	Industrial chemical	Yes	Yes
RDX (Hexahydro-1,3,5-trinitro-1,3,5-triazine)	3.0E+02	Explosive residue; low likelihood to occur in recycled water at elevated concentrations	No	No
Terbufos	3.5E+02	Pesticide; low likelihood to occur in recycled water at elevated concentrations	No	No
Terbufos sulfone	3.5E+02	Pesticide; low likelihood to occur in recycled water at elevated concentrations	No	No
Triphenyltin hydroxide (TPTH)	1.9E+00	Pesticide; low likelihood to occur in recycled water at elevated concentrations	No	No

6.0 Screening Unknown CECs in Recycled Water to Assess Exposure

6.1 Introduction

For unknown CECs (e.g., CECs that may be unknowingly released into the environment and for which there are currently no known methods for their quantification), biological monitoring or chemical screening methods could be used to quantify effects/equivalents or identify unknown chemicals and thus may offer an additional safeguard for human health (Figure 6.1). The main advantage of bioassays is that they are able to detect the presence of chemicals based on their bioactivity rather than on their detection by analytical chemistry. For this to work, however, robust, reproducible and high throughput assays need to be developed. This is one of the primary ways to evaluate the occurrence of unknown/unknown CECs. It is imperative to specify the endpoint of concern in this process. Several examples are discussed in Appendix L. The USEPA has focused on compounds that interfere with estrogen, androgen and thyroid hormone responses. Other potential candidate endpoints of concern include genotoxicity and steroidogenesis.

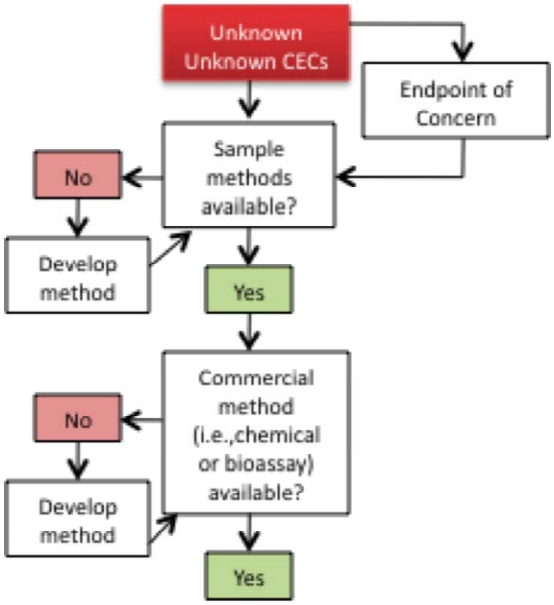


Figure 6.1. Screening approach for unknown unknown CECs in recycled water.

Advances in qualitative determination of unknown chemicals (i.e., chemical screening with high resolution mass spectroscopy) can be linked with biological effects to help identify agents, which can subsequently be evaluated for exposure or effects (see Figure 6.1). For biological monitoring there are both *in vivo* and *in vitro* assays that have been developed. Their use in the regulatory context was the topic of a debate sponsored by the Society of Toxicology in 2008 (Hartung & Daston, 2009). There are advantages and disadvantages to each of these monitoring systems, and possibly a mixture of both *in vivo* and *in vitro* testing systems will be necessary. A distinct advantage of *in vivo* tests is that the chemical exposure is to the whole animal where all the tissues and toxicity pathways are equally exposed; however, the apical end points that are normally measured including survival, reproduction and growth, are not specific to a mechanism of action (Snyder *et al*. 2008b). However, research has demonstrated that sometimes extreme differences within and among species confound the use of *in vivo* assays especially for prediction of human health (i.e., strain differences in mice and rats seen during the Endocrine Disruptors Screening Program (EDSP)). *In vitro* tests, on the other hand, are very specific for a mechanism of action, but are artificial and non-physiological representations of what may be happening *in vivo*. Novel methods in genomics and proteomics show great promise to bridge the advantages of both the *in vivo* and *in vitro* methods, by allowing the

exposures to occur *in vivo* but analyzing the effects to provide mechanistic information through systems toxicology approaches. The genomics and proteomics methods promise to be sensitive and accurate in determining the presence of possible hazards to human health in drinking water and conversely of clearly showing no observable toxicity. Genomic methods are still being developed in research laboratories and are not currently used for regulatory applications. However, USEPA has proposed that these methods will eventually be utilized to "fingerprint" biological responses (adverse outcome pathways) (Bennett *et al.*, 2010), which will be employed in risk assessment paradigms in the future.

An added benefit of bioassays is they can be used to measure synergistic, additive, and antagonistic interactions between compounds that may be present in a mixture. Toxicity evaluations based on single-chemical analyses will generally miss the synergistic, additive, or antagonistic potential found in mixtures, thus providing a false sense of security or false indication of a potential risk.

6.2 Bioanalytical Screening Tools

Bioanalytical screens can be used to develop integrated approaches that a capable of targeting a wide spectrum of CECs, and when calibrated, may also provide some indication of adverse effect. While analytical chemistry requires the availability of standards and known compounds, bioanalytical methods include the ability to integrate unknown compounds and mixture interactions within an environmental matrix. In addition, with recent movement by regulatory agencies toward a mode of action approach in risk assessment paradigms, several bioassays have recently been developed for the screening of compounds for specific biological target activities such as dioxin-like activity (e.g., toxic equivalents (TEQ)) (Van den-Berg *et al*., 1998), endocrine responses (i.e., estrogen, androgen, thyroid), and genotoxicity.

After nearly 10 years of scientific evaluation, the USEPA has recently announced the EDSP Tier I bioassays recommended by the Endocrine Disruptors Screening and Testing Advisory Committee (EDSTAC) (USEPA, 2009b). Many of these methods are now commercially available and have adequate quality assurance guidelines (Table 6.1). In the case of chemicals that behave as hormone mimics (e.g., estrogen, androgen, thyroid hormones), these bioassays could play a role as an initial screening tool for CECs, which could then direct specific analytical chemistry measurements. For example, if a water sample failed to demonstrate estrogenic activity in one of the assays described below, the measurement of difficult analytes by analytical methods may not be necessary. Thus, exposure could be described in terms of equivalent mass of estradiol (EEQ) per unit volume using a derived EEQ value (e.g., ng/L). Although a high degree of correlation exists between chemically derived EEQ and bioassay derived EEQ (Figure 6.2), false negatives may be present in a small percentage of samples that possess antagonistic activity, particularly in the yeast estrogen screening (YES) assay. Consequently, it may be prudent to use more than one bioassay (MCF-7; ER-CALUX) to confirm negative results.

Table 6.1. Commercially available EDSP Tier I Bioassays with adequate quality assurance guidelines (http://www.epa.gov/scipoly/oscpendo/pubs/assayvalidation/tier1battery.htm#assays).

Test Environment	Endpoint	Assay
In vitro	Estrogen receptor (ER) binding	Rat uterine cytosol
	Estrogen receptor (hERα) transcriptional activation	Human cell line (HeLA-9903)
	Androgen receptor (AR) binding	Rat prostate cytosol
	Steriodogenesis	Human cell line (H295R)
	Aromatase	Human recombinant microsomes
In vivo		Uterotrophic (rat)
		Pubertal female (rat)
		Pubertal male (rat)
		Amphibian metamorphosis (frog)
		Fish short-term reproduction

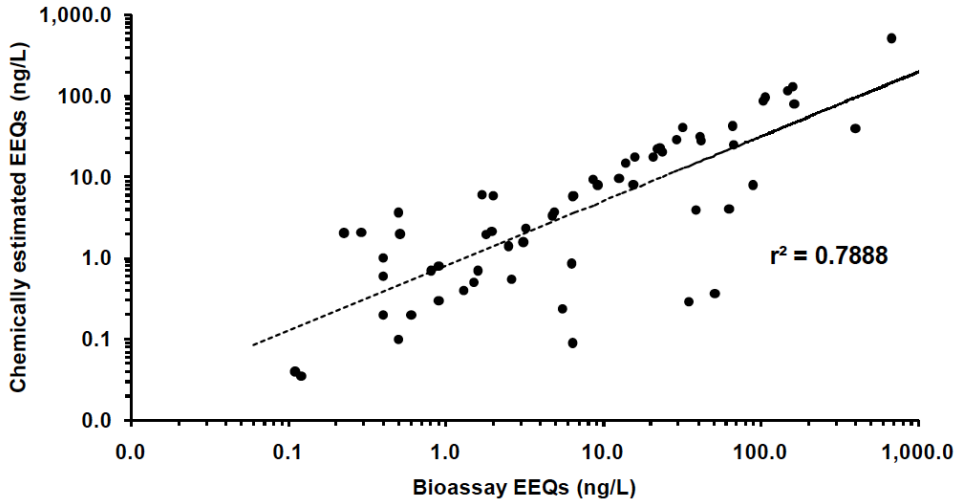


Figure 6.2. Correlation between chemically estimated EEQs and bioassay EEQs (Bulloch *et al*., in press).

6.3 Strengths and Weaknesses of Bioassays

6.3.1 Strengths

Bioassays that measure binding equivalency (i.e., EEQ, TEQ) are very powerful because they can be used to determine the bioactivity of a water extract on specific biological endpoints and, thus provide information on unknown/unknown CECs. Seldom are chemicals present alone and rarely can all be measured. For example, an extract that contains low levels of 17α-ethinyl estradiol EE2 (< 1 ng/L), which by itself may be below the threshold for biological or toxic responses, and also other estrogenic chemicals that act via the same soluble sex steroid receptors, can increase the activity above the threshold (Brian *et al*., 2007). For maximum protection of human health, one needs to group chemicals by their modes of action and test them in bioassays that have been calibrated to mammalian toxicity *in vivo* and clearly distinguish biological effects attributed to potential mixtures. This is especially true if it is possible that unknown chemicals are present in the treated water.

Bioassays can be very useful to evaluate active constituents of unknown chemical structure in TIE methods. For this to be practical, high throughput *in vitro* assays should be used to reduce the amount of time required for TIE procedures. Some of the assays mentioned above can be done in a matter of hours.

Another important aspect of bioassays is that they can be used in mode of action assessments of individual chemicals and in cell-based assays to help distinguish agonist from antagonist activities. Some cell types also allow metabolism to occur within the test, thus including health assessment tests for potent metabolites of chemicals, which may on their own be much less toxic. Several *in vitro* bioassays have undergone round robin testing including those for estrogenic activity, steroidogenic impacts, and genotoxicity. The USEPA and the National Institute of Environmental Health Sciences/National Toxicology Program (NIEHS/NTP) are using these assays in screening tiers for testing purposes.

6.3.2 Weaknesses

While strengths include exposure assessment for unknown/unknown CECs, the primary weakness of using bioassays is the uncertainty surrounding the potential for quantifying adverse effects in humans associated with a positive response. Few of these bioassays have been calibrated to higher order effects (i.e., adverse effects in humans). There is a possibility of false positives especially for low concentrations of chemicals (i.e., *in vitro* the chemicals signal activity but *in vivo* they fail to do so, or vice versa). The most likely explanation for these inconsistencies is metabolism and whole organism integrated responses compared to specific bioassay response. In addition, extraction procedures have not been evaluated in round-robin intercalibration studies. For the most part, the *in vitro* assays rely on chemical extraction of the contaminants from the water column, without knowing if the extraction methods reliably obtain the chemical contaminant or not. For example, perchlorate would have been missed by these assays. And, there is uncertainty as to the proper volumes of water to extract to get an *in vitro* response and how these concentrations can be extrapolated to human health.

Few commercial testing companies currently have the equipment and trained staff to perform bioassays creating a significant need for training. But, this should not stop the process. It is likely that suppliers of the biological test systems and kits (such as Invitrogen) would provide courses for personnel in testing companies to teach them how to run the assays under GLP conditions. Alternatively, continuing education courses associated with the Society of Toxicology (SOT) or Society of Environmental Toxicology and Chemistry (SETAC) could provide this service. As with medical tests for human disease, commercial companies can hire medical technicians that are adequately trained to run the tests.

Another short-term problem with bioassays is that many, particularly *in vivo* and microarray assays, still need to be vetted in round-robin studies to determine the limits of the methodology, the variability of response and the robustness and sensitivities of the assays. In addition, special emphasis should be placed on extraction procedures since most round robin tests were carried out on a common extract. This level of quality assurance/quality control (QA/QC) validation will require resources in parallel with other tests that are ongoing. While in the short run these additional resources will cost more than just performing chemical analyses, in the long run, the bioassays may help reduce the overall costs of monitoring reuse projects. In this scenario, the bioassays could indicate which analytical methods one must employ to identify the chemicals of greatest concern.

Thus, bioassay methods hold great promise for monitoring the safety of recycled water. However, in the Panel's view several steps of the process still need to be developed. These include:

- Development of bioassay methods that measure the critical human health endpoints/mechanisms of action. Currently, bioassays measuring estrogenic effects appear closest to being ready. These should be implemented as soon as possible to begin evaluating the efficacy of bioassays in CEC monitoring;
- Developing a trigger level for bioassay response linked to effects in humans. Again, given that human health ADIs exist of estrogen exposure and can be expressed on an estrogen-equivalent basis, suggests that at least for bioassays the measure estrogen response, relatively rapid development of human health-based trigger levels may be be possible. For full application of bioassay-based screening, such trigger levels would be needed for all key human health endpoints; and
- Developing a response to the exceedance of a trigger level. The Panel believes such a response can take one of two forms. One response could be to conduct a TIE to identify the compound(s) responsible for the exceedance of the trigger. That compound(s) could then be included in the CEC monitoring program. Given that monitoring safety of water supplies still relies on compound-by-compound evaluations, this is the most likely near-term response. An alternate response would be developing an understanding of how the measured biologic activity in water leaving a treatment plant is linked to treatment methods within the treatment plant. Such an understanding might lead to the reduction in biologic activity of an effluent through modifications in treatment methods, without the need to conduct chemical-specific measurements.

The Panel believes full implementation of bioassay screening methods is still several years away and, thus, the Panel is not recommending the adoption of such methods at this time. However, the Panel does recommend that development of such methods be given high priority and that the State should charge the next independent advisory panel with developing a pilot program that documents the efficacy of bioassays as monitoring tools, assuming bioassay methods are commercially available, and compares their predictions to those of a chemical-by-chemical monitoring program.

6.4 Quantifying Unknown Known CECs in Recycled Water

Many of the compounds used in commerce, or that are known or suspected of being excreted by humans, occur at concentrations too low to be detected by currently available analytical methods. Such compounds can be included in the CEC screening process recommended by the Panel, if PECs can be developed (Figure 6.3). The Panel believes developing a process that allows for estimating the possible concentration of CECs in recycled water is key to determining whether compounds for which MECs are not available or for which available analytical detection limits are well above the MTL, have the potential to pose a human health risk. In concept, a process to develop screening level predicted concentrations of CECs in recycled water is fairly simple. One simply needs to know how much of the compound is used each year in a household or per capita, make an assumption about how much water a person or household uses every day, estimate the amount entering a treatment plant, decide how many possible loss mechanisms during the use, transport and treatment process one wants to account for, and then predict a concentration in recycled water. Hannah *et al*. (2009) describe such a process to develop PECs for ethinyl estradiol in US surface waters.

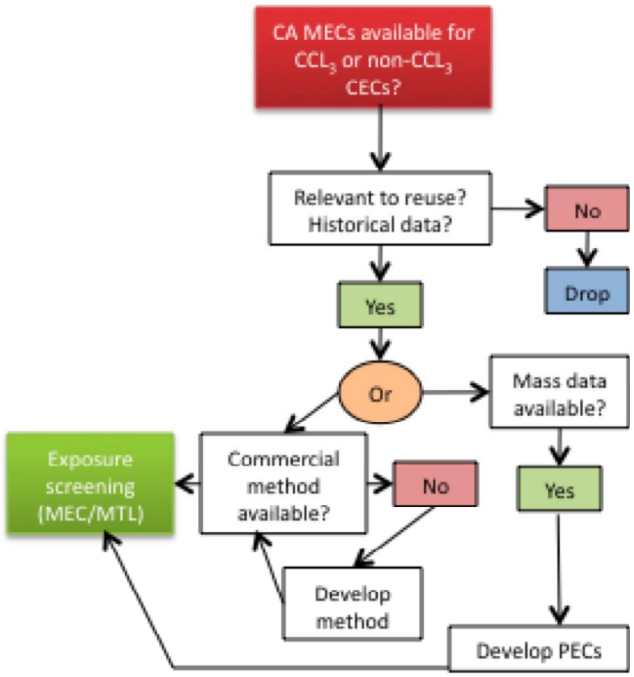


Figure 6.3. Estimating PECs for unknown known CECs.

The greatest challenge to implementing a production- or use-based model to predict concentrations of known unknowns in recycled water is developing an estimate of the mass of a compound used and released into the waste water system. Such data are available; for most compounds they just may not have been compiled in a readily accessible location. If the compound in question is in commerce, the amount sold every year should be available from manufacturers who know how much of compound they sell. If the compound in question is a

metabolite, information on its excretion may be available in the scientific literature or could be estimated based upon intake and information about metabolism.

The value of developing a simple model to predict concentrations of compounds in reused water is that comparisons to MTLs can be conducted even for compounds that do not yet have analytical methods. The availability of such a production-based screening system would allow for the screening of far more compounds than we currently have analytical methods for. Results of such a screening analysis could then be used to prioritize the development of analytical methods for CECs. The Panel recommends that the State charge the next independent advisory panel with evaluating a production volume-based system to prioritize known unknown CECs for a monitoring program.

7.0 Prerequisites for Monitoring CECs in Recycled Water

7.1 Background and Analytical Components for Monitoring CECs in Recycled Water

Although the term "emerging contaminants" has often been applied to chemicals that have been recently detected in the environment, the analysis of EDCs and PPCPs has been ongoing for decades. Despite several early reports of EDCs and pharmaceuticals in the environment, they received little attention until researchers in the United Kingdom and United States linked the occurrence of trace steroids to biological activity in fish and cellular bioassays (Desbrow *et al*., 1998; Routledge *et al*., 1998; Snyder *et al*., 2001) and the oft-cited study published in 2002 by the US Geological Survey (Kolpin *et al*., 2002), titled "*Pharmaceuticals, hormones, and other organic waste contaminants in US streams, 1999-2000: a national reconnaissance*". This latter manuscript reported summed steroid hormone concentrations as high as several µg/L and maximum EE2 and 19-norethisterone concentrations of 831 and 872 ng/L, respectively (Kolpin *et al*., 2002).

These developments, along with advances in analytical instrumentation, have led to a rapid increase in the number of analytical techniques used to study steroid hormones and other exogenous agents such as PPCPs in water. Analytical techniques have increased the sensitivity and accuracy of CEC analysis, allowing ultra-trace levels of a wide variety of contaminants to be identified and quantified in, for instance, US drinking water (Benotti *et al*., 2009; Quinones & Snyder, 2009).

Because CECs represent an extremely broad spectrum of compounds, developing a single all-encompassing technique for their analysis is highly unlikely. These chemicals vary widely in their physico-chemical properties (e.g., polarity, molecular weight, pKa, water solubility, etc.) making analysis by traditional analytical techniques difficult. Additionally, the concentration of many CECs in the environment can be quite low, typically sub-µg/L, which further increases the complexity of analysis by necessitating extraction and concentration steps. In general; however, a plan for the analysis of target CECs encompasses similar primary steps, including: sample collection/preservation, analysis, and quantification.

7.2 Sample Collection/Preservation

7.2.1 Sample Collection

Due to the common use of pharmaceuticals, the ubiquitous nature of personal care products, and the common occurrence of nearly ubiquitous commercial products containing flame retardants, plasticizers, and other industrial chemicals, great care must be taken to avoid contamination of samples by samplers, sampling equipment and laboratory personnel. Communication between the laboratory and those collecting samples regarding the list of target compounds is important to help prevent contamination by identifying and eliminating possible undesired sources of target analytes. In general, nitrile gloves should be worn at all times during the collection and handling of samples to prevent contamination with personal care products applied directly to the skin (such as triclosan, DEET, and various sunscreen

agents). Similarly, smoking and handling or ingesting pharmaceuticals or caffeinated beverages should be avoided shortly before and during sampling programs designed to detect trace levels of PPCPs. To monitor background levels of the target CECs, travel blanks should always be included.

It is generally recommended to collect samples in amber, glass bottles to prevent analyte loss due to photodegradation, contamination with various plasticizers, and adsorption to the walls of plastic sampling bottles (Vanderford *et al*., 2006). Special attention must be given to compounds such as fluorochemicals, which are known to be present in Teflon lined bottle caps and which can bind strongly to glass (Quinones & Snyder, 2009). Sample bottles should also be cleaned thoroughly with applicable solvents (e.g., water, methanol, acetone, dichloromethane, hexane) to ensure the cleanliness of the bottles prior to sampling. Furthermore, sampling equipment should be composed of materials such as stainless steel that will not leach target CECs and should be cleaned with solvent between sample locations to prevent cross contamination.

7.2.2 Preservation

At the time of collection, samples are generally preserved to reduce microbial degradation, hydrolysis, and adsorption of the target analytes. This is typically accomplished through lowered temperature and/or chemical preservatives. However, it must be noted that preservative selection depends greatly on the CECs selected for analysis. For example, some CECs may have an adverse reaction with a chemical preservative; therefore, it is advisable to test the target analytes with the selected preservative in a controlled experiment before using it in the field.

After samples are collected, they should be cooled to prevent analyte degradation. This usually involves placing the sample in a cooler with ice while other samples are taken and when they are transported back to the laboratory. If samples are to be transported over long distances, it is recommended that blue ice be used to maintain sample temperature during shipment. Once samples have been received by the laboratory, they may then be stored at 4°C or less until analysis. It is strongly advised to conduct holding studies using the matrices of interest to verify the maximum holding time without degradation.

Chemical preservatives are often used to prevent analyte degradation. Several have been commonly used including reducing the sample pH to 2 or below using either sulfuric (Vanderford *et al*., 2003) or hydrochloric acid (Hernando *et al*., 2006), adding formaldehyde to a final concentration between 1 – 4 percent (Baronti *et al*., 2000; Ferguson *et al*., 2001), or adding sodium azide to a final concentration of 1 g/L (Vanderford & Snyder, 2006). As stated above, care must be taken to ensure the preservative of choice does not interfere with the target analytes. For example, formaldehyde has been extensively used to preserve samples for steroid analysis; however, Vanderford *et al*. (2003) reported that using formaldehyde for the preservation of pharmaceuticals resulted in significant changes in their concentrations over time.

Although sample preservatives can reduce the amount of degradation that occurs before the samples are extracted and/or analyzed, it is recommended that samples be extracted as soon as possible after they are received. Long storage times can result in sample adsorption to both the bottle and suspended/dissolved organic matter in the sample. Typical holding times range from 24 to 7 days (Hernando *et al*., 2006; Miao & Metcalfe, 2003; Moldovan, 2006; Vieno *et al*., 2006).

7.2.3 Residual Oxidant Quenching

When collecting and analyzing samples from drinking water-treatment or potable reuse facilities, it is important to know whether residual oxidants, such as free chlorine, may be present. If the residual oxidants are not quenched, target analytes will continue to be exposed to chlorine until the samples are extracted. Analytes that are susceptible to oxidation will be further degraded due to this increase in contact time, leading to misinterpretation of analyte concentrations present at the time of sampling. Therefore, residual oxidants must be quenched using suitable chemical agents.

Commonly used quenching agents include sodium thiosulfate (Acero *et al*., 2005), sodium sulfite (Ho *et al*., 2006), ammonium chloride (Pepich *et al*., 2004), and ascorbic acid (Ye *et al*., 2007). However, researchers have found that some quenching agents react adversely with various target analytes (Trenholm *et al*., 2006; Ye *et al*., 2007). Therefore, it is essential that, like the preservation agents, tests are performed to ensure the selected quenching agent does not interfere with the target analytes. Furthermore, adverse reactions between preservatives and quenching agents should be explored, especially with regard to safety.

7.3 Instrumental Analysis

The combination of techniques of chromatographic separation and detection is the standard for detection of environmental contaminants. The two most powerful and most widely used combined techniques are gas chromatography-mass spectrometry (GC-MS) and liquid chromatography-mass spectrometry (LC-MS) due to their robustness, sensitivity and selectivity.

7.3.1 GC-MS

Because MS separates and detects an analyte based on mass to charge ratio (m/z), the compound must be charged (ionized) before it enters the MS. In GC-MS, there are two common ionization techniques: electron ionization (EI) and chemical ionization (CI). In EI, the GC column eluent is directed through a beam of electrons created by a filament that produces electrons having an energy of 70 eV. The electron interacts with analyte molecules in the gas phase, resulting in the loss or gain of an electron by the analyte creating a positively or negatively charged molecule, respectively. This type of ionization results in molecular fragmentation, which is related to the structural properties of the compound. Thus, each compound has a unique MS “fingerprint” that allows for the identification of the compound based on its fragmentation pattern. However, because the analyte is fragmented before it reaches the

detector, a loss in sensitivity results. In CI, a gas (typically methane or ammonia) is first ionized and then interacts with the analyte, resulting in the gain (positive ionization) or loss (negative ionization) of a proton. CI is considered a "soft" ionization process because it generally results in less fragmentation than EI, resulting in the potential for increased sensitivity. In contrast, CI often provides less structural information.

7.3.2 LC-MS

Unlike GC-MS, the separation of analytes in LC-MS occurs in the liquid phase. Thus, analytes reach the MS as dissolved solutes in the liquid phase rather than in the gaseous phase. Ionization of the target analyte in LC-MS also differs from GC-MS in that there are three common ionization techniques: electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI), and atmospheric pressure photoionization (APPI). By far the most utilized form of LC-MS ionization, ESI produces a fine mist of charged droplets containing the analyte of interest. Droplets are reduced in size until the charged analyte escapes the droplet (ion desorption) or the solvent has evaporated to leave the charged analyte in the gas phase. This process can form positive and negative ions based on the polarity of applied voltages. The terms ESI+ and ESI- refer the polarity of ionization imparted to the fragment ion. In APCI, the eluent from the LC column is nebulized and heated to completely vaporize the solvent and target analytes. The evaporated solvent then becomes a reagent gas which is then ionized and whose charge is then transferred to the target analyte, creating charged ions for detection by MS. APPI is similar to APCI, except a photon-emitting krypton lamp is used to directly ionize the target analyte. APCI and APPI are generally only used for compounds found to be less amenable to ionization by ESI.

7.3.3 GC-MS vs. LC-MS

In general, GC-MS is more amenable to volatile, thermally stable, less polar compounds. Therefore, it has been the method of choice in the past for legacy pollutants such as polychlorinated biphenyls (PCBs), polycylic aromatic hydrocarbons (PAHs), and dichlorodiphenyltrichloroethane (DDT). However, newly discovered contaminants, such as PPCPs, are often polar and non-volatile. This has, in part, led to the surge of popularity for the use of LC-MS to monitor emerging contaminants. For many of these compounds to be monitored by GC-MS, they need to be derivatized prior to analysis. This process can be painstaking, labor-intensive and ineffective. On the other hand, LC-MS has the ability to analyze a wide variety of compounds without the need for derivatization.

However, the ESI process that is most frequently used during LC-MS analysis can be susceptible to matrix effects. During the ionization process, non-target analytes at a greater concentration and/or that have a higher affinity for becoming charged will exhaust the available charge and leave target analytes uncharged. If uncorrected, matrix effects may result in improper data interpretation because the effects can vary substantially between matrices and lead to the reporting of artificially low concentrations. Researchers have tried to minimize matrix effects using various extraction, cleanup, and elution techniques (Kloepfer *et al*., 2005; Quintana *et al*., 2004; Reemtsma, 2003) or compensate for them using different calibration

techniques (Ferguson *et al*., 2000; Lindsey *et al*., 2001). However, most calibration techniques become problematic when applied to the simultaneous analysis of a broad range of compounds that encompass many different classes and structures in matrices having varying degrees of suppression and enhancement (Vanderford & Snyder, 2006).

7.3.4 Isotope Dilution LC-MS

Perhaps the most promising method to date is the use of isotope dilution to correct for matrix effects. In this method, isotopically-labeled versions of each analyte are added to all samples prior to solid phase extraction (SPE). Results obtained for unlabeled target analytes are corrected for matrix effects based on the recovery of the labeled version. This method has shown promise when applied to the analysis of a varied group of PPCPs, pesticides and EDCs (Vanderford & Snyder, 2006).

7.3.5 Quality Assurance/Quality Control Measures

A comprehensive, performance-based QA/QC approach for CECs such as EDCs and pharmaceuticals is critical in generating high quality data for decision making purposes. Because CEC concentrations are often less than 100 ng/L, extensive care must be taken to prevent accidental contamination by sampling and laboratory personnel (see Section 7.2 of this report). In a report following their national reconnaissance of US streams, the US Geological Survey reported a significant number of episodes of blank contamination (Barnes *et al.*, 2002), suggesting that even the most experienced laboratories encounter blank-related issues. Thus, blanks should be an integral portion of every sampling event and analytical batch to ensure that reported concentrations are present in the environment and, if contamination is suspected, to help determine a source of contamination. Frequent travel, field, and laboratory reagent blanks, as well as instrument blanks, are recommended.

The laboratory fortified blank, used to evaluate the performance of the total analytical system, including all preparation and analysis steps, is highly recommended for CEC analysis. Results of the laboratory fortified blank are compared to established criteria and, if found to be outside these criteria, indicate that the analytical system is not performing correctly and may not be producing acceptable results. Fortified blanks are typically prepared using a standard spike from a different source/batch from the one used to calibrate the instrument. To account for matrix effects, matrix spikes are also recommended to monitor the accuracy and quantitative recovery of target analytes. In this manner, deficiencies in the method can be revealed and corrected by techniques such as isotope dilution (Vanderford & Snyder, 2006). Duplicate matrix spikes are also recommended to provide an indication of precision.

7.3.6 Method Detection Limits

The limits of detection and quantification define the lowest levels at which an instrument can differentiate between a signal and noise and the lowest level at which a value may be reported, respectively. The determination of these values is especially important for the analysis of CECs, as many of these compounds occur at trace levels (sub-µg/L). Formal detection

and reporting limit studies are highly recommended (Glaser *et al.*, 1981; USEPA, 1984; Martin *et al.*, 2007; Winslow *et al.*, 2006). In addition, every effort should be made to determine and verify the reporting limit in the matrices to be analyzed. This should include analyzing sample matrices fortified at or slightly above the determined reporting limit of the method to detect the presence of potential interferences that may lead to false negative or positive results. Furthermore, reporting limits should be re-evaluated frequently as sample matrices change or instrumental performance varies.

7.4 Requirements for CEC Monitoring

Public water systems are responsible for complying with all regulations, including monitoring, reporting, performing treatment techniques, record keeping, and public notice requirements. States, in turn, keep the data for public water systems in the state data files. States report violations of MCLs, as well as monitoring violations, to the USEPA.

Compliance is based on a number of factors and depends on the individual contaminant. These factors are summarized in Appendix M using atrazine as an example.

7.5 Monitoring for CECs using Commercially Available Methods

Approved analytical methods must be used when analyzing water samples to meet federal monitoring requirements or to demonstrate compliance with drinking water regulations. Approved methods are listed in the Code of Federal Regulations after publication in a final rule or as part of an expedited approval. They are developed by the USEPA, other government agencies, universities, consensus methods organizations, water laboratories, and instrument manufacturers. Laboratories that analyze compliance samples must be certified by the USEPA or each individual state, although recently there has been movement to nationalize accreditation through the creation of the National Environmental Laboratory Accreditation Conference Institute (TNI). TNI is an organization that 1) develops and adopts for use into its programs consensus standards for accreditation of environmental testing laboratories and other organizations directly involved in the environmental measurement process; 2) implements a national program for the accreditation of environmental laboratories; 3) develops and maintains a national proficiency test program; 4) develops and maintains a national database of accredited laboratories; and 5) provides training and technical support to facilitate the implementation of a national accreditation program by accreditors (e.g., state agencies) and those entities pursuing accreditation (e.g., environmental laboratories). To ensure the quality of the data, methods approved by the USEPA demand rigorous QA/QC measures. These guidelines can be found in Appendix M.

7.5.1 Availability of Commercial Laboratories for CEC Analyses

During the course of this study, the Panel contacted five commercial laboratories in order to evaluate the commercial availability of CEC analyses. From the data received, it was obvious that there was relatively little consistency in compounds and method reporting limits among the laboratories surveyed. The Panel strongly recommends that once the initial priority list of

CECs is implemented by the State, commercial laboratories again be surveyed for capability of analysis of the initial CEC list. Additionally, it is recommended that the State conduct an initial performance evaluation of all laboratories, who respond by providing a series of blinded samples of recycled waters from the state, both unspiked and spiked with target CECs. Moreover, the initial performance testing should include randomized blanks and several replicate samples. From these data, the State will better be able to gauge the robustness of analytical methods available for indicator CECs.

A currently ongoing study sponsored by the Water Research Foundation (WRF #4167) lead by the Southern Nevada Water Authority is evaluating several commercial and academic laboratories with respect to analysis of a specific group of pharmaceuticals and suspected endocrine disrupting compounds. Data collected thus far for spiked laboratory purified water has shown that variability is both laboratory and compound specific. Moreover, the rate of false positives (blank contamination) and false negatives (spiked but not detected) also was related to both laboratory performance and MDLs, as well as being compound dependent.

The Panel also recognizes that variability and false positive/negative issues likely confound the MECs considered for the development of their CEC priority list (see Section 5). However, a detailed evaluation of the performance standards utilized by laboratories reporting measured CECs in California was beyond the scope of this project. It was obvious that some compounds in this dataset were more variable than others. In summary, the Panel believes that laboratory validation studies are of the utmost importance should the exposure screening approach proposed by this Panel be adopted by the State.

7.6 Selection/Establishment of Appropriate Method Reporting Limits

The Panel recognizes that monitoring at the lowest possible analytical detection limit is often not productive and often leads to erroneous data. Analytical variability and influence of false positive/negative results becomes a more significant issue at minute levels. This Panel recommends that for health-based values, or MTLs, a MRL of 10x lower than MTL be utilized (Table 7.1). However, in many cases, a 10x lower MDL may not be achievable using currently available methodologies. For instance, the MTL of NDMA is 1 ng/L, which would result in a suggested MRL of 0.1 ng/L, far below commonly employed analytical methods for NDMA. In these cases, the Panel suggests the use of the MRL that is closest to the MRL-goal and has proven reliability. For CEC performance indicators, the Panel recommends MRLs that are of sufficient sensitivity to monitor attenuation yet provide robust analytical results. Therefore, the Panel has collected recommended approximate MRLs for performance indicators, yet suggests that these values are not prescriptive and should be based on method performance measurements. The Panel stresses that accurate and precise QA/QC is vital in all monitoring programs. The Panel strongly recommends the inclusion of field blanks, laboratory blanks, replicate samples, and matrix spikes within each sampling event. The Panel also advises that the samples be sent to the analytical laboratories as anonymous randomized samples, that is, samples should not indicate the source and should provide information that allows them to be identified as blanks or matrix spikes. A monitoring program truly is only as good as the

reliability of the data collected. Therefore, it is vital that a robust QA/QC program be utilized at all stages of the monitoring program.

Table 7.1. Recommended MRLs for health and performance based indicator CECs.

Compound	Health-based MRL (ng/L)	Health-based $MRL_{practical}$ (ng/L)	Performance indicator MRL (ng/L)
17beta-estradiol	0.09	1	1
NDMA	0.1	2	2
Caffeine	35	50	50
Triclosan	50	50	50
Sucralose	N/A	N/A	100
Iopromide	N/A	N/A	50
DEET	N/A	N/A	50
Gemfibrozil	N/A	N/A	50

8.0 Monitoring Program for CECs in Water Reuse Leading to Urban Irrigation and Drinking Water Augmentation

8.1 The Proposed Prioritization Scheme for CECs in Recycled Water

The conceptual design of the Panel's approach in prioritizing CECs for monitoring programs is illustrated in Figure 8.1.

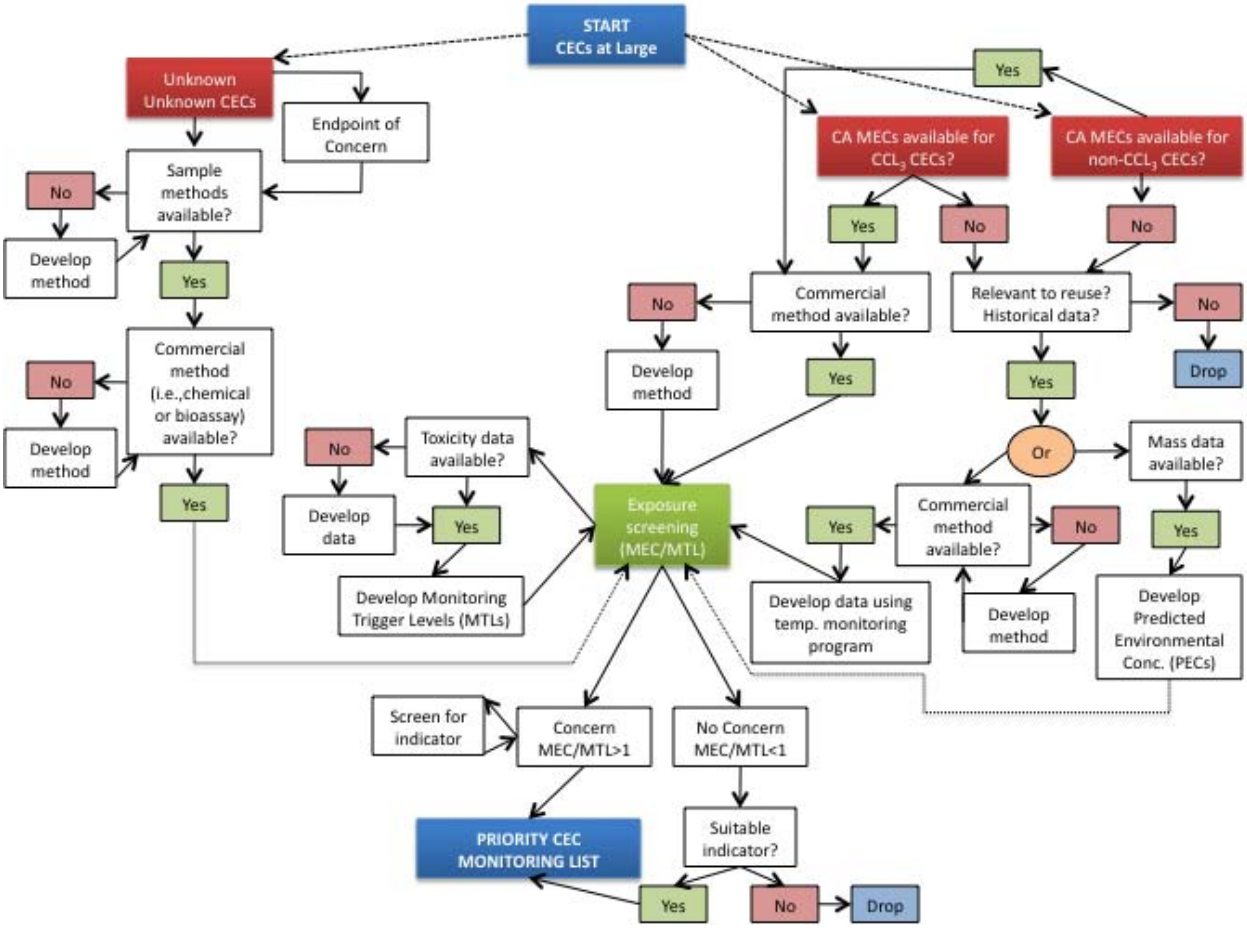


Figure 8.1. Conceptual CEC prioritization scheme.

