University of Colorado at Boulder

Center for Environmental Mass Spectrometry
Civil, Environmental and Architectural Engineering
ECOT 441, 428 UCB
Boulder, CO, 80309

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To: State Water Resources Control Board

The following review addresses the **"Requirements for Monitoring Emerging Constituents/Constituents of Emerging Concern for Recycled Water"** and the Final Report, "**Monitoring Strategies for Chemicals of Emerging Concern (CECs) in Recycled Water"**, which are the recommendations of a Science Advisory Panel whose members include: Paul Anderson, Nancy Denslow, Jorg E. Drewes, Adam Olivieri, Daniel Schlenk, and Shane Snyder. The panel and report was convened by the State Water Resources Control Board of California of June 25, 2010 in Sacramento, California. The panel, formed in May of 2009, includes six national experts in the field of chemistry, biochemistry, toxicology, epidemiology, risk assessment, and engineering.

The charge to the panel, as outlined on page 2 of the Final Report, includes five specific charge questions, which are written below. Furthermore, the Panel was 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.
3. Urban landscape irrigation with recycled water.

The five specific charges include:

1. What are the appropriate constituents to be monitored, including analytical methods and method detection limits?

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2. What is the known toxicological information for the above constituent?
3. Would the above lists of constituents change based on level of treatment and use? If so, how?
4. What are possible indicators that represent suites of CECs?
5. What levels of CECs should trigger enhanced monitoring of CECs in recycled water, groundwater, and/or surface waters?

Based on these charges and the guidelines of Attachment 2, the following review is written. The comments address each of the questions in light of the three reuse practices outlined by the Panel above, with the information from the review of the occurrence, relevance, and quantification of CECs in recycled water in the State of California, as well as my considerable knowledge on CECs in wastewater and surface water.

Yours sincerely,

Imma Ferrer

Dr. Imma Ferrer
Center for Environmental Mass Spectrometry
University of Colorado
Boulder, CO 80309

Scientific Issues to be Addressed by Peer Reviewers

1) Sufficiency of potential water contaminants lists of CECs.

I noticed that in this section it specifically says that "the approach for selecting CECs to screen relied on the United States Environmental Protection Agency (USEPA) Candidate Contaminant List 3 (CCL3) selection process". I only see two compounds from this list on the requirements (17β-estradiol and NDMA), which is surprising taking into account all the other potential contaminants that are included in the EPA list. But I agree with the Panel, that the CCL3 list is not inclusive of a diversity of monitoring data that has been collected in California, especially pharmaceutical compounds, thus should only be a guide in the selection process.

Three different lists of CECs (CCL3 from EPA, UCMR and CDPH lists) were used. However, it is not clear how all these lists were taken into account in the Report. According to Sections 4 and 5, only those CECs for which measured environmental concentrations (MECs) were available were considered for the calculation of monitoring trigger levels (MTLs). And from those, only the ones exhibiting a ratio of MEC/MTL higher than 1 were considered health CECs. In my opinion this is a limited view of what is out there in the environment and what are the important issues to be addressed, which I discuss later.

When talking about degradation products that occur in recycled water, the panel states that the concentrations at which they occur have not yet been quantified. I personally know of many studies (including USGS and NAWQA data) that report these types of degradation products in surface and groundwater in the state of California. Maybe some of these lists should have been used for the selection process as well.

Regarding unknown unknowns in Section 2 of the Report is a bit ambiguous since there are no data, not even an example of what these types of compounds can be. Moreover, when using terms such as "unknown unknowns" and "known unknowns" I would appreciate seeing a reference to the author who first reported and defined these terms in a peer review Journal: *James L. Little, Identification of "Known Unknowns" Utilizing Accurate Mass Data and Chemical Abstracts Service Databases , Journal of the American Society for Mass Spectrometry, vol. 22, 348-359.*

Overall, I think there are sufficient water contaminant lists that have been considered here. However, I would have appreciated seeing some of the proprietary and relevant environmental lists that a few scientists have reported in the last few years in well-known peer reviewed Journals, as well as extensive USGS environmental monitoring programs.

