Learned Discourses

setac@setac.org

Timely Scientific Opinions

Intent. The intent of Learned Discourses is to provide a forum for open discussion by and for SETAC members. These articles reflect the professional opinions of the authors regarding scientific issues. They do not represent SETAC positions or policies. And, although they are subject to editorial review for clarity, consistency, and brevity, these articles are not peer reviewed.

The Learned Discourses date from 1996 in the North America SETAC News; however, their continued success depends on our contributors. We encourage timely submissions that will inform and stimulate discussion. We expect that many of the articles will address controversial topics, and we promise to give dissenting opinions a chance to be heard. If you disagree with an opinion expressed here, don't complain–submit a reply!

Rules. All submissions must be succinct: no longer than 1000 words, no more than 6 references, and at most one table or figure. Reference format must follow that of the journal *Environmental Toxicology and Chemistry* except that text citations are by author and date, rather than numeric. Topics must fall within SETAC's sphere of interest. And, most importantly, respect and courtesy must prevail; personal attacks and other unprofessional behavior will not be tolerated.

Submissions. Send submissions as email attachments to Peter Chapman (pchapman@attglobal.net).

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Although preparation artifacts render previous studies suspect, concerns remain

Learned Discourses Editor

Peter M. Chapman Golder Associates Ltd. 195 Pemberton Avenue North Vancouver, BC V7P 2R4 Canada T 1-604-904-4005 F 1-604-662-8548 pmchapman@golder.com



APPLIED SCIENCE

Science and Politics: SETAC and the 'Untreated Sewage' Issue in Western Canada

P.M. Chapman

A report not provided, a political decision made then overruled, future environmental initiatives in doubt

Bioaccumulation Reality Check

Frank A.P.C. Gobas¹, Margo M. Moore¹, Joop L.M. Hermens², Jon A. Arnot³ ¹Simon Fraser University, Burnaby, BC, Canada; ²Utrecht University, Utrecht, The Netherlands; ³Trent University, Peterborough, ON, Canada <gobas@sfu.ca>

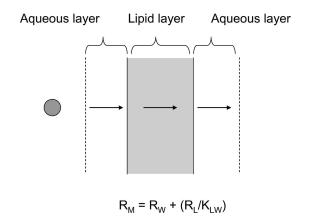
In SETAC Globe 7(2), Escher & Weisbrod discussed Lipinski et al.'s (1997) "rule of five" as an example of pharmaceutical research that could be used to improve bioconcentration assessment in aquatic species. Lipinski et al. (1997) proposed the "rule of five" to assess the oral absorption rate of pharmaceuticals by humans. According to these guidelines, a chemical is unlikely to cross biological membranes in quantities sufficient to exert a pharmacological or toxic response if it has a log K_{ow} > 5, a molecular weight (MW) > 500 g/mol, more than 5 Hbond donors, and the sum of N's and O's is over 10. Molecular weight cut-offs and size limits for membrane permeation have also repeatedly been suggested for bioaccumulation assessment and one POPs profiler restricts the uptake of large diameter molecules in its BCF-max assessment. This issue is of relevance as 6% of commercial organic chemicals on the Canadian Domestic Substances List (DSL) are of high K_{OW} (i.e., log K_{OW} > 5) and high molecular weight (MW > 500 g/mol). Chemicals with log K_{OW} values > 5 include some of the most bioaccumulative chemicals known to man. Of the 10 chemicals in our empirical BCF-BAF database with log $\rm K_{OW}$ > 5 and MW > 500, 4 chemicals have a BAF or BCF > 5,000. This class of high molecular weight, high K_{ow} chemicals also includes certain polybrominated diphenyl ethers and perfluorinated alcohols and sulphonamides. Bioaccumulative chemicals may be erroneously excluded in preliminary screening for bioaccumulation potential if principles developed for pharmaceuticals are erroneously applied to environmental chemicals. In this Learned Discourse, we present a bioaccumulation reality check in which we will briefly revisit the membrane permeation theory of hydrophobic organic chemicals in relation to bioaccumulation, point out key differences in the absorption of pharmaceutical drugs and environmental contaminants, and provide suggestions for simple (non- K_{OW}) rules than can be used to identify bioaccumulative substances.