This prioritization scheme provides guidance on how to select suitable, toxicologically relevant chemicals for monitoring purposes and considers that recycled water contains an unknown pool of CECs at large. CECs are classified into chemicals that have not been previously identified ("unknown unknowns") and those that have been previously identified, some of which appear on the USEPA's CCL3 list and others do not. For previously identified CECs the selection approach consists of four steps:

- Compile environmental concentrations of either measured or predicted environmental concentrations of CECs in recycled water that is the source for water reuse projects;
- Develop a MTL for each of these compounds (or groups thereof) based on toxicological relevance;
- Compare the environmental concentration (e.g., MEC, PEC) to the MTL. CECs with a MEC/MTL ratio greater than "1" should be prioritized for monitoring. Compounds with a ratio of less than "1" should only be considered if they represent viable treatment process performance indicators; and
- Screen the priority list to ensure that a commercially available, robust analytical method is available for that compound.

For *"known unknown"* CECs concentrations potentially present in reused water can be estimated using information on per capita use or production volume and combined with information on per capita water use to develop a PEC as discussed in Section 6. The PECs for *"known unknowns"* can then be compared to MTLs to identify the CECs with the greatest urgency to develop analytical methods and confirm the PECs.

For *"unknown unknown"* CECs, bioanalytical and chemical screening methods should be employed, when commercially available, to quantify effects or equivalent concentrations and identify chemicals for which there is the greatest urgency in developing MEC and MTL data for further assessment (Figure 8.1). As discussed in Section 6, bioanalytical methods are currently being used by several federal agencies to evaluate chemical safety, which will likely diminish input of hazardous chemicals into wastewater. Federal agencies have expressed similar concerns as the state regulatory entities regarding their inability to keep up with the regulation of CECs on a chemical-by-chemical basis using current risk assessment guidelines. Federal agencies have provided new risk assessment paradigms that incorporate high throughput models and bioanalytical assays to screen chemicals with specific animal testing directed only at chemicals that impair "critical modes of action". Due to the urgency presented by the regulatory community and the current development and testing of bioanalytical methods, the Panel estimates that bioanalytical methods will eventually be formally utilized for chemical and mixture assessments within the next 3 to 10 years. Since these methods are still in development, it is recommended that future science advisory panels (i.e., review panel suggested for 2013) update the prioritization framework as bioanalytical methods become specifically engineered for the evaluation of "unknown unknown" CECs in recycled water.

A number of conservative assumptions are embedded within the framework utilized to identify potential CECs for monitoring in recycled water. The assumption category and an estimated level ("order of magnitude") of conservatism compared to typical or commonly

expected exposures include the following:

- Selection of the MEC as the combined secondary/tertiary treated effluents for a particular reuse practice will result in MECs that are on the order of 40 to 800 times higher than what is likely observed at the POM since no credit was given for consistent tertiary treatment or for advanced treatment processes required for direct injection groundwater recharge projects (Drewes *et al*., 2008). For example, the MEC_{90th} for triclosan was reported as 485 ng/L; however, both SAT and RO can reduce this concentration to less than 50 ng/L reducing the MTL/MEC ratio from 1.39 to 0.14.
- For groundwater recharge projects, no credit was included to address dilution provided by mixing with native groundwater, and/or incidental treatment provided by the soil-aquifer system. Dilution credit for this assumption could provide an estimated safety factor of two-fold (e.g., based on the assumption of 50:50 dilution of recycled water with native groundwater). Treatment credit in the soil-aquifer system (e.g., adsorption, biodegradation) could provide a safety factor on the order of 10- to 90-fold (Drewes *et al*., 2008).
- For the environmental exposure concentrations, the 90th percentiles of MECs were utilized which provides a safety factor of approximately 10-fold (e.g., based on comparison of the ratio of the 90th percentile to median concentrations contained in Appendix K).
- For CECs with MECs below detection limits, the value of the reported MDL was used to represent the MEC providing an additional margin of safety;
- Chemical toxicity assumptions included total uncertainty/safety factors that generally range from 100 to 10,000 and, thus, added additional degrees of conservatism (see Section 4).
- Overall, the assumptions utilized to identify potential CECs for monitoring include between 4 to 6 orders of magnitude of conservatism for landscape irrigation projects and between 6 to 11 orders of magnitude of conservatism for indirect potable reuse projects.

8.2 Application of the CEC Prioritization Scheme to Identify Chemicals that should be Monitored at the Present Time

To assist the State in near-term program implementation, the Panel compiled available California MEC data and derived initial MTLs from drinking water benchmarks to apply the proposed scheme and to identify the chemicals that should be prioritized for present CEC monitoring. In applying the framework and in recognition of the time and resource constraints faced by the Panel for the purposes of this report, the Panel made of the following assumptions:

- The environmental concentrations compiled from the Panel's survey results represent secondary/tertiary treated effluent quality across the state;

- The MECs of CECs reported to the Panel were derived using validated and robust analytical methods;
- The Panel used the benchmarks summarized in Appendix J to develop initial MTLs for the purpose of identifying an initial list of CECs to be included in a monitoring program. The Panel wishes to point out that the MTLs presented in Tables 8.1 and 8.2 are provided as initial values, based in part on the safety factors and assumptions identified above, to the State for the purpose of establishing interim recycled water monitoring plans. The Panel, as is discussed below in Section 8.3 urges the State to reconvene the Panel to periodically update the initial MTLs, as well as any subsequently developed MTLs, using ADIs developed by the State, or if such are not available, based upon further review of toxicity information using the process outlined in this report; and
- For compounds with multiple drinking water benchmarks, initial MTLs were selected in the order of priority described below:
  - Given that the Panel's charge was to develop recommendations for monitoring for the State of California, the drinking water benchmarks developed by CDPH were given highest priority. Thus, when a CEC has a CDPH derived benchmark, that benchmark formed the basis for the initial MTL for that CEC, regardless of whether other sources also had a benchmark that could have been used to derive an initial MTL for that CEC;
  - Given that the drinking water benchmarks presented in the preliminary CCL and CCL3 lists were derived by a regulatory agency (see Section 2), those were given the next highest priority. Thus, for compounds without a CDPH drinking water benchmark but with a benchmark presented in the USEPA CCL dossiers, the CCL dossier benchmark was employed, regardless of whether the remaining sources also had a drinking water benchmark for that CEC; and
  - For CECs without either a CDPH or USEPA CCL benchmark, the lowest drinking water benchmark from the remaining five potential sources was used as the basis for the initial MTL.

The initial MTLs selected as described above were compared to MECs for recycled water in California to determine whether or not a CEC should be included in a monitoring program for potable and non-potable reuse systems. To derive the initial MTLs for landscape irrigation, the Panel multiplied potable use initial MTLs by 100 to account for the assumed reduced amount of water ingestion in a landscape irrigation setting (as described in Section 4). Given that the expected ingestion of water associated with landscape irrigation is 100-fold lower than that assumed for potable water use, and that is the only difference between the two sets of MTLs for the two scenarios, the landscape irrigation initial MTLs are 100 times greater than the initial MTLs for potable use.

For the CCL3 CECs for which MECs were available in California (considering data available to the Panel), only two CECs exceeded a ratio of "1" while comparing the MEC with the MTL for potable reuse applications, which were E2 and NDMA (see Section 5, Table 5.1). For the non-CCL3 CECs for which MECs and MTLs were available, only caffeine and triclosan exceeded a

MEC/MTL ratio of "1" (see Table 5.2). For the non-potable reuse practices, none of the CCL3 CECs and non-CCL3 CECs exceeded a MEC/MTL ratio of 1.

The Panel wishes to reiterate the conservative nature of the initial MTLs for the CECs indentified for inclusion on a monitoring list (Table 8.1).

- 17β-estradiol is a steroid estrogen, the majority of which has been reported to occur in wastewater as a result of natural excretion by humans rather than use of pharmaceuticals and that it is not predicted to be associated with adverse effects in drinking water (Caldwell *et al*. 2010). The primary reason that E2 had a MEC/MTL > 1.0 is that the initial MTL was based on the California Office of Environmental Health Hazard Assessment (OEHHA) cancer slope factor, as opposed to the ADI developed by the World Health Organization(WHO), which has been used by Australia (Australian-guideline, 2008) to develop its drinking water guidelines (see text box in Section 4). Had the Australian guidelines been used to develop the initial MTL, E2 would not be identified as a CEC to include in a monitoring program in California.
- Caffeine is a stimulant naturally present in virtually everyone's diet, including coffee, tea, chocolate, as well as in some pharmaceutical products. The initial MTL for caffeine of 0.35 µg/l is the drinking water guideline established by Australia (Appendix J). Based upon the chemical structure of caffeine, Australia assumes that caffeine is a Threshold of Toxicological Concern Structural Class III Compound ("chemicals for which structural features or likely metabolic pathways either permit no strong presumption of safety, or actually suggest significant toxicity." (Australian-guideline, 2008). Australia derives the caffeine drinking water guideline by dividing the NOAEL for chemicals in Structural Class III by a safety factor of 1,500. Both the assumption that caffeine is a Structural Class III compound and the use of an uncertainty factor of 1,500 result in an exceptionally conservative guideline and initial MTL. A sense of the degree of conservatism of the initial MTL of 0.35 µg/l is provided by a comparison of the initial MTL to the concentration of caffeine in brewed coffee, which can range between 250,000 and 500,000 µg/l and in black tea is about 200,000 µg/L. Thus, the concentration of caffeine in coffee is approximately one million (1,000,000) times greater than the initial MTL and in black tea is about 500,000 times greater than the initial MTL. Given that the MEC for caffeine only exceeds the initial MTL by about 2.6-fold, had caffeine been assigned to a different Threshold of Toxicological Concern Structural Class, for example to Class I, to which are assigned "substances of simple chemical structure with known metabolic pathways and innocuous end products that suggest a low order of toxicity" (Australian-guideline, 2008), the initial MTL would have been 20 times greater and caffeine would not be considered a initial CEC for monitoring.
- Triclosan is an antibacterial and antifungal agent used in a variety of consumer products, including toothpastes, deodorants, and soaps. As with caffeine the initial MTL of 0.35 µg/L for triclosan is based on the drinking water guideline established by Australia (Appendix J). Based upon the chemical structure of triclosan, Australia assumes that triclosan is a Threshold of Toxicological Concern Structural Class III Compound and then applies the safety factor of 1,500 to the NOEL described above to derive their guideline

(Australian-guideline, 2008). Unlike caffeine, two of the other sources of drinking water benchmarks reviewed by the Panel had drinking water benchmarks for triclosan. Snyder *et al.* (2008a) report a drinking water benchmark of 2,600 µg/L derived from by applying a safety factor of 1,000 to a NOEL of 75 mg/kg-day for systemic effects in hamsters. Cotruvo *et al*. (2010) report a drinking water benchmark of 500 µg/L. These benchmarks are between more than 1,000 to nearly 10,000 times greater than Australian benchmark and more in line with the widespread use of triclosan at levels of between 0.1 and 1.0% in common consumer products such as soaps and toothpastes. Had either of these alternative benchmarks been used, triclosan would not have been identified as a initial CEC for monitoring.

- NDMA is a disinfection byproduct that also occurs in various foods and alcoholic beverages. California has established a notification level of 0.01 µg/L for NDMA based upon on an excess lifetime cancer risk level of 3.3×10^{-6}, which is similar to the USEPA's cancer risk benchmark of one in one million.

Table 8.1. Exposure screening for CCL3 and non-CCL3 CECs in recycled water.

	Secondary/Tertiary Treated MEC 90th (ng/L)	Initial MTLs		MEC/MTLs	
		Potable Reuse	Irrigation	Potable Reuse	Irrigation
CCL3 CECs					
17β-estradiol	8.4	9.0E-01	9.0E+00	9.33	0.93
NDMA	68	1.0E+01	1.0E+02	6.8	0.68
Non-CCL3 CECs					
Caffeine	900	350	3500	2.57	0.26
Triclosan	485	350	3500	1.39	0.14

These brief summaries presented above of the background exposures and toxicological bases for the indicator CECs point to the need to fully understand the conservative nature of the initial MTLs. It is for these reasons that the Panel urges people interpreting the results of the exposure screening that forms the core of the CEC prioritization framework shown in Figure 8.1, to always keep in mind that the exposure screening was developed to prioritize CECs for a monitoring program; not to conduct an evaluation of potential risk. Inclusion of a CEC on the priority monitoring list does not mean the CEC poses a health risk. Further analyses outside of the framework proposed by the Panel are needed to evaluate the potential for a health threat.

The overarching goal of a CEC monitoring program is to ensure that the expected performance of a recycled water treatment plant operates consistently over extended periods of time and, thus, reliably produces recycled water that matches, or is superior to predetermined standards and thus, can be used as source water for indirect potable reuse projects. Since water quality standards for CECs are not currently available, reliability then must

be defined as the likelihood of achieving a consistent effluent quality[5]. For the purposes of developing the CEC monitoring program (i.e., start-up and baseline defined as the monitoring program conducted after DPH approval of indirect potable reuse project operation), consistent effluent quality is defined as the final recycled source water containing ≤5 times the ratio of the MEC/MTL for the indicator CECs listed in Table 8.1. It should be noted again, that the CECs listed in Table 8.1 represent an initial list of monitoring compounds based on a number of qualifying assumptions previously discussed. As such, while the indicator CECs were selected using the screening approach developed and applied by the Panel, they can also be used in preliminary screening evaluations of effluent quality.

8.3 Indicator Compounds and Surrogate Parameters for Treatment Performance Assessment

As previously described, a conservative regulatory approach for the design and operation of potable reuse systems has evolved that employs multiple barriers of treatment processes with a demonstrated ability to remove contaminants (see Section 3). The treatment processes are subjected to intensive water quality monitoring programs designed to detect failures in system performance. Traditional water quality methods of measuring bulk organic matter in wastewater, such as measurements of chemical oxygen demand (COD), total organic carbon (TOC), total organic halides (TOX), or conductivity, continue to be used in monitoring programs, even though their ability to serve as surrogates for CECs has only been demonstrated very recently (Drewes *et al.*, 2008; Dickenson *et al*. 2009; Drewes *et al*., 2010b). These studies demonstrate that changes in bulk parameters do correlate with changes of indicator chemicals in the subsurface or during RO treatment leading to direct injection (Drewes *et al*. 2010a). Thus, to ensure proper performance of unit operations regarding the removal of CECs, a combination of appropriate surrogate parameters and performance indicator CECs should be selected that are tailored to monitor the removal efficiency of individual unit processes comprising an overall treatment train. Performance indicator CECs and surrogate parameters are defined as follows:

- Indicator -- An indicator compound is an individual CEC occurring at a quantifiable level that represents certain physicochemical and biodegradable characteristics of a family of trace organic constituents that are relevant to fate and transport during treatment. It provides a conservative assessment of removal.

- Surrogate -- A surrogate parameter is a quantifiable change of a bulk parameter that can measure the performance of individual unit processes (often in real-time) or operations in removing trace organic compounds.

An indicator and surrogate approach utilizes only a limited set of analytes for the evaluation of potable reuse projects. The selection of a practical set of indicator compounds is driven by

[5] The definition of performance reliability only encompass the variability associated with effluent quality related to by in-plant treatment processes and assumes that the plant is properly designed, operated and maintained.

treatment performance and less so by toxicological relevance. Thus, selecting multiple indicators representing a broad range of properties will allow accounting for compounds currently not identified ("unknowns") and new compounds synthesized and entering the environment in the future (i.e., new pharmaceuticals) provided they fall within the range of properties covered. The underlying concept is that absence or removal of an indicator compound during a treatment process would also ensure absence or removal of unidentified compounds with similar properties. Table 8.2 lists health-based indicator CECs along with performance-based indicator CECs for the two groundwater recharge practices of interest to the Panel. Please note that certain health-based indicator CECs are also fulfilling the function of performance-based indicators (e.g., caffeine, NDMA). For these reuse practices as well as urban irrigation, performance surrogate parameters are also listed. It is noteworthy, that performance-based measures (using the select indicator CECs and surrogates) are differential measures (i.e., difference between the influent and effluent of a process). For both the health- and performance-based indicator CECs; MRLs are provided

Table 8.2. Health-based and performance based indicator CECs and performance surrogates for potable and non-potable reuse practices.

Reuse Practice	Health-based Indicator	MRL (ng/L)	Performance-based Indicator	Expected Removal[8]	MRL (ng/L)	Surrogate	Method	Expected Removal[8]
Groundwater Recharge	17β-estradiol[1]	1	Δgemfibrozil[5]	>90%	10	Δammonia	SM	>90%
SAT	Triclosan[2]	50	ΔDEET[6]	>90%	10	Δnitrate	SM	>30%
	Caffeine[3]	50	ΔCaffeine[3]	>90%	50	ΔDOC	SM	>30%
	NDMA[4]	2	Δiopromide[5]	>90%	50	ΔUVA	SM	>30%
			ΔSucralose[7]	<25%	100			
Direct Injection	17β-estradiol[1]	1	ΔDEET	>90%	10	Δconductivity	SM	>90%
	Triclosan[2]	50	ΔSucralose	>90%	100	ΔDOC	SM	>90%
	Caffeine[3]	50	ΔNDMA	25-50%	2			
	NDMA[4]	2	ΔCaffeine	>90%	50			
Landscape Irrigation	None		None			Turbidity	SM	
						Cl2 Residual	SM	
						Total Coliform	SM	

[1]Steroid hormones; [2]Antimicrobial; [3]Stimulant; [4]Disinfection byproduct; [5]Pharmaceutical residue; [6]Personal care product; [7]Food additive; [8]travel time in subsurface two weeks and no dilution, see details in Drewes *et al*. 2008; SM – Standard Methods

The determination of these differentials (for performance indicator CECs and surrogates) for individual unit processes comprising an overall treatment train is distinguished into two phases: piloting/start-up and full-scale operation monitoring (Table 7.3). In order to apply the surrogate/indicator framework to a given or proposed treatment train, first operational boundary conditions of treatment processes need to be identified, ensuring the performance of

each unit process according to their technical specifications. During a piloting/start-up phase for each unit process, the surrogate or operational parameters that demonstrate a measurable removal (differential) under normal operating conditions ($\Delta X = [X_{in} - X_{out}]/X_{in}$) need to be identified. In parallel, an occurrence study is to be performed confirming the presence of the proposed performance indicator CECs in the feedwater of each unit process (in the case of a surface spreading facility, recycled water prior to and after SAT; in case of direct injection, recycled water prior to and after RO/AOP). During piloting or start-up of a new treatment process, monitoring for a short time period should be conducted with the proposed performance-based indicator CECs to determine the removal differential ΔY under normal operating conditions. For the full-scale operation, the operational boundary conditions and removal differential ΔX and ΔY for selected surrogate and operational parameters and indicator compounds should be confirmed. To ensure the proper performance of each full-scale unit operation, select surrogate and operational parameters should be measured on a regular basis. While it is implied that proper performance of the full-scale treatment train will ensure appropriate removal of CECs, the proposed performance based indicator compounds for each water reuse practice should be monitored at frequencies in the order of semiannually or annually.

Table 8.3. Application of surrogate/indicator framework to an overall treatment train (adopted from Drewes *et al*. 2010b).

	Surrogate Parameters	Performance Indicator CECs
Piloting and/or Start-up		
Step 1	Define operational boundary conditions for surface spreading (SAT) or direct injection (RO/AOP) for proper operation according to technical specifications	
Step 2	For each unit process, identify those surrogate or operational parameters that demonstrate a measurable removal under normal operating conditions and quantify their removal differential ($\Delta X = [X_{in} - X_{out}]/X_{in}$)	Conduct occurrence study to confirm presence of performance based indicator CECs in the feedwater of each unit process
Step 3	Select viable surrogate and operational parameters for each unit process	Monitor for performance indicator CECs during pilot scale or start-up to determine the removal differentials under normal operating conditions ($\Delta Y = [Y_{in} - Y_{out}]/Y_{in}$)
Full-Scale Operation and Performance Monitoring		
Step 4	Confirm operational boundary conditions of full-scale operation and removal differential ΔX for selected surrogate and operational parameters	
Step 5	Monitor differential ΔX of select surrogate and operational parameters for each unit process on a regular basis (daily, weekly)	Monitor differential ΔY of selected indicator compounds for each unit process semiannually/annually

In addition to identifying the surrogate, real-time or on-line water quality monitoring represents an issue of concern and uncertainty. On-line monitoring involves constant *in-situ* measurement of a body of water as opposed to analyzing samples in the laboratory. As California and worldwide reuse treatment plant performance and reliability requirements become more stringent the topic will require an increasing level of investigation and development. Faced with compliance with more stringent environmental regulations, plant operators as well as instrument manufacturers will need new standards and improved techniques. Currently available methods tend to focus on on-line monitoring on a small subset of general organic parameters (e.g., BOD, COD, TOC) and some physical parameters (e.g., volume, flow, pH, turbidity, salinity). Currently, biosensors, optical sensors and sensor arrays as well as virtual sensors for the monitoring of wastewater organic load and other chemical constituents are under investigation/development. As reliable methods and equipment become available, they should be incorporated into the water reuse regulatory and industry standards of practice.

8.4 Monitoring Program and Suggested Response(s) for Indirect Potable Reuse Projects

Due to time and resource constraints, the guidance provided regarding a start-up and baseline monitoring program does not address all situations that the regulator and regulated entity will need to address. Under these circumstances, the Panel recommends that the affected stakeholders consult experts to recommend a plant or regional-specific solution.

To carry out the monitoring program for the indicator CECs identified above, the Panel recommends a multi-tiered approach for implementing and interpreting results from CEC monitoring programs for recycled water. While the Panel provides recommended thresholds for each of these tiers, conservative values were selected because of the limited toxicological information available and the interim nature of the initial MTLs. When drinking water benchmarks or ADIs derived by the State are available, those should be used to update and establish MTLs. The Panel also understands that differences in recycled water quality and facility operations will occur by region and that investigation of chronic exceedances will need to be tailored on a region-by-region or case-by-case basis.

The following discussion provides the Panel's recommended guidance on the monitoring, response and the subsequent review/updating of those plans for groundwater recharge projects used for drinking water augmentation.

8.4.1 Guidance on Start-up and Baseline CEC Monitoring Programs for Groundwater Recharge Projects

The sampling location, type of IPR project (including treatment processes), CEC constituent(s), and frequency of sampling all depend on the sampling objective. Two types of monitoring are suggested, start-up and baseline monitoring. Also, the suggested constituents contained in Table 8.2 have been identified as either an indicator of health relevance, overall

plant efficacy or a surrogate to represent treatment process performance. Based on the above, the Panel provides the following guidance:

- Overall Treatment Plant Efficacy - In general, sampling for CECs indicators should occur at the POM (as discussed in Section 1). To meet the draft CDPH groundwater recharge reuse regulations additional sampling is typically necessary from downgradient wells, from monitoring wells representing the underlying groundwater and/or from shallow lysimeter wells. The location and monitoring criteria for selection and use of these sampling locations are site-specific and need to be defined on a case-by-case basis. The guidance provided within this report should be used to supplement the monitoring conducted as part of compliance with the draft CDPH regulations;
    - Plant Start-up Monitoring Frequency - Initial start-up monitoring should include, at a minimum, quarterly analyses of the compounds identified as Indicator CECs (see Table 8.2) for the first year of project operation. The surrogates identified in Table 8.2 should be monitored using online devices, where feasible.
    - Baseline Monitoring Frequency - Baseline monitoring should occur twice per year for all indicator CECs at the POM for a minimum of three years. Consistent water recycle plant operation should produce final effluent IPR project source water containing Table 8.2 CEC concentrations that are consistently less than 5 times the ratio of MEC/MTL. The surrogates identified in Table 8.2 should be monitored using online devices, where feasible.
- Treatment Unit Process Performance - The following guidance is provided for monitoring the surrogates and indicators during start-up and baseline operations.
    - Plant Start-up Monitoring Frequency - Initial start-up monitoring should include, at a minimum, quarterly analyses of the compounds identified as indicator CECs (see Table 8.2) for the first year of project operation. The surrogates identified in Table 8.2 should be monitored using online devices, where feasible. To provide certainty that the individual treatment processes are performing according to their technical specifications, monitoring (depending on the type of IPR project) should occur at the following representative locations. The following example is for a direct injection based IPR (i.e., using RO/AOP). Duplication of effort at the POM is not the intent, but just shown for completeness.
        - Between secondary and membrane treatment processes;
        - Between membrane and advanced oxidation treatment; and
        - Final effluent after advanced oxidation and prior to groundwater injection (POM).

    The following sampling locations are suggested for an IPR using surface spreading. As noted above the selection of monitoring and lysimeter wells are site-specific and need to be selected consistent with DPH regulations.

        - Final effluent after tertiary treatment and prior to release to the groundwater spreading basin (e.g., POM).

    - At monitoring wells representing the underlying groundwater and/or from shallow lysimeter wells.
    - At down-gradient well(s) representing the potable source water prior to the potable water treatment plant.
  - Baseline Monitoring Frequency - Baseline monitoring should occur twice per year for all indicator CECs at the POM for a minimum of three years. Consistent water recycle plant operation should produce final effluent IPR project source water containing Table 8.2 CEC concentrations that are consistently less than 5 times the ratio of MEC/MTL. The surrogates identified in Table 8.2 should be monitored at the various treatment unit locations noted above using online devices, where feasible.
- Increasing Monitoring: If indicator CECs exceed the suggested thresholds during start-up or baseline monitoring, the Panel recommends that the recharge agency work with DPH and the RWQCBs to identify the need for and extent of increased monitoring to confirm the presence of problematic CEC(s), source identification studies, and/or toxicological studies. If appropriate, increased monitoring might involve engineering removal studies and/or modification of plant operation if found to be warranted.
- Commercial Laboratory Conditions: Methods used to quantify indicator CECs need to meet stringent QA/QC measures, including blanks, replication, and matrix spikes. The Panel recommends the use of isotope-dilution and tandem mass spectrometry whenever possible. A detailed description of analytical considerations is provided in Section 7 and Appendix M.

8.4.2 Response to Monitoring Results

Should there be positive baseline monitoring results, the recharge agency, RWQCBs and CDPH needs to consider whether the result is of concern. Consideration should entail topics such as: review of the basis of the (initial) MTL; what is known and what is not known about the particular chemical, the chemical's potential health effects at the given concentration, the source of the chemical, as well as possible means of better control to limit its presence, treatment strategies if necessary, and other appropriate actions.

The Panel provides the following guidance relative to defining positive monitoring results and the potential associated follow-up action(s). While the Panel provides guidance on thresholds for each of these tiers, conservative values were selected because of the limited toxicological information available. The guidance is provided based on the assumption that the Panel's conceptual framework, utilized within this report, include a minimum safety factor of approximately 10,000-fold. The Panel recommends that the recharge agency confer with the DPH and the appropriate RWQCB to develop a response plan with specific actions to be implemented by the recharge agency as part of interpreting appropriate responses to the monitoring results.

- If no more than 25 percent of the samples during phase-2 monitoring exceed a MEC/MTL ratio of 0.1, the Panel recommends that the DPH consider deleting the compound from further monitoring, if requested by the permitted agency. In cases where a reduction of monitoring is requested, the MTL(s) should be updated, if feasible, as part of reviewing the request.
- If 1<MEC/MLT< 10: data check, continue to monitor, until 1 year and the MEC/MLT < 1 and preferably is consistently less than 5 times the ratio of MEC/MTL.
- If 10<MEC/MLT< 100: data check, immediate re-sampling and analysis to confirm MEC, continue to monitor, until 1 year and the MEC/MLT< 1 and preferably is consistently less than 5 times the ratio of MEC/MTL.
- If 100<MEC/MLT< 1000: all of the above plus enhance source identification program. Also monitoring at a point in the distribution system closer to the POE to confirm attenuation of the CEC is occurring and to confirm the magnitude of assumed safety factors associated with removal efficiency. The POE should be selected consistent with the DPH regulations[6].
- MEC/MTL>1000: all of the above plus immediately confer with the CDPH and the RWQCBs to determine the required response action. Confirm plant corrective actions through additional monitoring that indicates the CEC levels are below at least an MEC/MTL of 100.)

Please note that the baseline monitoring recommended by the Panel and additional follow-up monitoring to investigate and address positive findings should not be considered for compliance and/or regulatory purposes, but for investigation and potential use for additional follow-up actions only as part of conferring with the CDPH and the RWQCBs.

8.4.3 Review/Update of Monitoring and Response Plans

In addition to the above suggested monitoring and results-based responses, the Panel suggests the following actions relative to updating and confirming the plant data as well as the list of indicator CECs for monitoring purposes.

- Once every five years, one additional round of CEC monitoring should be conducted to confirm monitoring results. The monitoring list should reflect suggestions of an independent panel, preferably a single non-project based State panel, following a selection process outlined in this report. The monitoring results should be submitted, along with all of the previous monitoring data, as part of the five year CDPH report (see draft CDPH regulations, section 60320.090).
- The State independent panel should review and update the list of indicator CECs at least triennially. The review and update should include the following:

[6] Refer to draft CDPH regulations sections 60320.070 and 60320.090, for example.

- Collect and review readily available toxicity data and update MTLs;
- Collect and review California advanced treatment plant effluent data including IPR monitoring data collected as part of CDPH permitted projects and update MECs;
- Update list of indicator CECs to include newly identified CECs where the MEC/MTL>1 and remove CECs where updated data indicate that the current MEC/MTL<1;
- Review CECs that have come off the monitoring list to see whether use patterns have changed and whether this change warrants their re-listing for monitoring;
- Review and update guidance on sampling frequency and location;
- Review and update conclusions regarding laboratory analytical methods;
- Review and update biological and chemical screening methods, as discussed in Section 6, and provide guidance on potential new monitoring methods/tools that would significantly enhance chemical conventional chemical monitoring methods;
- Develop guidance to the State for updating the monitoring requirements in groundwater recharge project permits; and
- Review and update Panel guidance on selecting viable surrogate parameters and performance indicator CECs.

8.5 Monitoring for Additional CECs with Insufficient MECs

As pointed out repeatedly, the Panel selected the indicator CECs for a monitoring program based on MEC data available to the Panel. As some of the CCL3 CECs did not have any California MEC data, the Panel reviewed the entire data base of CCL3 CECs and short-listed those CECs with MTLs of less than 500 ng/L that could have the potential to trigger a MEC/MTL ratio of larger than "1" (see Table 5.3, Section 5). To provide the State with guidance on the relevance of these CECs to the water recycling practices of interest, the Panel suggests monitoring select CCL3 CECs for which currently no California MECs are available in secondary/tertiary treated effluent representing the feed water quality to either surface spreading or advanced water treatment (i.e., RO/AOP) ahead of direct injection. Monitoring should occur quarterly for one year. Table 8.4 lists these suggested CCL3 CECs for which commercial methods are available and their corresponding method reporting limits.

In order to fill data gaps regarding CECs with limited or no information on MECs in California, the Panel also suggests that the State initially conduct a more thorough review of CECs likely to occur in recycled water using MEC and PEC data from the peer-reviewed literature and occurrence studies outside California. Those CECs that exhibit high MECs and PECs could be placed on a secondary monitoring list that is measured less frequently to confirm either presence or absence of these CECs in recycled water in California providing commercial

analytical methods are available. Results of this effort will provide the basis for revising the proposed initial monitoring list during the next triennial review.

Table 8.4. Suggested CECs with limited MEC for additional monitoring.

CECs for Additional Monitoring	MTL	MRL (ng/L)
1,2,3-Trichloropropane	5.0E+00	5
Hydrazine	1.0E+01	1
Quinoline	1.0E+01	1

9.0 Recommendations

Because the science of CEC investigation is still in its early stages and the Panel was limited in both time and resources, the State can undertake several activities to improve the quality of future monitoring and toxicological information that feeds into the process that the Panel has identified for this inaugural CEC monitoring effort. The State should utilize a Science Advisory Panel to conduct and oversee these activities. This Expert Panel provides a number of recommendations that are geared toward ensuring that monitoring data is of appropriately high quality and identifying those CECs in recycled water that are of greatest concern and relevance to ecosystems and human health, including:

1) In order to populate a recycled water data base of CECs with MEC and PEC data, conduct a comprehensive review of CECs likely to occur in recycled water based on peer-reviewed literature and occurrence studies outside California;
2) Develop robust and reproducible analytical methods to measure CECs in recycled water;
3) Perform laboratory performance and analytical method validation studies for CECs adopted by the State as monitoring priorities;
4) Develop a detailed procedure to estimate PECs for CECs for which MECs are currently not available based on production, use and environmental fate;
5) The SWRCB should convene and charge a Science Advisory Panel to scope out an investigative, short-term monitoring study (e.g. quarterly sampling over a one-year period) for CECs that exhibit relatively low MTLs (e.g. < 500 ng/L), but for which no or little MEC or PEC information is available for secondary/tertiary effluents used for the water reuse practices of interest; and
6) Encourage development of bioanalytical screening techniques that include CECs currently not identified but potentially present in recycled water ("unknown unknown" chemicals). Develop appropriate trigger levels for these bioanalytical screening techniques that correspond to a response posing a concern from a human health standpoint.

The Panel emphasizes that the compounds selected for monitoring in indirect potable reuse applications represent a preliminary list based on the limited data that are presently available in California and on a number of qualifying assumptions discussed in the report. While they represent a conservative screening of "CECs at large", the information available for such screening is growing rapidly as is the sheer volume of monitoring and supporting toxicological information. Thus, in addition to the research recommendations from above, the Panel urges the State to:

1) Develop a process to rapidly compile, summarize and evaluate monitoring data as they become available. Identify trends in occurrence pattern as a function of time and sampling locations;
2) Reapply the prioritization process at least on a triennial basis; and

3) Establish a State independent review panel that can provide a periodic review to the proposed selection approach, reuse practices, and MECs of ongoing CEC monitoring efforts.

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Appendix A - Biographies of Panel Members

HUMAN HEALTH TOXICOLOGIST

Dr. Paul Anderson

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Postdoctoral Fellowship, Harvard School of Public Health, Interdisciplinary Programs in Health

Postdoctoral Fellowship, Harvard University, Biology Department

Ph.D., Biology, Harvard University

M.A., Biology, Harvard University

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Dr. Anderson has over 20 years of experience in human health and ecological risk assessment. Since 2000, Dr. Anderson has led several research efforts investigating the potential presence and effects of active pharmaceutical ingredients (APIs) and personal care products in surface water as well as other environmental media. His research in the area of constituents of emerging concern (CECs) began with the development of a screening level model (the Pharmaceutical Assessment and Transport Evaluation (or P*h*ATE™) model) that predicts the concentration in surface water of human-use pharmaceuticals and other compounds released from sewage treatment plants across the United States (including the Sacramento and Lower Colorado Rivers). The model has since been corroborated and was published in Environmental Science and Technology in 2004. Additionally, Dr. Anderson helped develop and continues to oversee the use of a database that summarizes the English language peer-reviewed literature on aquatic toxicity, environmental fate in surface water and treatment plant removal of pharmaceuticals. The database is designed to make all historical information easily accessible to users as well as providing them with up-to-date information. Dr. Anderson and his colleagues have used these tools to conduct several evaluations, including an assessment of the potential human health effects of several therapeutic classes of pharmaceuticals in US surface waters; the development of a predicted no effect concentration for protection of aquatic receptors from ethinyl estradiol (EE2); a comparison of predicted to measured concentrations of EE2 in surface water to establish the range of likely EE2 concentrations (submitted for publication); an evaluation of the potential for estrogens (both prescribed and naturally occurring) in drinking water to pose a potential risk to humans in the United States (submitted for publication); and characterization of the potential ecological risk associated with EE2 in surface water (manuscript in preparation). More recently, Dr. Anderson has expanded his research in the area of trace compounds in surface waters to include two comprehensive reviews of existing

information and ongoing research efforts. The first was a review of the state-of-the-science of endocrine disrupting compounds (EDCs) and the implications of the presence of such compounds for wastewater treatment, published by the Water Environment Research Foundation in 2005. It described the sources of EDCs in wastewater, their fate in wastewater treatment plants, and impacts in the environment as a result of discharges. The second project, published in 2008, updated and expanded the 2005 work on EDCs to include the full range of organic compounds that may occur at trace levels in wastewater treatment plant effluents. The research included: a review of the different sources and categories of trace organic compounds; how they are measured; their removal in treatment plants; an introduction to the potential ecological and human health effects associated with trace organics in treated wastewater, recycled water, and receiving streams; and an overview of current research needs including a summary of web-links describing major current research initiatives. Dr. Anderson is also an adjunct professor in the Center for Energy and Environmental Studies within Boston University's Geography Department.

ENVIRONMENTAL TOXICOLOGIST

Dr. Daniel Schlenk

Professor

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Education:

Postdoctoral Fellow, Duke University

Ph.D., Biochemical Toxicology, Oregon State University

B.S., Toxicology, Northeast Louisiana University

The overall focus of Dr. Schlenk's laboratory has been to evaluate mechanisms of action of chemicals in aquatic and marine organisms. For the past 15 years, Dr. Schlenk has been interested in the estrogenic effects of legacy and emerging chemicals of concern. Initial work began with exploring the stereoselective biotransformation and activation of the legacy contaminant, methoxychlor. His lab helped develop a method to measure the egg yolk protein, vitellogenin in channel catfish and Japanese medaka. This metric was used to evaluate estrogenic activity in wastewater treatment plants in the south and east coasts and waterways of the United States. From there, his laboratory evaluated the effects of ß-adrenergic antagonists and other pharmaceutical agents on aquatic fish and invertebrates. Dr. Schlenk's research in California has focused on the impacts of feminization on marine fish reproduction and populations as well as the identification of causal agents in sediments and water receiving oceanic discharge from municipal wastewater treatment facilities, particularly off the coast of Orange County. In addition, his laboratory conducted studies evaluating the long-term effects of

recycled water on fish health. Current studies are underway to identify unknown estrogenic compounds in surface waters of the Central Valley and Santa Ana River. Specific agents that have been examined include current use pesticides (such as pyrethroids and herbicides), surfactants and UV-sunscreen agents. It is his goal to understand the modes of action of these compounds alone and in mixtures to determine the interactive roles each may have in endocrine disruption. In 2008, Dr. Schlenk served on the USEPA Science Advisory Board to evaluate potential changes to the Aquatic Life Criteria for Compounds of Emerging Concern. From 2003-2006, he was a member of the Board of Directors for the North American Society of Environmental Toxicology and Chemistry. He is the co-Editor-in Chief of *Aquatic Toxicology* and serves on the editorial boards of *Toxicological Sciences*, *The Asian Journal of Ecotoxicology* and *Marine Environmental Research*. He has been a permanent member of the USEPA FIFRA Science Advisory Panel since 2007, and has participated in proposal review panels for the USEPA, NOAA, and the National Institute of Environmental Health Sciences.

EPIDEMIOLOGIST/RISK ASSESSOR

Dr. Adam Olivieri, P.E.