2) Appropriateness of the approach for selecting CECs of toxicological relevance to monitor for recycled water uses.

a) Compilation of CEC occurrence data for municipal recycled water in California.

The compilation of data itself of CEC occurrence seems well done and results are clearly shown in the Report. But, as the Panel states, the list of non-CCL3 MECs shown here does NOT represent the entire spectrum of non-CCL3 compounds potentially present in recycled water. More studies are needed to screen (later commented in the methods section) for potential new emerging contaminants. Furthermore, it is interesting to note that no halogenated pharmaceuticals (which would be expected to have more toxicity) were included in previous monitoring programs. This pre-selection was made from a narrow list that did not include many of the potential contaminants that could be present in municipal wastewater. I think other resources, such as USGS or EPA monitoring data, could have been considered here to expand the scope of CECs. I will make specific comments later on this.

I assume the concentrations reported in Figures from Appendix K were ng/L, they were not specified anywhere in the Report. It would be useful to report the screening level ADIs for each one of the compounds reported in Tables 5.1 and 5.2. As shown it is a bit confusing how those levels were achieved.

b) Assignment of a toxicologically relevant concentration level, referred to as an initial monitoring trigger level (MTL), to individual CEC for each recycled water exposure scenario.

I assume the concentrations reported in Figures from Appendix K were ng/L, they were not specified anywhere in the Report. It would be useful to report the screening level ADIs for each one of the compounds reported in Tables 5.1 and 5.2. As shown it is a bit confusing how those levels were achieved.

First of all, what are the units for MTL's? As presented in Eq. 4.1 of the report and taking the example for 17β-estradiol presented, the units are ug/L. Later in Table 5.2, it seems that the units are ng/L for MTL's, but it does not mention it specifically.

There are a lot of assumptions about potential toxicity of a given CEC and the ADI values derived from different sources (or drinking water benchmarks). In some cases (e.g. DEET, ibuprofen, triclosan…) the derived MTL values vary a lot. Taking the most conservative values might not be the best choice to include or not to include a specific contaminant in the monitoring lists.

I have a hard time understanding why the MTL for caffeine is so much lower than let's say atenolol or fluoxetine. Likewise, a value of 350000 (0.35 ppm!) for Bisphenol A or a value of 500000 (0.5ppm!) for 4-nonylphenol, both of which

have been previously reported as carcinogenic compounds/endocrine disruptors by several studies, seems unreasonable to me. The model used here is a cancer/toxicological model, but does not take into account endocrine disruption at very low levels of concentration (1-10 ng/L) that has been proven in several studies (Kidd et al. 2007). Using a cancer/toxicological model, pharmaceuticals (prescribed for human intake) are automatically excluded from the CEC list, because the doses at which they are prescribed are high enough that the MTL level will always exceed the MEC level monitored; so in a way this pre-selection is somehow exclusive of important CECs that are present in the environment and could potentially be endocrine disruptors (see my comment on ethinylestradiol in the next section) or developmental disruptors for infants (e.g. brain function).

I have a major criticism to Table 5.3 in the Report. In the column where it says "available analytical method", what different sources were investigated? For example, there is an EPA method for Alachlor OA, and other EPA methods as well as for the majority of the organophosphate compounds included in this list. Moreover, why did the panel decided not to recommend gathering MEC information for most of them? I think it would be important to gather MEC for some of the high use pesticides (e.g. alachlor, terbufos, etc) in the state of California, as well as recognize that there are available analytical methods (official and non-official) for most of the compounds shown in this list.

c) Comparison of the MEC to the MTL.

The MTL is based on several factors including toxicity and intake volume. If MEC is higher than MTL then a compound is considered potentially toxic and becomes a candidate for monitoring. But this calculation does not take into account synergistic effects, such as sum of related CECs (anti-depressants, hormones, endocrine disruptor compounds…) in the same parcel/volume of water. I think that in certain cases the MTL is a value that will work to trigger specific potential health risk compounds, but as a whole picture scenario it might be too limited and it might not reflect the real environmental potential risk.