Membrane Permeation and Bioaccumulation

To better understand the role of molecular weight and K_{OW} on the membrane permeation of non-ionic organic chemicals, it is informative to describe the two-film membrane permeation model (Flynn and Yalkowski 1972) shown in Figure 1. It illustrates that as chemicals become more hydrophobic (i.e., KLW increases), the membrane permeation rate becomes increasingly controlled and ultimately dominated by aqueous boundary layer transport rather than phospholipid bilayer permeation. This model explains why gill uptake rate constants and efficiencies increase with increasing K_{OW} for low K_{OW} chemicals (i.e., lipid layer diffusion or convection control) and then become constant once log K_{OW} reaches approximately 3 to 4 as chemical transport through aqueous layers (i.e., diffusion and ventilation) dominates the kinetics (Gobas et al. 1986; Gobas and Mackay 1987). This model also explains why the dietary uptake efficiency falls with increasing K_{OW} for chemicals with log K_{OW} > 7 as intestinal uptake is aqueous-diffusion-layer controlled (Gobas et al. 1989). The implication of the membrane permeation model for bioaccumulation assessment of high K_{OW} chemicals is that permeation or transport in water layers (not lipid layers) controls membrane permeation and bioaccumulation uptake kinetics from water and food for high K_{OW} chemicals.

Pharmaceuticals vs. Environmental contaminants

One of the key differences between pharmaceuticals and environmental contaminants is that pharmaceuticals are often used in solid form (e.g., a pill) and must dissolve to become available within a short time (i.e., the gut transit time). In contrast, environmental contaminants are already dissolved in or sorbed to environmental media such as water, air or particulate matter, and can provide a source of exposure throughout the animal's lifetime. It is therefore important to distinguish between processes controlling dissolution (solubility) and membrane permeation when extrapolating the behavior of pharmaceuticals to environmental contaminants. Many pharmaceuticals have molecular weights greater than 500 g/mol and are readily absorbed by tissues. For example, cyclosporine (MW=1202.64 g/mol), a hydrophobic immunosuppressive agent is efficiently absorbed orally and plasma concentrations peak within 3-4 hours. Erythromycin and rifampin (MW 733.94 and 822.95 g/mol, respectively) are also absorbed in the intestines and diffuse across the bacterial plasma membrane to target intracellular receptors. This illustrates that large, high molecular weight substances are able to permeate through membranes and can be efficiently absorbed orally because of their moderate K_{OW} which makes them sufficiently soluble in water and membranes to diffuse quickly through aqueous and lipid phases. Higher Kow substances with high molecular weights also permeate through membranes but at slower rates due to their lower solubility in water layers. It is the slow rate of elimination that gives high K_{OW} chemicals (in



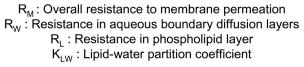


Figure 1 : Conceptual diagram of the permeation of a solute through a biological membrane consisting of lipid and aqueous diffusion layers and the corresponding membrane mass transfer model after Flynn and Yalkowski (1972). aquatic species) and high octanol-air partition coefficient K_{OA} chemicals (in air-breathing organisms – Arnot and Gobas 2003) their inherent bioaccumulative potential. These substances indeed make bad pills (because of their slow absorption kinetics) but very bioaccumulative environmental contaminants if they are not appreciably metabolically transformed (because of their slow elimination kinetics). It is also important to emphasize that there is no recognized molecular weight cut-off for membrane permeation that can be applied to assess bioaccumulation.