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M.S., Civil and Sanitary Engineering, University of Connecticut

B.S., Civil Engineering, University of Connecticut

Dr. Olivieri has over 30 years of experience in the technical and regulatory aspects of water recycling, groundwater contamination by hazardous materials, water quality and public health risk assessments, water quality planning, wastewater facility planning, urban runoff management, and on-site waste treatment systems. He is a Registered Civil Engineer and a Registered Environmental Assessor with the State of California. Dr. Olivieri has extensive experience in the area of microbial risk assessment and the application of such models to make engineering and public policy decisions. Recently he served as Principal Investigator on the development of a user friendly microbial risk assessment tool (MRAIT) for the Water Environment Research Foundation. Dr. Olivieri served as the co-project director at the Public Health Institute/Western Consortium for Public Health, where he directed the City of San Diego's Health Effects Studies at Mission Valley and San Pasqual, investigating the health risks of potable reuse of

recycled San Diego municipal wastewater. The overall research plan was developed to address the fundamental issues raised by the 1982 National Research Council, and consistent with their recommendations involved a comprehensive investigation and comparison of both a recycled and a current potable water supply. The research project involved developing research plans and managing research across a wide base of California's prestigious universities including Berkeley, Davis, Los Angeles, San Francisco, and Scripps (San Diego), San Diego State University and several laboratories of the California Department of Public Health Services. The project involved research in the following major areas: a) Infectious Disease Agents – pathogenic viruses, parasites, and bacteria (including indicator organisms), b) Chemical Screening – volatile and semi-volatile organics, metals, PCBs, dioxins, TOC, and TOX, c) Genetic Toxicity Bioassay – Ames Assay, Micronucleus tests, 6-Thioguanine Resistance Assay, and Cellular Transformation Assay, d) Fish Biomonitoring, e) Plant Reliability – performance and mechanical reliability analysis and chemical and microbial agent unit and plant spiking studies, f) Chemical Risk Assessment – carcinogenic and non-carcinogenic, g) Epidemiology – baseline information (reproductive outcomes, vital statistics, and neural tube defects), and h) a Long-Term Health Effects Monitoring Plan. The San Diego Health Effects investigations have been recognized by the Science Advisory Board and a special publication by the Water Environment Federation and the American Water Works Association covering the use of recycled water to augment potable water resources. The San Diego Health Effects investigations have also been recognized and used by the Australian government and the University of New South Wales in the development of water reuse guidelines. Dr. Olivieri has and continues to serve on a number of national technical review panels. Currently he serves on two National Water Research Institute technical review panels, one for Orange County (CA) evaluating the alternative disinfection options for the wastewater treatment plant along with potential public health implications related to recreation exposure. The second is for Monterey County (CA), which is evaluating groundwater recharge using recycled water. At the request of the USHouse of Representatives – Subcommittee on Water Resources and Environment, he provided testimony on April 13, 2005 on microbial agents and risk assessment relative to the national wastewater blending issue.

BIOCHEMIST

Dr. Nancy Denslow
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Education:
Postdoctoral Fellow, University of Florida
Ph.D., Biochemistry and Molecular Biology, University of Florida
M.S., Biochemistry and Molecular Biology, Yale University
B.S., Chemistry, Mary Washington College

Dr. Denslow's research involves environmental toxicology with a special focus on endocrine disruptors and pharmaceuticals in the environment. Her interests include defining molecular mechanisms of action of endocrine disrupting chemicals that adversely affect reproduction in fish that are exposed to the

contaminants in surface waters. Her research covers both sex hormone receptor mediated and independent mechanisms. Favorite model systems include largemouth bass, fathead minnow, sheepshead minnow and zebrafish. Common research tools include traditional toxicology assays, biochemical pathways, histopathology, microarrays, real time PCR, proteomics, tissue culture based assays, transfections and in vivo determination of reproductive endpoints. In addition, Dr. Denslow has initiated research to understand the effect of nanomaterials on fish health. These experiments are integrated to look at gill function, histopathology, nanomaterial uptake and nanomaterial characterization. In addition, microarrays and proteomics tools are used to characterize the effects of the exposures. She has published more than 120 peer-reviewed publications and has led research projects supported by NIH/NIEHS, NSF, USEPA, and the USArmy Corps of Engineers. Dr. Denslow also serves as Associate Editor for *Comparative Biochemistry and Physiology Part D Toxicogenomics* and *Ecotoxicology and Environmental Safety*, and received the Pfizer Award for Research Excellence in 2007 and a UFRF professor designation for 2009-2012. Dr. Denslow previously served for 15 years as the Director of the Protein Chemistry and Molecular Biomarkers Core Facility at the University of Florida. She has served on the Executive Board of the Association for Biomolecular Research Facilities (ABRF) and is a member of the Society of Environmental Toxicology and Chemistry (SETAC) and the Society of Toxicology (SOT) serving as senior councilor in the Molecular Biology Specialty Section. She is also a member of the American Association for Biochemistry and Molecular Biology (ASBMB).

CIVIL ENGINEER FAMILIAR WITH THE DESIGN AND CONSTRUCTION OF RECYCLED WATER TREATMENT FACILITIES

Dr. Jörg E. Drewes *(Panel Chair)*

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Dr. Drewes has been actively involved in research in the area of water treatment and non-potable and potable water reuse for more than 18 years. For the last 14 years, Dr. Drewes has been conducting research on indirect potable reuse projects in the State of California, including surface spreading as well

as direct injection projects. The main focus of these studies has been the fate and transport of trace organic chemicals in these systems. He has led research as the principal investigator (PI) or Co-PI to better understand the rejection of trace organic chemicals during high-pressure membrane treatment (nanofiltration, reverse osmosis) as well as the fate and transport of micropollutants in soil-aquifer treatment systems. A common theme in all these projects was to identify meaningful trace organic compounds that can serve as indicator compounds for system performance assessments. He has also conducted tailored studies to further develop this concept for multiple treatment processes commonly employed in indirect potable reuse followed by more focused efforts for surface spreading and direct injection projects. This indicator concept has been adopted in the Australian Water Recycling Guidelines for Drinking Water Augmentation in 2008. In addition, he has been involved in several studies addressing the occurrence of emerging contaminants in recycled water and to provide guidance to the water industry regarding occurrence, fate and transport, health effects, analytical methods and communication. Dr. Drewes research group is currently working on developing more predictive tools for the fate of trace organic chemicals in various reuse schemes using quantitative structural property relationships (QSPRs) coupled with process models. Dr. Drewes has published more than 160 journal papers, book contributions, and conference proceedings. He was awarded the 2007 AWWA Rocky Mountain Section Outstanding Research Award, the 2003 Dr. Nevis Cook Excellent in Teaching Award, the Quentin Mees Research Award in 1999, and the Willy-Hager Award in 1997. In 2008, he was appointed to the National Research Council Committee on Water Reuse as an Approach for Meeting Future Water Supply Needs. Since 2007, Dr. Drewes has held an Adjunct Professor appointment at the University of New South Wales, Sydney, Australia.

CHEMIST FAMILIAR WITH THE DESIGN AND OPERATION OF ADVANCED LABORATORY METHODS FOR THE DETECTION OF EMERGING CONSTITUENTS

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Dr. Shane Snyder is the co-founder and vice president of Total Environmental Solutions Inc (TES). TES was founded in 1999 as a solutions-based company offering consulting and laboratory services to a diversity of government, municipal, and private sector clients. Dr. Snyder also served as the R&D Project

Manager for the Southern Nevada Water Authority (SNWA) for over a decade. He has published more than 90 manuscripts on the occurrence and fate of emerging contaminants in water. In 1998, he was credited with the first discovery of natural and synthetic estrogens in North American waters. Dr. Snyder also linked the occurrence of steroids in wastewater to potential endocrine impacts in fish in the late 1990's. In 2002, he was awarded one of the most comprehensive studies investigating the efficacy of conventional and advanced water treatment processes for the removal of endocrine disruptors and pharmaceuticals (AwwaRF 2758). Dr. Snyder serves as an Associate Adjunct Professor of Chemistry at the University of Nevada, Las Vegas. He has served two terms on the USEPA Federal Advisory Committee for the Endocrine Disruptor Screening Program and has served on two expert panels for USEPA's Candidate Contaminant List III. He is a member of the Research Advisory Council for the WateReuse Foundation and is a member of the American Water Works Association's Water Science & Research Division Board of Trustees. Dr. Snyder was one of six experts to testify before the US Senate regarding pharmaceuticals in US waters in April of 2008. In 2009, Dr. Snyder's research team published the first national survey of pharmaceuticals in US drinking water. Beginning in 2010, Dr. Snyder has accepted the position of Professor of Chemical and Environmental Engineering at the University of Arizona. He is also the Co-Director of the Arizona Laboratory for Emerging Contaminants at the University of Arizona.

Appendix B - Ecotoxicology Assessment

Most water reuse practices tend to have limited impact on ecological receptors. Based upon the conceptual models discussed in Section 1 and reuse practices of interest to this Panel, urban irrigation and groundwater recharge operations are discussed for potential ecotoxicological effects.[7] The two potential ecological receptors of interest identified in the conceptual models for groundwater recharge are fish and birds (Figures 1.1 and 1.2). The stocking of recharge basins with fish, which is not common practice, represents a unique potential exposure pathway for migratory birds and humans to CECs. Fish clearly represent a "worst-case" scenario for exposure to CECs based upon constant immersion within water, which may contain CECs. As such, fish are typically viewed as excellent bioindicators of exposure (through bioaccumulation) and direct adverse effects of compounds in water.

Two CECs have received extensive attention in the ecotoxicology community: the synthetic estrogen 17α-ethinylestradiol (EE2) and the non-steroidal anti-inflammatory pharmaceutical diclofenac. Experimental exposure of fish to EE2 in a Canadian lake caused significant population declines in fish and dramatic declines in South Asia vulture populations were observed following use of diclofenac in cattle rearing. EE2 is a potent feminizing agent in egg-laying vertebrates. Studies in Canadian lakes indicated exposure to 5-6 ng/L to EE2 significantly diminished populations of fathead minnow after one year of exposure (Kidd, Blanchfield *et al*. 2007). Although laboratory studies have indicated other CECs may possess similar estrogenic activities, with the exception of EE2, no single CEC has demonstrated significant population declines in the field. However, based upon a recent review of measured and predicted concentrations of EE2 in surface water, it appears that the exposure concentration of 5-6 ng/l of EE2 in the Canadian lake experiment was five to ten times higher than the highest concentrations expected in US surface water and that typical concentrations are substantially lower than that (Hannah, D'Aco *et al*. 2009). Consequently, the experimental Canadian Lake observations are not likely to be representative of conditions in most US surface waters and the dramatic effects observed in that experimental setting are not expected in US surface waters as a result of normal human-use of EE2.

Because several species of fish are sometimes stocked within recharge basins that also serve recreational purposes (e.g., rainbow trout, largemouth bass, channel catfish), it is unclear whether fish populations are impaired within these systems. However, fish and other invertebrates within recharge basins may provide a means for dietary exposure to consumers in that "ecosystem". Given the relatively rapid half-life of EE2 in fish (~50 hr with a 1 mg/kg intravenous dose) (Schultz, Orner *et al*. 2001), accumulation would not be likely unless fish were undergoing continual exposure, which may result in "pseudo-persistent" conditions

[7] However, uncertainty exists with regard to the potential effects of CEC concentrates (aka "brine") resulting from reverse osmosis or other physical separation processes. In many cases, the brine streams are commonly blended with treated wastewater effluents prior to discharge to the ocean and virtually no published studies exist on their potential impacts. As noted above, the State Board, in cooperation with the Packard Foundation, established another Science Advisory Panel that was charged in January of 2010 to address questions related to CEC discharge to the ocean and exposure to human health and ocean life.)

(Daughton and Ternes 1999). Thus, although other species-dependent differences may be present, avian receptors should be free from risk due to dietary consumption of fish containing EE2. However, additional studies to confirm this hypothesis are necessary.

While limited ecological risk may exist from EE2 in natural settings, dietary exposure of avian receptors to other CECs in contaminated prey has been reported in Pakistan and India where populations of endangered vultures (*Gyps sp*.) were significantly impacted by the consumption of carrion derived from livestock treated with the non-steroidal anti-in flammatory drug diclofenac (Oaks, Gilbert *et al*. 2004). Daily intake concentrations necessary to exceed LD_{50} values in these species were approximately in the mg/kg range. However, relative to North American species of turkey vulture or other species of birds which are more resistant than *Gyps sp.*, more than 20-100 times greater concentrations of diclofenac would be necessary to observe similar pathological effects noted in *Gyps sp.* (Hussain, Khan *et al*. 2008). Given the ng/L concentrations of diclofenac observed in surface water or recycled water, and concentration-dependent bioconcentration factors (BCF) of 12–2732 in the liver, 5–971 in the kidney, 3–763 in the gills, and 0.3–69 in the muscle, respectively in rainbow trout (Schwaiger, Ferling *et al*. 2004), deterministic evaluations of exposure to effect indicate little risk to bird populations from diclofenac in the US. However, uncertainty continues to surround the potential risk of other CECs recently reported in fish across North America (Mottaleb, Usenko *et al*. 2009). While several recent studies have evaluated the effects of non-steroidal anti-in flammatory drugs in avian species, the effects of other CECs that accumulate in fish are limited. CECs that have shown elevated accumulation in fish are the synthetic fragrance musks of which galaxolide is a representative. Of additional concern is the effect of contaminant mixtures and unknown transformation products.

Irrigation of urban landscapes (e.g., golf courses and sports fields, and parks) with recycled water is a common practice in California. For example, one Northern California community typically utilizes 4,110 gallons/acre/day (0.15 inches/day[8]) applied from April to November (214 days) for golf-course and sports fields (California 2009)[9]. Assuming concentrations of ng/L of CECs, approximately 3.5 mg of CEC could be loaded to each acre in a given year. CECs with high K_{oc} values could bind to soils with high organic carbon content resulting in exposure to terrestrial organisms. Kinney *et al*. (2006a) evaluated the fate of 19 pharmaceutical residues in soils from 3 sites in Colorado irrigated with recycled water and reported loadings in the ng-μg level with measured concentrations ranging from 0.02 to 15 μg/kg dry soil. Several of the selected pharmaceuticals increased in total soil concentration at one or more of the sites. The four most commonly detected pharmaceuticals were erythromycin, carbamazepine, fluoxetine, and diphenhydramine. Given the low concentrations, uptake into terrestrial organisms, such as earthworms, would likely be limited. Kinney *et al*. (2008) evaluated uptake of multiple CECs

[8] Application rates will vary across the State (as well as across the nation) with more water utilized in dryer and hotter southern California climate conditions and less in northern climates. For comparison purposes, information from Texas regarding landscape irrigation indicates that application rates vary from roughly 1,500 gallons/acre/day to 5,000 gallons/acre/day (USDA, 1994).

[9] The City of Sunnyvale is located in the San Francisco Bay area. Sunnyvale has a mediterranean climate, with mild, moist winters and warm, very dry summers.

from biosolids into earthworms, bioaccumulation factors (BAFs) were relatively low and ranged from 0.05 (galaxolide) to 27 (triclosan). When concentrations of CEC in biosolids (mg/kg) are compared to concentration of soils treated with recycled water (μg/kg), bioaccumulation into terrestrial organisms seems unlikely especially with the limited BAFs. However, additional studies are needed to confirm these predictions and to better understand the effects of these compounds in trophic food webs.

Appendix C - Antibiotic Resistant Bacteria and Antimicrobials of Concern in Recycled and Drinking Water

The cause of the prevalence of drug resistant bacteria in the United States is controversial and drug resistance in bacteria may in fact have many origins. The Panel was not charged with this important question and suggests that further research into this problem is necessary and may require resources at the Federal level. Concerns that California drinking water augmentation projects may add to the problem of antibiotic-resistant bacteria containing antibiotics and antimicrobials in trace amounts are not likely to be a problem in California water recycling programs, but they are addressed specifically below. The antibiotics of most concern due to their persistence in water reclamation processes include sulfamethoxazole, trimethoprim, and erythromycin, while the antimicrobials include triclosan and triclocarban (Al-Ahmad, Daschner *et al*. 1999; Phillips, Casewell *et al*. 2004). The concentrations of these antibiotics and antimicrobials, and others, in finished water that is used for recharge projects are below levels that cause resistance to occur de novo (Watkinson, Murby *et al*. 2007) and thus are not likely to be the source of antibiotic resistance.

There is keen interest in the potential health effects of drug resistant microbes, which are already present in the environment, potentially becoming resistant because of exposure to low concentrations of antibiotics. At sub-inhibitory doses, antibiotics may lead to increased resistance in bacteria – but the concentrations found in recycled water are at least three orders of magnitude lower than the concentrations needed for resistance (Watkinson, Murby *et al*. 2007). Special interest has been focused in methicillin-resistant *Staphylococcus aureus* (MRSA), in which the mecA gene mediates resistance (Börjesson, Melin *et al*. 2009). The dynamics of how MRSA and other antibiotic resistant microbes may flourish in wastewater treatment plants has been the concern of many health providers and the public at large. Treatment processes at reclamation facilities effectively reduced the amount of both MRSA and the mecA gene, however, did not eliminate them (Börjesson, Melin *et al*. 2009). In terms of public health concerns, the MRSA is the most feared. However, other bacteria, such as *lysteria* or *E. coli*, can also impact human health, thus forms of these microbes that are resistant to antibiotics should also be investigated. There is no doubt that treatment through wastewater plants reduces the number of pathogenic bacteria (Harwood, Levine *et al*. 2005; Rijal, Zmuda *et al*. 2009; Zhang, Marrs *et al*. 2009); however, there is controversy in the literature as to whether the reduction is sufficient (Harwood, Levine *et al*. 2005; *Chang*, *Toghrol et al*. 2007)) and whether the coliform assays used as surrogates are sufficient (Zhang, Marrs *et al*. 2009).

In a study by Vilanova *et al*. (Vilanova, Manero *et al*. 2004) the structure and composition of fecal coliforms and enterococcal bacterial populations were investigated in wastewater from five treatment plants employing conventional processes to gauge the extent of forms that were resistant to vancomycin and erythromycin. The origin of waste and sewershed size varied for the five plants. Bacterial populations were similar at all five of the plants that were tested, including the fraction of bacteria that were resistant to antibiotics. The antibiotic resistant bacteria were not selectively eliminated by conventional treatment but they were reduced.

Advanced treatment processes were not tested in this study. Oxidation as well as low- and high-pressure membrane filtration are likely to remove more than 99% of the bacteria (Bockelmann, Dorries *et al*. 2009).

Findings from another study, conducted by the Metropolitan Water Reclamation District of Greater Chicago, supported the conclusion that secondary wastewater treatment effectively reduced the number of antibiotic resistant coliform bacteria and that the environments in the wastewater treatment facilities were not supportive of their growth (Rijal, Zmuda *et al*. 2009).

People who consume antibiotics can and will excrete some of the antibiotics consumed, but more importantly they will also excrete antibiotic resistant bacteria. Thus the presence of these bacteria in the influents is probably from human sources. The amount of antibiotics excreted by humans is diluted in the receiving waters to concentrations that are not likely to convert the bacteria in wastewater treatment plants to antibiotic resistance. But this point is controversial (Rijal, Zmuda *et al*. 2009; Zhang, Marrs *et al*. 2009) and deserves more study. The possibility exists for antibiotic resistant bacteria that are excreted from humans to either evade treatment or to transfer antibiotic resistance to other bacteria within the water reclamation plant (Zhang, Marrs *et al*. 2009). Clearly the existence and raising concentrations of antibiotic-resistant bacteria in the environment are a national problem that requires further study to understand their origins and how to control them, however, it is the view of the Panel that the specific water reuse practices described in this report do not cause the problem nor add to it at the present time.

Appendix D - Federal Paradigm for Regulating CECs in Drinking Water

History of Federal Regulation of Drinking Water

The US Congress enacted the Public Health Service Act in 1912, which initiated studies to elicit the link between clean drinking water and human health. In 1962 this legislation was revised as the US Public Health Services Drinking Water Standards Revisions, which established regulations for 28 contaminants. The American Water Works Association endorsed the 1962 standards as "minimum standards for all public water supplies". Subsequently, all 50 states accepted these standards as either guidelines or regulations. The 1962 drinking water standards also provided some insight into concerns related to impaired waters from unintentional water reuse. While the standards specifically state that "The water supply should be obtained from the most desirable source which is feasible", the document goes on the say that *"If the source is not adequately protected by natural means, the supply shall be adequately protected by treatment"*. Interestingly, the 1962 standards included alkyl benzene sulfonate (ABS), an anionic surfactant that was commonly used in detergents. The statement is made that *"waters containing ABS are likely to be at least 10 percent of sewage origin for each mg ABS/liter present".* Also of pertinent interest was the use of carbon chloroform extract (CCE) in the 1962 standards as an indicator of organic compounds in water. The CCE standard of 200 µg/L was established to *"represent an exceptional and unwarranted dosage of the water consumer with ill-defined chemicals"*. The ABS and CCE standards promulgated in 1962 demonstrate that the federal government understood that unintentional water reuse was indeed occurring and that the contamination of drinking water from a diversity of organic contaminants was possible. Moreover, these early standards began to pave the way for the use of chemical indicators and surrogate measurements in a regulatory framework. Congress created the USEPA in 1970 and subsequently authorized this branch of the federal government to ensure drinking water safety.

The Safe Drinking Water Act

In 1974, Congress passed the Safe Drinking Water Act (SDWA) to protect public health by regulating drinking water supplies. Throughout the United States, there were concerns that drinking water supplies were becoming tainted by industrial activities, agriculture, and wastewater effluents. The SDWA provides authority to the USEPA to establish and enforce national standards to protect against chemical and microbial health risks from drinking water. These national standards set enforceable maximum contaminant levels (MCLs) for biological and chemical contaminants, as well as treatment technologies in some cases, deemed to necessary for the protection of public health. The EPA drinking water standards require regular testing to assure that contaminants do not exceed their MCLs.

States can apply to the USEPA for primacy, which grants the particular state the right to implement the SDWA requirements within the state. Every state in the US except for Wyoming and the District of Columbia have applied for and been subsequently granted primacy. This means that the state will enforce SDWA compliance and has the right to require more stringent

regulations than those specified in the SDWA. For instance, the state of California recently established an enforceable drinking water MCL of 6 µg/L for perchlorate in the absence of a federal MCL.

The USEPA establishes national standards based on occurrence and risk to public health. The risk is estimated by establishing a health-based maximum contaminant level goal (MCLG) for the most sensitive population (i.e., children, pregnant women, the elderly, etc.). The MCLG is the level of a contaminant in drinking water below which no known or expected risk exists. The MCLG includes uncertainty factors (or safety factors) that are used to adjust for uncertainties or inadequacies in the data set used to develop the MCLG. The EPA then evaluates the types and costs of treatment to reduce the contaminant concentration and performs a cost-benefit analysis to identify an enforceable MCL as close to the MCLG as possible. The availability and reliability of analytical methods for detection and quantification of a contaminant may also influence the promulgated MCL. Additionally, every six years the EPA reviews the existing MCLs to determine if modifications are required based on new data or technology advancements.

Safe Drinking Water Act and Unregulated Contaminants

In order to assess the occurrence of contaminants suspected to impact drinking water, the USEPA established an Unregulated Contaminant Monitoring (UCM) program. The initial UCM round took place between 1988 and 1993, when 62 contaminants were monitored in 40 states. The resulting data became part of the Unregulated Contaminant Monitoring Information System (URCIS). The second round of UCM occurred between 1993 and 1997 and included data from 35 states on 48 (then) unregulated contaminants. In 1996, the SDWA was amended and the UCM program was significantly revised and a new Unregulated Contaminant Monitoring Regulation (UCMR) established. Under the UCMR the USEPA requires all large systems (>10,000 customers) and a representative number of small systems (<10,001 customers) to monitor for no more than 30 unregulated contaminants specified by the EPA. Contaminants detected under the UCMR must be reported to customers in a Consumer Confidence Report issued by the system and reviewed by the state. The USEPA is required to review and update the UCMR every five years. The first UCMR (UCMR1) was issued in September 1999 and the second UCMR (UCMR2) was issued in January 2007. UCMR data are entered into the National Contaminant Occurrence Database (NCOD).

The 1996 SDWA Amendments also mandated that the EPA publish a Candidate Contaminant List (CCL) every five years. The CCL contains contaminants that are known, or anticipated, to occur in US drinking waters and that may require future regulation. Specifically, the CCL must address contaminants that:

1) are not currently regulated under the SDWA
2) may have adverse health effects
3) are known or anticipated to occur in public water systems
4) may require regulation under the SDWA

The USEPA selects up to 30 contaminants from the CCL for the UCMR; however, other contaminants may be added to the UCMR that were not included on a CCL. Every five years the USEPA must repeat the cycle of revising the CCL, make regulatory determinations for at least five of the CCL contaminants, and identify up to 30 contaminants for the UCMR. The USEPA released the first CCL (CCL1) containing 60 contaminants (50 chemical and 10 biological) in March 1998. The CCL1 specifically deferred the listing of 21 contaminants identified in the draft CCL as endocrine disruptors since the 1996 SDWA amendments specifically provided for the establishment of the Endocrine Disruptor Screening Program (EDSP). After the release of CCL1, the USEPA asked the National Research Council (NRC) for guidance in establishing a system to prioritize contaminants listed on the CCL (NRC 1999). The USEPA also asked the NRC to provide advice regarding the development of subsequent CCL's by systematically identifying and prioritizing emerging contaminants. The NRC suggested that within one year of a CCL release, the USEPA use a three-part assessment for each contaminant listed. The suggested process would: 1) review existing health effects data, 2) review existing exposure data, and 3) review existing data on treatment and analytical methods. From these data, the NRC suggested that USEPA should then conduct a preliminary risk assessment followed by a separate decision document which indicates whether a contaminant is to be dropped from the list, be slated for additional research, or will be considered for regulation. The NRC further advised USEPA to conduct health advisories for all compounds that will remain on the CCL within three months after completion of initial decision documents.

The NRC held a workshop on emerging drinking water contaminants in December of 1998 in conjunction the NRC Committee on Drinking Water Contaminants. The purpose of the workshop was *"to present and discuss a dozen papers on emerging microbial and chemical drinking water contaminants, associated analytical and treatment methods, and existing and proposed environmental databases for their proactive identification and evaluation"*. In 1999, the NRC published a report based on the workshop and subsequent deliberations of the committee (NRC 1999). The committee suggested that ideal CCLs should include the following:

- Meet the statutory requirements of the 1996 SDWA amendments;
- Identify the *"entire universe of drinking water contaminants"* before ranking;
- Consider all routes of exposure, including dermal, inhalation, and ingestion;
- Use the same identification and selection process for chemical and microbial contaminants;
- Include mechanisms to identify similarities among contaminants and contaminant classes that can be used for evaluation of individual chemicals; and,
- Result in a CCL that contains only contaminants that are truly relevant to human health.

The committee recommended a two-step process that would prioritize chemicals from a broad universe to a preliminary CCL (PCCL) through screening criteria and expert judgment followed by use of a prioritization tool and expert judgment to develop the final CCL. The

committee estimated that the number of contaminants in the "chemical universe" could be close to 100,000 considering that the Toxic Substances Control Act inventory alone includes approximately 72,000 substances produced or imported at greater than 10,000 pounds/year. In 2001, the NRC published a report that provided more detailed information regarding the suggested approaches for moving contaminants from the universe to the PCCL and eventually to the CCL (NRC 2001). This NRC report suggested the use of selected attributes to evaluate the likelihood of a particular contaminant occurring at a concentration pose risk to public health through drinking water. This report also suggested the use of an algorithm in conjunction with expert opinion to more quickly and efficiently sort through vast amounts of data. In relationship to water reuse, the NRC committee specifically recommended the inclusion of *"any constituent of wastewater treatment of septage"* within the chemical universe. The committee also recommended the use of virulence-factor activity relationships, within which microorganisms, which have the *"ability to survive wastewater treatment and to reenter drinking water"*, are specifically addressed. The NRC reports became the foundation for the USEPA's CCL process, but were not adopted in time for the development of the second CCL (CCL2).

The CCL2 was published in February 2005 and contained 51 of the original 60 contaminants from CCL1. The USEPA determined that regulations were not required for the nine compounds, which were removed from CCL1. In order to move a contaminant from the CCL into regulation, the USEPA must show that regulation would provide a meaningful opportunity to reduce health risk. While the NRC emerging contaminant identification and prioritization scheme was not utilized for CCL2, the process would become largely utilized for the generation of the third CCL (CCL3).

The Candidate Contaminant List 3

The process used to develop the CCL3 was far more systematic and objective than the more subjective selection of contaminants used for CCL1 and CCL2. The CCL3 selection process utilized the expert opinions provided by the NRC as well as the National Drinking Water Advisory Council (NDWAC). This multi-step process includes three key elements:

- Identification of a broad universe of potential biological chemical and chemical contaminants (CCL Universe);
- Application of screening criteria based on potential occurrence and human health relevance (preliminary CCL or PCCL); and,
- Selection of priority contaminants based on more detailed occurrence and health effect data as well as expert judgment, public comment, and external advisory committees (draft and final CCL).

CCL3 Universe

A draft of the CCL3 was released in February of 2008 and the final CCL3 was published in October of 2009 (Table D-1). Figure D.1 in the main text illustrates the general process utilized in the development of the CCL3. The CCL3 Universe is to encompass a wide array of potential

water contaminants, both chemical and microbial. The Universe includes not only compounds known or anticipated to occur in water supplies, but also releases to the environment and production volume. Additionally, the Universe is to include contaminants with demonstrated or adverse health effects, regardless of occurrence data. Due to the wide array of potential data, the USEPA chose to follow the advice of the National Drinking Water Advisory Council, in relying primarily on easily accessible databases for the information that would be used to generate the CCL3 Universe. The accessibility became a highly limiting factor, as any database to be used must be electronically accessible and free of charge. The EPA initially identified some 284 potential databases from which they could rely for populating the CCL3 Universe (http://www.epa.gov/safewater/ccl/pdfs/ccl3_docs/CCL3_Chemicals_Universe_08-31-09_508_v3.pdf); however, these databases were culled based on relevance, completeness, redundancy, and retrievability (Figure D-1). Of the 284 databases initially identified, 142 were eliminated due to relevance, 12 eliminated due to completeness, 26 eliminated due to redundancy, and 64 eliminated due to retrievability. In terms of relevance, several databases were found to contain only descriptive data such as used for pesticide labeling or nomenclature that is not related to occurrence or toxicity were not utilized. Completeness was gauged based on minimum documentation and quality requirements, such as contact information, description of data elements, information on how data were obtained, and whether or not data were peer-reviewed. Redundancy was assessed to avoid duplication and when redundant data was found, the more comprehensive database was utilized. Retrievability was a major limitation for database inclusion, and databases that provided information in tabular format that could be extracted and formatted was used while databases providing information in text format were generally not considered. However, databases with simple lists in text format that could be easily imported were sometimes used. Due to transparency concerns, databases that were available only by subscription (fees) or were proprietary were not utilized. Ultimately only 40 databases were utilized (Table D-2). The limitations on the databases that were screened are likely the greatest hindrances in utilizing the CCL3 for prioritization of CECs in reuse systems. While some databases are clearly relevant, much of the data published in peer-reviewed literature and in various reports would not have been considered in the CCL3 Universe.

Table D-1. List of Contaminants on USEPA's CCL3

Common Name - Registry Name
1,1,1,2-Tetrachloroethane
1,1-Dichloroethane
1,2,3-Trichloropropane
1,3-Butadiene
1,3-dinitrobenzene
1,4-Dioxane
17-a-estradiol
17-b-estradiol
1-Butanol
2-Methoxyethanol
2-Propen-1-ol
3-Hydroxycarbofuran
4,4'-Methylenedianiline
Acephate
Acetamide
Acetochlor
Acetochlor ethane sulfonic acid (ESA)
Acetochlor oxanilic acid (OA)
Acrolein
Alachlor ethanesulfonic acid (ESA)
Alachlor OA
alpha.-Hexachlorocyclohexane
Aniline
Bensulide
Benzyl chloride
bromochloromethane
Captan
chlorate
Chloromethane (Methyl chloride)
Clethodim
Cobalt
Cumene hydroperoxide
Cyanotoxins
Dicrotophos
Dimethipin
Dimethoate
Disulfoton
Diuron
equilenin
equilin
Erythromycin

estriol
estrone
ethinyl estradiol
Ethoprop
Ethylene glycol
Ethylene oxide
Ethylene thiourea
Fenamiphos
Formaldehyde
Germanium
HCFC-22
Hexane
Hydrazine
Methamidophos
Methanol
Methyl bromide Bromomethane
Methyl tert-butyl ether
Metolachlor
Metolachlor ESA
Metolachlor OA
mestranol
Molinate
Molybdenum
Nickel
Nitrobenzene
Nitroglycerin
N-Methyl-2-pyrrolidone
N-Nitrosodiethylamine
N-nitrosodiethylamine (NDEA)
N-nitrosodimethylamine (NDMA)
N-nitroso-di-n-butylamine (NDBA)
N-nitroso-di-n-propylamine (NDPA)
N-nitrosomethylethylamine (NMEA)
N-nitrosopyrrolidine (NPYR)
norethindrone
n-Propylbenzene
o-Toluidine
Oxirane, methyl-
Oxydemeton-methyl
Oxyfluorfen
Perchlorate
Permethrin
PFOA
PFOS
Profenofos

Quinoline
RDX (Hexahydro-1,3,5-trinitro-1,3,5-triazine)
sec-Butylbenzene
Strontium
Tebuconazole
Tebufenozide
Tellurium
Terbufos
Terbufos sulfone
Thiodicarb
Thiophanate-methyl
Toluene diisocyanate
Tribufos
Triethylamine
Triphenyltin hydroxide (TPTH)
Urethane
Vanadium
Vinclozolin
Ziram

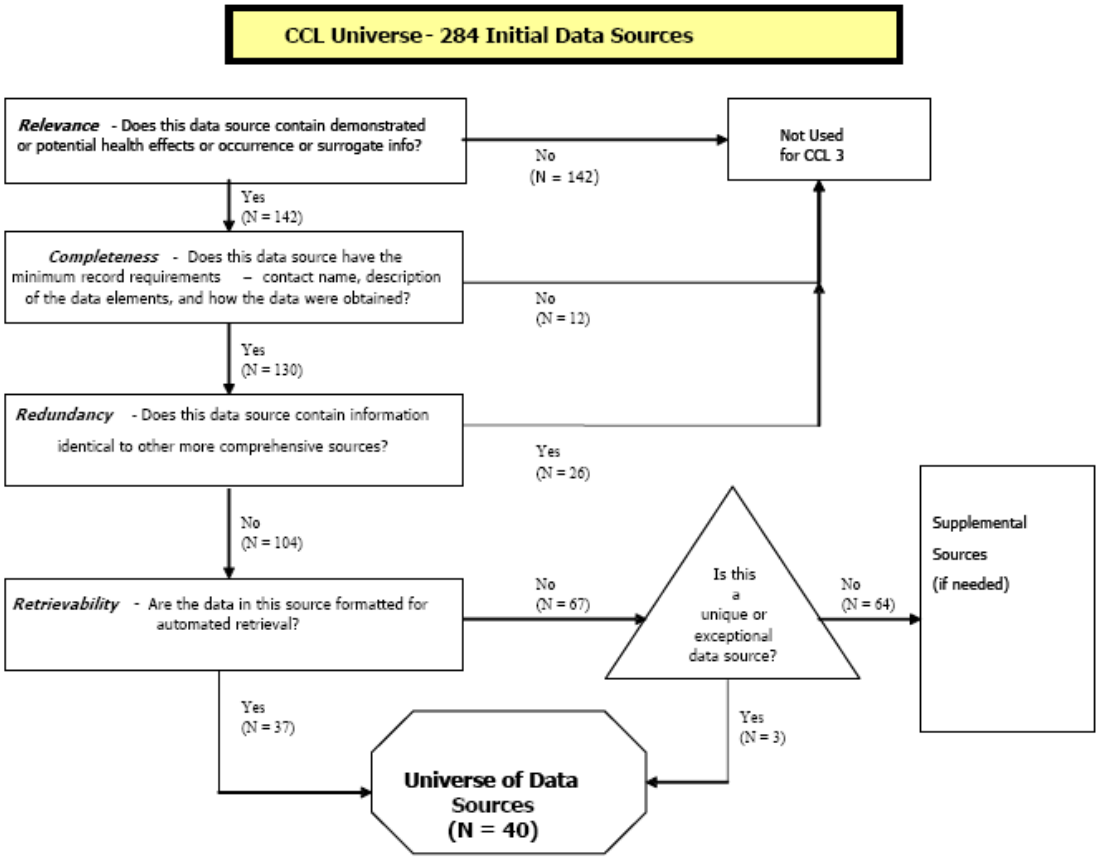

Figure D-1. Databases utilized in the CCL3 selection process

Table D-2. Data sources utilized for defining the USEPA CCL3 universe

	Name of Data Source
1	Agency for Toxic Substances and Disease Registry (ATSDR) Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) Priority List
2	ATSDR Minimal Risk Levels (MRLs)
3	Chemical Toxicity Database - Ministry of Health and Welfare, Japan
4	Chemical Update System/Inventory Update Rule (CUS/IUR) – EPA
5	Cumulative Estimated Daily Intake/Acceptable Daily Intake (CEDI/ADI) Administration (FDA) Database – US Food and Drug
6	Database of Sources of Environmental Releases of Dioxin-Like Compounds in the United States – EPA
7	Distributed Structure Searchable Toxicity Public Database Network (DSSTox) – EPA
8	Everything Added to Food in the United States (EAFUS) Database – FDA
9	Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) List – EPA
10	Generally Regarded As Safe (GRAS) Substance List – FDA
11	Guidelines for Canadian Drinking Water Quality (CADW): Summary of Guidelines – Health Canada
12	*Hazardous Substances Data Bank (HSDB) – National Library of Medicine (NLM)*
13	Health Advisories (HA) Summary Tables – EPA
14	High Production Volume (HPV) Chemical List – EPA
15	Indirect Additives Database – FDA
16	Information Collection Rule (ICR) Federal Database (DBP ICR) – EPA
17	Integrated Risk Information System (IRIS) – EPA
18	*International Agency for Research on Cancer (IARC) Monographs*
19	International Toxicity Estimates for Risk (TERA) (ITER) Database – Toxicology Excellence in Risk Assessment
20	Joint Meeting On Pesticide Residues (JMPR) - 2001 Inventory of Pesticide Evaluations – Organization (WHO), Food and Agriculture Organization (FAO)
21	National Drinking Water Contaminant Occurrence Database (NCOD) - Round 1&2 – EPA
22	NCOD - Unregulated Contaminant Monitoring Regulation (UCMR) – EPA
23	National Inorganics and Radionuclides Survey (NIRS) – EPA
24	National Pesticide Use Database – National Center for Food and Agricultural Policy (NCFAP)
25	National Reconnaissance of Emerging Contaminants (NREC) Toxic Substances Hydrology Program – United States Geological Survey (USGS)
26	*National Toxicology Program (NTP) Studies*
27	National Water Quality Assessment (NAWQA) – USGS
28	OSHA 1988 Permissible Exposure Limits (PELs) – National Institute for Occupational Safety and Health (NIOSH)
29	Pesticide Data Program (PDP) – United States Department of Agriculture (USDA)
30	Pesticides Pilot Monitoring Program (PPMP) - USGS/EPA
31	Risk Assessment Information System (RAIS) - Department of Energy - Chemical Factors
32	RAIS - Department of Energy - Health Effects Data
33	State of California Chemicals Known to the State to Cause Cancer or Reproductive Toxicity
34	Substances Registry System (SRS) – EPA
35	Syracuse Research Corporation (SRC) – BIODEG
36	The Toxics Release Inventory (TRI) – EPA
37	Toxic Substances Control Act (TSCA) List – EPA
38	Toxicity Criteria Database - California Office of Environmental Health Hazard Assessment (OEHHA)
39	University of Maryland - Partial List of Acute Toxins/Partial List of Teratogens
40	WHO Guidelines for Drinking Water Quality: Summary Tables

From the 40 databases screened, nearly 26,000 substances were identified. Therefore, USEPA developed a pre-Universe selection process to evaluate those compounds that were most suitable for inclusion in the Universe (Figures D-2 and D-3). The initial process essentially determined whether or not a contaminant had health effects (HE) and occurrence data. If only HE data were available, these contaminants would be screened to determine if the contaminant was toxicologically relevant (see section of PCCL process regarding relevance). Chemicals for which only occurrence data were available were sequentially evaluated for finished or ambient source water data, release data, or production of over 1 billion pounds/year (Table D-3). This pre-Universe selection process identified 7,720 chemicals, which went on to the final selection process shown in Figure D-3. The final selection process first evaluated whether or not primary drinking water standards already existed, which eliminated 1,009 chemicals (mostly radionuclides and compounds with multiple isomers, such as PCBs). Four hundred and thirty substances that are considered mixtures, such as petroleum products and resin acids, were eliminated from further consideration. Also, substances that are not "chemically defined" (such as wood dust and surgical implants) were eliminated. Lastly, two substances were removed because they are considered biological and would not be considered within the chemical Universe. The USEPA also considered 174 contaminants that were nominated through the public input process and 132 of those nominated were already considered. The remaining nominations were evaluated through the same criteria as all other chemicals for consideration of the CCL3 Universe. Once the draft CCL3 was released in February of 2008, USEPA subsequently received 177 comments. From these comments, 30 additional contaminants were added to the Universe.