My final comment here is that MECs and MTLs were compared for a selected list of compounds that were included in previous monitoring programs (Section 5). So, again, the scope is narrowed to only include these analytes and does not consider other relevant environmental contaminants that are present in recycled municipal wastewater.

d) Evaluation of robust analytical method availability.

It is unfortunate not to have the names of the CECs that were excluded because the Panel considered that they did not have commercially available analytical methods. Also, were these methods based on U.S. EPA guidelines? It is not clear how this issue can be reviewed if only limited information is available in the Report. Furthermore, not much has been described in the Report related to

analytical methodologies for the identification/determination of environmental contaminants, other than in Section 7.3. I would like to add here that the use of high resolution-mass spectrometry techniques would be an invaluable addition to the described instrumentation, especially for the identification of newly and relevant non-target/unknown contaminants (Ferrer & Thurman, 2009).

In the next revision, I would encourage the Panel to comment more specifically about the different analytical approaches that can be used and are currently used for the detection of environmental contaminants. I noticed that tandem mass spectrometry (MS-MS) is not mentioned and it is a very important technique to confirm the identity/presence of detected analytes. Likewise, multiple reaction monitoring (MRM) techniques are now used to identify emerging contaminants in the environment and there are a set of regulations (e.g. ion ratios, ion intensities) established for the confirmation of the presence/non-presence of individual compounds in water samples (Ferrer & Thurman, 2010). There is extensive literature information nowadays on "classic" (GC-MS and LC-MS) and state-of-the-art (GC/TOF-MS, LC/TOF-MS, LC/MS-MS) methodologies for organic contaminants in water samples. I feel like this issue was skipped somehow in the Report, as well as in the water policy requirements.

Also, recently, direct injection methods (without sample preparation) have been reported for the analysis of pharmaceutical and related compounds in water samples, thus avoiding potential losses and/or matrix effects by LC-MS analyses (as stated by the Panel Report, page 54). I would expect these types of methods to become popular over the next few years, and this could be an alternative to the "classic" methods reported here.

And, again, in Table 5.3 many of the compounds shown do have an available analytical method for their determination. This should be clarified, if the Panel meant there is no EPA method or there is no official method whatsoever.

I want to emphasize one of the sentences used by the Panel in the Report: *"A monitoring program truly is only as good as the reliability of the data collected"*. Totally true and I would even add that the monitoring should be performed with the best analytical tools available at present.

3) Determination of initial MTLs for the landscape irrigation.

No comments on this section. It is well explained in the Report how MTLs are developed for landscape irrigation. Just a note: in Tables 5.1 and 5.2 the difference between potable reuse MTLs and irrigation MTLs is a factor of 10, not a 100 as described in page 34 of the Report.

However, I can not imagine that drinking 5 ppm (or is it 50 ppm?) of 4-nonylphenol in a swimming pool or irrigation canal is safe!

4) Adequacy of the selected performance indicator CECs.

I will comment on both types of CECs here: health and performance indicators.

CECs Selected to be Monitored. The panel selected four health relevant compounds based on toxicological relevance. They are N-nitrosodimethylamine (NDMA), 17-β-estradiol, caffeine, and triclosan. In addition, four additional CECs were identified for surface spreading and direct injection operations as viable performance indicator compounds (i.e. they represent a family of CECs with similar chemical structure and attributes). These compounds are N,N-diethyl-meta-toluamide (DEET), gemfibrozil, iopromide, and sucralose. The 8 compounds are discussed by compound, their analytical methods, detection limits, and toxicology.