Conclusion

We should be especially cautious when assessing the bioaccumulation behavior of high K_{OW}, high molecular weight chemicals. The guidelines that refer to these properties for developing good oral drugs in humans are not applicable to determine the bioaccumulation behavior of these substances. Rather than considering limits on membrane permeation or uptake, we suggest focusing on the role of excretion and metabolism. Potentially bioaccumulative chemicals which are quickly metabolized or otherwise eliminated do not biomagnify in food-chains. Foodweb bioaccumulation models show that irrespective of uptake and internal distribution, a total elimination rate greater than approximately 0.1 d-1 in invertebrate and vertebrates is sufficient to make a chemical non-biomagnifying in simple aquatic food-webs. To obtain these rates, simple elimination tests can be performed which avoid the difficult water concentration measurements of BCF tests, and methods for the estimation of these rates using in-vitro tests should be explored.

References

- Arnot JA, Gobas FAPC. 2003. A generic QSAR for assessing the bioaccumulation potential of organic chemicals in aquatic foodwebs. QSAR Comb Sci 22: 337-345.
- Flynn GL, Yalkowsky SH.1972. Correlation and prediction of mass transport across membranes I: Influence of alkyl chain length on flux determining properties of barriers and diffusants. J Pharm Sci 61:838-852.
- Gobas FAPC, Mackay D. 1987. Dynamics of hydrophobic organic chemical bioconcentration in fish. Environ Toxicol Chem 6, 495 504.
- Gobas FAPC, Opperhuizen A, Hutzinger O.1986. Bioconcentration of hydrophobic chemicals in fish: relationship with membrane permeation. Environ Toxicol Chem 5: 637 646.
- Gobas FAPC, Muir DCG, Mackay D. 1989. Dynamics of dietary bioaccumulation and faecal elimination of hydrophobic organic chemicals in fish. Chemosphere 17: 943-962.
- Lipinski CA, Lombardo F, Dominey BW, Feeney PJ. 1997. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development setting. Adv Drug Delivery Rev 23: 3-25.

Probabilistic Risk Assessment of Pesticides: Is It Working?

Jeffrey M. Giddings¹, William Warren-Hicks² ¹Compliance Services International, Rochester, MA, USA, ²EcoStat, Mebane, NC, USA, <jgiddings@ComplianceServices.com>

What are the benefits and drawbacks of probabilistic risk assessment (PRA) of pesticides as practiced today? Does PRA serve a useful purpose in the regulatory framework? We posed these questions to an informal cross-section of experts from industry, academia, and regulatory agencies, and in this Learned Discourse we summarize their responses, supplemented by insights gleaned from a recent U.S. EPA review of an industrysubmitted PRA.

First we must be more specific about what is meant by "working." Several interrelated criteria might be considered: Does PRA give a more complete, accurate picture about risk than "traditional" deterministic approaches? Does PRA make registration decisions easier? Are we learning where additional research would be most productive? Does PRA help the public understand the risks of pesticides? Are we better able to balance environmental goals with the benefits of pesticide use?

We asked each expert to consider these questions from the viewpoint of science, regulatory decisions, and public interest. Although we deliberately included individuals with a range of opinions, there was general agreement about the perceived benefits and drawbacks of PRA, summarized as follows:

Scientific View: Benefits. PRA provides a more realistic description of temporal and spatial aspects of pesticide risk. More data are brought to bear in reaching a conclusion. PRA properly accounts for uncertainty that we know exists. Issues of concern are brought into sharper focus, and the findings help us design research to address remaining uncertainties.

<u>Scientific View</u>: Drawbacks. PRA requires a high quality Problem Formulation. (Indeed, Problem Formulation accounts for a substantial fraction of the total effort.) More species toxicity testing is required than is generally available. PRA often requires other data that are not readily available and need to be gathered—for example, information about actual pesticide use in the field. Like any complex scientific application, PRA can be done badly or misapplied.

<u>Regulatory View:</u> Benefits. PRA separates science from decision making and improves the scientific credibility of the decisions. PRA enables efficient targeting of higher tier studies, aids in the design of stewardship programs, and supports appropriate options for risk mitigation.