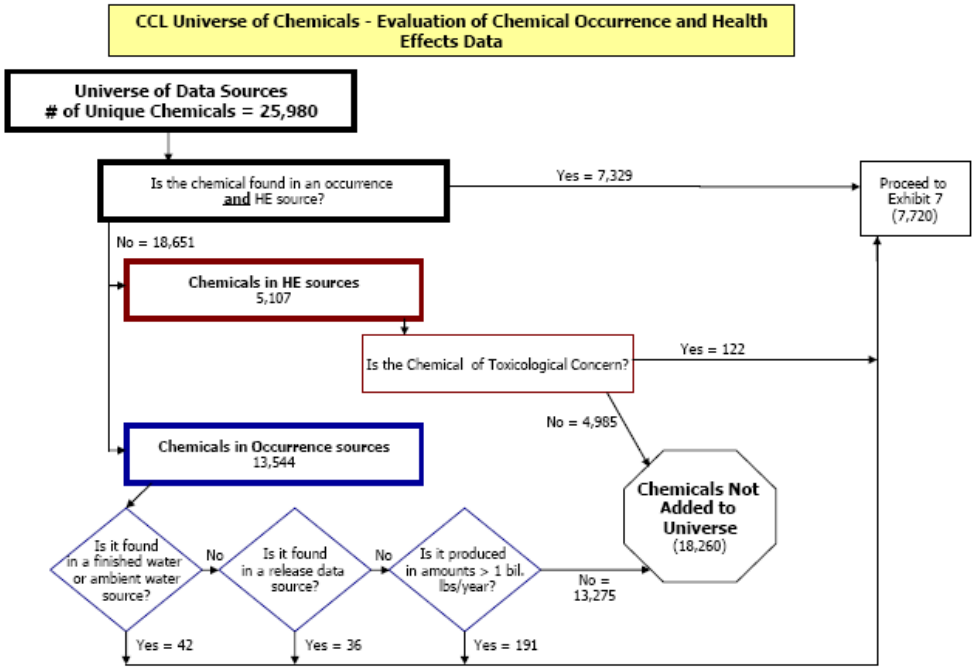

Figure D-2. Initial process for selecting the CCL3 Universe

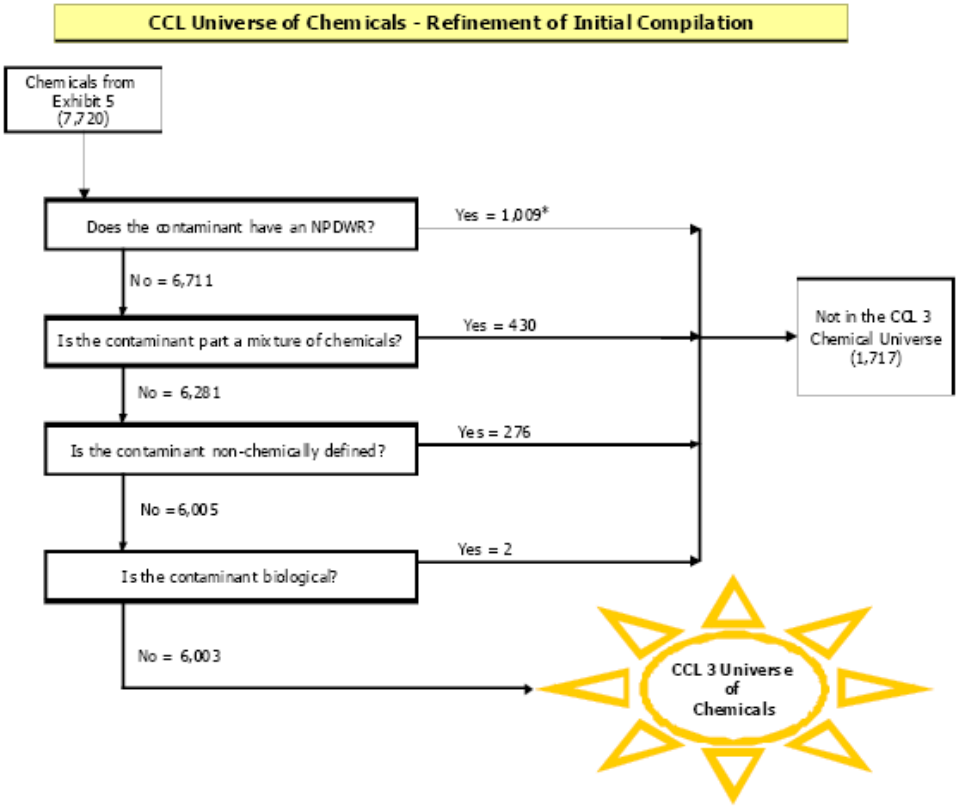

Figure D-3. Final selection process for CCL3 Universe (Exhibit 7)

Table D-3. Occurrence data sources without health effects

Occurrence Data Type	Type of Data; Typical Source	Number of Chemicals without Health Effects
Finished and ambient water quality data	Measured water occurrence; UCMR; NAWQA	42
Environmental release	Amount released; TRI; pesticide application	36
Production	Annual production volume; CUS/IUR	9,344
Listed as food additive or only on list with general physical or chemical properties	Generally regarded as safe substance list (FDA); RAIS (DOE)	4,122

The PCCL screening process

The next stage in the development of the CCL3 was the screening of the chemical universe to create a preliminary candidate contaminant list (PCCL) based on health and occurrence data. The PCCL prioritization scheme categorizes the information available from the Universe into toxicity and occurrence data elements, which are subsequently weighed on a variety of key factors. For health effects data elements, the two key categories are potency (dose-response) and severity (mostly carcinogenic potential). Although the availability of a lowest observed adverse effect level (LOAEL) was most desirable, other types of data were also considered for the PCCL. The health effects data were segregated into five toxicity categories based upon the type of data and potency (Table D-4). For carcinogens, the USEPA relied upon categorical data for the probability of cancer and usually included slope factors. These data also were segregated into toxicity categories for inclusion in the PCCL selection process (http://www.epa.gov/safewater/ccl/pdfs/ccl3_docs/CCL3Chem_Screening_to_PCCL_08-31-09_508v2.pdf).

Table D-4. Potency Measures for toxicity categories

(from http://www.epa.gov/safewater/ccl/pdfs/ccl3_docs/CCL3Chem_Screening_to_PCCL_08-31-09_508v2.pdf)

	RfD	NOAEL	LOAEL	MRDD	LD_{50}
Toxicity Category 1	<0.0001	<0.01	<0.01	<0.01	<1
Toxicity Category 2	0.0001 - <0.001	0.01 - < 1	0.01 - <1	0.01 - < 1	1 - <50
Toxicity Category 3	0.001 - <0.05	1 - <10	1 - <10	1 - <10	50 - <500
Toxicity Category 4	0.05 - <0.1	10 - < 1000	10 - <1000	10 - < 1000	500 - <5000
Toxicity Category 5	≥0.1	≥1000	≥1000	≥1000	≥5000

In order to evaluate occurrence, the USEPA considered data from measured concentrations in ambient and finished water, total releases to the environment (from state data), pesticide application rates, and production volume. The USEPA also considered descriptive data, which includes compounds, such as disinfection byproducts and drinking water treatment chemicals. For both finished and ambient water quality data, the USEPA considered the percent of samples with detections, percent of sites with detections, and the median, maximum, and mean concentrations detected. In addition, the USEPA considered Toxics Release Inventory and the National Pesticide Use Database to determine total releases to the environment (lbs/year), number of states with documented releases, pesticide application (lbs/year), and number of states with pesticide application. Data from the Toxic Substances Control Act (TSCA) production volume data reported in the Chemical Update System/Inventory Update Rule, which includes USEPA's High Production Volume chemicals list, was also considered in the exposure assessment. Disinfection byproducts and water treatment chemical information was gathered from DSS-Tox database and he NSF standard 60, respectively. Because of the high propensity for DBPs and water treatment chemicals to persist in drinking water, the USEPA moved these categories forward for consideration to PCCL even when limited occurrence data were available (as long as they fell into toxicity categories 1 or 2). Because occurrence data often fall into

multiple categories (i.e., finished water concentration and production volume data), the USEPA established the following hierarchy:

Finished Water = Ambient Water > Environmental Release Data > Production Data

This hierarchy becomes especially important in the discussion of the inclusions of steroid hormones in the final CCL3, since finished drinking water measurements were essentially non-detectable (Benotti *et al*. 2009) yet ambient water concentrations used by USEPA were extremely large. This means that water treatment is not considered in the selection of the CCL3 and the most conservative values are used in the prioritization.

An integrated assessment combining the occurrence and health effects data are provided in Table D-5. The asterisks in Table D-5 signify where calculated drinking water equivalent levels (DWEL) thresholds fell within each toxicity category. For instance, for category 1 toxicity (most toxic), any concentration or even non-detect would move the chemical into the PCCL. While in toxicity category three, the DWEL threshold was calculated to be 40 µg/L. Therefore, the bold line that separates the grey from the white area in Table D-5 is the dividing line between PPCL inclusion (white) and PPCL exclusion (grey).

Table D-5. Comparing health effects to ambient & finished water concentrations for PCCL (from http://www.epa.gov/safewater/ccl/pdfs/ccl3_docs/CCL3Chem_Screening_to_PCCL_08-31-09_508v2.pdf)

Screening Health Effects Categories	Occurrence – Finished Water – Concentration (µg/L)						
	0-<0.1	0.1-<1	1-<10	10-<100	100-<1,000	1K-<10K	≥10K
Toxicity Category 1							
Toxicity Category 2			*				
Toxicity Category 3				*			
Toxicity Category 4						*	
Toxicity Category 5						*	

A similar PPCL inclusion/exclusion scenario was developed for comparing release data to toxicity categories (Table D-6). Again, the shaded area indicates compounds not included in the PCCL while the white areas indicate inclusion on the PCCL. For instance, a compound released at 900,000 lbs/year in toxicity category 4 would not be considered for the PCCL, while a compound with the same release but in toxicity category 3 would be included.

Table D-6. Comparing health effects to release data for PCCL (from http://www.epa.gov/safewater/ccl/pdfs/ccl3_docs/CCL3Chem_Screening_to_PCCL_08-31-09_508v2.pdf)

Screening Health Effects Categories	Occurrence – Environmental Release Category – Total Environmental Releases (lbs/year)							
	0 - <10	10 - <100	100 -<1K	1K - <10K	10K - <100K	100K<1M	1M - <10M	≥10M
Toxicity Category 1								
Toxicity Category 2								
Toxicity Category 3								
Toxicity Category 4								
Toxicity Category 5								

An analogous assessment was performed for production volume data (Table D-7). Once again, the shaded area represents compounds that would not be considered for PCCL while the white areas indicate compounds that would be included on the PPCL.

Table D-7. Comparing health effects to production data for PCCL (from http://www.epa.gov/safewater/ccl/pdfs/ccl3_docs/CCL3Chem_Screening_to_PCCL_08-31-09_508v2.pdf)

Screening Health Effects Categories	Occurrence - Production Category (lbs/year)								
	<10K	10K-500K	>500K-1M	>1M-10M	>10M-50M	>50M-100M	>100M-500M	>500M-1B	>1B
Toxicity Category 1									
Toxicity Category 2									
Toxicity Category 3									
Toxicity Category 4									
Toxicity Category 5									

After the initial screening, USEPA applied quality assurance measures and conducted detailed evaluations of those chemicals falling near the border between inclusion and exclusion on the PPCL. Using this approach, the USEPA screened the chemical Universe of more than 6,000 compounds and selected 561 for consideration on the PCCL. The complete list of PCCL chemicals along with their corresponding data sheets can be found at http://www.epa.gov/safewater/ccl/pdfs/ccl3_docs/Final%20PCCL%203%20Contaminant%20Information%20Sheets.pdf.

From PCCL to CCL

From the 561 chemicals included on the PCCL, the USEPA applied classification models based on past expert decisions and advice from the NRC and NDWAC. The USEPA classified chemicals based on attributes based on similarities of qualities or traits that are indicative of propensity for occurrence and health effects. Several algorithms were then developed and evaluated to provide for rapid and reproducible prioritization. Once attributes were established and a suitable algorithm applied, the USEPA used expert review as a final analysis prior to releasing the draft CCL.

The USEPA used the attributes of potency and severity to describe health effects and the attributes of prevalence and magnitude to describe occurrence. In the absence of occurrence data, the USEPA sometimes used persistence and mobility environmental fate properties. Attributes given a numerical scoring system (where higher numbers equate to greater concern) in order to assess the relative importance of a particular attribute for each chemical.

Health effects attributes of severity and potency are interrelated. Potency represents the lowest dose of a chemical that induces an adverse effect, while severity is the adverse health effect and is ranked according to significance (i.e., cancer versus skin irritation). A rather detailed and lengthy description of how potency and severity attribute scores were determined is provided at http://www.epa.gov/safewater/ccl/pdfs/ccl3_docs/CCL3_PCCLtoCCL_08-31-09_508.pdf. In brief, potency scores ranged from 1 – 10 and were generally based upon reference doses (RfD), LOAEL/NOAEL, LD_{50}, and cancer risk (Table D-8). The severity attribute scoring is far more complex and perhaps more subjective (Table D-9). For detailed descriptions regarding severity scoring, see Exhibit A.3 at http://www.epa.gov/safewater/ccl/pdfs/ccl3_docs/CCL3_PCCLtoCCL_08-31-09_508.pdf.

For occurrence attributes, both prevalence and magnitude are considered. Prevalence scoring is essentially the frequency of occurrence or release/production, and is based upon both a hierarchy as discussed previously (Table D-6). Magnitude is essentially the quantity of concentrations reported, application/release data, or persistence/mobility data (Table D-10). In order to determine the persistence/mobility score, the corresponding value from Table D-11 and Table D-12 are averaged and the averaged value multiplied by 10/3 in order to determine persistence/mobility attribute score (Table D-13).

Table D-8. Potency attributes

(from http://www.epa.gov/safewater/ccl/pdfs/ccl3_docs/CCL3_PCCLtoCCL_08-31-09_508.pdf)

SCORE	RfD mg/kg-day	LOAEL/NOAEL mg/kg-day	LD50 mg/kg	10^{-4} Cancer Risk
10	0 - 0.000000316	0 - 0.000316	0 - 0.0316	0 - 0.00000316
9	0.000000317 - 0.00000316	0.000317 - 0.00316	0.0317 - 0.316	3.17E-06 - 0.0000316
8	0.00000317 - 0.0000316	0.00317 - 0.0316	0.317 - 3.16	3.17E-05 - 0.000316
7	0.0000317 - 0.000316	0.0317 - 0.316	3.17 - 31.6	0.000317 - 0.00316
6	0.000317 - 0.00316	0.317 - 3.16	31.7 - 316	0.00317 - 0.0316
5	0.00317 - 0.0316	3.17 - 31.6	317 - 3,160	0.0317 - 0.316
4	0.0317 - 0.316	31.7 - 316	3,170 - 31,600	0.317 - 3.16
3	0.317 - 3.16	317 - 3,160	31,700 - 316,000	3.17 - 31.6
2	3.17 - 31.6	3,170 - 31,600	317,000 - 3,160,000	31.7 - 316
1	31.7 - >31.7	31,700 - >31,700	3,170,000 - >31,700,000	317 - >317

Table D-9. Severity attribute generalize scoring

Severity Score	Score Definition
1	No Adverse Effect
2	Cosmetic Effect
3	Reversible Effects
4	Cellular/Physiological Changes that Could Lead to Disorders
5	Significant Functional Changes that are Reversible or Permanent Changes that are of Minimal Toxicological Significance
6	Significant, Irreversable, Nonlethal Conditions or Disorders
7	Developmental or Reproductive Effects Leading to Major Dysfunction
8	Tumors or Disorders Likely Leading to Death
9	Death

Table D-10. Hierarchy and attribute score for prevalence

	Hierarchy				
	1	2	3	4	5
Prevalence Score	% Finished Water PWSs with detections of contaminant All PWSs	% Ambient water sites with detections of contaminant All sites/samples	# States Reporting Pesticide in Use	# of States Reporting TRI total releases	CUS/IUR (production data) Number of pounds (by category) produced
1	<=0.10	<=0.10	--	1	<500K
2	0.11-0.16	0.11-0.16	--	2	--
3	0.17-0.25	0.17-0.25	Default for any pesticide in non-environmental use	3	>500K-1M
4	0.26-0.44	0.26-0.44	--	4	--
5	0.45-0.61	0.45-0.61	Default for any pesticide in environmental use without data	5	>1M-10M
6	0.62-1.00	0.62-1.00	<6	6	>10M-50M
7	1.01-1.30	1.01-1.30	6-10	7-10	>50M-100M
8	1.31-2.50	1.31-2.50	11-15	11-15	>100M-500M
9	2.51-10.00	2.51-10.00	16-25	16-25	>500M-1B
10	>10.00	>10.00	>25	>25	>1B

Table D-11. Hierarchy and attribute score for magnitude

	Hierarchy				
	1	2	3	4	5
Magnitude Scale	Finished Water Occurrence Scale	Ambient Water Occurrence Scale	Pesticide Use Scale	TRI Total Releases Scale	Persistence/ Mobility
Data Used to Score	Median of detections - all PWSs	Median of detections - all sites/samples	Number of pounds applied	Total number of pounds released	
Units	µg/L	µg/L	lbs	lbs	Used when Production data are used to score for prevalence. See Persistence/ Mobility protocol (Exhibit A.8)
Score					
1	<0.003	<0.003	<10,000	<300	
2	0.003 - 0.01	0.003 - 0.01	- -	301-1,000	
3	>0.01 - 0.03	>0.01 - 0.03	10,000-30,000	1,001-3,000	
4	>0.03 - 0.1	>0.03 - 0.1	30,001-100,000	3,001-10,000	
5	>0.1 - 0.3	>0.1 - 0.3	100,001-300,000	10,001-30,000	
6	>0.3 - 1	>0.3 – 1	300,001-1M	30,001-100,000	
7	>1 - 3	>1 – 3	1M - 3M	100,001-300,000	
8	>3 - 10	>3 – 10	3M - 10M	300,001-1M	
9	>10 - 30	>10 – 30	10M - 30M	1M - 3M	
10	>30	>30	>30M	>3M	

Table D-12. Mobility scale

	Units	1 (Low)	2 (Medium)	3 (High)
Organic Carbon Partitioning Coefficient (Koc)	mL/g	>1,000	100-1,000	<100
Log Octanol/Water Partitioning Coefficient (Kow)	dimensionless	>4	1-4	<1
Soil/Water Distribution Coefficient (Kd)	mL/g	>10	1-10	<1
Henry's Law Coefficient (Kh)	atm-m3/mol	$>10^{-3}$	10^{-7} - 10^{-3}	$<10^{-7}$
Henry's Law Coefficient (Kh)	dimensionless	>0.042	$0.042\text{-}4.2\times10^{-6}$	$<4.2\times10^{-6}$
Solubility	Mg/L	<1	1-1,000	>1,000
Percent in water (PBT Profiler)	dimensionless	≤ 25	>25-50	> 50

Table D-13. Persistence scale

	Units	1 (Low)	2 (Medium)	3 (High)
Half Life ($t_{1/2}$)	Time	days	months	recalcitrant
Measured Degradation Rate	Time	days	months	recalcitrant
Modeled Degradation Rate (PBT Profiler)	Time	days	months	recalcitrant

Once the attributes had been assigned for all PCCL chemicals, these attributes were evaluated using three preferred models to determine list, no list, or questionable status for CCL3. The three models were Artificial Neural Network (ANN), Classification Tree with Linear Nodes (Quest), and Linear Regression (Linear). USEPA experts then evaluated the model output and further evaluated the chemicals by calculation of a health reference level (HRL). Table D-14 provides the equations used by the EPA, with corresponding uncertainty factors, for the calculation of the HRL. Note that a relative source contribution of 0.2 is used in each of the non-cancer equations. The HRL is then compared to the 90th percentile concentration in ambient or finished water. For compounds without measured data (primarily pesticides) the USEPA would use an estimated environmental concentration calculated from models. If the corresponding ratio between the HRL and the occurrence value was less than or equal to 10, the USEPA would list the contaminant on the draft CCL3.

Another post-model evaluation was the relative ranking of certainty of the data into low, medium, and high certainty based upon the type of data that was used to assign attributes. For instance, measured concentrations coupled with reference doses or cancer slope factors were considered high certainty, while health effects based on LD_{50} and occurrence based on production volumes were considered low certainty.

The draft CCL3 was reviewed by an external panel of experts and stakeholders, and then published on February 21st, 2008 in Federal Register. The final CCL3 included 106 chemicals, including:

- 36 chemicals in the high certainty bin;
- 23 pesticides in the medium certainty bin (with modeled occurrence data);
- 26 pesticides and chemicals in the medium certainty bin (with application or release occurrence data); and,
- 19 chemicals originally in the low or medium certainty bin that USEPA reevaluated using supplemental data (including data from commentators)

Table D-14. Derivation of the health reference level (HRL) (from http://www.epa.gov/safewater/ccl/pdfs/ccl3_docs/CCL3_PCCLtoCCL_08-31-09_508.pdf)

Non-Cancer Equations
$\text{HRL, mg/L} = \frac{\text{RfD (mg/kg/day) x BW (70 kg) x RSC (0.2)}}{\text{2 L/day}}$
$\text{HRL, mg/L} = \frac{\text{NOAEL (mg/kg/day) x BW (70 kg) x RSC (0.2)}}{\text{2 L/day x UF (1,000)}}$
$\text{HRL, mg/L} = \frac{\text{LOAEL (mg/kg/day) x BW (70 kg) x RSC (0.2)}}{\text{2 L/day x UF (3,000)}}$
$\text{HRL, mg/L} = \frac{\text{LD}_{50}\text{ (mg/kg)) x BW (70 kg) x RSC (0.2)}}{\text{2 L/day x UF (100,000)}}$
Cancer Equations
$\text{HRL, mg/L} = \frac{\text{Risk } (10^{-6}) \text{ x BW (70 kg)}}{\text{Slope Factor x 2 L/day}}$
$\text{HRL, mg/L} = 10^{-4}\text{ Cancer Risk (mg/L) x 0.01}$

The Panel found the CCL process utilized by USEPA, and developed in consultation with the NAS, NDWAC, SAB, and various expert panels, to be rigorous and transparent. However, the Panel recognizes that the key missing elements are mostly related to the data appropriate to California recycled water. The CCL databases would not have commonly captured the MEC data from California utilities nor have captured the majority of water reuse literature such as WateReuse Foundation and NWRI reports. When toxicological data were available within the CCL dossiers they were considered by the panel. However, for CECs with measured environmental concentrations in California that were not considered in the CCL process, the Panel recognizes the need to utilize other databases or screening tools described later.

Appendix E - Summary of California Water Recycling Regulations and Additional Discussion of California Department of Health Groundwater Recharge Reuse Regulations

The following is a more detailed discussion the key California regulations (i.e., current and draft), criteria, and policy that impact reuse projects.

Summary of California Enabling Legislation for Recycling Schemes

- Porter-Cologne Water Quality Control Act of the California Water Code (CWC) - The Porter-Cologne Act of the CWC is the main regulation that gives the authority and responsibility to the RWBs to establish water quality objectives, to prescribe and enforce requirements for waste discharge to protect surface and groundwater quality, and, in consultation with DPH, prescribe and enforce reclamation requirements. Under the CWC, Waste Discharge Requirements (WDRs) are issued by the RWBs that contain the water quality objectives, effluent limits, and other requirements that are used to regulate reclamation projects. The State has a policy to promote the use of recycled water to the maximum extent in order to supplement existing surface and ground water supplies to help meet water needs (CWC sections 13510-13512). One of the primary conditions on the use of recycled water is protection of public health (CWC sections 13521, 13522, 13550(a)(3)). In addition, the 1977 amendments to the CWA required publicly owned treatment works (POTWs) to ensure compliance with the pretreatment standards by each significant local source introducing pollutants subject to pretreatment standards into a POTW. To meet the requirements of the 1977 amendments, the USEPA developed the General Pretreatment Regulations for Existing and New Sources of Pollution, which are further discussed in Appendix H.

- SWRCB Recycled Water Policy - In February 2009, the SWRCB adopted an updated Recycled Water Policy (Resolution No. 2009-0011). The goal of the Policy is to increase the use of recycled water while protecting groundwater quality. The Policy states that local water and wastewater entities, together with salt/nutrient contributing stakeholders, will fund locally driven and controlled collaborative processes open to all stakeholders to develop salt/nutrient management plans for each groundwater basin /sub-basin in California. The policy also attempts to incorporate the most current state-of-the-science on CECs into regulatory policies for use by various state agencies. As a part of this policy, Southern California Coastal Water Research Project (SCCWRP) was asked to convene a Science Advisory Panel of six experts to provide recommendations to the SWRCB. The plan development processes must include compliance with California Environmental Quality Act (CEQA) and participation by the RWB staff. Each plan's complexity depends on a variety of site-specific factors including, but not limited to, size and complexity of the basin, source water quality, stormwater recharge, hydrogeology, and aquifer water quality. The policy recommends that priority be given to those basins

identified as priority basins by the Groundwater Ambient Monitoring Assessment (GAMA) program.

- SWRCB Nondegradation Policy - In 1968 the SWRCB adopted Resolution No. 68-16, entitled " Statement of Policy with Respect to Maintaining High Quality Waters in California". This policy requires the continued maintenance of existing high quality waters, and provides conditions under which a change in water quality is allowable. A change must be consistent with maximum benefit to the people of the State, not unreasonably affect present and anticipated beneficial uses of water, and not result in water quality less than that prescribed in water quality control plans or policies.

- RWB Basin Plans - The CWC requires all RWBs to develop, adopt and implement a Water Quality Control Plan (Basin Plan). The Basin Plan includes three basic components: waters of the state and associated beneficial uses (potential and existing); water quality objectives necessary to protect the uses; and, an implementation plan and time schedule for achieving the water quality objectives. Some of RWBs have specific water recycling guidance and/or implementation criteria designed to enhance the feasibility of water recycling projects (e.g., relax surface and groundwater quality objectives based on technical reports demonstrating that the revised objectives would still protect existing beneficial uses fully while minimizing the need for unnecessary treatment, and streamflow augmentation to enhance or add riparian habitat and fisheries beneficial uses by relying on streambeds for transporting and/or recharging recycled water).

California Department of Public Health

The RWBs must consult with and consider recommendations of the Department of Public Health (DPH) when issuing waste discharge/water recycling requirements (CWC section 13523). The statute requires the DPH is to establish uniform statewide recycling criteria for the various uses of recycled water to assure protection of public health where recycled water use is involved (CWC section 13521). DPH has promulgated regulatory criteria in Title 22, Division 4, Chapter 3, section 60301 et seq. of the CCR. DPH regulatory criteria include specified approved uses of recycled water, numerical limitations and requirements, treatment method requirements and performance standards. DPH regulations allow use of alternate methods of treatment in some cases, so long as the alternate methods are determined by DPH to provide equivalent treatment and reliability.

A 1996 Memorandum of Agreement (MOA) between the DPH, State Water Resources Control Board, and the regional water boards on the use of recycled water allocates primary areas of responsibility and authority between these agencies. The MOA provides methods and mechanisms necessary to assure ongoing and continuous future coordination of activities relative to the use of recycled water in California.

To protect public drinking water supplies, the DPH also has regulations to prevent cross connections between recycled water systems and potable water systems. Local health departments and the DPH have enforcement authority over these cross connection prevention

regulations. The California Building Standards Commission sets plumbing standards for use of recycled water in buildings and industries. A summary of key regulations is provided below.

- California Code of Regulations (CCR), Title 22 - The CWC requires the DPH to establish statewide reclamation and public health criteria for each type of recycled water use (Section 13521). DPH Wastewater Reclamation Criteria are contained in Title 22, Division 4 of the CCR. A summary of the Title 22 criteria is presented in Table 3.1. Title 22 criteria cover three basic areas: standards for bacterial quality, levels and types of treatment required for a specific recycled water use, and standards for reliability of the reclamation plant. The DPH is responsible for the review of all proposed reclamation projects and discharge permits for consistency with Title 22 criteria. In addition, although the quality of recycled water can be produced at a level that is acceptable for full body contact activities and the irrigation of food crops, a number of additional precautions are also implemented to protect public health. For example:

    - Recycled water pipes are colored purple and appropriately marked;
    - Exposed air vents and appurtenances are labeled;
    - Sprinkler heads and valves are marked indicating recycled water;
    - Hose bibs are generally made inaccessible to the public;
    - Irrigation times are adjusted and overspray minimized to reduce public contact;
    - Signage and postings are provided to notify the public;
    - Back-flow prevention devices and where necessary air-gaps are provided to protect potable water; and,
    - Cross-connection inspections are conducted to protect potable water supplies.

- *DRAFT* Groundwater Recharge Reuse Regulations (CDPH 2008) - The draft recharge regulations address the supplementing of groundwater through surface or subsurface application of treated municipal wastewater prior to eventual extraction via drinking water wells for potable use. The proposed California criteria for groundwater recharge reflect a cautious approach toward potential short and long-term health concerns. The criteria rely on a combination of controls intended to maintain a microbiologically and chemically public health protective groundwater recharge operation and protect current and future potable groundwater supplies. The criteria specify source control, wastewater treatment processes, water quality, recharge methods (i.e., surface spreading versus direct injection), dilution, extraction well location, and monitoring frequency and location. DPH requires monitoring of additional constituents for unregulated chemicals (e.g., chromium-6, diazinon, 1,4-dioxane, the nitrosamine N-nitrosodimethylamine (NDMA), and 1,2,3-trichloropropane) using drinking water analytical methods, where available and practicable, and will specify other methods

where necessary (e.g., for certain endocrine disrupting chemicals, pharmaceuticals, personal care products). DPH notes that monitoring for these chemicals—or categories of chemicals—is a diligent way of assessing and verifying recycled municipal wastewater quality characteristics, which can be useful in addressing issues of public perception about the safety of recharge projects. The proposed regulations have undergone several modifications since the early 1990's (see additional discussion is contained in Appendix E).

- Basis of DPH Approval of Surface Water Augmentation with Recycled Water - The Department of Public Health and the Department of Water Resources convened the California Potable Reuse Committee, following the initial approval of the San Diego indirect potable reuse proposal to augment a surface water reservoir, to identify the conditions necessary for safe surface water augmentation throughout California. "A Proposed Framework for Regulating the Indirect Potable Reuse of Advanced Treated Recycled Water by Surface Water Augmentation" (Framework) was produced by the committee. The California Recycled Water Task Force was created by statute in 2001 and was tasked, in part, to evaluate the need to reconvene the California Potable Reuse Committee to update their findings in the Framework. The Task Force concluded (Water Recycling 2030 – Recommendations of California's Recycled Water Task Force, State of California, 2003, Recommendation 6.3) that it was not necessary to revisit the Framework and that the State should be able to make determinations regarding indirect potable reuse based on the following publications:

  - "Report of the Scientific Advisory Panel on Groundwater recharge with Reclaimed Water", State of California, 1987;
  - "Issues in Potable Reuse", NRC, 1998;
  - "A Proposed Framework for Regulating the Indirect Potable Reuse of Advanced Treated Reclaimed Water by Surface Water Augmentation", State of California, 1996; and,
  - DPH draft groundwater recharge regulations (August 5, 2008).

- Proposed 1996 Framework for Regulating Indirect Potable Reuse by Surface Water Augmentation - In May 1993 a California Potable Reuse Committee was formed by the DPH and the California Department of Water Resources to look into the feasibility and safety of potable reuse of recycled water following advanced treatment. The members concluded that planned indirect potable reuse of advanced treated recycled water using surface water reservoirs is feasible under the following six specific criteria:

1. Application of Best Available Technology in advanced wastewater treatment with the treatment plants meeting operating criteria;
2. Maintenance of appropriate retention times based on reservoir dynamics;

3. Maintenance of advanced wastewater treatment plant reliability to consistently meet primary microbiological, chemical, and physical drinking water standards;
4. Surface water augmentation projects using advanced treated recycled water must comply with applicable State of California criteria for groundwater recharge for direct injection with recycled water;
5. Maintenance of reservoir quality; and,
6. Provision for an effective source control program.

Other project approval considerations identified in the Framework include:

1) Independent Monitoring Oversight Authority. This authority would be appointed by the CDPH and RWQCB to provide a third-party review of operational, regulatory, and environmental issues associated with the project;

2) Coordination. Coordination between water reclamation agencies, regulatory agencies, and agencies responsible for public water systems should be instituted in both formal and informal channels;

3) Operator Training and Certification. Operator training and certification programs must assure reliable operation of advanced treatment facilities; and,

4) Source Aesthetic Quality. Use of advanced treated recycled water should not negatively impact the aesthetics (taste, odor, and appearance) or consumer acceptance of the public drinking water supply.

Additional Discussion of California Department of Health Groundwater Recharge Reuse Regulations[10]

In the late 1980s, the California Department of Public Health (CDPH), formerly known as California Department of Health Services (CalDHS), developed draft criteria for the use of recycled municipal wastewater to recharge groundwater basins that are sources of domestic water supply (Crook *et al*., 2000). The CDPH criteria, which set forth the agency's approach to writing permits for indirect potable reuse systems, have been updated several times but have never been approved or finalized. The CDPH draft groundwater recharge criteria are designed to ensure a groundwater supply that meets all the drinking water standards and other requirements more specific to water derived from wastewater effluent (CDPH, 2007b). In formulating the proposed criteria, CDPH considered both acute health effects from microbial pathogens and potential long-term health effects associated with chemical constituents, particularly trace organics (Geselbracht and Crook 2000). After receiving the final report prepared by a science advisory panel (SAP) submitted to the state in 1987, CDPH selected TOC limits in wastewater effluent prior to recharge as a means of ensuring the lowest possible concentration of unregulated wastewater-derived organic contaminants (Robeck 1987). In its summary report, the SAP concluded that organic carbon should be removed to "…below 1 mg/L

[10] Excerpted from Drewes *et al*. 2008.

by reverse osmosis and essentially all identifiable trace organic compounds of significance should be absent in detectable concentrations."

The current draft criteria (CDPH 2008) couple an even more stringent TOC limit with the fraction of the drinking water supply that is derived from wastewater effluent as a factor in determining system performance requirements (quantified as TOC). This fraction is referred to as the "recycled water contribution" (RWC). The current draft regulations require that subsurface injection projects produce water with TOC of wastewater origin less than or equal to 0.5 mg/L at the point where the recycled water (with or without dilution water) mixes with native groundwater. Subsurface injection projects are required to treat 100% of the recycled water by RO to provide sufficient removal of organics and must meet the TOC limit at the point of injection. If the RWC exceeds 50%, advanced oxidation processes (AOPs) using UV/AOP must be employed following RO treatment. For surface spreading operations, TOC must be equal to or less than 0.5 mg/L divided by the RWC at the point where the recycled water meets the groundwater. Therefore, surface spreading projects can receive credit for TOC removal that occurs within the vadose zone.

In recognition of the possible shortcomings of using TOC as a surrogate for wastewater-derived contaminants, CDPH also included additional monitoring requirements in the 2003 draft criteria (CDPH 2003).

Appendix F - Recycled Water: Case Examples

The following is a brief summary of the two key indirect potable reuse projects in California. Case Examples for landscape irrigation projects are also provided. As discussed in Section 3.4, the groundwater recharge case examples are provided to illustrate the extent of implememtation of the key recommendations from both the 1998 NRC report and the California's 1996 surface water augmentation framework document. The two irrigation examples are provided to illustrate that the DPH Title 22 regulations are sufficient and appropriate.

Orange County Water District - Groundwater Replenishment via Direct Injection and Surface Water Augmentation (DDB Engineering 2008, Mills et.al. 1998)

Orange County Water District (OCWD) is located in southern California where historic agriculture water use has been replaced with water demands from urbanization. OCWD was formed in 1933 by the California legislature to manage northern Orange County's groundwater supply. Currently, over 200 groundwater production wells exist within the OCWD service area and supply roughly 75% of the water demand. The remaining water supply demand is met through importing water from the Colorado River and northern California.

OCWD operated the original Water Factory 21 (WF-21) from 1975 to 2004 and Interim Water Factory 21 (IWF-21) from 2004 to 2006. WF-21 was an advanced water treatment facility that recycled secondary-treated wastewater from Orange County Sanitation District's (OCSD) in Fountain Valley, California. WF-21 produced up to 15 million gallons per day (mgd) of highly treated recycled water for injection into the Talbert Gap Seawater Intrusion Barrier (Talbert Barrier) to prevent the inflow of seawater into the Orange County Groundwater Basin. IWF-21 was a transitional advanced water treatment facility during construction of a new full-scale groundwater replenishment system (GWR) that produced up to 5 mgd of high quality recycled water for injection at the barrier. Without the barrier, seawater can, if the groundwater basin level is low, migrate inland through the shallow, highly permeable, sandy, fresh water aquifers at the Talbert Gap near the Santa Ana River (SAR) and contaminate the deeper potable aquifers in the groundwater basin.

The GWR System is a water supply project jointly sponsored by OCWD and OCSD to supplement existing water supplies by providing a new, reliable, high-quality source of water to recharge the Orange County Groundwater Basin and protect the Basin from further degradation due to seawater intrusion. The GWR System is located in central Orange County and extends from Fountain Valley and Huntington Beach near the coast to Santa Ana, Orange, and Anaheim, generally near the Santa Ana River.

A pump station conveys recycled water via a pipeline to a series of 36 injection well sites that comprise the Talbert Barrier. Another pump station conveys recycled water via the 13-mile long GWR Pipeline to the Kraemer/Miller Spreading Basins in the Anaheim Forebay area. The GWR System is being implemented in phases, with the initial design capacity rated at 70 mgd (or roughly 72,000 acre-feet per year (afy), allowing for downtimes).

The barrier water demands are considered "first priority" and generally require an estimated annual average water demand of approximately 30 to 32 mgd. The balance of the AWTF recycled water production that is not used at the barrier is pumped to the Kraemer/Miller Spreading Basins. Diluents (which are waters of non-wastewater origin) include captured Santa Ana River storm water and purchased imported water from the Metropolitan Water District of Southern California (MWD) that is recharged at the nearby OCWD spreading basins.

The State permit allows 75 percent of the water injected at the Talbert Barrier to be recycled water based on a monthly running average over the past 60 months. This requirement allows for flexibility to inject only recycled water at times when the MWD potable water supply may be unavailable. The permit also includes provisions for a phased approach to injection of 100 percent recycled water at the barrier, or a maximum RWC limit of 100 percent on a monthly running average basis over the preceding 60 months. Following a demonstration period, OCWD anticipates injecting only recycled water at the Talbert Barrier.