N-Nitrosodimethylamine (NDMA). N-Nitrosodimethylamine is a member of a family of extremely potent carcinogens, the N-nitrosamines, a family of compounds found in food and known about since the early 1990s. A recent review by Mitch et al. (2003) points out that NDMA is a drinking water contaminant resulting from reactions occurring during chlorination or via direct industrial contamination, typically with dimethylamine. Also Mitch et al. (2003) notes that relatively high concentrations of NDMA will form during wastewater chlorination. Furthermore, the intentional or unintentional reuse of municipal wastewater is a particularly important area of concern since NDMA may be mobile and transported in groundwater. Thus, this compound merits its selection on the list as the first and most important compound for monitoring based on toxicity. I definitely agree that this compound should be chosen for future monitoring based on toxicity and it does represent a class of chlorinated N-nitrosoamines of interest of which there are at least 7 compounds that have been reported. A quick literature search shows that there are both GC-MS and LC-MS methods available for detection of NDMA at the 1 ng/L limit of detection. However, these methods recommend the use of high resolution and accurate mass analysis, not the conventional simpler GC-MS and LC-MS methods (Taguchi et al. 1994; Krauss and Hollender, 2008) although an LC-MS method has been reported (Zhao et al., 2006). Appendix K in the final report shows that NDMA has been measured in California reuse waters with an N of 92 times, median concentration of 29 ng/L and a maximum of 330 ng/L. Thus, a LOD of 1 ng/L should be adequate for a monitoring study of this compound in groundwater and reuse waters.

17-β-Estradiol. The compound, 17-β-estradiol, is a human (animal) sex hormone. 17-β-Estradiol is abbreviated E2 as it has 2 hydroxyl groups in its molecular structure. Estrone has 1 (E1) and estriol has 3 (E3). estradiol (E2) is about 10 times as potent as estrone and about 80 times as potent as estriol in its estrogenic effect. Estradiol (E2) is the predominant estrogen during reproductive years both in terms of absolute serum levels as well as in terms of estrogenic activity. During menopause, estrone is the predominant circulating estrogen and during pregnancy estriol is the predominant circulating estrogen in terms of serum levels. Estradiol is also present in males, being produced as an active metabolic product of testosterone. The serum levels of estradiol in males (14 - 55 ng/L) are roughly comparable to those of postmenopausal women (~35 ng/L). Estradiol *in vivo* is interconvertible with estrone; estradiol to estrone conversion being favored.

Referring to Appendix K in the final report, there are only nine measurements of 17-β-estradiol, one measurement of 17-α-ethinylestradiol (EE2, birth control pill active ingredient), and one measurement of estriol, and 11 measurements of estrone. Thus, there are very little data available on this family of compounds in reuse waters of California. However, the available data does show that estrone is the most abundant of the four compounds that represent this family of compounds. I think that 17-α-ethinylestradiol though is the compound that would be most important to monitor since it is not a natural compound, it is used in the birth control pill (a pharmaceutical and a potent endocrine disruptor); thus, it would be a much better choice than the 17-β-estradiol. Also I know that this compound has generated a tremendous amount of literature over the past 12 years on endocrine disruption, especially in fish.

In fact, one panel member, Nancy Denslow, has published on estrogenic effects and the production of vitellogenin in fish (Folmar et al. 2000) and perhaps the most important paper is that of Kidd et al. (2007) showing the total collapse of a fish population on exposure to 17-α-ethinylestradiol (EE2) at 5-10 ng/L level in water. Given this important information and the fact that only one sample has been analyzed according to Appendix K, I think that it is critically important to look at EE2 rather than E2 as proposed by this panel. Furthermore, I would suggest the addition of estrone as an indicator compound as well to go along with the EE2. The reason being that it will occur at higher concentration levels based on both our experience and that which is shown in Appendix K and that its removal should mimic EE2 and E2 giving confidence to treatment procedures. The fact that E2 is produced naturally in the body of both men and women at levels considerably greater than what appears to occur in wastewater, it seems more relevant to select EE2 as a toxic indicator compound over E2. Furthermore, the fact that E2 occurs naturally in our bodies it is difficult to call this a CEC, whereas EE2 definitely fits the description of a CEC of highest toxic concern. The same methods available for E2 will work equally well for EE2, a suggestion is LC-MS-MS in negative ion mode.