<u>Regulatory View:</u> Drawbacks. PRA changes the risk assessment paradigm, and doesn't fit into the standard testing program. PRAs are time consuming to conduct and review. There is little established guidance for interpretation of a PRA, which can lead to inconsistency in decision making. PRA may demonstrate a high degree of uncertainty about an assessment, thereby undermining the legitimacy of regulatory decisions based on that assessment. <u>Public View:</u> Benefits. Advocates and critics of PRA agreed that the public perceives little benefit in PRA of pesticides. However, to an objective public stakeholder, PRA can provide a more realistic estimate of risk. PRA also allows more informed comparison of risks and benefits, so public funds can be applied to the most pressing issues and not wasted on activities that do little to reduce actual risk.

<u>Public View:</u> Drawbacks. PRA is difficult to understand and interpret. The public is suspicious about statistics and ignorant about probability. PRA is seen as enabling more "lenient" decisions rather than greater environmental protection. PRA also demonstrates that risk is rarely zero, a fact that makes many people uncomfortable.

Although we included individuals from all three of SETAC's traditional sectors in our informal survey, most of the replies summarized above came from industry and academia. Although the EPA is developing PRA methods for pesticides (U.S. EPA 2004), the Agency's perspective on PRA has not often been articulated. For insight, we turned to a recent review by EPA of one of our own PRAs submitted in support of a product registration. From the review, we extracted comments that revealed, by implication, elements EPA considers important in a pesticide PRA. What we found is summarized below:

<u>Scope.</u> The PRA should address all issues of regulatory concern. The temporal and spatial scale must be appropriate, and spatial and temporal variability must be considered. Surrogate species used in the analysis must represent all the species of concern.

<u>Model.</u> The risk model used in the PRA must adequately represent the assessment scenario, and must account for all factors that affect exposure and effects. Toxicokinetics must be accurately simulated. Input variables must be selected carefully, and their range must represent all scenarios of interest.

<u>Assumptions.</u> Model assumptions must be plausible and supported by reference to published research. Assumptions about distributions must be justified. The sensitivity of the model to the assumptions should be explored. The assumptions should not limit the range of predicted outcomes.

<u>Data.</u> The data used in the PRA must be complete and consistent. Data quality must meet EPA standards. All relevant data should be incorporated into the model. The data must represent the situations being assessed.

<u>Uncertainties.</u> A quantitative uncertainty analysis is needed. Uncertainties stemming from assumptions must be clearly presented. Risk often depends on local conditions that are difficult to quantify on a national scale; depending on the assumptions used, risk could range from minimal to high. Bayesian approaches are "innovative and creative" but their limitations are unknown to the Agency.

<u>Risk Characterization.</u> The PRA should not understate the risk. Model predictions should be compared with field observations of effects.

In this particular case, EPA concluded that the PRA was insufficient to alter the conclusions reached by previous deterministic assessments. Given the regulatory outcome, did this PRA "work"? In our view, and the view of the companies that sponsored the assessment, the answer is "yes." Most of EPA's concerns can be addressed, without altering the model or the approach, by correcting misunderstandings, modifying data selection, and extending the scope to other species and scenarios. More importantly, the PRA resulted in a better understanding of the sources of uncertainty affecting the risk estimation. Discussion can now focus on assumptions that most affected the outcome, and additional data can be sought to address those assumptions.

References

U.S. EPA. 2004. A discussion with the FIFRA Scientific Advisory Panel regarding the terrestrial and aquatic Level II refined risk assessment models (Version 2.0). U.S. Environmental Protection Agency, Office of Pesticide Programs, Washington, DC. http://www.epa. gov/scipoly/sap/meetings/2004/index.htm#march.

Fragrance materials and the environment - is there a risk?