Besides water supply, another purpose of the GWR System is to provide peak flow relief for OCSD during peak wet weather flow conditions. During peak wastewater flow events, the AWTF will provide peak flow discharge relief for the OCSD ocean outfall by discharging up to 100 mgd of microfiltered, disinfected recycled water to the Santa Anna River.

Best Available Technology and Multiple Barriers: Secondary-treated wastewater that is normally be discharged to the ocean is diverted from OCSD Plant to the GWR System AWTF, where it is treated to drinking water standards using microfiltration (MF), reverse osmosis (RO), advanced oxidation/disinfection (ultraviolet (UV) irradiation and hydrogen peroxide, also called AOP) processes, decarbonation, and lime stabilization post-treatment.

Plant Monitoring and Performance Evaluation/Control: The GWR System includes plans to conduct performance monitoring at multiple points or steps as the water is treated and recharged, and thus, allow for action if certain performance requirements are not met. Critical control point monitoring includes: continuous on-line instrument monitoring, feedback to allow for control evaluation, corrective action for failure, and records management.

Recycled water produced by the AWTF must comply with drinking water standards and other water recycling and discharge requirements established by CDPH and the RWQCB. On March 12, 2004, the RWQCB issued Order No. R8-2004-0002 entitled "Producer/User Water Recycling Requirements for the Orange County Water District Interim Water Factory 21 and Groundwater Replenishment System, Groundwater Recharge and Reuse at Talbert Gap Seawater Intrusion Barrier and Kraemer/Miller Recharge Basins". (RWQCB, 2004)

OCSD Peak Wet Weather Flow Relief: The GWR System will provide peak wet weather flow relief for the OCSD ocean outfall. It is anticipated that peak storm events occur about once

every three years, and create high wastewater flows that could exceed the capacity of the OCSD ocean outfall. During these storm events, the GWR System will provide up to 100 mgd of peak wet weather flow relief for OCSD treating peak secondary effluent flows using MF and UV disinfection (bypassing RO) for discharge to the SAR.

Source Control: The Orange County Sanitation District has expanded their source control program as an integral part of the multi-barrier system that protects the quality of the product water of the Groundwater Replenishment System (GWRS).

The scope and purpose of the expanded source control program was defined by the California Department of Public Health, Santa Ana Regional Water Quality Control Board, GWRS Expert Panel, and GWRS Public/NGO Panel and appears in the California Department of Public Health: California Code of Regulations Title 22 - Draft Groundwater Recharge Reuse, Section 60320 General Requirements, and Santa Ana Regional Water Quality Control Board: Regional Order No. R8-2008-0058 - Producer/User Water Recycling Requirements.

Under the Title 22 Draft regulations, recycled municipal wastewater used for a Groundwater Recharge Reuse Project shall be from a wastewater management agency that:

(1) administers an industrial pretreatment and pollutant source control program;

(2) implements and maintains a source control program that includes at a minimum:

(A) an assessment of the fate of Department-specified contaminants through the wastewater and recycled municipal wastewater treatment systems,

(B) contaminant source investigations and contaminant monitoring that focus on Department-specified contaminants,

(C) an outreach program to industrial, commercial, and residential communities within the sewage collection agency's service area for the purpose of managing and minimizing the discharge of contaminants of concern at the source, and

(D) an up-to-date inventory of contaminants discharged into the wastewater collection system so that new contaminants of concern can be readily evaluated.

(3) is compliant with the effluent limits established in the RWQCB permit for the Groundwater Recharge Reuse Project.

Regional Order No. R8-2008-0058 states that the scope and purpose of this OCSD source control program need to be expanded to include not only contaminants that may be detrimental to the facilities or environment, but also to include contaminants specified by CDHS that may be harmful to human health and drinking water supplies. In addition to OCSD's Federal Pretreatment Program, key elements of the expanded source control program include:

• **Pollutant Prioritization**. OCSD's CEC monitoring began in March 2007 with an initial list of 500 constituents developed by stakeholders including regulators, NGO's, and staff. Monitoring included the source water, unit processes, and product water in three phases over a two-year period. The prioritization program reduced the list of 500

constituents to a short list of 22 based on 1) concentration and mass, 2) toxicity, numerical limits or standards, 3) treatment removal effectiveness using an on probabilistic parametric model, and 4) action levels or triggers. Continual monitoring for existing and new CEC's is done periodically for program effectiveness.

• **Pharmaceutical Program.** Source Control permits industrial pharmaceutical manufacturers through the Federal Pretreatment Program. Pharmaceutical manufacturers' wastewater disposal practices are being re-evaluated to coincide with the overall pharmaceutical strategy. To address commercial facilities, Source Control is currently developing a Health Service Facilities (HSF) program. A study of several HSF commercial sectors is currently being performed. The practices and impacts of pharmaceutical disposal by HSFs will be determined so that a comprehensive program can be administered which will complement the residential and industrial programs.

• **Commercial Sector Program**. Using the pollutant prioritization results, Source Control is tracing the sources of the prioritized CEO's based on mass emission level (versus concentration). In this manner, significant dischargers are located from functional use of CEC ingredients in consumer products. Since there are over 20,000 commercial businesses in the Orange County service area, the significant dischargers are prioritized using a sector impact analysis. The level of regulation will be established in a tiered implementation program. If an action level or trigger is reached, the tier of regulation is increased until reduction goals are satisfied. Initial commercial sectors include: cleaners and degreasers, coatings, coloring agents and dyes, pesticides, disinfection byproducts, fuels additives and byproducts. Domestic and trunkline sampling are essential to characterizing the sources of the CEC's.

• **Countywide Pollution Prevention Partnership Program C4P**. C4P is OCSD's new Countywide Pollution Prevention Partnership Program. This partnership was solidified on March 28, 2008 when OCSD's Board of Directors adopted Resolution 08-02 that supports an Enhanced Source Control Program to reduce emerging pollutants of concern. Source control of emerging pollutants of concern from nonindustrial sources will be accomplished primarily through countywide public education, targeting residential and commercial entities within OCSD's service area. Many people are not well informed about the water quality impacts that can result from certain everyday behavioral practices, such as flushing unused medicines down the toilet, pouring volatile chemicals down the sink, or by applying excessive amounts of fertilizers to their lawns and gardens. OCSD's close involvement and support with individual citizens and businesses are absolutely essential in controlling pollutants of concern, since nonindustrial water pollution commonly originates from their combined activities of improperly disposing harmful pollutants into the sewer system. Unlike source control of industrial facilities where permits are issued to regulate dischargers, implementation of a source control program for domestic and commercial sources may be implemented through a voluntary pollution prevention outreach program designed to change improper waste disposal practices. OCSD has partnered with its 25 member agencies to disseminate outreach materials provided by OCSD using their existing media outlets. Focused outreach materials will support various Nonindustrial Source Control Programs

including Pharmaceutical, Emerging Pollutants of Concern (support GWR System), Fats, Oils, and Grease; and Urban Runoff/Nonpoint Source Pollution.

• **Chemical Inventory and Chemical Fact Sheets.** Chemical inventories used by businesses within the OCSD services area are being tracked leveraging off existing databases of other agencies such as Fire Departments and the Toxic Release Inventory by Source Control. The inventories are geo-positioned to facilitation source identification searches and fast response. Chemical fact sheets of CEC also facilitation fast response or coordination with other agencies.

(Source: Attachment-I Orange County Sanitation District Source Control Program (OCSD letter from Ed Torres, May 14, 2010)

Staffing and Quality Assurance: OCWD plans call for the plan to be continuously manned, 24 hours per day, 7 days per week. In addition to the Chief Operator, there are approximately 16 plant operators who each work 12-hour shifts, daytime and nighttime. There are approximately 11 I&E Technicians and 17 Maintenance Technicians who also work alternating shifts. OCWD has an on-site state-certified laboratory that operates in accordance with the Orange County Water District, Laboratory Quality Assurance Manual (OCWD, 2004).

Contingency Plans: The GWR System contingency plans call for operation on the condition that it causes no impairment to the groundwater basin. In the event of emergencies, the GWR System can be shutdown, stopping production of recycled water. The Talbert Barrier can be partially maintained using potable MWD water only, if necessary. Recharge via spreading at the Anaheim Forebay can be sustained, if necessary, using only imported water and/or captured stormwater. In addition, the OCWD plant has a dual feed power supply makes the likelihood of electrical power outages extremely rare.

Coordination: OCWD and the OCSD recognize the importance of interrelationship between the GWR System and the OCSD wastewater treatment plant and have a formal agreement (OCWD and OCSD, 2002) memorializing the understanding between the two agencies under which the GWR System is operated and maintained. The GWR System Steering Committee, which is comprised on Directors from both the OCWD and OCSD Boards of Directors, meets regularly to review matters and make recommendations to the full Boards on issues pertaining to the GWR System. The Joint Operations Committee, which consists of OCWD and OCSD staff, meets on a regular basis to communicate operations and maintenance plans, implement joint policies and procedures, cross-train operations staff, and address issues that arise to optimize both the GWR System and OCSD treatment plant.

Montebello Forebay Groundwater Recharge Project (Hartling and Nellor 1998)

Since 1962, recycled water provided by the County Sanitation Districts of Los Angeles County (LACSD) has been used to replenish the Central Groundwater Basin as part of the Montebello Forebay Groundwater Recharge Project. Other sources of replenishment water are imported river water (Colorado River Water and State Project Water) supplied by the Metropolitan Water District of Southern California (MWD) and storm water. The waters used for recharge meet primary drinking water standards. Replenishment water is applied at two spreading grounds owned and operated by the Los Angeles County Department of Public Works (LACDPW): the Rio Hondo Coastal Spreading Grounds and the San Gabriel Coastal Spreading Grounds (Figure F.1). In addition, the San Gabriel River channel itself is unlined (soft natural bottom) and is also used for recharge. Each spreading ground is subdivided into an organized system of smaller ponds that can be filled or dried alternatively to allow maintenance in some while others are being used. The spreading basins are operated under a wetting/drying cycle designed to optimize inflow and discourage the development of vectors.

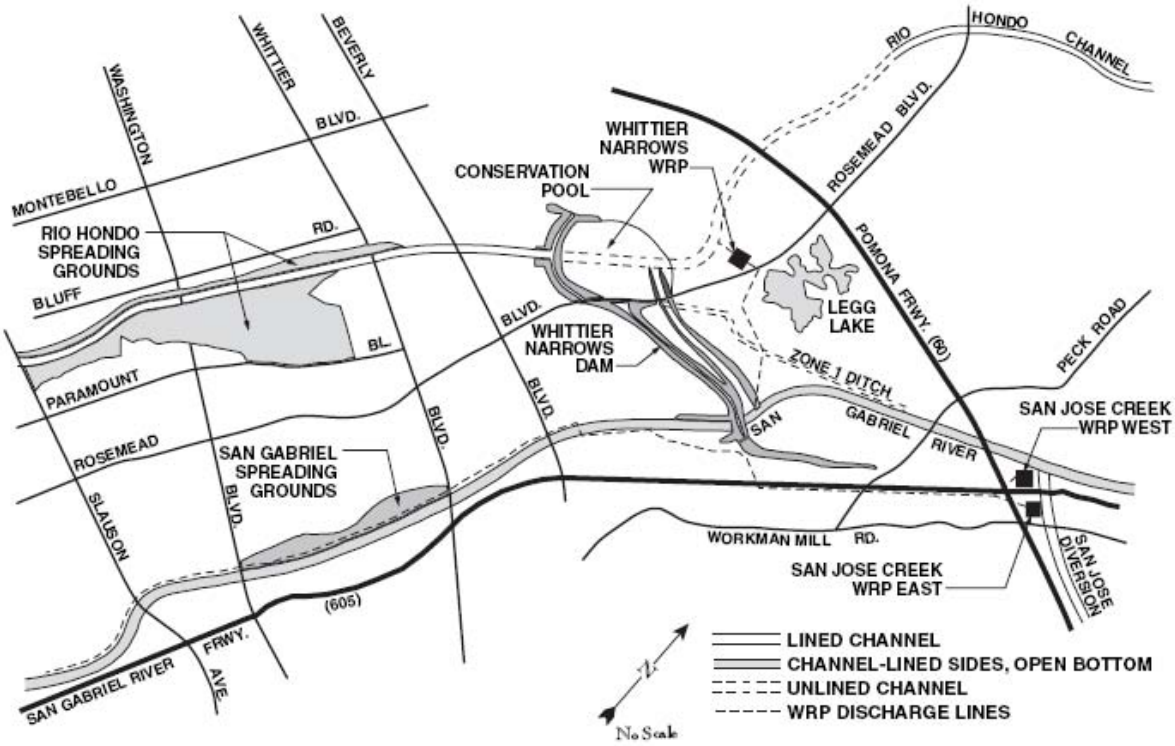

Figure F.1 Groundwater Recharge Locations

The Central Groundwater Basin is adjudicated and has been governed as part of a controlled replenishment and water withdrawal framework for over 50 years to prevent salt water from the ocean from contaminating local supplies due to overdraft of the aquifer and to ensure a high quality and reliable source of groundwater[11]. The Montebello Forebay Project is the oldest and best characterized groundwater recharge project in California. The project is the

[11] Research has been conducted on the ability of soil to treat recycled water as it percolates to groundwater via the soil aquifer treatment (SAT) process. The investigation found that SAT is an effective and sustainable process to remove organic compounds such as pharmaceuticals, personal care products, and endocrine disrupting compounds (Fox *et al*., 2001; Fox *et al*, 2006).

joint responsibility of the Water Replenishment District of Southern California (WRD), LACSD, and LACDPW.

Over several State permit cycles allowable recharge has been increased to allow up to 60,000 AFY of recycled water to be used for recharge and up to 50 percent recycled water in any one year as long as the running 3-year total did not exceed 150,000 AFY or 35 percent recycled water. The recycled water percentage was based on the combined total inflow to both spreading grounds where total inflow included all waters spread, rainfall, and the underflow from the Main San Gabriel Groundwater Basin. Typically, the amount of recycled water has averaged 40,000 AFY.

The State permit was recently amended (April 2009) to make a change in the averaging period for the calculation of the recycled water allowance to ensure that an adequate and reliable source of groundwater was available due to the lack of MWD imported water that could be used for replenishment. The 2009 permit amendment allows an increase in the amount of recycled water by removing the running 3-year allowable annual quantity limit and annual volume caps of recycled water. It allows the maximum quantity of recycled water spread to be 35 percent based on the combined total inflow to both spreading grounds during a period of five years instead of three years and thus will allow for additional recycled water to be spread to account for wet years and to provide more flexibility in operations.

In addition, local water agencies are looking at a possible project in the Central Groundwater Basin including expanding the role of storm water and recycled water. One option would be to provide an advanced level of treatment to the tertiary effluent from the San Jose Creek WRP for groundwater replenishment.

Best Available Technology and Multiple Barriers: The recycled water provided by LACSD comes from three water reclamation plants (WRPs): the Pomona WRP, Whittier Narrows WRP, and San Jose Creek WRP. The treatment system for these facilities, as shown in Figure F.2, consists of primary treatment, nitrification/denitrification nitrification activated sludge biological treatment, granular media filtration, disinfection using sequential chlorination, and dechlorination. The change to from chloramination to sequential chlorination has occurred over the past few years in response to the goal of minimizing disinfection byproduct formation. Sequential chlorination involves the application of chlorine to fully nitrified secondary effluent upstream of the granular media filters (to form free available chlorine), and subsequent addition of chloramines (ammonia followed by chlorine) downstream of the filters.

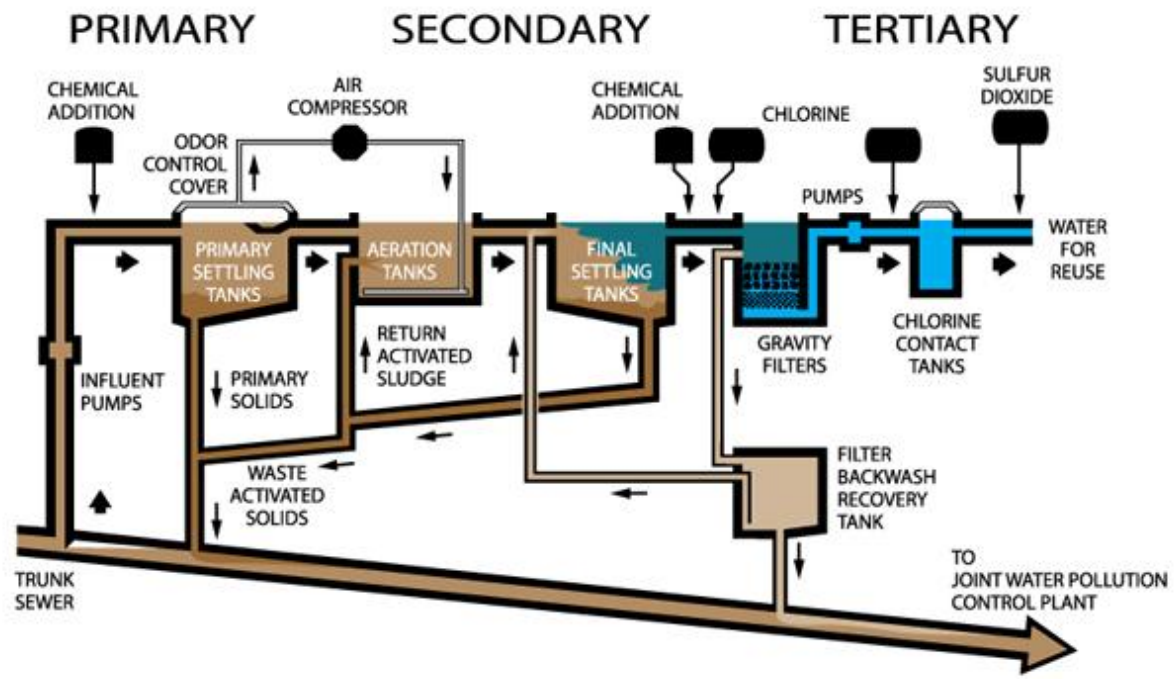

Figure F.2 Schematic of LACSD WRP Treatment System

<u>Plant Monitoring and Performance Evaluation/Control</u>: The WRPs ensure plant performance reliability through various in-plant control parameters, redundancy capabilities, and emergency operation plans. In-plant control parameters include the following:

- Mixed liquor DO – indicates possible high load or high industrial waste which impacts secondary quality
- Secondary turbidity – reflects secondary treatment and loading on the filters
- Filter effluent turbidity – early warning for final turbidity, provides time to react (notify reusers to shutdown)
- Final effluent turbidity – indicates when to turn reusers back on
- Pre-chlorine residual analyzer – ensure free chlorine residual before filtration (1 mg/L)
- Post-chlorine residual analyzer – ensure disinfection of effluent (4-6 mg/L)
- Out-chlorine residual analyzer – ensure adequate disinfection (2.5 mg/L)
- Final chlorine residual analyzer – verify adequate de-chlorination (<0.1 mg/L)
- Secondary effluent ammonia analyzer – indicates ammonia bleed through
- Filter structure overflow indication – warning on impending effluent filter bypass

Department of Public Health Reliability Requirements are addressed by the WRPs through having enough tankage to operate in an emergency with one unit out of service if flows are normal. The WRPs have adequate storage and standby feeders for coagulation with auto controls, the filtration system has alarms for high head loss and high filter effluent turbidity, and the disinfection system has standby storage tanks, automatic residual controls, recorders, alarms, and multipoints for addition. Although the WRPs have no long or short-term storage, they do have the ability to bypass flow.

The recharge project is subject to a complex water quality monitoring and compliance program that assesses all of the waters used for replenishment and in the groundwater system. Effluent samples from the WRPs are collected monthly, bimonthly, and quarterly. Recycled water produced by the WRPs complies with the primary drinking water standards, and meets total coliform and turbidity limits of 2.2/100 mL and 2 NTU, respectively. Additionally, extensive virus and parasite sampling indicates that the recycled water is essentially free of measurable levels of pathogens.

Six spreading ground monitoring wells are specified for bimonthly sampling under the project's monitoring program. In addition, nineteen production wells in the vicinity of the Montebello Forebay are specified for semiannual sampling and the headworks at both of the Rio Hondo and San Gabriel spreading facilities are sampled on a quarterly basis (Figure F.3).

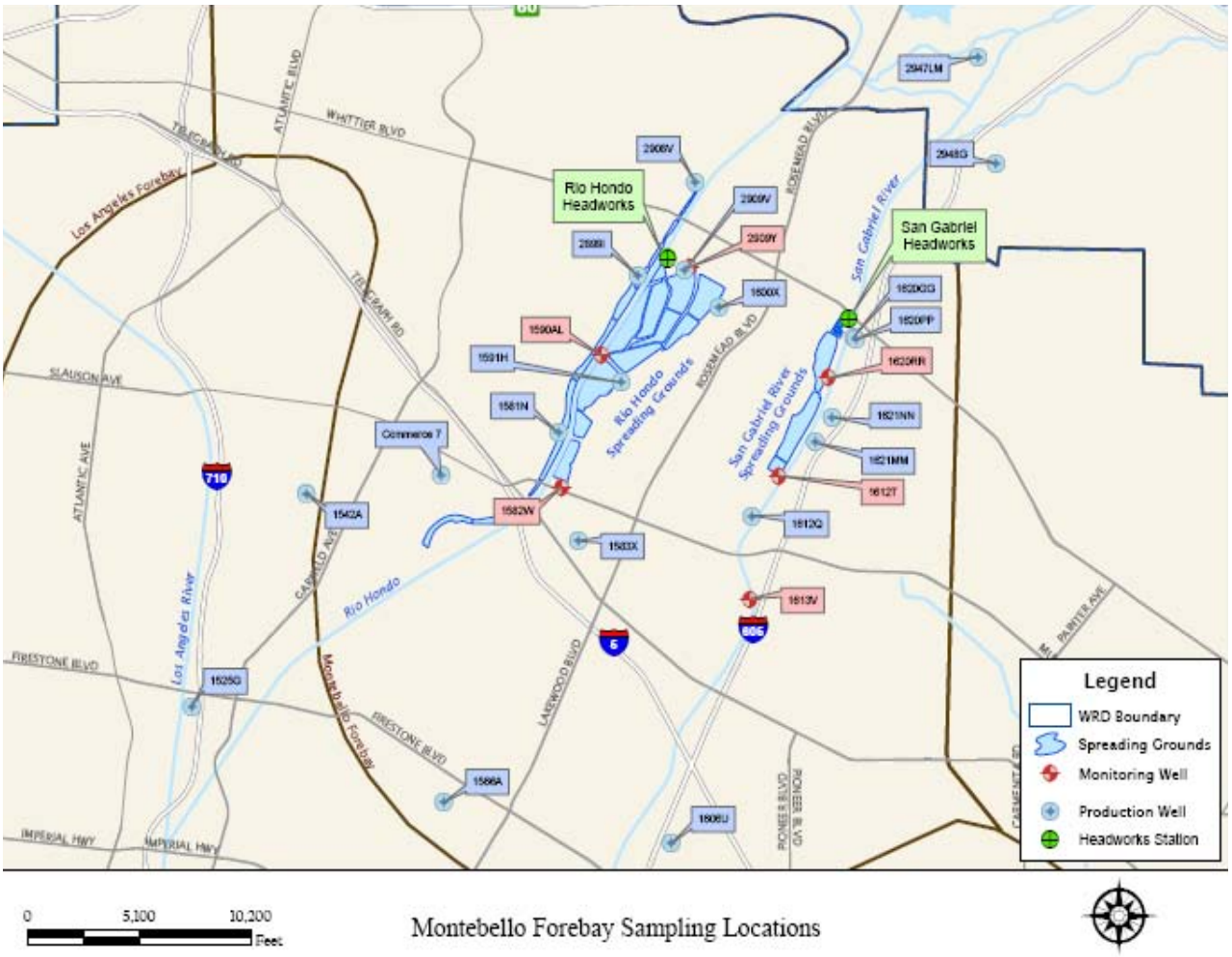

Figure F.3 Montebello Forebay Sampling Locations

Source Control: The three WRPs that provide recycled water for the recharge project are part of LACSD's Joint Outfall System, which is an integrated network of the Joint Water Pollution Control Plant (JWPCP), six WRPs, and collection systems. LACSD, primarily through its source control program, takes steps to prevent contaminants that might adversely impact the quality of the recycled water being produced from entering the sewer system. Industrial facilities with discharges to WRPs that are not compatible with the Districts' reuse goals may be given stringent limits or even required to reroute their flows around the WRPs for treatment at JWPCP and ocean disposal. The WRPs treat mainly residential and commercial waste, with generally less than 10% of the influent coming from industrial sources.

The industrial source control program was established to ensure that all of LACSD's treatment facilities are able to comply with waste discharge requirements; to protect the public and the environment; and to protect personnel and facilities from potentially harmful industrial

wastes. To achieve these objectives, a system-wide pretreatment program was created in 1972, beginning with the adoption of the *Wastewater Ordinance*. This document establishes the legal authority to enforce LACSD's local requirements as well as all appropriate state and federal regulations. LACSD's source control program presently regulates an extensive and varied industrial base consisting of over 2,600 industrial users (IUs).

The key elements of the source control program include:

- **Permitting.** Industrial wastewater discharge permits are issued jointly with the city in which the industry is located or the LACDPW for a period of five years.
- **Industrial Wastewater Monitoring.** The industrial wastewater monitoring program provides data for the evaluation of regulatory compliance (federal, state and local); wastewater treatment plant loadings and operation; and the discharge of illegal or incompatible wastes. Industrial wastewater dischargers are monitored through three separate mechanisms: 1) industrial user self-monitoring; 2) LACSD monitoring via onsite composite or grab sampling; and 3) surveillance sampling.
- **Inspection.** LACSD has developed an active industrial waste inspection program that includes frequent inspections and coordination with emergency response and other regulatory agencies.
- **Enforcement.** LACSD has established a tiered enforcement program to respond to pretreatment violations. Industries are required to address each violation and implement corrective actions. Follow-up inspection and/or sampling is conducted to confirm that the corrective actions taken were successful in achieving compliance. Each subsequent violation leads to escalation of enforcement action, including legal action if necessary.
- **Pollution Prevention.** LACSD participates in the statewide No Drugs Down the Drain program, which is a public outreach program to alert California residents living in specific regions about the problems associated with flushing unused, unwanted, and expired medications down the toilet or drain and to provide them with other, safe and proper disposal choices. In addition, the LACSD is involved with a number of local and statewide pollution prevention initiatives including working with the local air regulatory agency to ensure that mandated, widespread conversion to aqueous cleaners does not result in additional pollutant discharges.

<u>Staffing and Quality Assurance:</u>

<u>Contingency Plans</u>: In case of plant failure or disruption, the Pomona and Whittier Narrows WRPs can be completely bypassed in certain cases. Additionally the secondary effluent from the Pomona and Whittier Narrows WRPs can be diverted back to the sewer if needed. The San Jose Creek West WRP can divert the secondary effluent back to the sewer and the San Jose Creek East WRP can divert the final effluent back to the sewer. Flow can also be sent

interchangeably to or from both the San Jose Creek WRPs. The ability to divert or bypass flow depends on time of day and sewer conditions down stream of the WRPs.

Except at the San Jose Creek WRPs, the WRPs have enough standby emergency power to operate all plant process equipment. The San Jose Creek WRPs have enough power to operate all plant equipment except the process air compressors. The San Jose Creek WRP can pump and disinfect the water but not biologically treat it.

Coordination: The project is permitted by the Los Angeles Regional Water Quality Control Board (RWQCB) under Water Reclamation Requirements (WRRs) (Order No. 91-100), which were amended in April 2009 via Order No. R4-2009-048. The permit was jointly issued to LACSD, WRD, and LACDPW.

Case Examples - Summary of Non-potable reuse (Restricted and Unrestricted Irrigation) Projects in California (excerpted from Olivieri and Seto 2007)

Case study 1: City of Sunnyvale, CA

The City of Sunnyvale Water Pollution Control Plant (WPCP) is located in Sunnyvale, California. The plant provides advanced secondary treatment of wastewater from domestic, commercial and industrial sources within the City of Sunnyvale, Rancho Rinconada and Moffett Field. The service area has a population of approximately 127,000. The plant has an average dry weather flow design capacity of 29.5 MGal/d and a peak flow capacity of 40 MGal/d. Disinfected tertiary recycled water is produced intermittently to meet user demand and to fill a 2 million gallon storage tank, which then serves as a supply source. The recycled water is distributed throughout the northern portion of the City of Sunnyvale, where it is used mainly for irrigation purposes.

The wastewater treatment process consists of influent grinding, pre-aeration/grit removal, primary sedimentation, secondary biological treatment (oxidation ponds), fixed-film reactor nitrification, dissolved air flotation with coagulation, dual media filtration, chlorination and dechlorination. During periods of recycled water production, plant operating conditions are adjusted to meet California's *Water Recycling Criteria* for disinfected tertiary recycled water (average turbidity less than 2 NTU prior to chlorination, chlorine contact (CT) of > 450 mg-min/L (as estimated by residual chlorine concentration (mg/L) times contact time (min)) with 90 minutes minimum modal chlorine contact time, and median total coliform <2.2 MPN. These conditions are achieved through changes in dissolved air flotation polymer dose, chlorine dose, and flow rates through the contact basins used for recycled water. Filtered water turbidity, final chlorine residual, and CT are monitored continuously by the control system. If turbidity or CT exceed the regulatory limits, the control system will automatically divert water from the recycled water pump station to the NPDES "normal" discharge. CT values are normally much higher than the minimum requirement.

The recycled water flow from the contact tanks to the recycled water pump station is partially dechlorinated with sodium bisulfite to maintain a chlorine residual of approximately 2-3 mg/L. The calculated CT does not include any additional contribution from the chlorine residual in the distribution system.

During the peak recycled water production season (April-October) the plant effluent is highly nitrified. Between May and July, ammonia levels prior to chlorination are typically below 0.5 mg/L, indicating that chlorine is mostly likely initially present in the free residual form during this period. During the late summer, fall, and winter, some or all of the chlorine is likely present in the form of a combined residual.

In 2005, 265 million gallons of recycled water was distributed to customers throughout the northern portion of the City of Sunnyvale. In 2004 the total recycled water distributed was 306 million gallons. A summary of recycled water usage by reuse application category for 2005 is provided in Table F.1. Review of the table clearly indicates that landscape and park irrigation accounts for the vast majority of recycled water use.

<u>Available Data</u>: Data for flow, filtered water turbidity, chlorine residual, and CT are recorded continuously by the plant's Supervisory Control and Data Acquisition (SCADA) system. Grab

samples collected during each recycled water production run are analyzed for total coliform and dissolved oxygen as required by the City's permit (Water Reuse Order). During the summer of 2006, 19 samples were also analyzed for enterococcus. Those results varied from <1to 3/100mL (MPN). Additional water quality monitoring is conducted to track long-term trends and to provide information to interested recycled water customers. The parameters analyzed include chloride, bicarbonate, sulfate, nitrate, phosphate, calcium, magnesium, sodium, TDS, conductivity, hardness, alkalinity, salinity, boron, ammonia and pH.

Table F.1 Summary of 2005 Recycled Water Usage for City of Sunnyvale Water Pollution Control Plant

Reuse Application[4]	No. of Sites	Area Applied (acres)	Volume Delivered[8] (MG)	% of Total Reuse Flow
Landscape Irrigation				
Parks[5]	3	65	36.8	13.9
Golf Courses	1	100	78.8	29.8
Green Belts[7]	12	10	5.8	2.2
Other[6]	68	150	134.6	50.8
Industrial[1]	2	-	8.4	3.2
Dual Plumbing[3]	1	-	0.30	0.11
TOTAL	88	325	265	100

Notes:

1. Industrial processes receiving recycled water include cooling, construction applications, soil compaction and dust control, etc. (Note: RW is supplied to one cooling tower site as a backup supply, but no water is actually used).
2. Environmental Enhancement includes wildlife habitat, wetland/marsh applications, etc.
3. As defined in Title 22
4. Two sites are listed under two categories because of multiple uses
5. Parks category includes County park, large sports complex, and baseball fields.
6. Primarily comprised of landscaping at commercial/industrial office buildings. Some use in fountains.
7. Consists of freeway interchange and street median sites.
8. Based on totals recorded at each site's meter (water billing records) reduced by 16 percent to account for average system-wide potable water fraction.

Recycled Water Use Management Concerns: In the early days of the program, concerns regarding the safety of recycled water used in golf course water features were raised by golf course maintenance staff. Similar concerns are typically raised when use of recycled water at parks and playgrounds is proposed. Parks Department staff has also raised concerns about potential exposure to recycled water that may be on picnic tables as a result of irrigation overspray or drift.

Interpretation of Risk Matrix with Case Study Context: The City of Sunnyvale produces a disinfected tertiary recycled water that is consistent with and meets California's water reuse regulations. Data provided by the City indicate that the most common end use of the recycled water is for landscape irrigation and reported concerns regarding the safety of recycled water are also related to that use.

Based on the results of the MRA simulations it could be expected that the median risk of infection from human enteric viruses, *Cryptosporidium*, or *Giardia* would each be on the order of 10^{-5} per exposure with 90-percent confidence intervals ranging from 10^{-6} to 10^{-3} per exposure, provided that the WPCP is operating in a manner consistent with planned operations.

Case study 2: City of San Jose, CA

The San Jose/Santa Clara (SJ/SC) WPCP is located in San Jose, CA. The plant provides tertiary treatment of wastewater from domestic, commercial and industrial sources from the cities of San Jose, Santa Clara, and Milpitas; County Sanitary Districts 2 and 3; the West Valley Sanitation District including Campbell, Los Gatos, Monte Sereno and Saratoga, and the Cupertino, Burbank and Sunol Sanitary Districts. The service area has a population of approximately 1,300,000.

The wastewater treatment process consists of screening and grit removal, primary sedimentation, secondary (biological nutrient removal) treatment, secondary clarification, filtration, disinfection with chlorine and dechlorination. The WPCP has an average dry weather flow design capacity of 167 Mgal/d and a peak hourly flow capacity of 271 Mgal/d. The secondary treatment process is a biological nutrient removal process that consists of anoxic, aerobic, anoxic and aerobic zones in sequence. The mean cell residence time in summer is 6-10 days and in winter is 8-12 days. The multi-media gravity filters with 22 inches of anthracite, 12 inches of sand and 12 inches of gravel are divided into filters which produce plant effluent discharged to the receiving water (at hydraulic loading rates between 5.3 and 7.2 gpm/ft^2) and filters which produce recycled water (at hydraulic loading rates between 4.3 and 4.8 gpm/ft^2). Chlorine is used for intermittent prefilter chlorination. The filters are backwashed every 24 to 25 hours on average using 0.28 Mgal of filtered plant effluent per backwash. Aluminum sulfate is used for backwash water treatment.

Recycled water from the plant is delivered to customers in the service area by the South Bay Water Recycling Program (SBWR). Treated water from the SJ/SC WPCP plant is redirected from the South San Francisco Bay discharge to an effluent diversion structure and pipe, where it receives an additional chlorine dose to achieve a CT of 450 mg-min/L (5 mg/L after 90 minutes contact time), and then flows into the recycled water distribution system via a transmission

pump station (TPS). The recycled water production quality is monitored continuously via an on-line system for turbidity and chlorine residual.

In 2005 the total recycled water production was over 2.6 billion gallons and the WPCP discharged 100 Mgal/d to the receiving water. The average peak summer months recycled water production is 12 Mgal/d and the annual average monthly supply is 8-10 Mgal/d. A summary of recycled water usage by reuse application category for 2005 is provided in Table F.2. There are currently 541 customers served through SBWR's four retailers, San Jose Municipal Water System, San Jose Water Company in the City of San Jose, City of Milpitas and the City of Santa Clara.

Available Data: Daily data from 2005 are available for flow, total coliform, dissolved oxygen, pH, chlorine residual, plant effluent enterococcus, filter effluent turbidity, and total CT. Median total coliform sample results were 1.0 MPN/100mL for 2005. The chlorine residual ranged from 3.5 to 9.0 mg/L with an average value of 5.8 mg/L and a standard deviation of 0.95 mg/L. The total CT ranged from 938 to 7,607 mg-min/L with an average value of 2,472 mg-min/L and a standard deviation of 1,233 mg-min/L. The filter effluent turbidity ranged from 0.02 to 2.2 NTU with an average value of 0.6 NTU and a standard deviation of 0.25 NTU

Table F.2 Summary of 2005 Recycled Water Usage for South Bay Water Recycling

Reuse Application	No. of Sites[4]	Volume Delivered[5] (MG)	% of Total Reuse Flow
Landscape Irrigation[1]	501	1687	67
Agriculture	3	0.9	0
Industrial[2]	8	823.5	33
Dual Plumbing[3]	5	3.7	0
TOTAL	517	2515.1	100

Notes:

1. Landscape irrigation includes parks, golf courses, green belts and schools.

2. Industrial processes receiving recycled water include cooling, construction applications, soil compaction and dust control, etc.

3. Commercial buildings.

4. Customers that used recycled water for beneficial use during 2005.

5. Amount distributed represents the amount of recycled water used by customers

Recycled Water Use Management Concerns: Concerned citizens have occasionally contacted the SBWR Program regarding public contact with recycled water from irrigation sprinklers, wet grass in parks and/or golf courses, condenser drift from cooling towers, overspray from decorative fountains, and by other incidental means of public contact. In most cases, they have been satisfied to learn that recycled water provided by the SBWR program meets the full body contact requirements contained in the California *Water Recycling Criteria* (State of California 2000).

Interpretation of Risk Matrix within Case Study Context: The City of San Jose produces a disinfected tertiary recycled water that is consistent with California's water reuse regulations. Data provided by the City indicate that the most common end use of the recycled is for landscape irrigation and reported concerns from concerned citizens regarding the safety of recycled water are most often related to that use.

Based on the results of the MRA simulations it could be expected that the median risk of infection from human enteric viruses, *Cryptosporidium spp*., or *Giardia spp*. would each be on the order of 10^{-5} per exposure with 90% confidence intervals ranging from 10^{-6} to 10^{-3} per exposure, provided that the WPCP is operating in a manner consistent with planned operations.

Appendix G - Concept of Reliability

Failure of municipal wastewater treatment plant processes used to reclaim wastewater for potable reuse could result in exposure of the user population to considerable disease risk. It is therefore desirable to minimize the probability of failure at such a reclamation facility, or, in other words, to increase reliability. Quantification of reliability is an important element in assessing the potential health risks of water reuse.

The definition of treatment plant processes could be broadened to include those of an entire water reuse scheme plan (i.e., municipal wastewater plant, the holding reservoir, the groundwater basin, and the potable water treatment plant). These additional treatment operations/processes within an entire reuse plan would add redundancy and a degree of fail safety to the reuse plan. However, the focus of the discussion within this report is on the treatment plant processes affecting the advanced wastewater treatment plant effluent.

Treatment plant reliability is defined as the probability that a system can operate consistently over extended periods of time. In the case of a water reclamation plant, which produces an effluent for potable reuse, reliability might be defined as the likelihood of the plant achieving an effluent that matches, or is superior to predetermined standards. Where predetermined standards are not available, reliability might be defined as the likelihood of achieving a consistent effluent. The above definitions only encompass the variability associated with effluent quality related to by in-plant treatment processes and assume that the plant is properly designed, operated and maintained.

The above definition also includes the determination of the probability that the plant will be non-functional at any given time. Expansion of the definition of reliability to include this factor requires an evaluation of plant operational reliability, separate from effluent quality variability, that is caused by mechanical, design, process, or operational failures.