Caffeine. Caffeine is a bitter, white crystalline xanthine alkaloid that acts as a stimulant drug and a reversible acetylcholinesterase inhibitor. In humans, caffeine acts as a central nervous system stimulant, temporarily warding off drowsiness and restoring alertness. It is the world's most widely consumed psychoactive drug, but, unlike many other psychoactive substances, it is both legal and unregulated in nearly all parts of the world. Beverages containing caffeine, such as coffee, tea, soft drinks, and energy drinks, enjoy great popularity; in North America, 90% of adults consume caffeine daily. My daily consumption which includes one double espresso each day is 100 mg, which is consumed in approximately 20 mL for a concentration of 5000 ppm! This amount is typical of most coffee drinkers; however, a typical Americano Coffee is 100 mg in 300 mL for a concentration of 330 ppm. Either way of consumption this dose concentration is much greater than values found in reuse waters of California.

For example, Appendix K shows 19 measurements for caffeine with a median of 280 ng/L and a maximum of 2.7 μg/L or ppb. This highest value is more than 10,000

lower than a Coffee Americano and 150,000 lower than my double espresso! My point is that this is a ridiculous compound to be monitoring under the CEC list of toxic compounds. It is not on the same toxic par as NDMA or EE2, not in any shape or form. Furthermore, it does not represent a class of compounds reported. The only other compound similar is its degradate, 1,3-dimethylxanthine, which is not a compound typically on the CEC list. Rather it is the human metabolite of caffeine. Furthermore, caffeine, has other sources than wastewater, i.e. food and drinks. Finally, it does degrade in the body and would not be a good tracer for groundwater recharge. I highly think that this compound should be removed from the list and another more relevant compound substituted. For example, there is a long list of psychoactive drugs that are true pharmaceuticals (CECs) that are widely found in reuse waters, such as carbamazepine, venlafaxine, lamotrigine, and fluoxetine to name just a few. Carbamazepine occurs at a median level of 200 ng/L similar to caffeine (Appendix K), is known to be present in all wastewaters, and is relatively toxic. I suggest that caffeine be replaced by carbamazepine in order to have at least one pharmaceutical as an indicator compound. It does not escape my notice that none of the four compounds are pharmaceuticals, including the next compound, triclosan. Carbamazepine works quite well by LC-MS-MS in positive ion mode with detection limits in the 1-10 ng/l range.

Triclosan. Triclosan is an antibacterial and antifungal agent. It is a polychloro phenoxy phenol. It used in many consumer products, such as toothpaste to prevent gingivitis and deodorants to control bacterial odors. Appendix K shows that it has been measured 19 times with a median of 25 ng/L and a maximum concentration of 510 ng/L. A quick literature survey shows that triclosan was considered a safe compound (Bhargava et al. 1996) and more recently triclosan levels in mother's breast milk was not considered toxic to infants (Dayan, 2007). Therefore, the selection of this compound for monitoring on toxicity basis seems weak. Also in our experience, triclosan is detected much less frequently than many CECs and has a strong sorption to soil and presumably to aquifer solids. Thus, it should show removal in groundwater. It does not represent a class of compounds, as this is the only CEC of this type. Thus, I suggest again that this is not a good choice for a health relevant compound. Other important classes of compounds that could be considered include: antibiotics such as sulfamethoxazole and trimethoprim, which are found ubiquitously in reuse water and much higher median concentrations, i.e. 295 ng/L for sulfamethoxazole and 44 ng/L for trimethoprim. These two compounds are widely used and sulfamethoxazole represents a large class of antibiotics. I suggest both of these compounds would be a much better choice than triclosan. Again, LC-MS methods using triple quadrupole are available at the 1-10 ng/L level, which are entirely suitable for these compounds.

Summary of 4 health revelevant CECs for Groundwater Recharge Projects. In summary, I suggest that NDMA is a good CEC as presented by the Panel, that 17-β-estradiol is not a good CEC and should be replaced by a more estrogenic, man-made pharmaceutical hormone, 17-α-ethinylestradiol. Next, caffeine, is a very poor choice and should definitely be replaced by another psychoactive compound, such as carbamazepine. Lastly, triclosan is a poor choice also for an antimicrobial and should be replaced by sulfamethoxazole.

The methods required to monitor for these CECs involve LC-MS with triple quadrupole mass spectrometry, which can easily reach the 1-10 ng/L level in all cases, with perhaps the exception of 17-α-ethinylestradiol, which is much more difficult to measure at these low levels. Thus, the idea to substitute estrone was suggested in order to easily reach the 1 ng/L limits of detection. The four compounds would require two methods, a GC-MS high resolution method for NDMA and a LC-MS-MS method for 17-α-ethinylestradiol (negative ion), carbamazepine (positive ion), and sulfamethoxazole (positive ion). Given that the cost of analysis for LC-MS-MS involves the same procedure, it seems like a good idea to monitor at least 10 to 15 more analytes as part of this method. Why not gain as much information as possible? Why only four analytes, when it is possible to have 20 analytes at the 1 ng/l level for water reuse and indicator compounds? This would give a much better idea of what is in the water and how the compounds are being removed. My fear is that the original four compounds will give many non-detections and nothing much will be learned from these negatives for water treatment studies. A longer list of 20 compounds would be quite easy to setup and monitor for the **same cost**! We routinely look at more than 20 compounds (CECs) at the 1-10 ng/l level using LC-MS-MS and these data are quite helpful in understanding sources and movement of CECs in the environment. Finally, to re-emphasize the fact that over the past ten years there has been considerable and widespread interest in pharmaceuticals and hormones in the environment (the USGS survey by Kolpin et al. 2002 has been cited nearly 2,400 times!). I think it is paramount, even necessary, that the CECs chosen by the State of California should include man-made pharmaceuticals and man-made hormones, which the four compounds chosen are not.

Four Performance Indicator CECs. The four compounds, DEET, gemfibrozil, iopromide and sucralose, were chosen as four performance indicator compounds. They are discussed next.

DEET. N,N-Diethyl-meta-toluamide known as DEET is an insect repellant developed during World War II and used commercially after 1957. DEET serves as a true repellent in that mosquitoes intensely dislike the smell of the chemical repellent. Apparently a type of olfactory receptor neuron in special antennal sensilla of mosquitoes is activated by DEET, which acts as a powerful repellant for mosquitoes. Given the current fear of West Nile Virus, the use of DEET has increased. It is banned in Europe. Human toxicity to DEET is considered small since we are able to apply this to skin surfaces as a neat material at 100% strength. However, DEET has been found to inhibit the activity of a central nervous system enzyme, acetylcholinesterase, in both insects and mammals. DEET does not represent any other class of compounds based on pesticide structures. DEET was found in 12 samples (Appendix K) with a median concentration of 137 ng/L and the maximum concentration of 1700 ng/L. I think that DEET is a good candidate for monitoring with one caveat. It is sorbed strongly onto surfaces and we have noticed some carryover with DEET in methods. Thus, a LOD of 1 ng/L is probably not possible because of carryover issues and a more reasonable value would be 20-30 ng/L based on our current work. This compound is very easy to monitor and detect by either GC-MS or LC-MS with solid phase extraction for sample preparation.

I have noticed that there are no pesticides as part of the 8 compounds selected by the Panel. I think that this is a mistake since pesticides are an important part of California application, both in urban and agricultural settings. For example, the triazines, especially simazine and atrazine, are used and detected in California both groundwater and surface waters (NAWQA reports of the USGS). Furthermore, simazine is used as a roadside herbicide across much of the state of California and can then easily makes its way into reuse water. I strongly urge the state to consider adding the two triazines, atrazine and simazine, along with the two soil degradates, deisopropylatrazine and deethylatrazine, to their monitoring list of CECs. They are toxic compounds with EPA limits of 3 and 2 μg/L each. Although not strictly CECs, they would be quite useful in monitoring treatment facilities in California. Finally, I would point out that DEET is not a pesticide as such, but an insect repellant used on humans.