Reliability analysis itself can not only be used to quantify the reliability of a plant but also to find ways of increasing the reliability by revealing weak points in the process so that (often simple) corrections and/or modifications can be made. Even a well maintained, well operated plant is not perfectly reliable. Some variation will necessarily be inherent in the system. Variations in influent flow and quality which differ markedly from design values, as well as many inexplicable factors, create variation in effluent characteristics. In addition to variation inherent in the treatment system itself, other factors contribute to the plant unreliability. These factors include power outages, equipment failure, and operational (human) error, all of which must be incorporated into the reliability analysis.

Source: (Olivieri, Eisenberg *et al*. 1987)

Appendix H - Current Pretreatment Regulatory Authority for Source Control

"A component of the National Pollutant Discharge Elimination System (NPDES) Program, the National Pretreatment Program was developed by USEPA to control the discharge of pollutants from POTWs [publically owned treatment works]. The statutory authority for the National Pretreatment Program lies in the Federal Water Pollution Control Act of 1972, which was amended by Congress in 1977 and renamed the Clean Water Act (CWA). Under Section 307(b), [US]EPA must develop Pretreatment Standards that prevent the discharge of pollutants that pass through, interfere with, or are otherwise incompatible with POTWs. The 1977 amendments to the CWA required POTWs to ensure compliance with the pretreatment standards by each significant local source introducing pollutants subject to pretreatment standards into a POTW. To meet the requirements of the 1977 amendments, [US]EPA developed the General Pretreatment Regulations for Existing and New Sources of Pollution [40 Code of Federal Regulations(CFR) Part 403]." (Local Limits Development Guidance, EPA 833-R-04-002A, Office of Wastewater Management 4203, July 2004, page 1-1)

"Section 13240 of the Porter-Cologne Water Quality Control Act requires each Regional Board to formulate and adopt water quality control plans, or basin plans, for all areas within the Region. The Porter-Cologne Act also requires each Regional Board to establish water quality objectives to ensure the reasonable protection of beneficial uses and a program of implementation for achieving water quality objectives within the basin plans. Title 40, Code of Federal Regulations, Part 131 requires each State to adopt water quality standards by designating water uses to be protected and adopting water quality criteria that protect the designated uses. In California, the beneficial uses and water quality objectives are the State's water quality standards." (Central Valley Regional Water Board Executive Officer's Report 5 August 2005, Program Reports, Basin Planning Program, http://www.waterboards.ca.gov/centralvalley/water_issues/basin_plans/planning_overview.pdf, November 16, 2009)

"To protect its operations and to ensure that its discharges comply with State and Federal requirements, a POTW will design its local limits based on site-specific conditions. Among the factors a POTW should consider in developing local limits are the following: the POTW's efficiency in treating wastes; its history of compliance with its NPDES permit limits; the condition of the water body that receives its treated effluent; any water quality standards that are applicable to the water body receiving its effluent; the POTW's retention, use, and disposal of sewage sludge; and worker health and safety concerns. The General Pretreatment Regulations require the following:

- POTWs that are developing pretreatment programs must develop and enforce specific limits on prohibited discharges, or demonstrate that the limits are not necessary [40 CFR 403.8(f)(4)].
- POTWs that have approved pretreatment programs must continue to develop and revise local limits as necessary [40 CFR 403.5(c)(1)].

- POTWs that do not have approved pretreatment programs must develop specific local limits if pollutants from non-domestic sources result in interference or pass through and such occurrence is likely to recur [40 CFR 403.5(c)(2)].

[US]EPA and the States have approved more than 1,400 POTW pretreatment programs. Each program must develop, implement, and enforce technically based local limits. Because most of the POTWs that require pretreatment programs now have them, only a few new programs are approved each year. Work on local limits continues, however, because POTWs with approved programs must periodically review these local limits. [US]EPA regulations require that POTWs with approved programs must "provide a written technical evaluation of the need to revise local limits under 40 CFR 403.5(c)(1), following permit issuance or reissuance" [40 CFR 122.44(j)(2)(ii)]. Additionally, [US]EPA recommends that Control Authorities review the adequacy of local limits if current wastewater treatment plant performance fails or will fail to attain applicable NPDES, State, or local permit requirements or other operational objectives, including water quality objectives of receiving waters; and if the performance shortcomings may be reasonably attributed to pass through or interference caused by a POC [pollutant of concern]. Finally, Control Authorities may find it beneficial to re-evaluate their local limits when a change in POTW operations results in a significant change in operational objectives; when the POTW experiences a significantly different influent flow or pollutant characteristics; or when a significant alteration of key environmental criteria occurs. . . .

The National Pretreatment Program consists of three types of national pretreatment standards established by regulation that apply to industrial users (IUs). These include prohibited discharges, categorical standards, and local limits. Prohibited discharges, comprised of general and specific prohibitions, apply to all IUs regardless of the size or type of operation. Categorical standards apply to specific process wastewater discharges from particular industrial categories. Local limits are site-specific limits developed by the POTW to enforce general and specific prohibitions on IUs." (Local Limits Development Guidance, July 2004, page 1-1 to 1-2)

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The following are definitions included in the Local Limits Development Guidance cited above:

- Interference. [US]EPA uses the term "interference" in its regulations to describe a discharge that, alone or with discharges from other sources, inhibits or disrupts a POTW, its treatment processes and operations, or its sludge processes, use, or disposal and, therefore, causes a violation of the POTW's NPDES permit, increases the magnitude or duration of such a violation, or prevents the proper use or disposal of sewage sludge in compliance with the Clean Water Act, Solid Waste Disposal Act, Toxic Substance Control Acts, or the Marine Protection, Research and Sanctuaries Act.

- Pass Through. A discharge that enters the waters of the United States from a POTW in quantities or concentrations that, alone or with discharges from other sources, either causes a violation of any requirement of the POTW's NPDES permit, or increases the magnitude or duration of a violation of the POTW's NPDES permit.
- Pollutant of Concern (POC). Any pollutant that might reasonably be expected to be discharged to the POTW in sufficient amounts to pass through or interfere with the works, contaminate its sludge, cause problems in its collection system, or jeopardize its workers.

Appendix I - Overview and Summary of Key Studies of the Toxicological Relevance of Reused Water

In evaluating the toxicological relevance of recycled water to human health, the Panel relied primarily upon sources that had already compiled, reviewed and summarized findings from many of the key studies conducted over the past 40 years. Those studies include epidemiological studies examining effects in humans directly, studies in which laboratory animals have been exposed to recycled water, bio-analytical screening studies and risk assessments that predict the potential effects to humans of individual CECs in recycled water (e.g., Schwab *et al* 2005, Schriks *et al*. 2009). The Panel's review was greatly facilitated by a summary of historic studies developed by Ms. Margaret H. Nellor and forwarded to the Panel by Mr. David Smith of WaterReuse California. Table I.1 (A summary of Epidemiology Studies) and Table I.2 (Summary of Bio-analytical Screening Studies) were taken directly from the materials Ms. Nellor provided to Mr. Smith (Nellor 2009). Additionally the Panel found the summaries of previous studies in both NRC(NRC 1998) and Sloss *et al*. (Sloss, Geschwind *et al*. 1996) to be very helpful.

Based upon its review of this information, the Panel believes the findings of the epidemiological studies of recycled water are very encouraging from a human health risk perspective. The earliest studies were conducted in the 1970's and 1980's with a focus on the potential effects of disinfection byproducts produced following disinfection of drinking water with chlorine. Whilst most of these early studies find no clear association between recycled water use and adverse health outcomes in humans, some of the early studies report an increase in bladder and rectal cancers possibly associated with chlorination byproducts (see summary in Sloss *et al*., (Sloss, Geschwind *et al*. 1996)). More recent studies of recycled water find, essentially, no adverse health outcomes in populations using recycled water (see Table I.1). The virtual absence of adverse health outcomes from the early epidemiological studies is encouraging, in that treatment methods at that time were less sophisticated and their efficacy at removing trace chemicals was not well understood. Over the past decades, those methods have been refined and the amount of disinfection byproducts present in recycled water has decreased. Thus, if very few effects were found in recycled water in the 1970's and 80's, when disinfection byproduct concentrations were higher, than even fewer effects would be expected today, at least from these byproducts.

These epidemiological findings are particularly robust because they span decades. While CECs have come to the forefront of public health scrutiny within the last decade, a great deal of that scrutiny owes to the improvements in analytical detection methods. Many of what are today considered CECs have likely been present in recycled water for decades (Okun 1980). Epidemiological studies conducted in the past likely included potential effects associated with CECs, even though CECs were not the focus, or even mentioned, in the studies. Indeed, as noted above, the earliest of those studies focused on the potential effects of disinfection by products because the drinking water providers and the public health community wished to better understand what effects, if any, were associated with what were, at that time, novel or new water treatment methods, including chlorination, for example.

That the most recent epidemiological studies find even fewer adverse effects than historic studies is not surprising for several reasons. Wastewater and drinking water treatment processes are more refined than they were two or three decades ago. Product and chemical registration requirements are much stricter. Compounds and products are developed with much greater focus on environmental stewardship. We also know a great deal more about chemicals and moieties that cause adverse effects, so developers are likely producing and using fewer chemicals with known adverse impacts, or that we have a strong suspicion might cause such impacts. While it seems likely the diversity and number of chemicals with an anthropogenic origin has increased over the past 50 years, it also seems likely that the knowledge we have acquired over that time about the mechanisms through which adverse effects are caused, may mean that the chemicals that are present may have fewer unintended consequences that chemicals used 50 years ago. We should also not loose site that it is not just man-made chemicals that are present in recycled water. Such water contains many naturally occurring chemicals and always has, including hormones that humans synthesize and excrete naturally, phytoestrogens present in our diets that we excrete naturally, as well as many other compounds present in foods that we also excrete.

Thus, the findings about that absence of adverse health effects associated with recycled water use is very encouraging. However, it is important to keep in mind that all studies (epidemiological, laboratory animal, bio-analtycial, and risk assessments) have limitations. Interpretation of the results of epidemiological studies is complicated by confounding factors. These can include movement of people into and out of the community being studied and uncertainty about the exact level of exposure to compounds in recycled water (e.g., in most communities only a fraction of potable water is comprised of recycled water) (NRC 1998).

A shortcoming of human health risk assessments is that most of those are conducted on a chemical-by-chemical basis. The effects of each individual chemical can be summed to derive an estimate of the effect from all the chemicals included in the evaluation but in most cases, information on non-additive effects of the chemicals is not available. This has led to concerns that mixtures of CECs may have greater effects than can be discerned by or are predicted by risk assessments that simply add the effects of chemicals. Another limitation of risk assessments is that they only evaluate the potential effects of chemicals known or suspected to be present in recycled water and are limited to chemicals for which toxicity information is available. Recycled water almost certainly has a great many more chemicals than we are able to identify or have toxicity information for. The negative findings of the epidemiological studies are, therefore, particularly important in addressing these limitations of risk assessments. By their very nature, epidemiological studies look at the mixture of compounds that may be present in recycled water.

The Panel also appreciates that over the last several years awareness has grown that certain chronic adult diseases (such as diabetes, obesity, anxiety) may be related to exposure to environmental contaminants while in utero. This is has led to the field of epigenetics (Bateson, Barker *et al*. 2004; Dolinoy, Weidman *et al*. 2007; Jirtle and Skinner 2007). Epigenetic changes are heritable changes in gene expression that do not involve mutation of DNA, but instead involve changes in the signals that are used to identify genes that should be temporally expressed in different tissues, especially during development of the fetus. It is now clear that

hormones play a significant role in early fetal development and disregulation of this process can lead to adult disease. Chemicals that behave as hormones can also influence this process and there have been reports of epigenetic effects from exposure of mice to bisphenol A (an estrogen mimic, (Dolinoy, Weidman *et al*. 2007), vinclozlin (an anti-androgen,(Skinner, Anway *et al*. 2008)) and other environmental factors (Guerrero-Bosagna and Skinner 2009). However, the concentrations of chemicals that are necessary to produce these changes are several tens of orders of magnitude higher than concentrations found in drinking water. For bisphenol A, maternal exposure of rats to 50 mg/Kg/day throughout gestation and lactation influenced heritable epigenetic changes in the pups (Dolinoy, Weidman *et al*. 2007). Vinclozolin was administered as an intraperitoneal injection at a concentration of 100 mg/kg/day for 8 days during embryogenesis (Skinner, Anway *et al*. 2008). This exposure influenced the gene expression in the brain of third generation pups and significantly influenced the behavior of the animals causing female rats to have higher anxiety-like behavior. The reported 90th percentile concentration of bisphenol A in water is 286 ng/L, and there are no reported measurements for vinclozlin.

The Panel felt it important to provide a brief overview of the emerging field of epigenetics because of its potential relevance to the assessment of chemicals in the environment. However, it must be pointed out that the concentrations required to cause the changes in above referenced studies are several orders of magnitude higher than would be found in treated water. While more research to determine whether chronic exposure to very low levels of chemicals, as found in treated water, have any epigenetic effects would provide additional insight, at the time of the writing of this report, such a scenario seems unlikely. In particular, the general absence of adverse human health effects reported by epidemiological studies of recycled water suggest that increased incidence of various diseases, regardless cause, is not occurring.

Combined, the Panel views the predominantly negative findings of the epidemiological studies, laboratory rodent studies, bio-analytical screening studies and risk assessments as robust evidence that recycled water represents a source of safe drinking water.

Table I.1 Summary of Epidemiology Studies

Project	Description	Studies/Results
Montebello Forebay Groundwater Recharge Study, Los Angeles County, CA (Nellor *et al.* 1984; Sloss *et al*. 1996; Sloss *et al*. 1999)	Recycled water has been used as a source of replenishment since 1962; other replenishment sources are imported river water (Colorado River and State Project water) and local storm runoff. Water is percolated into the groundwater using two sets of spreading grounds. From 1962 to 1977, the water used for replenishment was disinfected secondary effluent. Filtration (dual-media or mono-media) was added later to enhance virus inactivation during final disinfection. During this time period, the amount of recycled spread annually averaged 27,000 acre-feet (AF), which was 16% of the inflow to the groundwater basin. At that time an arbitrary cap of 32,700 AFY of recycled water had been established. In 1987, the project was allowed in increase the amount of recycled water to 50,000 AFY. The current permit allows for a maximum recycled water contribution of 35% based on a five-year running average.	The studies have looked at health outcomes for 900,000 people that received some recycled water in their household water supplies in comparison to 700,000 people in a control population. Three sets of studies have been conducted: 1) the Health Effects Study, which evaluated mortality, morbidity, cancer incidence, and birth outcomes for the period 1962-1980 (see Attachment 2); 2) the Rand Study, which evaluated mortality, morbidity, and cancer incidence for the period 1987-1991; and 3) the second Rand Study, which evaluated adverse birth outcomes for the period 1982-1993. Health Effects Study (1962-1980): the epidemiological studies focused on a broad spectrum of health concerns that could potentially be attributed to constituents in drinking water. Health parameters evaluated included: mortality (death from all causes, heart disease, stroke, all cancers and cancers of the colon, stomach, bladder and rectum); cancer incidence (all cancers, and cancers of the colon, stomach, bladder, and rectum); infant and neonatal mortality; low birth weight; congenital malformations; and selected infectious diseases (including hepatitis A and shigella). Another part of the study consisted of a telephone interview of adult females living in recycled water and control areas. Information was collected on spontaneous abortions and other adverse reproductive outcomes, bed-days, disability-days, and perception of well-being. The survey was able to control for the confounding factors of bottled water usage and mobility. Rand (1987–1991): the study study evaluated cancer incidence (all cancers, and cancer of the bladder, colon, esophagus, kidney, liver, pancreas, rectum, stomach); mortality (death from all causes, cancer, cancer of the bladder, colon, esophagus, kidney, liver, pancreas, rectum, stomach, heart disease, cerebrovascular disease); and infectious diseases (including giardia, hepatitis A, salmonella, shigella). Rand (1982–1993): the evaluation focused on two types of adverse birth outcomes: (a) prenatal development and infant mortality (including: low birth weight (full term only), low birth weight (all births), very low birth weight, preterm birth, infant mortality); and (b) birth defects (all defects, neural tube defects, other nervous system defects, ears, eyes, face, neck defects; major cardiac defects, patent ductus arteriosus, other cardiac defects, and respiratory system defects; cleft defects, pyloric stenosis, intestinal artesias, other digestive system defects; limb, other musculoskeletal, integument and all other defects; chromosomal syndromes and syndromes other than

Project	Description	Studies/Results
		chromosomal). The results from these studies found that after almost 30 years of groundwater recharge, there was no association between recycled water and higher rates of cancer, mortality, infectious disease, or adverse birth outcomes.
Total Resource Recovery Project, City of San Diego (Cooper *et al.* 1992 and 1997); (NRC 1998)	This is a proposed surface water augmentation project that would utilize advanced treated recycled water to supplement the Miramar raw reservoir water (current drinking water supply). The project and treatment system are currently being re-evaluated.	Baseline reproductive health and vital statistics data were assembled. The reproductive data were collected from telephone interviews of 1,100 women. Vital statistics data were collected on mortality, birth outcomes, and infectious disease. Data were also collected on neural tube birth defects from 1979 – 1985.
Windhoek, South Africa – direct reuse (Isaacson and Sayed, 1988)	This is a direct reuse project. At the time the studies were conducted, the recycled water was treated using sand filtration and granular activated carbon, and the recycled water was added to drinking water supply system. The treatment system for this project has been revised since this work was conducted.	The study, which was conducted for the period 1976–1983, looked at cases of diarrheal diseases. For the Caucasian population of similar socio-economic status studied, disease incidence was marginally lower in persons supplied with recycled water than those with water from conventional sources. Incidence rates were significantly higher in black populations, all of whom received conventional water only. Age-specific incidence rates in children of the various ethnic groups also showed differences characteristically associated with socio-economic stratification. It was concluded that the consumption of recycled water did not increase the risk of diarrheal diseases caused by waterborne infectious agents.
Chanute, Kansas (Metzler *et al.* 1958)	Emergency use of recycled water during a drought for 150 days during 1956-57. The Neosho River was dammed below the outfall of the sewage treatment plant and the treated effluent backed up to the water intake. The impounding acted as waste stabilization and water was chlorinated prior to service. The use ended when heavy rains washed out the temporary dam. The river water source already contained wastewater prior to this event.	An epidemiology study showed fewer cases of stomach and intestinal illness during the period recycled water was used than the following winter when Chanute returned to using river water.

Table I.2 Summary of Bio-analytical Screening Studies

Project	Types of Water Studied	Health-effects data
Montebello Forebay Groundwater Recharge Study, Los Angeles County, CA (Nellor *et al.* 1984)	Disinfected tertiary effluent, storm water, and imported river water used for groundwater replenishment; also recovered groundwater.	Ames *Salmonella* test and mammalian cell transformation assay. 10,000 to 20,000 x organic concentrates were used in Ames test and mammalian cell assays, and subsequent chemical identification was attempted using the Ames assays. Samples were collected from the late 1970s to the early 1980s. The level of mutagenic activity (in decreasing order) was storm runoff > dry weather runoff > recycled water > groundwater > imported water. No relation was observed between percent recycled water in wells and observed mutagenicity of residues isolated from wells. The residues did not yield significant cytotoxicity in the mammalian cell assays To facilitate the isolation and identification of the components in sample concentrates, the residues were first fractionated by high performance liquid chromatography (HPLC), followed by testing of the fractions for mutagens and analysis of the mutagenic fractions by gas chromatography-electron ionization mass spectrometry (GC-EIMS). Results indicated that mutagenicity generally occurred in the least polar (most hydrophobic) fractions of each sample. In most cases, the sum of TA98 mutagenicity in sample fractions was similar in magnitude to that observed in the whole sample. There was no evidence of synergistic effects in these assays. Analysis by GC-EIMS of mutagenic fractions from 34 samples yielded only four known Ames mutagens in six samples (fluoranthene, benzo(a)pyrene, N-nitrosomorpholine, and N-nitrosopiperidine). However, these compounds were considered to contribute little to the observed overall mutagenicity of the samples. Several unknown compounds detected in the mutagenic fractions could not have caused the mutagenicity in all of the samples, because their frequency of occurrence, distribution in the fractions, and concentrations were not consistent with the bioassay results. Selected sample residues were then evaluated qualitatively by chemical derivatization techniques to determine which classes of compounds might be contributing to the mutagenic activity. Since mutagens are considered to be electrophilic, two nucleophilic reagents were used to selectively remove epoxide and organohalide mutagens from the residues. Analysis of mutagenic residues of groundwater and replenishment water by negative ion chemical ionization (NICI) GC-MS and Ames assay before and after derivatization supported (but did not unequivocally prove) the role of at least these two classes of electrophiles in the observed mutagenicity. Several samples had more than 100 reactive components, containing chlorine, bromine, iodine, or epoxides, with concentrations at the part-per-trillion level. However, the structures of these compounds could not be

Project	Types of Water Studied	Health-effects data
		determined by NICI, nor were the sources of the compounds identified. Because positive chemical identifications of specific mutagens could not be made and because the estimated concentrations of the components were so low, the biological significance of these materials remained in doubt. Follow-up toxicity testing of recycled water residues in the mid-1990s (not published) showed no Ames test response, while preserved residues from the earlier testing still showed a response indicating that the character of the recycled water has changed over time, perhaps as a result of increased source-control activities.
Denver Potable Water Reuse Demonstration Project (Lauer *et al*. 1996; NRC (NRC 1998)	AWT effluent (with ultrafiltration or reverse osmosis) and finished drinking water (current supply). The purpose of the project was to evaluate the feasibility of direct reuse by producing high quality recycled water; it was not implemented.	150 to 500 x organic residue concentrates used in 2-year *in vivo* chronic/carcinogenicity study in rats and mice and reproductive/teratology study in rats. No treatment-related effects observed.
Tampa Water Resource Recovery Project (CH2M Hill, 1993, Pereira *et al*. undated; NRC, 1988)	AWT effluent (using GAC and ozone disinfection) and Hillsborough River water using ozone disinfection (current drinking water supply). The proposed project involved augmentation of the Hillsborough River raw water supply; it was not implemented.	Up to 1,000 x organic concentrates used in Ames *Salmonella*, micronucleus, and sister chromatid exchange tests in three dose levels up to 1000 x concentrates. No mutagenic activity was observed in any of the samples. *In vivo* testing included mouse skin initiation, strain A mouse lung adenoma, 90-day subchronic assay on mice and rats, and a reproductive study on mice. All tests were negative, except for some fetal toxicity exhibited in rats, but not mice, for the AWT sample.
Total Resource Recovery Project, City of San Diego (Cooper *et al.* 1992 and 1997); (NRC 1998)	AWT effluent (reverse osmosis and GAC) and Miramar raw reservoir water (current drinking water supply). This is a proposed surface water augmentation project that would utilize AWT recycled water to supplement the Miramar raw reservoir water. The project and treatment system are currently being re-evaluated.	150–600 x organic concentrates used in Ames *Salmonella* test, mouse micronucleus, 6-thoguanine resistance, and mammalian cell transformation assays. The Ames test showed some weak mutagenic activity, but recycled water was less active than drinking water. The micronucleus test showed positive results only at the high (600x) doses for both types of water. The 6-thoguanine assay run on whole samples and fractions of each type of water showed no mutagenic effect. The mammalian cell transformation assay, showed a strong response for the Miramar sample, but the single test may not have been significant. *In vivo* fish biomonitoring using fathead minnows (28-day

Project	Types of Water Studied	Health-effects data
		bioaccumulation and swimming tests) showed no positive results. There was greater evidence of bioaccumulation of pesticides in fish exposed to raw water than recycled water.
Potomac Estuary Experimental Wastewater Treatment Plant (James M. Montgomery, Inc., 1983; NRC, 1998)	Study of the wastewater-contaminated Potomac River Estuary; 1:1 blend of estuary water and nitrified secondary effluent, AWT effluent (filtration and GAC), and finished drinking waters from three water treatment plants.	150 x organic concentrates used in Ames *Salmonella* and mammalian cell transformation tests. Results showed low levels of mutagenic activity in the Ames test, with AWT water exhibiting less activity than finished drinking water. The cell-transformation test showed a small number of positive samples with no difference between AWT water and finished drinking water.
Windhoek, South Africa – direct reuse (NRC, 1998)	AWT effluent (sand filtration, GAC). This is a direct reuse project with the recycled water was added to drinking water supply system. The treatment system has been revised since this work was conducted.	Ames test, urease enzyme activity, and bacterial growth inhibition. *In vivo* tests include water flea lethality and fish biomonitoring (guppy breathing rhythm).
Singapore Water Reclamation Study (Khan and Roser 2007)	AWT effluent (microfiltration, reverse osmosis, UV irradiation) and untreated reservoir water. The largest amount of Singapore's NeWater is currently used for industrial (semi-conductor manufacturing) and commercial use. A smaller amount is blended with raw water in reservoirs, which is then treated for domestic use.	Japanese medaka fish (Oryzias latipes) testing over a 12-month period with two generations of fish showed no evidence of carcinogenic or estrogenic effects in AWT effluent; however, the study was repeated owing to design deficiencies. The repeated fish study was completed in 2003 and confirmed the findings of no estrogenic or carcinogenic effects. Groups of mouse strain (B6C3F1) fed 150 x and 500 x concentrates of AWT effluent and untreated reservoir water over 2 years. The results presented to an expert panel indicated that exposure to concentrated AWT effluent did not cause any tissue abnormalities or health effects.
Santa Ana River Water Quality Monitoring Study (Woodside, 2007)	Shallow groundwater adjacent to the SAR and control water. This is an unplanned indirect potable reuse project where OCWD diverts SAR water for recharge into the Orange County Groundwater Basin. The SAR base flow is comprised primarily of tertiary-treated effluent.	Three rounds of testing were conducted in 2004 and 2005. In the first two rounds, Japanese Medaka fish were analyzed for tissue pathology, vitellogenin induction, reproduction, and gross morphology. In the third round, fish were analyzed for vitellogenin induction, reproduction, limited tissue pathology, and gross morphology. In the first two rounds, no statistically significant differences in gross morphological endpoints, gender ratios, tissue pathology, or reproduction were observed between the test water (shallow groundwater adjacent to the SAR) and the control water. In the third round, no statistically significant differences were observed in reproduction, tissue pathology (limited to evaluation of

Project	Types of Water Studied	Health-effects data
		gonads and ovaries), or vitellogenin induction between the test water and the control water.
Soil Aquifer Treatment Study (Fox *et al*. 2006)	Wastewater (various facilities), soil aquifer treatment water, storm water	The study used a variety of analytical methods to characterize and measure chemical estrogenicity: *in vitro* methods (estrogen binding assay, glucocorticoid receptor competitive binding assay, yeast-based reporter gene assay ,and MCF-7 cell proliferation assay); *in vivo* fish vitellogenin synthesis assay; enzyme-linked immunosorbent assays (ELISAs); and gas chromatography–mass spectrometry (GC/MS). Procedures were developed to extract estrogenic compounds from solids, liquid/liquid methods for direct extraction from aqueous suspensions such as primary and secondary effluents, and concentration of estrogenic (and other) organics on hydrophobic resins followed by organic fractionation during elution in a solvent (alcohol/water) gradient. Field applications of these techniques were designed to measure estrogenic activity derived from conventional wastewater treatment and from soil aquifer treatment (SAT). The stability of estrogenic contaminants that are removed on soils SAT was investigated by extracting and measuring nonylphenol from infiltration basin soils as well as by measuring total estrogenic activity in soil extracts. The researchers attempted to separate and measure estrogenic and anti-estrogenic activities in wastewater effluent and conducted a multi-laboratory experiment in which a variety of wastewater effluents and effluents spiked with known concentrations of specific estrogenic chemicals were tested for estrogenic activity. Significant variability in recycled water estrogenicity was observed in bioassay results. Facilities with the longest hydraulic retention times tended to have the lowest observed levels of estrogenicity. Estrogenicity was efficiently removed during SAT. The study also presented information on the advantages and disadvantages of the bioassay test procedures evaluated.
Toxicological Relevance of EDCs and Pharmaceuticals in Drinking Water – Water Research Foundation #3085 (Snyder *et al*. 2007; 2008)	Drinking water (20 facilities), wastewater (4 facilities - raw and recycled), and food products.	The researchers used an in vitro cellular bioassay (E-screen) with a method reporting limit (MRL) of 0.16 ηg/L; results were also converted to estradiol equivalents. The results showed that the vast majority of drinking waters were less than the MRL. The level of estrogenicity (in decreasing order) was food and beverage products (particularly soy based products) > raw wastewater > recycled water > finished drinking water.

Appendix J - Summary of Drinking Water Benchmarks for CECs

CEC	Summary of Drinking Water Benchmarks for Contaminants of Emerging Concern (CECs)											
	California Drinking Water Notification Levels (2007)[a] (ng/L)	USEPA CCL 3 List/PCCL[b]		Schwab (2005)[c]		Australia (2008)[d]		AwwaRF (2008)[e]		Schriks et al. (2009)[f]		Cotruvo et al. (2010)[g]
		ADI or RfD (µg/kg/day)	PNEC (ng/L)	ADI (µg/kg/day)	$PNEC_{dw}$ (ng/L)	ADI (µg/kg/day)	DWG (ng/L)	ADI (µg/kg/day)	DWEL (ng/L)	TDI, ADI, or RfD (µg/kg/day)	PGV (ng/L)	Lowest Guideline Value (ng/L)
1,1,1,2-Tetrachloroethane		30	1.0E+03									
1,1,1-Trichloroethane												2.0E+05
1,1-Dichloroethane		200	6.1E+03									
1,1-Dichloroethene						na	3.0E+04					
1,2,3,4,6,7,8-Heptachlorodibenzo-1,4-dioxin												3.0E+00
1,2,3,4,6,7,8-Heptachlorodibenzofuran												3.0E+00
1,2,3,4,7,8,9-Heptachlorodibenzofuran												3.0E+00
1,2,3,6,7,8-Hexachlorodibenzo-1,4-dioxin												3.0E+00
1,2,3,7,8-Pentachlorodibenzofuran												6.0E-02
1,2,3-Trichloropropane (1,2,3-TCP)	5.0E+00	6	5.0E+00									
1,2,4-Trimethylbenzene	3.3E+05	50	3.5E+05									
1,2-Dibromo-3-chloropropane												2.0E+02
1,3,5-Trimethylbenzene	3.3E+05											
1,3-Butadiene		na	1.0E+01									
1,3-Dinitrobenzene		0.1	7.0E+02									
1,4-Dichlorobenzene												7.5E+04
1,4-Dioxane	3.0E+03	na	3.0E+03							na	3.0E+04	3.0E+04
1,7-Dimethylxanthine (Paraxanthine)						na	7.0E+02					
17 α-ethinyl estradiol		na	2.8E+02			0.000043	1.5E+00	0.0001	3.5E+00			

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	California Drinking Water Notification Levels (2007)[a] (ng/L)	USEPA CCL 3 List/PCCL[b]		Schwab (2005)[c]		Australia (2008)[d]		AwwaRF (2008)[e]		Schriks et al. (2009)[f]		Cotruvo et al. (2010)[g]
		ADI or RfD (µg/kg/day)	PNEC (ng/L)	ADI (µg/kg/day)	$PNEC_{dw}$ (ng/L)	ADI (µg/kg/day)	DWG (ng/L)	ADI (µg/kg/day)	DWEL (ng/L)	TDI, ADI, or RfD (µg/kg/day)	PGV (ng/L)	Lowest Guideline Value (ng/L)
17α-estradiol		0.05	3.5E+02			na	1.8E+02					
17β-estradiol		0.05	9.0E-01			0.05	1.8E+02	0.05	1.8E+03			
1-Butanol		100	7.0E+05									
2,3,4,7,8-Pentachlorodibenzofuran												6.0E-03
2,3,7,8-Tetrachlorodibenzo-1,4-dioxin												6.0E-03
2,3,7,8-Tetrachlorodibenzofuran												3.0E-01
2,4,5-Trichlorophenol												1.8E+04
2,4,6-Trichlorophenol						na	2.0E+04					1.8E+04
2,4,6-Trinitor-1,3-dimethyl-5-tert-butylbenzene (musk xylene)						100	3.5E+05					
2,4,6-Trinitrotoluene (TNT)	1.0E+03											
2,4-D (2,4-Dichlorophenoxyacetic acid)						na	3.0E+04			10	3.0E+04	
2,4-Dichlorophenol						na	2.0E+05					1.8E+04
2,4-Dimethylphenol												1.0E+05
2,5-Dihydroxybenzoic acid						na	7.0E+03					
2,6-Dichlorobenzamide (BAM)										15	5.3E+04	
2,6-Dichlorophenol						3	1.0E+04					
2,6-Dinitrotoluene												6.0E+03
2,6-di-tert-butyl-1,4-benzoquinone (2,6-bis(1,1-dimethylethyl)-2,5-Cyclohexadiene-1,4-dione)						na	1.4E+01					

CEC	Summary of Drinking Water Benchmarks for Contaminants of Emerging Concern (CECs)											
	California Drinking Water Notification Levels (2007)[a] (ng/L)	USEPA CCL 3 List/PCCL[b]		Schwab (2005)[c]		Australia (2008)[d]		AwwaRF (2008)[e]		Schriks et al. (2009)[f]		Cotruvo et al. (2010)[g] Lowest Guideline Value (ng/L)
		ADI or RfD (µg/kg/day)	PNEC (ng/L)	ADI (µg/kg/day)	$PNEC_{dw}$ (ng/L)	ADI (µg/kg/day)	DWG (ng/L)	ADI (µg/kg/day)	DWEL (ng/L)	TDI, ADI, or RfD (µg/kg/day)	PGV (ng/L)	
2,6-di-tert-butylphenol (2,6-bis(1,1-dimethylethyl)phenol)						na	2.0E+03					
2,7-Dichlorodibenzo-p-dioxin (DCDD)						0.02	1.6E-02					
2-Butanone												3.6E+06
2-Butoxyethanol												3.0E+06
2-Chloronaphthalene												4.8E+05
2-Chlorotoluene	1.4E+05	20	1.4E+05									
2-Methoxyethanol		3	2.1E+04									
2-Phenylphenol						na	1.0E+03					
2-Propen-1-ol		5	3.5E+04									
3-Hydroxycarbofuran		0.06	4.2E+02									
4,4'-DDE						na	2.0E+04					
4,4'-DDT						na	2.0E+04					
4,4-Methylenedianiline		na	2.2E+01									
4-Acctyl-6-t-butyl-1,1-dimethylindan						na	7.0E+03					
4-Chloro-3-methylphenol												7.0E+05
4-Chlorophenol						3	1.0E+04					
4-Chlorotoluene	1.4E+05	20	1.4E+05									
4-Cumylphenol						na	3.5E+02					
4-Isopropyltoluene												3.0E+03
4-Methyl-2-Pentanone												7.0E+06
4-Methylbenzenesulfonamide										750	2.6E+06	

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	California Drinking Water Notification Levels (2007)[a] (ng/L)	USEPA CCL 3 List/PCCL[b]		Schwab (2005)[c]		Australia (2008)[d]		AwwaRF (2008)[e]		Schriks et al. (2009)[f]		Cotruvo et al. (2010)[g]
		ADI or RfD (µg/kg/day)	PNEC (ng/L)	ADI (µg/kg/day)	$PNEC_{dw}$ (ng/L)	ADI (µg/kg/day)	DWG (ng/L)	ADI (µg/kg/day)	DWEL (ng/L)	TDI, ADI, or RfD (µg/kg/day)	PGV (ng/L)	Lowest Guideline Value (ng/L)
4-Methylphenol (p-cresol)						170	6.0E+05					3.0E+05
4-Nitrophenol						8	3.0E+04					
4-Nonylphenol (4NP)						150	5.0E+05	50	1.8E+06			
4-tert octylphenol						15	5.0E+04					
5-methyl-1H-benzotriazole						na	7.0E+00					
6-Acetyl-1,1,2,4,4,7-hexamethyltetraline						na	4.0E+03					
Acephate		1.2	4.0E+03									
Acetaldehyde		10000	2.3E+04									1.0E+04
Acetamide		na	5.0E+02									
Acetaminophen		50	3.5E+05	340	5.0E+06							
Acetochlor		20	1.4E+05									
Acetochlor ethane sulfonic acid (ESA)		na	1.6E+05									
Acetochlor oxanilic acid (OA)		na	1.6E+05									
Acetone												5.4E+06
Acetophenone						100	4.0E+05					
Acrolein		0.5	3.5E+03									3.0E+03
Alachlor (Lasso)						na	2.0E+03					
Alachlor ethanesulfonic acid (ESA)		na	1.1E+06									
Alachlor OA		na	4.0E+02									
Albuterol				2.8	4.1E+04							
Aldicarb sulfone												6.0E+03
Aldicarb sulfoxide												6.0E+03

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		ADI or RfD (µg/kg/day)	PNEC (ng/L)	ADI (µg/kg/day)	$PNEC_{dw}$ (ng/L)	ADI (µg/kg/day)	DWG (ng/L)	ADI (µg/kg/day)	DWEL (ng/L)	TDI, ADI, or RfD (µg/kg/day)	PGV (ng/L)	Lowest Guideline Value (ng/L)
Alpha-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA)										300	9.0E+05	
Alprazolam						0.0071	2.5E+02					
Aluminum						na	2.0E+05					
Amidotrizoic acid (diatrizoic acid)										na	2.5E+08	
Amoxycillin						0.43	1.5E+03					
Anatoxin-a		0.5	3.5E+03									
Androsterone						na	1.4E+04					
Anhydro-erthromycin A						5	1.8E+04					
Aniline		7	6.0E+03									4.2E+04
Anthracene						na	1.5E+05					
Antipyrine						28.4	1.0E+06					
Aspirin						8.3	2.9E+04			7	2.5E+04	
Atenolol								2	7.0E+04			
Atorvastatin						0.14	5.0E+03	0.54	1.9E+04			
Atrazine						na	4.0E+04	0.1	3.0E+03			2.0E+03
Azinphos-methyl						na	3.0E+03					
Azithromycin						11	3.9E+03					
Azobenzene												3.0E+03
Bensulide		5	3.5E+04									
Bentazone										100	3.0E+05	
Benzene										na	1.0E+04	3.0E+03
Benzo(a)pyrene						na	1.0E+01					

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		ADI or RfD (µg/kg/day)	PNEC (ng/L)	ADI (µg/kg/day)	$PNEC_{dw}$ (ng/L)	ADI (µg/kg/day)	DWG (ng/L)	ADI (µg/kg/day)	DWEL (ng/L)	TDI, ADI, or RfD (µg/kg/day)	PGV (ng/L)	Lowest Guideline Value (ng/L)
Benzoic acid												2.4E+07
Benzothiozole										26	9.0E+04	
Benzotriazole (1H-benzotriazole)										295	1.0E+06	
Benzyl alcohol												3.0E+06
Benzyl chloride		na	2.0E+02			na	2.0E+02					
Betaxolol						0.28	1.0E+04					
Bezafibrate(Benzafibrate)						8.6	3.0E+05					
Bis(2-ethylhexyl)adipate												2.4E+06
Bis(2-ethylhexyl)phthalate												2.4E+04
Bis(chloroisopropyl)ether (BCIPE)										40	1.4E+05	
Bisoprolol						0.018	6.3E+02					
Bisphenol A		50	3.5E+05			50	2.0E+05	50	1.8E+06			3.0E+05
Bisphenol A diglycidyl ether												1.0E+06
Boron	1.0E+06					na	4.0E+06					
Bromide						1000	7.0E+06					
Bromine						1000	7.0E+06					
Bromoacetic acid						na	3.5E+02					
Bromochloroacetonitrile						na	7.0E+02					
Bromochloromethane		10	7.0E+04			10	4.0E+04					9.0E+04
Bromodichloromethane						na	6.0E+03					1.8E+04
Bromoform						na	1.0E+05					1.0E+05
Bromomethane		1.4	9.8E+03									6.0E+03
Bromophos-ethyl						na	1.0E+04					