Gemfibrozil. Gemfibrozil is the generic name for an oral drug used to lower lipid levels. It belongs to a group of drugs known as fibrates. It is most commonly sold as the brand name, Lopid. Appendix K shows that the median value for this compound is 610 ng/L with a maximum value of 4300 ng/L, based on 22 samples. This compound would be a good indicator compound for the general class of lipids known as fibrates. It is relatively easy to monitor for; however, it gives only one good MRM transition for LC-MS-MS, making it somewhat difficult to have a good secondary ion for confirmation at low levels, i.e. 1-10 ng/L.

Iopromide. Iopromide is a molecule used as a contrast medium. It is marketed under the name Ultravist which is produced by Bayer Healthcare. It is a low osmolar, non-ionic contrast agent for intravascular use. It is commonly used in radiographic studies such as intravenous urograms and CT Brain scans. This unusual compound was first noted in wastewater by studies in Germany and has had some popularity in CEC studies, including several papers by one of the Panel, Jorg Drewes. It is not commonly monitored for and because of its chemical structure with three iodine functional groups is not thought to be a mobile compound in groundwater. Appendix K shows that it has been monitored in California samples for 9 samples with a median of 110 ng/L. It does not represent any other compounds or pharmaceuticals; thus, I consider it of limited value as an indicator compound. It is a poor choice because of difficulty of analysis. I would suggest other more common pharmaceuticals to take its place, such as a common over-the-counter medication, such as one of the analgesics, i.e. ibuprofen or diclofenac, with diclofenac my favorite choice based on analytical methodology and ease of detection and widespread use. Diclofenac has been reported in 18 samples with a median of 22 ng/L (Appendix K).

Sucralose. Sucralose is an artificial sweetener. The majority of ingested sucralose is not broken down by the body and therefore it is non-caloric. In the European Union, it is also known under the E number (additive code) E955. Sucralose is approximately 600 times as sweet as sucrose (table sugar), twice as sweet as saccharin, and 3 times as sweet as aspartame. Sucralose does not appear in Appendix K. Based on my experience it is present in wastewater at relatively high levels, 100s of ng/L and is always present.

However, it is marketed as a totally safe compound. It is not a tracer of wastewater, based on my experience, because it is used in many foods and drinks, as well as excreted; thus, it has multiple sources and falls into the same basket as caffeine. It is a bad choice for a monitoring program as an indicator compound since it, like caffeine, is consumed by the public in large quantities. For the sake of aesthetics it is a bad choice and does give credence to water quality studies when it is one of the major monitored compounds. Not that it is incorrect to monitor this compound but that it does not warrant a position as an important indicator compound. Again there are many CECs, pharmaceuticals or pesticides that could be substituted for this compound. Furthermore, like caffeine, sucralose does not represent a family of compounds, except of course for sucrose, which does not make any sense. I also don't see the point of using this compound as a performance indicator for treatment purposes since its removal is less than 25%. I suggest this compound be removed along with caffeine.

5) Adequacy of the selected surrogates for monitoring treatment process performance.

I think all the surrogates that the Panel proposed are reasonable and will work well when assessing the treatment process performance. Also these surrogates should be monitored on a regular basis to ensure proper functioning of the treatment operation, especially dissolved or total organic carbon.

6) Validity of expected percent removal of surrogates and performance indicator CECs for a treatment process.

No specific comments. Refer to my previous comments on the validity of each compound to represent a class of compounds.

7) Appropriateness of tiered risk quotient thresholds and corresponding degree of response for evaluating monitoring results for health-based CECs in recycled water.

No specific comments.

8) Adequacy of monitoring frequencies for CECs and surrogates and the phase monitoring approach.

I think all the monitoring frequencies as presented in the Report are reasonable and well-defined. However, as mentioned above, I do not see the use of sucralose as a performance indicator as its removal is less than 25%. This means that this compound would not be a good candidate after the initial assessment monitoring phase, as stated in Attachment A of the policy: *"only the performance indicators that demonstrate measurable removal for a given process shall be candidates for use in the monitoring programs for the baseline and standard operation phases"*. According to this, this compound would not be a good candidate.