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		ADI or RfD (µg/kg/day)	PNEC (ng/L)	ADI (µg/kg/day)	$PNEC_{dw}$ (ng/L)	ADI (µg/kg/day)	DWG (ng/L)	ADI (µg/kg/day)	DWEL (ng/L)	TDI, ADI, or RfD (µg/kg/day)	PGV (ng/L)	
Butylated hydroxyanisole (3-tert-butyl-4-hydroxy anisole) (BHA)		na	5.8E+02			500	1.8E+06					
Butylated hydroxytoluene (2,6-Di-tert-Butyl-p-Cresol)						300	1.0E+06					
Butylbenzyl phthalate								100	3.5E+06			1.2E+06
Caffeine						na	3.5E+02					
Captan		130	1.5E+04									
Carazolol						0.01	3.5E+02					
Carbamazepine						2.8	1.0E+05	0.34	1.2E+04	0.34	1.0E+03	
Carbendazim						na	1.0E+05			30	1.1E+05	
Carbon disulfide	1.6E+05	100	7.0E+05									6.0E+05
Carbon tetrachloride												4.2E+03
[(Carboxymethyl)imino bis(ethylenenitrilo)] tetra acetic acid						na	5.0E+03					
Cefaclor						7.1	2.5E+05					
Cephalexin						10	3.5E+04					
CFC-12		200	1.4E+06									
Chloral hydrate												6.0E+05
Chloramphenicol						5	1.8E+05					
Chlorate	8.0E+05	30	2.1E+05									4.2E+06
Chlordane (gamma-chlordane)						na	1.0E+03					
Chlorfenvinphos												4.2E+03
Chloridazon (pyrazon)										54	1.9E+05	

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		ADI or RfD (µg/kg/day)	PNEC (ng/L)	ADI (µg/kg/day)	$PNEC_{dw}$ (ng/L)	ADI (µg/kg/day)	DWG (ng/L)	ADI (µg/kg/day)	DWEL (ng/L)	TDI, ADI, or RfD (µg/kg/day)	PGV (ng/L)	
Chloroform						na	2.0E+05					6.0E+04
Chloromethane		4	2.7E+03									2.4E+04
Chlorophene						na	3.5E+02					
Chlorotetracycline						30	1.1E+05					
Chlorpropham												1.2E+06
Chlorpyrifos						na	1.0E+04					
Chlorpyrifos-methyl						na	1.0E+04					
Cholesterol						na	7.0E+03					
Cimetidine				29	4.2E+05	5.7	2.0E+05					
Ciprofloxacin				1.6	2.3E+04	7.1	2.5E+05					
Clarithromycin						7.1	2.5E+05					
Clenbuterol						4.2	1.5E+04					
Clethodim		10	7.0E+04									
Clindamycin						8.6	3.0E+05					
Clofibric acid (clofibrate)						21.4	7.5E+05			10	3.0E+04	
Cobalt		10	7.0E+04									
Codeine				2	2.9E+04	1.4	5.0E+04					
Copastanol						na	7.0E+02					
Cotinine						0.28	1.0E+04					
Coumarin						na	5.0E+02					
Cumene hydroperoxide		na	7.6E+04									
Cylcophosphamide						0.1	3.5E+03					
Cylindrospermopsin		0.03	2.1E+02									

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		ADI or RfD (µg/kg/day)	PNEC (ng/L)	ADI (µg/kg/day)	$PNEC_{dw}$ (ng/L)	ADI (µg/kg/day)	DWG (ng/L)	ADI (µg/kg/day)	DWEL (ng/L)	TDI, ADI, or RfD (µg/kg/day)	PGV (ng/L)	
Cypermethrin						na	5.0E+02					
Dalapon												1.8E+05
Dehydronifedipine				100	1.5E+06	0.57	2.0E+04					
Demeclocycline						8.6	3.0E+05					
Demeton-S						0.04	1.5E+02					
Diatrizoate sodium						na	3.5E+02					
Diatrizoic acid						na	3.5E+02					
Diazepam (Valium)						0.071	2.5E+03	1	3.5E+04			
Diazinon		0.2	1.4E+03			na	3.0E+03					1.2E+03
Dibromoacetonitrile												7.0E+04
Dibromochloromethane						na	1.0E+05					8.0E+04
Dibutyl phthalate												3.1E+05
Dibutyltin (DBT)						0.25	2.0E+03					
Dichloroacetic acid						na	1.0E+05					7.0E+03
Dichloroacetonitrile						na	2.0E+03					2.0E+04
Dichlorodifluoromethane (Freon 12)	1.0E+06											
Dichlorodiphenyldicloroethane (DDD)												1.0E+03
Dichlorvos						na	1.0E+03					
Diclofenac						0.5	1.8E+03	67	2.3E+06			
Dicrotophos		0.07	4.9E+02									
Dieldrin												3.0E+01
Diethyl glycol dimethyl ether										50	1.8E+05	

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		ADI or RfD (µg/kg/day)	PNEC (ng/L)	ADI (µg/kg/day)	$PNEC_{dw}$ (ng/L)	ADI (µg/kg/day)	DWG (ng/L)	ADI (µg/kg/day)	DWEL (ng/L)	TDI, ADI, or RfD (µg/kg/day)	PGV (ng/L)	Lowest Guideline Value (ng/L)
Diethyl phthalate										800	2.8E+06	8.0E+05
Diethylamine (DEA)										2140	7.5E+05	
Diethylene triamine penta acetic acid										100	3.5E+05	
Diethylhexyl phthalate								12	4.2E+05			
Digoxigenin				0.07	1.0E+03							
Digoxin				0.07	1.0E+03							
Diltiazem				14	2.0E+05	1.7	6.0E+04					
Dimethenamid										70	2.5E+05	
Dimethipin		21.8	1.5E+05									
Dimethoate		2.2	1.5E+04			na	5.0E+04					
Dimethyl phthalate												3.0E+03
Dimethylamine (DMA)										540	1.9E+05	
Di-n-butyl phthalate						10	3.5E+04					
Dipyrone						150	5.3E+05					
Disulfoton		0.13	9.1E+02									
Diuron		3	1.8E+03			na	3.0E+04			2	7.0E+03	1.8E+04
Dodecylguanidine acetate												2.4E+04
Doxycycline				30	4.4E+05	3	1.1E+04					
Enalaprilat (enalapril)				70	1.0E+06	0.036	1.3E+03	0.23	8.1E+03			
Endosulfan												3.6E+04
Endosulfan sulfate						na	3.0E+04					
Endrin												1.8E+03

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		ADI or RfD (µg/kg/day)	PNEC (ng/L)	ADI (µg/kg/day)	$PNEC_{dw}$ (ng/L)	ADI (µg/kg/day)	DWG (ng/L)	ADI (µg/kg/day)	DWEL (ng/L)	TDI, ADI, or RfD (µg/kg/day)	PGV (ng/L)	Lowest Guideline Value (ng/L)
Enrofloxacin						6.2	2.2E+04					
Equilenin		0.05	3.5E+02			0.00086	3.0E+01					
Equilin		0.05	3.5E+02			0.00086	3.0E+01					
Erythromycin-H_2O		0.7	4.9E+03	40	5.8E+05	5	1.8E+04					
Estriol		0.05	3.5E+02			0.0014	5.0E+01					
Estrone		0.05	3.5E+02			0.00086	3.0E+01	0.013	4.6E+02			
Ethion						na	3.0E+03					
Ethoprop		0.1	7.0E+02									
Ethoprophos (Mocap)						na	1.0E+03					
Ethyl tert-butyl ether (ETBE)										150	5.3E+05	
Ethylene glycol	1.4E+07	2000	1.4E+07									
Ethylene oxide		na	1.1E+02									
Ethylene thiourea		0.2	6.0E+01									
Ethylenediaminetetraacetic acid (EDTA)						na	2.5E+05			1900	6.0E+05	
Fenamiphos		0.1	7.0E+02									
Fenoprofen						12.9	4.5E+05					
Fenthion (fenthion-methyl)						na	5.0E+02					
Fluorene												2.4E+05
Fluoxetine (Prozac)				2.9	4.2E+04	0.28	1.0E+04	0.97	3.4E+04			
Formaldehyde	1.0E+05	200	1.4E+06									1.2E+06
Fyrol FR 2 (tri(dichlorisopropyl phosphate)						na	1.0E+06					

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		ADI or RfD (µg/kg/day)	PNEC (ng/L)	ADI (µg/kg/day)	$PNEC_{dw}$ (ng/L)	ADI (µg/kg/day)	DWG (ng/L)	ADI (µg/kg/day)	DWEL (ng/L)	TDI, ADI, or RfD (µg/kg/day)	PGV (ng/L)	Lowest Guideline Value (ng/L)
Galaxolide						500	1.8E+06					
Gemfibrozil				55	8.0E+05	17	6.0E+05	1.3	4.5E+04			
Germanium		na	7.4E+02									
Glyoxal		200	1.4E+06									
Glyphosate										300	9.0E+05	
HCFC-22		na	3.2E+04									
Heptachlor												4.0E+02
Hexachlorobenzene												4.8E+03
Hexane		60	4.2E+05									
HMX	3.5E+05											
Hydrazine		na	1.0E+01									
Ibuprofen				110	1.6E+06	11.4	4.0E+05					
Imidacloprid										60	2.1E+05	
Indomethacin						0.71	2.5E+04					
Iodide						17	1.0E+05					
Iohexol						20.6	7.2E+05				3.8E+08	
Iomeprol (iomeron)										1900	6.7E+06	
Iopamidol						11.4	4.0E+05				4.2E+08	
Iopromide						21.4	7.5E+05				2.5E+08	
Isophorone												4.0E+05
Isophosphamide						0.1	3.5E+03					
Isopropylbenzene	7.7E+05											6.0E+05

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		ADI or RfD (µg/kg/day)	PNEC (ng/L)	ADI (µg/kg/day)	$PNEC_{dw}$ (ng/L)	ADI (µg/kg/day)	DWG (ng/L)	ADI (µg/kg/day)	DWEL (ng/L)	TDI, ADI, or RfD (µg/kg/day)	PGV (ng/L)	Lowest Guideline Value (ng/L)
Isoproturon										3	9.0E+03	
Ketoprofen						1	3.5E+03					
Lincomycin				25	3.7E+05	1000	3.5E+06					
Lindane (gamma-BHC)						na	2.0E+04	0.56	2.0E+04			2.0E+02
Linuron		2	5.6E+04					2	7.0E+04			
Malathion						na	9.0E+05					
Manganese	5.0E+05					na	5.0E+05					
m-Dichlorobenzene												5.4E+05
Meprobramate								7.5	2.6E+05			
Mestranol		na	2.8E+02			0.000071	2.5E+00					
Metformin				62	9.1E+05	7.1	2.5E+05					
Methamidophos		0.3	2.1E+03									
Methanol		500	3.5E+06									
Methomyl												1.5E+05
Methoxychlor								0.02	7.0E+02			2.0E+04
Methyl isobutyl ketone (MIBK)	1.2E+05											
Methyl tert-butyl ether (MTBE)		na	1.9E+04							300	9.4E+06	6.0E+04
Methylene chloride (dichloromethane)						na	4.0E+03					5.0E+03
Methyl-oxirane		1	2.3E+02									
Metolachlor		100	7.0E+05			na	3.0E+05					
Metolachlor (ESA)		na	7.0E+06									
Metolachlor (OA)		na	7.0E+06									
Metoprolol						0.71	2.5E+04			14	5.0E+04	

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		ADI or RfD (µg/kg/day)	PNEC (ng/L)	ADI (µg/kg/day)	$PNEC_{dw}$ (ng/L)	ADI (µg/kg/day)	DWG (ng/L)	ADI (µg/kg/day)	DWEL (ng/L)	TDI, ADI, or RfD (µg/kg/day)	PGV (ng/L)	Lowest Guideline Value (ng/L)
Microcystin-LR		0.003	2.1E+01									
Mirex												4.8E+03
Molinate		2	1.4E+04									
Molybdenum		5	3.5E+04			na	5.0E+04					
Monensin						10	3.5E+04					
Monobutyltin (MBT)						na	7.0E+02					
Monochloroacetic acid												6.0E+04
Musk ketone						100	3.5E+05					
Musk tibetene						na	3.5E+02					
N,N-diethyltoluamide (NN-diethyl-3-methylbenzamide (DEET)						750	2.5E+03			1800	6.3E+06	
Nadolol						0.57	2.0E+04					
Naladixic Acid						28.4	1.0E+06					
Naphthalene	1.7E+04					na	7.0E+04					1.2E+05
Naproxen						6.3	2.2E+05	570	2.0E+07			
n-Butylbenzene	2.6E+05											
n-Butylbenzenesulphonamide										83	2.9E+05	
Nicosulfuron										200	7.0E+05	
Nitrilotriacetic acid (NTA)						na	2.0E+05					2.0E+05
Nitrobenzene		2	1.4E+04									1.2E+04
N-methyl-2-pyrrolidone		600	4.2E+06									
N-nitrosodiethylamine (NDEA)	1.0E+01	na	2.0E-01			na	1.0E+01					

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		ADI or RfD (µg/kg/day)	PNEC (ng/L)	ADI (µg/kg/day)	$PNEC_{dw}$ (ng/L)	ADI (µg/kg/day)	DWG (ng/L)	ADI (µg/kg/day)	DWEL (ng/L)	TDI, ADI, or RfD (µg/kg/day)	PGV (ng/L)	
N-nitrosodimethylamine (NDMA)	1.0E+01	0.008	6.9E-01			na	1.0E+01			na	1.0E+02	
N-nitrosodi-n-propylamine (NDPA)	1.0E+01	na	5.0E+00									
N-nitrosomorpholine (NMOR)						na	1.0E+00					
N-nitrosopyrrolidine (NPYR)		na	2.0E+01									
N-Octadecane												3.0E+03
Norethindrone		16.7	4.0E+01			0.0071	2.5E+02					
Norfloxacin				190	2.8E+06	11.4	4.0E+05					
Norfluoxetine								0.97	3.4E+04			
n-Propylbenzene	2.6E+05	na	5.8E+03									
Octachlorodibenzo-4-dioxin												3.0E+02
Octachlorodibenzo-p-dioxin (OCDD)						0.02	1.6E-02					
Octylphenol								150	5.3E+06			
o-Dichlorobenzene												9.0E+04
o-Toluidine		na	1.9E+02									
Oxamyl												6.0E+03
Oxydemeton-methyl		0.13	9.1E+02									
Oxyfluorfen		3	4.8E+02									
Oxytetracycline				30	4.4E+05	30	1.1E+05					
p,p'-Sulfonyldiphenol										17	6.0E+04	
Paracetamol						50	1.8E+05					
Parathion (ethyl parathion)						na	1.0E+04					
Parathion-methyl (methyl parathion)						na	1.0E+05					

CEC	Summary of Drinking Water Benchmarks for Contaminants of Emerging Concern (CECs)											
	California Drinking Water Notification Levels (2007)[a] (ng/L)	USEPA CCL 3 List/PCCL[b]		Schwab (2005)[c]		Australia (2008)[d]		AwwaRF (2008)[e]		Schriks et al. (2009)[f]		Cotruvo et al. (2010)[g] Lowest Guideline Value (ng/L)
		ADI or RfD (µg/kg/day)	PNEC (ng/L)	ADI (µg/kg/day)	$PNEC_{dw}$ (ng/L)	ADI (µg/kg/day)	DWG (ng/L)	ADI (µg/kg/day)	DWEL (ng/L)	TDI, ADI, or RfD (µg/kg/day)	PGV (ng/L)	
Paroxetine metabolite				2.9	4.2E+04							
PCB 105						0.02	1.6E-02					
PCB 118						0.02	1.6E-02					
PCB 156						0.02	1.6E-02					
PCB 167						0.02	1.6E-02					
PCB 169						0.02	1.6E-02					
PCB 77						0.02	1.6E-02					
p-Dichlorobenzene												7.5E+04
Penicillin G						0.43	1.5E+03					
Penicillin V						0.43	1.5E+03					
Pentachlorophenol						na	1.0E+04					
Pentamethyl-4,6-dinitroindane						na	3.5E+02					
Perchlorate		0.7	4.9E+03									
Perfenofos		0.05	3.5E+02									
Perfluoroctane sulfonate (PFOS)		na	2.0E+02							0.15	5.0E+02	
Perfluorooctanoic acid (PFOA)		na	1.1E+03							1.5	5.3E+03	
Permethrin		50	3.7E+03									
Phenanthrene						na	1.5E+05					2.4E+05
Phenazone										36	1.3E+05	
Phenol						40	1.5E+05					2.4E+05
Phenytoin (Dilantin)		na	1.2E+04					0.19	6.8E+03			
Phthalic anhydride						2000	7.0E+06					
Progesterone						30	1.1E+05					

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		ADI or RfD (µg/kg/day)	PNEC (ng/L)	ADI (µg/kg/day)	$PNEC_{dw}$ (ng/L)	ADI (µg/kg/day)	DWG (ng/L)	ADI (µg/kg/day)	DWEL (ng/L)	TDI, ADI, or RfD (µg/kg/day)	PGV (ng/L)	
Prometon												9.0E+04
Propachlor	9.0E+04											
Propranolol						1.14	4.0E+04					
Propylenedinitrilotetraacetic acid (PDTA)						na	7.0E+02					
Pyrene						na	1.5E+05					
Pyridine												6.0E+03
Quinoline		na	1.0E+01									
Ranitidine				11	1.6E+05							
RDX	3.0E+02	3	3.0E+02									
Risperidone								0.014	4.9E+02			
Roxithromycin						4.3	1.5E+05					
Salbutamol						0.086	3.0E+03					
Salicylic acid						na	1.1E+05					
sec-Butylbenzene	2.6E+05	na	1.0E+04									3.0E+03
Silver						na	1.0E+05					
Simazine						na	2.0E+04			520	2.0E+03	
Simvastatin								0.54	1.9E+04			
Stigmastanol						28.4	1.0E+06					
Strontium		600	4.2E+06									
Sulfadimethoxine						10	3.5E+04					
Sulfamethazine						10	3.5E+04					
Sulfamethiazole						10	3.5E+04					

CEC	Summary of Drinking Water Benchmarks for Contaminants of Emerging Concern (CECs)											
	California Drinking Water Notification Levels (2007)[a] (ng/L)	USEPA CCL 3 List/PCCL[b]		Schwab (2005)[c]		Australia (2008)[d]		AwwaRF (2008)[e]		Schriks et al. (2009)[f]		Cotruvo et al. (2010)[g]
		ADI or RfD (µg/kg/day)	PNEC (ng/L)	ADI (µg/kg/day)	$PNEC_{dw}$ (ng/L)	ADI (µg/kg/day)	DWG (ng/L)	ADI (µg/kg/day)	DWEL (ng/L)	TDI, ADI, or RfD (µg/kg/day)	PGV (ng/L)	Lowest Guideline Value (ng/L)
Sulfamethoxazole				130	1.9E+06	10	3.5E+04	510	1.8E+07	130	4.4E+05	
Sulfasalazine						14.2	5.0E+05					
Sulfate						na	5.0E+08					
Sulfathiazole				50	7.3E+05							
Tebuconazole		29	2.1E+05									
Tebufenozide		18	1.3E+05									
Tellurium		na	1.8E+05									
Temazepam						0.14	5.0E+03					
Terbufos		0.05	3.5E+02									
Terbufos sulfone		0.05	3.5E+02									
Terbutaline						0.13	4.5E+03					
tert-Butylbenzene	2.6E+05	na	1.0E+04									
Tertiary butyl alcohol (TBA)	1.2E+04	na	6.3E+05									6.0E+06
Testosterone						2	7.0E+03					
Tetrachloroethylene												5.0E+03
Tetracycline				30	4.4E+05	30	1.1E+05					
Thiodicarb		30	1.9E+03									
Thiophanate						na	5.0E+03					
Thiophanate-methyl		80	3.0E+03									
Timolol						0.28	1.0E+04					
Tolfenamic acid						5	1.8E+04					
Toluene												4.8E+05
Toluene diisocyanate		na	9.0E+02									

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		ADI or RfD (µg/kg/day)	PNEC (ng/L)	ADI (µg/kg/day)	$PNEC_{dw}$ (ng/L)	ADI (µg/kg/day)	DWG (ng/L)	ADI (µg/kg/day)	DWEL (ng/L)	TDI, ADI, or RfD (µg/kg/day)	PGV (ng/L)	Lowest Guideline Value (ng/L)
Tolyltriazole										250	8.8E+05	
Tri(butyl cellosolve) phosphate (ethanol,2-butoxy-phosphate)						15	5.0E+04					
Tribufos		1	7.0E+03									
Tributyl phosphate						na	5.0E+02					
Tributyltin (TBT)						na	1.0E+03					
Tributyltin Oxide												9.0E+00
Trichloroacetic acid						na	1.0E+05					6.0E+04
Trichloroethene										1.5	2.0E+04	5.0E+03
Triclosan						na	3.5E+02	75	2.6E+06			5.0E+05
Triethylamine		na	2.3E+03									
Triethylphosphate (TEP)										560	2.0E+06	
Trifluralin						na	5.0E+04					
Trihalomethanes (total)												8.0E+04
Trimethoprim				4.2	6.1E+04	20	7.0E+04	190	6.7E+06			
Triphenyl phosphate						na	1.0E+03					
Triphenylphosphine oxide (TPPO)										8	2.8E+04	
Triphenyltin hydroxide (TPTH)		0.3	1.9E+00									
Tris(2-chloroethyl)phosphate (TCEP)		300	2.5E+03			Na	1.0E+03			22	7.7E+04	
Tylosin						300	1.1E+06					
Urethane		na	3.5E+01									
Urotropine										150	5.0E+05	

CEC	Summary of Drinking Water Benchmarks for Contaminants of Emerging Concern (CECs)											
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		ADI or RfD (µg/kg/day)	PNEC (ng/L)	ADI (µg/kg/day)	$PNEC_{dw}$ (ng/L)	ADI (µg/kg/day)	DWG (ng/L)	ADI (µg/kg/day)	DWEL (ng/L)	TDI, ADI, or RfD (µg/kg/day)	PGV (ng/L)	Lowest Guideline Value (ng/L)
Vanadium	5.0E+04	3	2.1E+04									
Vinclozolin		25	5.5E+02					12	4.2E+05			
Warfarin				0.16	2.3E+03							
Xylenes (total)												5.0E+05
Ziram		16	5.7E+02									
α-BHC						na	2.0E+04					
α-Hexachlorocyclohexane		na	6.0E+00									
β-BHC						na	2.0E+04					

Notes:

na = not available; an ADI or RfD is not available for this chemical

ADI = acceptable daily intake

$PNEC_{dw}$ = predicted no effect concentration in drinking water

DWG = drinking water guideline

DWEL = drinking water equivalent level

TDI = tolerable daily intake

RfD = reference dose

PGV = provisional guideline value

µg/kg/day = micrograms per kilogram per day

ng/L= nanograms per liter

Highlighted cells indicate selected DWEL based on the following heirarchy: CA, CCL, then lowest of the remaining values.

a. From CA Dept of Public Health. 2007. Drinking Water Notification Levels and Response Levels: An Overview.Drinking Water Program.

b. From USEPA CCL 3 and CA PCC Dossier of Chemicals

c. From Table 6 in Schwab et al. 2005. Human pharmaceuticals in US surface waters: a human health risk assessment. Regulatory Toxicology and Pharmacology 42: 296-312.
d. From Tables 4.4, A1, A2, A8a, and A8b in Environment Protection and Heritage Council et al. 2008. Australian Guidelines for Water Recycling. Augmentation of Drinking Water Supplies. May 2008.

e. From Tables 9.1 and 9.2 in Snyder et al. 2008. Toxicological Relevance of EDCs and Pharmaceuticals in Drinking Water. Awwa Research Foundation. 484 pp.
f. From Table 2 in Schriks et al. 2009. In Press. Toxicological relevance of emerging contaminants for drinking water quality. Water Research, doi: 10.1016/j.wateres.2009.08.023.
g. From Table 3.2 in Cotruvo et al. 2010. Identifying Health Effects Concerns of the Water Reuse Industry and Prioritizing Research Needs for Nomination of Chemicals for Research to Appropriate National and International Agencies

California Department of Public Health (2007). Drinking Water Notification Levels and Response Levels: An Overview. Drinking Water Program.

- Notification levels are calculated using standard risk assessment methods for non-cancer and cancer endpoints, and typical exposure assumptions, including a 2-liter per day Drinking Water Consumption (DWC) rate, a 70-kilogram adult body weight (BW), a 70-year lifetime, an RSC of 0.2, a 10^{-6} cancer risk, and the upper 95% confidence limit on the cancer Slope Factor in $(mg/kg\text{-}day)^{-1}$ (q_1*)
- Non-carcinogens: C = (NOAEL x BW x RSC)/(MF x UF x DWC)
- Carcinogens: C = (BW x 10^{-6})/(q_1* x DWC)

USEPA CCL 3 List/PCCL

- For the CCL process, HRLs were calculated by converting the RfD or other dose to µg/L, assuming 2 L/day of water consumed by a 70 kg adult, and a Relative Source Contribution (RSC) of 20%.
- For carcinogens, the concentration at the 10^{-6} cancer risk was used and no RSC was included, assuming a 70-year exposure.

Schwab *et al*. (2005). Human pharmaceuticals in US surface waters: a human health risk assessment. *Regulatory Toxicology and Pharmacology* 42: 296-312. Note that values provided in the summary table with benchmarks from all the studies are for child receptors (more conservative than adults), with exposure parameters as follows:

$$\mathrm{PNEC_{DW}} = \frac{1000 \times \mathrm{ADI} \times \mathrm{BW} \times \mathrm{AT}}{\mathrm{IngR_{DW}} \times \mathrm{EF} \times \mathrm{ED}},$$

- Body weight – 14 kg
- Water consumption – 1 L/day
- Exposure frequency – 350 days/year
- ADI averaging time – 2190 days

Environment Protection and Heritage Council *et al*. (2008). Australian Guidelines for Water Recycling. Augmentation of Drinking Water Supplies.

- assume a bodyweight of 70 kg for adult 2-year-old and 13 kg for a 2-year old child
- based on a risk of 10^{-6}
- 2 L/day for an adult and 1 L/day for a 2-year-old child
- Proportion (P) from water varies. For human-use pharmaceuticals P=1.0. For other CECs the default P=0.1.

Drinking water guideline (mg/L) = $\frac{\text{NOEL (mg/kg bw/day)} \times \text{bw (kg)} \times \text{P}}{\text{SF} \times \text{V (L/day)}}$ with SF = safety factor

For carcinogens: (mg/L) = $\frac{\text{Risk x P x BW (kg)}}{\text{SF (mg/kg-day) x V (L/day)}}$ with SF = slope factor

Snyder *et al*. (2008). Toxicological Relevance of EDCs and Pharmaceuticals in Drinking Water. Water Research Foundation.

- ADIs were converted to DWELs by multiplying the ADI by 70 kg BW and dividing by 2 L/day (average daily ingestion rate of water)
- Carcinogens assumed a cancer risk of 10^{-6}
- Noncarcinogens: DWEL = $\frac{\text{ADI*70 kg*1000000 ng/mg}}{\text{2 Liters/day}}$
- Carcinogens: $\frac{10^{-6} \text{ * 70kg * 25550 days * 1000000 ng/mg}}{\text{SF * 2 L/day * 30 years * 365 days}}$ with SF = slope factor

Schriks *et al*. (2009). Toxicological relevance of emerging contaminants for drinking water quality. Water Research.

- A drinking water equivalent level (DWEL) was calculated by multiplying the TDI by a typical average body weight of 70 kg and division by a daily water consumption of 2 liters. The DWEL was multiplied by a default allocation factor of 10%.
- Cancer risk to an individual = 10^{-5} over a 70-year lifetime

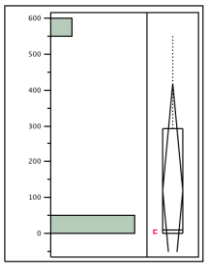
Cotruvo *et al*. (2010). Identifying Health Effects Concerns of the Water Reuse Industry and Prioritizing Research Needs for Nomination of Chemicals for Research to Appropriate National and International Agencies

- 60 kg = Default adult body weight
- 0.2 = Default Relative Source Contribution from drinking water of 20%
- 2 L/day = Default daily drinking water intake for a 60-kg adult

Action Level = $\frac{\text{ADI x 60 kg x 0.20}}{\text{2 L/day}}$

Appendix K - 90th Percentile MEC of CECs in Secondary/Tertiary Treated Effluents in California

Acetaminophen



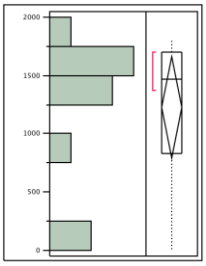
Quantiles

100.0%	maximum	550
99.5%		550
97.5%		550
90.0%		550
75.0%	quartile	292.95
50.0%	median	10
25.0%	quartile	1
10.0%		1
2.5%		1
0.5%		1
0.0%	minimum	1

Moments

Mean	119.58
Std Dev	241.03627
Std Err Mean	107.7947
Upper 95% Mean	418.86605
Lower 95% Mean	-179.7061
N	5

Atenolol



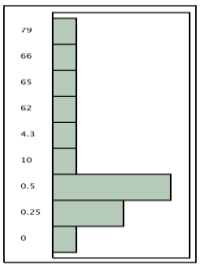
Quantiles

100.0%	maximum	1800
99.5%		1800
97.5%		1800
90.0%		1780
75.0%	quartile	1700
50.0%	median	1470
25.0%	quartile	830
10.0%		20.48
2.5%		5.6
0.5%		5.6
0.0%	minimum	5.6

Moments

Mean	1226.8727
Std Dev	641.19792
Std Err Mean	193.32845
Upper 95% Mean	1657.6354
Lower 95% Mean	796.1101
N	11

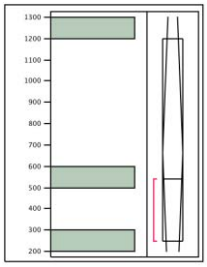
Atorvastatin



Frequencies

Level	Count	Prob
0	1	0.06667
0.25	3	0.20000
0.5	5	0.33333
10	1	0.06667
4.3	1	0.06667
62	1	0.06667
65	1	0.06667
66	1	0.06667
79	1	0.06667
Total	15	1.00000

Azithromycin



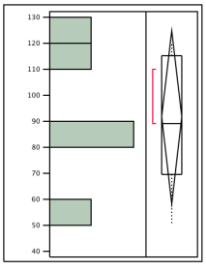
Quantiles

100.0%	maximum	1200
99.5%		1200
97.5%		1200
90.0%		1200
75.0%	quartile	1200
50.0%	median	540
25.0%	quartile	248
10.0%		248
2.5%		248
0.5%		248
0.0%	minimum	248

Moments

Mean	662.66667
Std Dev	487.7103
Std Err Mean	281.57967
Upper 95% Mean	1874.2062
Lower 95% Mean	-548.8729
N	3

Benzophenone



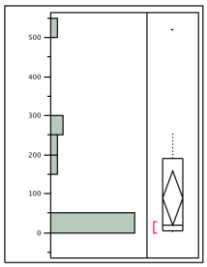
Quantiles

100.0%	maximum	120
99.5%		120
97.5%		120
90.0%		120
75.0%	quartile	115
50.0%	median	89
25.0%	quartile	69.5
10.0%		50
2.5%		50
0.5%		50
0.0%	minimum	50

Moments

Mean	91.6
Std Dev	26.87564
Std Err Mean	12.019151
Upper 95% Mean	124.97051
Lower 95% Mean	58.229486
N	5

Bisphenol A



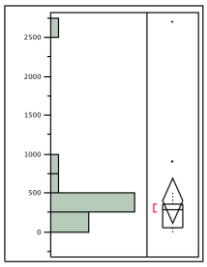
Quantiles

100.0%	maximum	520
99.5%		520
97.5%		520
90.0%		286
75.0%	quartile	191.25
50.0%	median	19
25.0%	quartile	5
10.0%		0
2.5%		0
0.5%		0
0.0%	minimum	0

Moments

Mean	88.883333
Std Dev	141.64005
Std Err Mean	33.38488
Upper 95% Mean	159.31927
Lower 95% Mean	18.447393
N	18

Caffeine



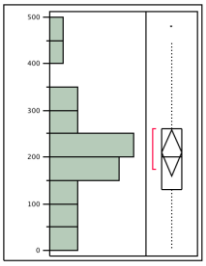
Quantiles

100.0%	maximum	2700
99.5%		2700
97.5%		2700
90.0%		900
75.0%	quartile	355
50.0%	median	280
25.0%	quartile	50
10.0%		3
2.5%		0
0.5%		0
0.0%	minimum	0

Moments

Mean	401.84211
Std Dev	596.49572
Std Err Mean	136.8455
Upper 95% Mean	689.34384
Lower 95% Mean	114.34037
N	19

Carbamezepine



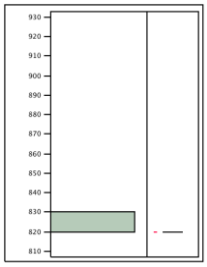
Quantiles

100.0%	maximum	480
99.5%		480
97.5%		480
90.0%		400.2
75.0%	quartile	260
50.0%	median	200
25.0%	quartile	130
10.0%		50
2.5%		1.1
0.5%		1.1
0.0%	minimum	1.1

Moments

Mean	209.3087
Std Dev	113.48913
Std Err Mean	23.664119
Upper 95% Mean	258.38508
Lower 95% Mean	160.23232
N	23

Clofibric acid



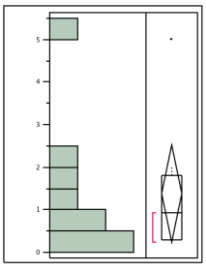
Quantiles

100.0%	maximum	820
99.5%		820
97.5%		820
90.0%		820
75.0%	quartile	820
50.0%	median	820
25.0%	quartile	820
10.0%		820
2.5%		820
0.5%		820
0.0%	minimum	820

Moments

Mean	820
Std Dev	.
Std Err Mean	.
Upper 95% Mean	.
Lower 95% Mean	.
N	1

Diazepam



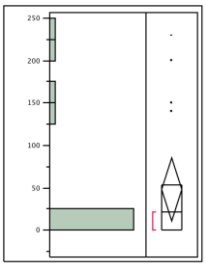
Quantiles

100.0%	maximum	5
99.5%		5
97.5%		5
90.0%		5
75.0%	quartile	1.8
50.0%	median	0.94
25.0%	quartile	0.3
10.0%		0.25
2.5%		0.25
0.5%		0.25
0.0%	minimum	0.25

Moments

Mean	1.3822222
Std Dev	1.4857134
Std Err Mean	0.4952378
Upper 95% Mean	2.5242427
Lower 95% Mean	0.2402018
N	9

Diclofenac



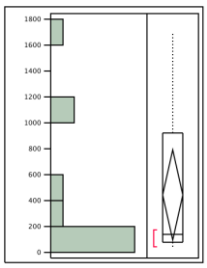
Quantiles

100.0%	maximum	230
99.5%		230
97.5%		230
90.0%		203
75.0%	quartile	53
50.0%	median	21.5
25.0%	quartile	0.5125
10.0%		0
2.5%		0
0.5%		0
0.0%	minimum	0

Moments

Mean	48.198333
Std Dev	75.303899
Std Err Mean	17.749299
Upper 95% Mean	85.646081
Lower 95% Mean	10.750585
N	18

DEET



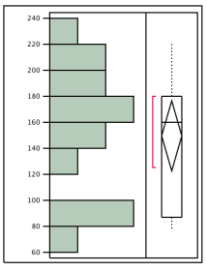
Quantiles

100.0%	maximum	1700
99.5%		1700
97.5%		1700
90.0%		1520
75.0%	quartile	925
50.0%	median	137
25.0%	quartile	81.775
10.0%		45.5
2.5%		44
0.5%		44
0.0%	minimum	44

Moments

Mean	446.55833
Std Dev	546.38599
Std Err Mean	157.72805
Upper 95% Mean	793.71543
Lower 95% Mean	99.401238
N	12

Dilantin



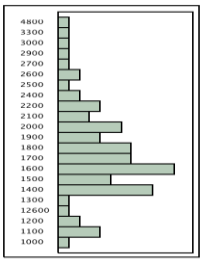
Quantiles

100.0%	maximum	220
99.5%		220
97.5%		220
90.0%		217
75.0%	quartile	180
50.0%	median	160
25.0%	quartile	87
10.0%		81.8
2.5%		77
0.5%		77
0.0%	minimum	77

Moments

Mean	149.73333
Std Dev	48.506946
Std Err Mean	12.52444
Upper 95% Mean	176.59558
Lower 95% Mean	122.87108
N	15

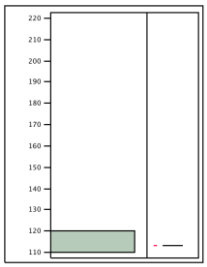
1,4-Dioxane



Frequencies

Level	Count	Prob
1000	1	0.01333
1100	4	0.05333
1200	2	0.02667
12600	1	0.01333
1300	1	0.01333
1400	9	0.12000
1500	5	0.06667
1600	11	0.14667
1700	7	0.09333
1800	7	0.09333
1900	4	0.05333
2000	6	0.08000
2100	3	0.04000
2200	4	0.05333
2400	2	0.02667
2500	1	0.01333
2600	2	0.02667
2700	1	0.01333
2900	1	0.01333
3000	1	0.01333
3300	1	0.01333
4800	1	0.01333
Total	75	1.00000

Erythromycin



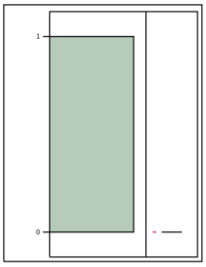
Quantiles

100.0%	maximum	113
99.5%		113
97.5%		113
90.0%		113
75.0%	quartile	113
50.0%	median	113
25.0%	quartile	113
10.0%		113
2.5%		113
0.5%		113
0.0%	minimum	113

Moments

Mean	113
Std Dev	.
Std Err Mean	.
Upper 95% Mean	.
Lower 95% Mean	.
N	1

17α-Estradiol



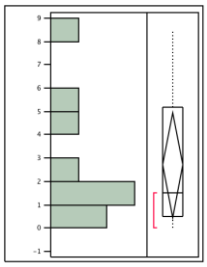
Quantiles

100.0%	maximum	0
99.5%		0
97.5%		0
90.0%		0
75.0%	quartile	0
50.0%	median	0
25.0%	quartile	0
10.0%		0
2.5%		0
0.5%		0
0.0%	minimum	0

Moments

Mean	0
Std Dev	.
Std Err Mean	.
Upper 95% Mean	.
Lower 95% Mean	.
N	1

17β-Estradiol



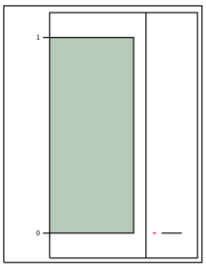
Quantiles

100.0%	maximum	8.4
99.5%		8.4
97.5%		8.4
90.0%		8.4
75.0%	quartile	5.2
50.0%	median	1.5
25.0%	quartile	0.5
10.0%		0
2.5%		0
0.5%		0
0.0%	minimum	0

Moments

Mean	2.7
Std Dev	2.9068884
Std Err Mean	0.9689628
Upper 95% Mean	4.9344322
Lower 95% Mean	0.4655678
N	9

Estriol



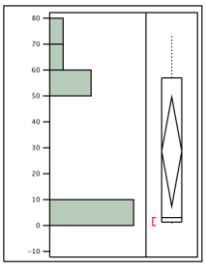
Quantiles

100.0%	maximum	0
99.5%		0
97.5%		0
90.0%		0
75.0%	quartile	0
50.0%	median	0
25.0%	quartile	0
10.0%		0
2.5%		0
0.5%		0
0.0%	minimum	0

Moments

Mean	0
Std Dev	.
Std Err Mean	.
Upper 95% Mean	.
Lower 95% Mean	.
N	1

Estrone



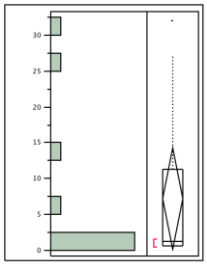
Quantiles

100.0%	maximum	73
99.5%		73
97.5%		73
90.0%		72.2
75.0%	quartile	57
50.0%	median	3
25.0%	quartile	1.2
10.0%		0.2
2.5%		0
0.5%		0
0.0%	minimum	0

Moments

Mean	28.654545
Std Dev	31.390329
Std Err Mean	9.4645402
Upper 95% Mean	49.742855
Lower 95% Mean	7.5662358
N	11

Fluoxetine



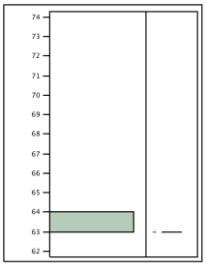
Quantiles

100.0%	maximum	32
99.5%		32
97.5%		32
90.0%		30.5
75.0%	quartile	11.325
50.0%	median	1.3
25.0%	quartile	0.6625
10.0%		0.5
2.5%		0.5
0.5%		0.5
0.0%	minimum	0.5

Moments

Mean	7.1916667
Std Dev	11.082754
Std Err Mean	3.1993155
Upper 95% Mean	14.233313
Lower 95% Mean	0.1500208
N	12

Furosemide



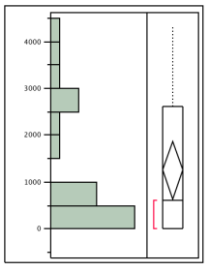
Quantiles

100.0%	maximum	63
99.5%		63
97.5%		63
90.0%		63
75.0%	quartile	63
50.0%	median	63
25.0%	quartile	63
10.0%		63
2.5%		63
0.5%		63
0.0%	minimum	63

Moments

Mean	63
Std Dev	.
Std Err Mean	.
Upper 95% Mean	.
Lower 95% Mean	.
N	1

Gemfibrozil



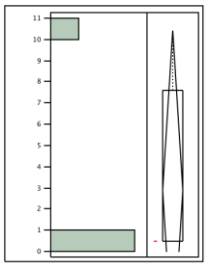
Quantiles

100.0%	maximum	4300
99.5%		4300
97.5%		4300
90.0%		3550
75.0%	quartile	2612.5
50.0%	median	610
25.0%	quartile	0.925
10.0%		0
2.5%		0
0.5%		0
0.0%	minimum	0

Moments

Mean	1252.4068
Std Dev	1411.3658
Std Err Mean	300.90419
Upper 95% Mean	1878.1713
Lower 95% Mean	626.64229
N	22

o-hydroxy atorvastatin



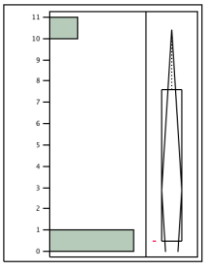
Quantiles

100.0%	maximum	10
99.5%		10
97.5%		10
90.0%		10
75.0%	quartile	7.625
50.0%	median	0.5
25.0%	quartile	0.5
10.0%		0.5
2.5%		0.5
0.5%		0.5
0.0%	minimum	0.5

Moments

Mean	2.875
Std Dev	4.75
Std Err Mean	2.375
Upper 95% Mean	10.43331
Lower 95% Mean	-4.68331
N	4

p-hydroxy atorvastatin



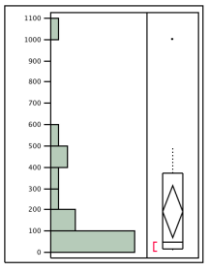
Quantiles

100.0%	maximum	10
99.5%		10
97.5%		10
90.0%		10
75.0%	quartile	7.625
50.0%	median	0.5
25.0%	quartile	0.5
10.0%		0.5
2.5%		0.5
0.5%		0.5
0.0%	minimum	0.5

Moments

Mean	2.875
Std Dev	4.75
Std Err Mean	2.375
Upper 95% Mean	10.43331
Lower 95% Mean	-4.68331
N	4

Ibuprofen



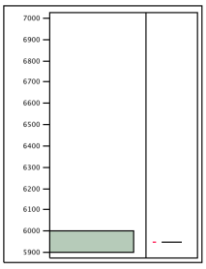
Quantiles

100.0%	maximum	1000
99.5%		1000
97.5%		1000
90.0%		500
75.0%	quartile	370
50.0%	median	50
25.0%	quartile	16
10.0%		10
2.5%		5.5
0.5%		5.5
0.0%	minimum	5.5

Moments

Mean	191.21053
Std Dev	253.12773
Std Err Mean	58.071484
Upper 95% Mean	313.21419
Lower 95% Mean	69.206866
N	19

Iohexal



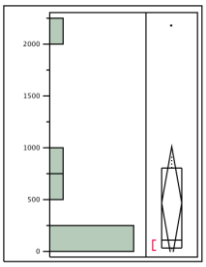
Quantiles

100.0%	maximum	5948
99.5%		5948
97.5%		5948
90.0%		5948
75.0%	quartile	5948
50.0%	median	5948
25.0%	quartile	5948
10.0%		5948
2.5%		5948
0.5%		5948
0.0%	minimum	5948

Moments

Mean	5948
Std Dev	.
Std Err Mean	.
Upper 95% Mean	.
Lower 95% Mean	.
N	1

Iopromide



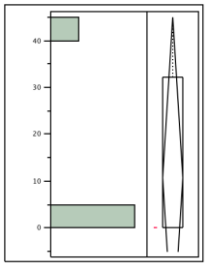
Quantiles

100.0%	maximum	2174
99.5%		2174
97.5%		2174
90.0%		2174
75.0%	quartile	800
50.0%	median	110
25.0%	quartile	30
10.0%		11
2.5%		11
0.5%		11
0.0%	minimum	11

Moments

Mean	462.88889
Std Dev	719.77539
Std Err Mean	239.92513
Upper 95% Mean	1016.1572
Lower 95% Mean	-90.37945
N	9

Ketoprofen



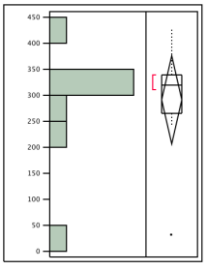
Quantiles

100.0%	maximum	43
99.5%		43
97.5%		43
90.0%		43
75.0%	quartile	32.25
50.0%	median	0
25.0%	quartile	0
10.0%		0
2.5%		0
0.5%		0
0.0%	minimum	0

Moments

Mean	10.75
Std Dev	21.5
Std Err Mean	10.75
Upper 95% Mean	44.961298
Lower 95% Mean	-23.4613
N	4

Meprobamate



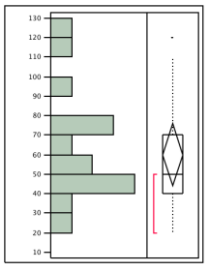
Quantiles

100.0%	maximum	430
99.5%		430
97.5%		430
90.0%		430
75.0%	quartile	340
50.0%	median	320
25.0%	quartile	265
10.0%		31
2.5%		31
0.5%		31
0.0%	minimum	31

Moments

Mean	292.22222
Std Dev	110.08948
Std Err Mean	36.696495
Upper 95% Mean	376.84449
Lower 95% Mean	207.59995
N	9

Methylisothiocyanate



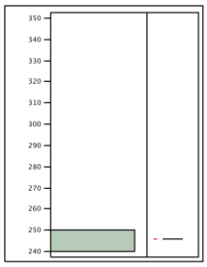
Quantiles

100.0%	maximum	120
99.5%		120
97.5%		120
90.0%		114
75.0%	quartile	70
50.0%	median	50
25.0%	quartile	40
10.0%		26
2.5%		20
0.5%		20
0.0%	minimum	20

Moments

Mean	60
Std Dev	28.784917
Std Err Mean	7.4322335
Upper 95% Mean	75.940556
Lower 95% Mean	44.059444
N	15

Metoprolol



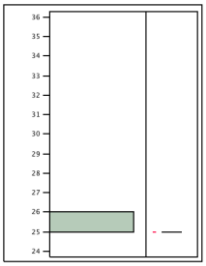
Quantiles

100.0%	maximum	246
99.5%		246
97.5%		246
90.0%		246
75.0%	quartile	246
50.0%	median	246
25.0%	quartile	246
10.0%		246
2.5%		246
0.5%		246
0.0%	minimum	246

Moments

Mean	246
Std Dev	.
Std Err Mean	.
Upper 95% Mean	.
Lower 95% Mean	.
N	1

Musk ketone



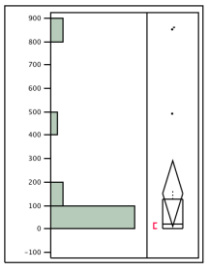
Quantiles

100.0%	maximum	25
99.5%		25
97.5%		25
90.0%		25
75.0%	quartile	25
50.0%	median	25
25.0%	quartile	25
10.0%		25
2.5%		25
0.5%		25
0.0%	minimum	25

Moments

Mean	25
Std Dev	0
Std Err Mean	0
Upper 95% Mean	25
Lower 95% Mean	25
N	6

Naproxen



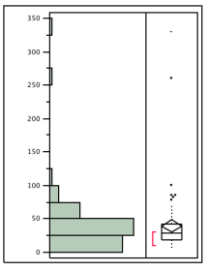
Quantiles

100.0%	maximum	860
99.5%		860
97.5%		860
90.0%		851
75.0%	quartile	126.25
50.0%	median	23
25.0%	quartile	1.175
10.0%		0
2.5%		0
0.5%		0
0.0%	minimum	0

Moments

Mean	150.03333
Std Dev	281.22278
Std Err Mean	66.284845
Upper 95% Mean	289.88213
Lower 95% Mean	10.184535
N	18

NDMA



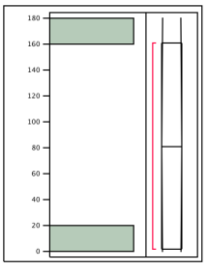
Quantiles

100.0%	maximum	330
99.5%		330
97.5%		208
90.0%		67.7
75.0%	quartile	42.5
50.0%	median	29
25.0%	quartile	19
10.0%		11.3
2.5%		7.5575
0.5%		6.6
0.0%	minimum	6.6

Moments

Mean	39.593478
Std Dev	43.414478
Std Err Mean	4.5262722
Upper 95% Mean	48.584362
Lower 95% Mean	30.602595
N	92

Nonylphenol



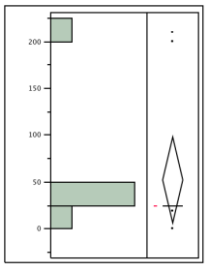
Quantiles

100.0%	maximum	161
99.5%		161
97.5%		161
90.0%		161
75.0%	quartile	161
50.0%	median	81.3
25.0%	quartile	1.6
10.0%		1.6
2.5%		1.6
0.5%		1.6
0.0%	minimum	1.6

Moments

Mean	81.3
Std Dev	112.71282
Std Err Mean	79.7
Upper 95% Mean	1093.9845
Lower 95% Mean	-931.3845
N	2

Octylphenol



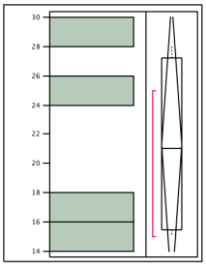
Quantiles

100.0%	maximum	210
99.5%		210
97.5%		210
90.0%		207
75.0%	quartile	25
50.0%	median	25
25.0%	quartile	25
10.0%		5.84
2.5%		0.2
0.5%		0.2
0.0%	minimum	0.2

Moments

Mean	52.433333
Std Dev	71.64939
Std Err Mean	20.683397
Upper 95% Mean	97.957184
Lower 95% Mean	6.9094825
N	12

PFOA



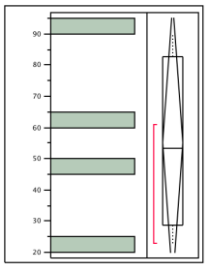
Quantiles

100.0%	maximum	28
99.5%		28
97.5%		28
90.0%		28
75.0%	quartile	27.25
50.0%	median	21
25.0%	quartile	15.5
10.0%		15
2.5%		15
0.5%		15
0.0%	minimum	15

Moments

Mean	21.25
Std Dev	6.2383224
Std Err Mean	3.1191612
Upper 95% Mean	31.176563
Lower 95% Mean	11.323437
N	4

PFOS



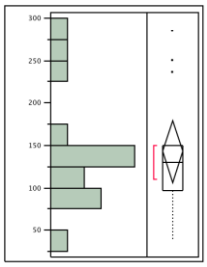
Quantiles

100.0%	maximum	90
99.5%		90
97.5%		90
90.0%		90
75.0%	quartile	82.75
50.0%	median	53.5
25.0%	quartile	28.75
10.0%		23
2.5%		23
0.5%		23
0.0%	minimum	23

Moments

Mean	55
Std Dev	28.08321
Std Err Mean	14.041605
Upper 95% Mean	99.686653
Lower 95% Mean	10.313347
N	4

Primidone



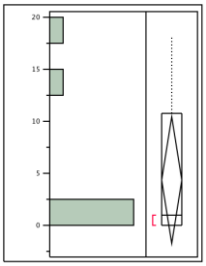
Quantiles

100.0%	maximum	285
99.5%		285
97.5%		285
90.0%		264
75.0%	quartile	150
50.0%	median	130
25.0%	quartile	97
10.0%		68.2
2.5%		40
0.5%		40
0.0%	minimum	40

Moments

Mean	143.06667
Std Dev	65.858579
Std Err Mean	17.004612
Upper 95% Mean	179.53793
Lower 95% Mean	106.5954
N	15

Progesterone



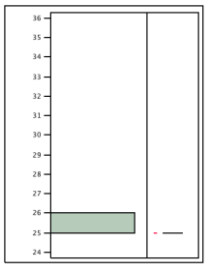
Quantiles

100.0%	maximum	18
99.5%		18
97.5%		18
90.0%		18
75.0%	quartile	10.75
50.0%	median	1
25.0%	quartile	0
10.0%		0
2.5%		0
0.5%		0
0.0%	minimum	0

Moments

Mean	4.375
Std Dev	7.2690636
Std Err Mean	2.5700021
Upper 95% Mean	10.452089
Lower 95% Mean	-1.702089
N	8

Propranolol



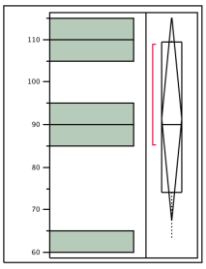
Quantiles

100.0%	maximum	25
99.5%		25
97.5%		25
90.0%		25
75.0%	quartile	25
50.0%	median	25
25.0%	quartile	25
10.0%		25
2.5%		25
0.5%		25
0.0%	minimum	25

Moments

Mean	25
Std Dev	.
Std Err Mean	.
Upper 95% Mean	.
Lower 95% Mean	.
N	1

Salicylic acid



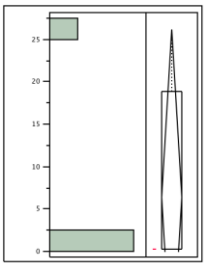
Quantiles

100.0%	maximum	110
99.5%		110
97.5%		110
90.0%		110
75.0%	quartile	109.5
50.0%	median	90
25.0%	quartile	74.1
10.0%		63
2.5%		63
0.5%		63
0.0%	minimum	63

Moments

Mean	91.44
Std Dev	19.382157
Std Err Mean	8.667964
Upper 95% Mean	115.50613
Lower 95% Mean	67.373874
N	5

Simvastatin hydroxyacid



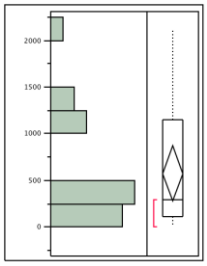
Quantiles

100.0%	maximum	25
99.5%		25
97.5%		25
90.0%		25
75.0%	quartile	18.8125
50.0%	median	0.25
25.0%	quartile	0.25
10.0%		0.25
2.5%		0.25
0.5%		0.25
0.0%	minimum	0.25

Moments

Mean	6.4375
Std Dev	12.375
Std Err Mean	6.1875
Upper 95% Mean	26.128887
Lower 95% Mean	-13.25389
N	4

Sulfamethoxazole



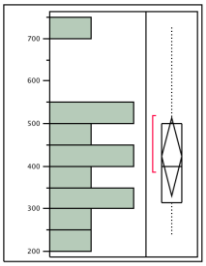
Quantiles

100.0%	maximum	2100
99.5%		2100
97.5%		2100
90.0%		1400
75.0%	quartile	1150
50.0%	median	295
25.0%	quartile	110
10.0%		5
2.5%		2.3
0.5%		2.3
0.0%	minimum	2.3

Moments

Mean	577.12105
Std Dev	603.79351
Std Err Mean	138.51973
Upper 95% Mean	868.14021
Lower 95% Mean	286.1019
N	19

TCEP



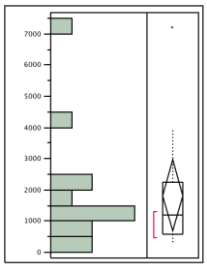
Quantiles

100.0%	maximum	730
99.5%		730
97.5%		730
90.0%		688
75.0%	quartile	500
50.0%	median	400
25.0%	quartile	314
10.0%		250.4
2.5%		240
0.5%		240
0.0%	minimum	240

Moments

Mean	422.54545
Std Dev	135.79497
Std Err Mean	40.943723
Upper 95% Mean	513.77375
Lower 95% Mean	331.31716
N	11

TCPP



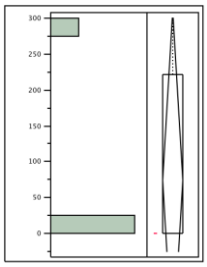
Quantiles

100.0%	maximum	7200
99.5%		7200
97.5%		7200
90.0%		5920
75.0%	quartile	2250
50.0%	median	1200
25.0%	quartile	572
10.0%		343.2
2.5%		270
0.5%		270
0.0%	minimum	270

Moments

Mean	1828.2308
Std Dev	1903.4643
Std Err Mean	527.92601
Upper 95% Mean	2978.4827
Lower 95% Mean	677.9788
N	13

TDCPP



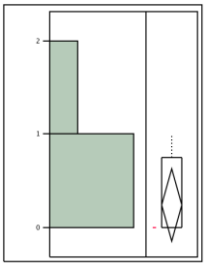
Quantiles

100.0%	maximum	296
99.5%		296
97.5%		296
90.0%		296
75.0%	quartile	222
50.0%	median	0
25.0%	quartile	0
10.0%		0
2.5%		0
0.5%		0
0.0%	minimum	0

Moments

Mean	74
Std Dev	148
Std Err Mean	74
Upper 95% Mean	309.50103
Lower 95% Mean	-161.501
N	4

Testosterone



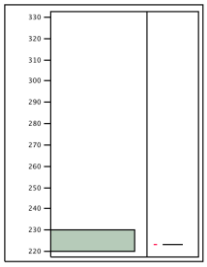
Quantiles

100.0%	maximum	1
99.5%		1
97.5%		1
90.0%		1
75.0%	quartile	0.75
50.0%	median	0
25.0%	quartile	0
10.0%		0
2.5%		0
0.5%		0
0.0%	minimum	0

Moments

Mean	0.25
Std Dev	0.46291
Std Err Mean	0.1636634
Upper 95% Mean	0.6370025
Lower 95% Mean	-0.137002
N	8

Triclocarban



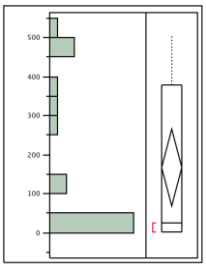
Quantiles

100.0%	maximum	223
99.5%		223
97.5%		223
90.0%		223
75.0%	quartile	223
50.0%	median	223
25.0%	quartile	223
10.0%		223
2.5%		223
0.5%		223
0.0%	minimum	223

Moments

Mean	223
Std Dev	.
Std Err Mean	.
Upper 95% Mean	.
Lower 95% Mean	.
N	1

Triclosan



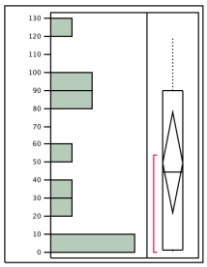
Quantiles

100.0%	maximum	510
99.5%		510
97.5%		510
90.0%		485
75.0%	quartile	380
50.0%	median	25
25.0%	quartile	1.9
10.0%		1.1
2.5%		1
0.5%		1
0.0%	minimum	1

Moments

Mean	168.37368
Std Dev	203.52077
Std Err Mean	46.690866
Upper 95% Mean	266.46755
Lower 95% Mean	70.279814
N	19

Trimethroprim



Quantiles

100.0%	maximum	120
99.5%		120
97.5%		120
90.0%		111.6
75.0%	quartile	89.5
50.0%	median	44.5
25.0%	quartile	1
10.0%		0.28
2.5%		0.25
0.5%		0.25
0.0%	minimum	0.25

Moments

Mean	49.883333
Std Dev	44.288334
Std Err Mean	12.784941
Upper 95% Mean	78.022798
Lower 95% Mean	21.743869
N	12

Appendix L - Assays currently Available Requiring Limited Quality Assurance/Quality Control Development

In vitro assays

Multiple *in vitro* assays are available for the assessment of specific biological responses. Receptor binding assays for the estrogen and androgen receptor have been approved for EDSTAC as has the H295R steroidogenesis assay (USEPA, 2009a). Alternative systems for estrogenic activity that have been also been evaluated include the MCF-7 cell line (E-screen), the Yeast Estrogen Screening (YES) bioassay, the Estrogen-Receptor-CALUX system (popular in Europe), and the rainbow trout tissue slice method (Developed by USEPA) (Leusch, 2008). Each of these assays can be calibrated against 17β-estradiol to provide EEQ (ng/L) of any water matrix.

A recent round robin experiment used five in vitro assays (YES, ER-CALUX, MELN, T47D-KBluc and E-Screen) to measure estrogen equivalence in the range of 0.1 to 320 ng/L EEq (Leusch, 2008). Tap water was spiked with chemicals that have estrogenic activity including hormones, alkylphenols, phthalates, pesticides, phytosterols. In addition, real environmental samples including sewage, river and groundwater were tested. The two assays that seemed to work the best were the ER-Calux and the E-screen assays and these also correlated the best with analytical chemistry results for spiked contaminants. The ER-Calux assay depends on T47D human breast cancer cells which contain a stably transfected ERE-Luciferase plasmid. These cells express both human ERs (ERα and ERβ). In the presence of estrogen, luciferase is expressed by the cells which can be read by a luminescence plate reader. The E-screen is an assay that depends on the proliferation of MCF-7 cells (another human breast cancer cell line) and tests the action of estrogen on both genomic and non-genomic modes of action (e.g., membrane signaling effects as well as direct gene expression effects through soluble estrogen receptors). Both assays were considered to be robust and reliable and worked well to screen the estrogenic compounds. Both of these assays could easily be performed in the commercial realm on aliquots of water extracts used for analytical chemistry measurements.

When evaluating nine studies over the last ten years where EEQ derived from in vitro assays and analytical chemistry for estrogenic compounds was conducted, a very strong correlation was observed (Figure 6.2). This plot compiled data from studies done around the world in a variety of water types, including river surface water, stream surface water and wastewater influents/effluents using four different in vitro bioassays (Bulloch, Lavado *et al*. in press). Consequently, a relatively inexpensive bioassay can be used to garner information about the occurrence of known and ***unknown*** compounds in water that have estrogen-like activity.

Another in vitro bioassay has recently been through an interlaboratory comparison and targets a highly conserved pathway involved in steroid biosynthesis in humans (Hecker, Giesy *et al*. 2008). The H295R steroidogenesis assay is based on a human adreno-carcinoma cell line and measures alterations of steroidogenesis. The H295R cells represent a unique *in vitro* system in that they have the ability to produce all of the steroid hormones found in the adult adrenal cortex and the gonads, allowing testing for effects on both corticosteroid synthesis and the production of sex steroid hormones such as progesterone, androgens and estrogens. This assay

is relatively new but has been validated in an initial round robin test by OECD (Hecker, Giesy *et al*. 2009) and approved for use for the EDSP (USEPA, 2009a).

There are also a number of genotoxic assays that have been used to test wastewater, surface water, and drinking water (Žegura, Heath *et al*. 2009). In particular, the AMES test (ISO 16240:2005), the SOS/umuC assay ((Hamer, Bihari *et al*. 2000) and ISO 13829:2000), and the in vitro micronucleus test that has been applied to wastewater samples ((Reifferscheid, Ziemann *et al*. 2008) and ISO 21427-2:2006). The first two are established assays that rely on genotoxicity to bacteria, while the micronucleus test uses a mammalian cell line, V79 cells. (See also the summary in Table I.2 of the results of several bioassays applied to recycled water.)

The use of genotoxic and cytotoxic assays may allow determination of potential harm to human health. The in vitro micronucleus test which uses mammalian cells to test for cytotoxicity and mutagenicity has recently undergone a round robin test (Reifferscheid, Ziemann *et al*. 2008; Bulloch, Lavado *et al*. in press). The test is simple in design and powerful to show effects of genotoxic chemicals. The round robin was performed by ten different laboratories representing government, industries and academic institutions. Cells were incubated with the test solutions for 24 hours and then fixed on slides for examination of micronuclei formation. Cytotoxicity must also be measured since this could confound the results. This was done by measuring the survival index (growth rate of treated cells versus control cells). This test could easily be done in commercial laboratories.

Another example is the use of a combination of the SOS/umuC assay with *Salmonella typhimurium* and the MTT cytotoxicity assay with human hepatoma HepG2 cells, respectively (Žegura, Heath *et al*. 2009). The SOS/umuC assay has been standardized and is currently used in many countries to test water effluents (Hamer, Bihari *et al*. 2000; Dizer, Wittekindt *et al*. 2002). HepG2 cells are of hepatic origin and therefore contain a variety of metabolizing enzymes and are therefore useful to also measure potential cytotoxic or genotoxic metabolites that may result from metabolism of xenobiotics (Mersch-Sundermann, Knasmuller *et al*. 2004). Using these assays, Žegura *et al*. (Žegura, Heath *et al*. 2009) demonstrated that none of the water extracts from potable sites were cytotoxic. These tests are relatively quick to perform and can give assurance of safety for human health.

In vivo assays

As indicated above, EDSTAC suggested several bioassays in rats, fish, and amphibians to evaluate the estrogenic, androgenic and thyroid receptor mediated effects in humans and wildlife. Two approved assays that lend themselves to the assessment of water include the Fathead Minnow recrudescence assay (Ankley, Jensen *et al*. 2001)and the FETAX assay (Hoke and Ankley 2005). The choice of these assays is not specifically geared to effects in wildlife, but may also be used to evaluate estrogenic and thyroid disruption to all vertebrates including humans.

For estrogenic activity, the Fathead minnow recrudescence bioassay has been specifically developed by EDSTAC and has undergone extensive review by the USEPA for chemical testing. This assay measures effects on reproduction (number of eggs produced, number of fertilized

eggs, number of hatched eggs and survival of fry) from endocrine disruptors that affect any point along the HPG axis. Likewise, FETAX (frog embryo teratogenesis assay xenopus) has been proposed for determining thyroid active compounds (USEPA 2009a). Two endpoints are assessed with the assay: mortality and malformation of embryos.

Assays requiring additional quality assurance/control development

In vitro assays

Nuclear Receptor Cell-Based Assays.

InVitrogen, Inc has developed commercial kits for 22 soluble hormone receptors that are implicated in toxicity pathways. The assays are for the following receptors: androgen receptor (AR), estrogen receptors alpha and beta (ERα, ERβ), estrogen related receptor alpha (ERRα), farnesoid x receptor (FXR), glucocorticoid receptor (GR), liver X receptors alpha and beta (LXRα, LXRβ), mineralocorticoid receptor (MR), peroxisome proliferator-activated receptors alpha, delta, and gamma (PPARα, PPARδ, PPARγ), progesterone receptor (PR), retinoic acid receptors alpha, beta, and gamma (RARα, RARβ, RARγ), retinoic acid related orphan receptor (ROR), retinoic X receptors alpha and beta (RXRα, RXRβ), thyroid receptors alpha and beta (TRα, TRβ) and vitamin D receptor (VDR). These assays are all validated and ready for high throughput screening. In fact, the National Toxicology Program in its Tox21 studies is in the process of using these assays to screen approximately 10,000 chemicals (Collins, Gray *et al*. 2008). These assays are using a 15 point dose response curve in the range of 5 nM to 100 µM. These assays should be immediately amenable to commercial laboratories. Of particular importance to drinking water would be the assays for soluble sex hormone receptors (AR, ERs, PR).

In vivo assays

Genomic Assays

USEPA has clearly stated that toxicology will eventually be assessed through *in silico* methods as data on the effects of compounds on biological systems become more available. Chemicals provide specific signatures or "fingerprints" of biological responses at the genomic level of biological organization. To evaluate these signatures, microarrays for transcriptome studies are commercially available for zebrafish, fathead minnows and a large assortment of mammalian models, including rat, mouse and human among others (Affymetrix and Agilent). Mammalian cell lines (for example HepG2) can be treated with waters in the laboratory to determine sublethal toxicity pathways that are changed upon exposure. Alternatively, small fish models such as zebrafish and fathead minnows can be exposed to waters for a short period (24 to 96 h) and relevant tissues excised and measured for adverse changes in gene transcription related to toxicity pathways. Once calibrated for specific mode of action, these assays should provide an indication of the "type" of compounds present within the matrix. With subsequent studies using refined *in vitro* assays in a Toxicity Identification Evaluation approach, specific compounds may eventually be identified. Even more importantly these assays may be used to determine the "no observable adverse transcription effect level (NOATEL)". To be fully useful for

regulatory use these assays must still be vetted in round robin tests and commercial laboratories will have to be trained in their proper use.

On-line fish bioassays

A National Research Council panel recommended flow-through biomonitoring systems as a potential tool for certain water quality situations (NRC 1998). To implement such a system, fish were utilized by the Orange County Water District as an investigative model to develop a standard test platform, and evaluate the water quality of shallow ground water originating from the Santa Ana River (Deng, Carney *et al*. 2008). The endpoinst focused upon chronic exposure (3 months) and included histopathology (i.e., cancer), endocrine and reproduction metrics. A more developed system has been employed in Singapore primarily for acute impacts of water quality (http://www.pub.gov.sg/mpublications/Pages/PressReleases.aspx?ItemId=178). Disadvantages of these systems are differentiating non-chemical and chemical stressors as well as appropriate controls for use in assessing potential adverse effects in humans.

Appendix M - Prerequisites for Monitoring CECs in Recycled Water

Background and History of Efforts to Monitor CECs in Recycled Water

Although the term "emerging contaminants" has often been applied to chemicals that have been recently detected in the environment, the analysis of endocrine disrupting compounds (EDCs) and pharmaceuticals and personal care products (PPCPs) has been ongoing for decades. In the 1960s, Stumm-Zollinger and Fair (Stumm-Zollinger and Fair 1965) used UV absorbance to study the biodegradation of steroid hormones in wastewater. In the 1970s, Tabak and Bunch (Tabak, Bunch *et al*. 1970) studied steroid hormones as water pollutant and Hignite and Azarnoff (Hignite and Azarnoff 1977) studied the presence of chlorophenoxyisobutyrate (a biologically active metabolite of clofibrate) and salicylic acid (commonly known as aspirin) in wastewater using gas chromatography-mass spectrometry (GC-MS). Despite these reports of EDCs and pharmaceuticals in the environment, they received little attention until researchers in the United Kingdom and United States linked the occurrence of trace steroids to biological activity in fish and cellular bioassays (Desbrow, Routledge *et al*. 1998; Routledge, Sheahan *et al*. 1998; Snyder, Villeneuve *et al*. 2001). The most prolific study was published in 2002 by the U.S. Geological Survey (Kolpin, Furlong *et al*. 2002), titled "*Pharmaceuticals, hormones, and other organic waste contaminants in US streams, 1999-2000: a national reconnaissance*". This manuscript reported summed steroid hormone concentrations as high as several µg/L and maximum 17α-ethynyl estradiol (EE2) and 19-norethisterone concentrations of 831 and 872 ng/L, respectively (Kolpin, Furlong *et al*. 2002). The USGS subsequently retracted some of the steroid hormone data stating that "*seven concentrations of EE2 (ranging from 0.023 to 0.831 µg/L) and four concentrations of mestranol (ranging from 0.034 to 0.197 µg/L) were erroneously published and should have been reported as nondetections*" (http://toxics.usgs.gov/regional/est_errata.html). However, even accounting for these corrections, the USGS data still indicate the highest concentrations of steroid hormones ever reported in environmental waters. Based on EPA dossiers for the nine steroid hormones included in Contaminant Candidate List 3 (CCL3), the Kolpin manuscript appears to have been the dominant factor in occurrence attributes used for the EPA's listing decision (see also discussion on CCL3 in Section 2). With regard to CCL3 dossier information, it is also of interest that the 10^{-6} calculated cancer risk level for 17β-estradiol (E2) is 0.9 ng/L, making the key endogenous estrogen almost as potent a carcinogen as N-nitrosodimethylamine (NDMA) (10^{-6} cancer risk at 0.7 ng/L). It is worth noting that the occurrence section of the E2 CCL3 dossier cites the Kolpin *et al*. (Kolpin, Furlong *et al*. 2002) maximum concentration of 200 ng/L as well as a reference to research showing no detectable E2 concentrations in U.S. finished drinking water (Snyder, Wert *et al*. 2007).

These developments, along with advances in analytical instrumentation, have led to a rapid increase in the number of analytical techniques used to study steroid hormones and other exogenous agents such as pharmaceuticals and personal care products (PPCPs) in water. Analytical techniques have increased the sensitivity and accuracy of CEC analysis, allowing ultra-trace levels of a wide variety of contaminants to be identified and quantified. For instance, a number of pharmaceuticals and perfluorinated organic compounds have been recently reported to occur in US drinking waters {Benotti, 2009; Quinones, 2009).

Because CECs represent an extremely broad spectrum of compounds, developing a single all-encompassing technique for their analysis is highly unlikely. These chemicals vary widely in their physico-chemical properties (e.g., polarity, molecular weight, pKa, water solubility, etc.) making analysis by traditional analytical techniques difficult. Additionally, the concentration of many CECs in the environment can be quite low, typically sub-μg/L, which further increases the complexity of analysis by necessitating extraction and concentration steps.

In general; however, a plan for the analysis of target CECs encompasses similar primary steps including: sample collection/preservation, analysis and quantification. Many excellent reviews exist that can be used for background information on this topic (Lopez de Alda and Barcelo 2001; Ternes 2001; Richardson 2002; Richardson 2004; Koester and Moulik 2005; Petrovic, Hernando *et al*. 2005; Richardson and Ternes 2005; Richardson 2006).

Example Requirements for Compliance Monitoring

Compliance is based on a number of factors and depends on the individual contaminant. Using atrazine as an example, compliance (per 141.24(h) is determined as follows for this chemical; note that some sections have been removed for brevity):

> (11) Compliance with § 141.61(c) shall be determined based on the analytical results obtained at each sampling point. If one sampling point is in violation of an MCL, the system is in violation of the MCL.
>
> (i) For systems monitoring more than once per year, compliance with the MCL is determined by a running annual average at each sampling point.
>
> (ii) Systems monitoring annually or less frequently whose sample result exceeds the regulatory detection level as defined by paragraph (h)(18) of this section must begin quarterly sampling. The system will not be considered in violation of the MCL until it has completed one year of quarterly sampling.
>
> (iii) If any sample result will cause the running annual average to exceed the MCL at any sampling point, the system is out of compliance with the MCL immediately.
>
> (iv) If a system fails to collect the required number of samples, compliance will be based on the total number of samples collected.
>
> (v) If a sample result is less than the detection limit, zero will be used to calculate the annual average.
>
> (16) The State has the authority to determine compliance or initiate enforcement action based upon analytical results and other information compiled by their sanctioned representatives and agencies.
>
> (20) All new systems or systems that use a new source of water that begin operation after January 22, 2004 must demonstrate compliance with the MCL within a period of time specified by the State. The system must also comply with the initial sampling frequencies specified by the State to ensure a system can demonstrate compliance with

the MCL. Routine and increased monitoring frequencies shall be conducted in accordance with the requirements in this section.

Recommended QA/QC Guidelines for Commercially Available Methods

To ensure the quality of the data, methods approved by USEPA demand rigorous quality assurance/quality control (QA/QC) measures. In general, QA/QC involves the following:

1. Detailed written protocols in place for positive and negative controls to monitor tests such as blanks, spikes, and reference materials;

2. Tests to define the variability and/or repeatability of the laboratory results such as replicates;

3. Measures to assess the accuracy of the test method including calibration and/or continuing calibrations, use of certified reference materials, and proficiency test samples;

4. Measures to evaluate test method capability, such as limit of detection and limit of quantification or range of applicability such as linearity;

5. Selection of appropriate formulae to reduce raw data to final results such as regression analysis, comparison to internal/external standard calculations, and statistical analyses;

6. Selection and use of reagents and standards of appropriate quality;

7. Measures to ensure the selectivity of the test for its intended purpose; and,

8. Measures to ensure constant and consistent test conditions.

Specific quality control practices generally involve an initial demonstration of capability (or proficiency) and then ongoing quality control measures that validate the data through acceptance criteria. A demonstration of capability may be required prior to using any test method and any time there is a change in instrument type, personnel, or test method. This typically involves the determination of the limit of detection and limit of quantification, an evaluation of precision and bias, and an evaluation of selectivity.

On-going quality control may involve the use of the following controls:

- Laboratory performance controls
- Method blank or laboratory reagent blank – This negative control is used to assess the sample batch for possible contamination during the preparation and processing steps.
- Laboratory control standard or laboratory fortified blank – The laboratory control standard is used to evaluate the performance of the total analytical system, including all preparation and analysis steps. Results of the laboratory control standard are compared to established criteria. Failure to meet these criteria indicates that the analytical system is not performing correctly and may not be producing acceptable results. Control

standards are typically prepared using a standard that differs from the one used to prepare the instrument calibration curve.

- Continuing calibration check – This standard is used to evaluate the reliability of the calibration curve.
- Sample-specific controls
- Matrix spikes or laboratory fortified sample matrix – Matrix-specific quality control samples indicate the effect of the sample matrix on the precision and accuracy of the results generated using the selected methods.
- Matrix duplicates – Matrix duplicates are replicate aliquots of the same sample taken through the entire analytical procedure. The results from this analysis indicate the precision of the results for the specific sample using the selected method. The matrix duplicate provides a usable measure of precision only when target analytes are found in the sample chosen for duplication.
- Surrogate spikes – Surrogates are chosen to reflect the chemistries of the targeted components of the method. Added prior to sample preparation/extraction, they provide a measure of recovery for every sample matrix. These are typically used in lieu of techniques like isotope dilution and when matrix characterization is not practical because the method is being used for large numbers of highly variable sample matrices.
- Limit of detection and limit of quantification – Limits of detection and quantification define the lowest levels at which the instrument can differentiate between a signal and noise and the lowest level at which a value may be reported, respectively. After the initial demonstration of capability, these limits are monitored and re-evaluated, as necessary.