Moreover, I am concerned that after the first and second monitoring phases no compounds would be left to monitor. I would suggest including more CECs in the monitoring program.

9) Additional consideration for the peer reviews.

Additional comments related to charges 3, 4 and 5:

Charge 3. Would the above lists of constituents change based on level of treatment and use? If so, how?

The eight compounds above would change based on the type of treatment applied. For example, simple sand filtration would not be effective for all eight of the compounds, at least with respect to sorption and biodegradation. Bank filtration studies show that the compounds are mobile in sand columns with only a slight chance of biodegradation, less than 5% degradation.

On the other hand, carbon filtration is highly effective for 6 of the eight compounds, only caffeine and sucralose would have rapid breakthrough on fresh carbon, based on our studies in the laboratory and my experience with solid phase extraction of these compounds, i.e. hydrophobicity and sorption potential.

I am not experienced with advanced oxidation processes for these compounds. This would require a literature search for all 8 compounds.

Charge 4. What are possible indicators that represent suites of CECs?

1. NDMA-is an indicator for other nitrosoamines, of which there are 7 compounds that have been easily studied. However, I am not aware that the other compounds are commonly found in wastewater; rather they are more commonly analyzed in food.
2. 17-β-estradiol is a good indicator of sex hormones, perhaps 6 or more that are commonly monitored.
3. Caffeine-is not an indicator compound of other CECs,. It is a one of kind compound with perhaps the exception of its human metabolite, 1,3-dimethylxanthine.
4. Triclosan is not an indicator of other CECs. It appears as a one of a kind compound
5. DEET is not an indicator of other CECs. It appears as a one of a kind compound.
6. Gemfibrozil is a lipid regulator and fibrate. I am not aware of other CECs that are similar to it. However, its chemical structure is similar to some over the counter analgesics and could perhaps be an indicator for those, but this is a bit of a stretch, so to speak.
7. Iopromide is a contrast medium and is not an indicator of other compounds in reuse water.

8. Sucralose is a sweetener and could be an indicator of other sweeteners, except for the fact that its chemical structure is not similar to any of the other sweeteners, only to sucrose itself, which is not a CEC.

Charge 5. What levels of CECs should trigger enhanced monitoring of CECs in recycled water, groundwater, and/or surface waters?

In my opinion, it is not so much the level of CECs that should trigger enhanced monitoring but the number of compounds that are present. For example, our lab monitors many CECs as part of routine water quality monitoring for drinking water. It is not uncommon for example to find both caffeine and sucralose in drinking water sources, especially reservoirs that have other activities, such as recreation. In these cases, we suspect that beverages and soft drinks may well be the source of these compounds at trace levels that is from 10-50 ng/L. Since both of these compounds are being considered by the State of California, it is imperative to understand that a suite of compounds may be much more important. For example, we commonly monitor about 25 compounds, CECs, by LC-MS-MS at the 1-10 ng/L concentration level. Finding only sucralose and caffeine (which are part of our suite) are not a cause for concern. However, in nearby streams and canals that we monitor we find a suite of CECs, from 5 to 10 compounds, mostly pharmaceuticals. This raises a red flag suggesting that further and more frequent monitoring may be necessary. Also it is important to consider looking for non-targeted compounds, what the Panel refers to as unknown unknowns. This is a good idea and requires other types of instrumentation, such as LC/Q-TOF-MS, the use of databases, and GC/Q-TOF-MS, also using databases. This type of monitoring would be worth considering by the State of California because there may be many CECs that are present. Scans of accurate mass could be used both before and after treatment or archived for future use. It is important to realize that state-of-the-art mass spectrometry is currently available for use on this project and should not be forgotten. The Panel does not discuss these methods in their report.

Some additional comments. There is no mention of trace metals, mainly arsenic and selenium, which are known water quality problems in California, especially for irrigation purposes.

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