Daniel Salvito¹, Ronald Senna^{2, 3}, Colin McIntosh⁴ ¹Research Institute for Fragrance Materials, Woodcliff Lake, NJ, USA, ²International Flavors and Fragrances Inc., Shrewsbury, NJ, USA, and ³International Fragrance Association, Brussels, Belgium, ⁴Firmenich Inc, Princeton, NJ, USA, <dsalvito@rifm.org>

Introduction

Over the past decade, there has been increasing interest among the academic, regulatory, and NGO communities concerning the environmental "risk" from non-traditional chemicals. These are chemicals that have not traditionally been used as the basis for our understanding of environmental "risk" and thus for the implementation of regulatory frameworks compared to substances such as pesticides, PCBs, and PAHs. Multiple terms are used to identify these chemicals: emerging pollutants and pharmaceutical and personal care products (PPCPs) are two examples of new nomenclature applied to some of these chemicals.

Many of these chemicals used today in commerce are neither "new" nor "emerging". They have been used for decades in a variety of consumer products and other industrial applications with no known adverse effects. Quite understandably, however, as it would appear that there is a dearth of environmental fate and effects information on these chemicals, questions arise as to their potential to incur a risk to the environment.

As fragrance materials are often cited as "emerging pollutants" or PPCPs, it is the intent of this Learned Discourse to outline our present understanding about these materials and their potential to affect the environment.

What are Fragrance Materials?

Typically, fragrance ingredients consist of organic molecules of low molecular weight (<300 mu) with vapor pressures less than 2 mm Hg. These chemicals represent a wide variety of chemical classes including esters, acids, aldehydes, ketones, etc. of varying physical-chemical properties. While the majority of these materials are used at very low commercial volumes; a few are higher tonnage materials. Fragrance materials consist of mixtures of these ingredients and can range from ten to several hundred individual ingredients, depending on the application (e.g., perfumes, soaps and detergents, cosmetics and other consumer products).

Currently available information

The nitromusk and polycyclic musk compounds are some of the most studied chemicals within the fragrance industry. These materials are often listed as PPCPs and, although they represent two different structural classes, are often collectively referred to as "musks". There are over 40 peer-reviewed publications on the nitromusks and 50 on the polycyclic musks, and the list continues to grow. Their risk assessments are currently under review by the European Union. Thus far, the European Chemicals Bureau has concluded that the polycyclic musks HHCB (1,3,4,6,7,8hexahydro-4,6,6,7,8,8-hexamethylcyclopenta-γ-2-benzopyran) and AHTN (6-acetyl-1,1,2,4,4,7-hexamethyltetraline) are not PBT (Persistent, Bioaccumulative, Toxic) substances, and the European Scientific Committee for Cosmetics and Non-Food Products has affirmed their continued safe use in consumer products (SCCNFP 2002a, SCCNFP 2002b). A recent summary of the environmental risk assessments of these materials is available in HERA (2004).

The difficulty arises within the literature and the popular press when the "discovery" of these chemicals in the environment is separated from an assessment of their potential risk; i.e., comparison to known, measured effects. While we acknowledge the great advances in analytical chemistry that have enabled us to find chemicals in the environment at ever decreasing concentrations, we encourage the comparison of these analytical measurements with the reported effects of the chemical in a risk assessment context. This context would further benefit from more thorough reviews of the existing literature and searches of regulatory databases for risk-based information. Identification and quantification is not risk assessment.

Risk assessment and fragrance materials

The fragrance material industry, through its non-profit research institute, the Research Institute for Fragrance Materials (RIFM), published an aquatic screening level risk assessment paradigm (Salvito et al. 2002) to establish research and testing priorities for over 2,000 discrete, organic chemicals used in fragrance compounds. The aquatic scenario is a reasonable worst case, because the major route of exposure for fragrance ingredients is in down-the-drain products. This screening tool provides for multiple tiers of assessment beginning with basic physical-chemical properties (molecular weight, octanol-water partitioning coefficient, and regional volume of use) and a quantitative structure-activity relationship to determine aquatic toxicity (applying a large application factor to determine the Predicted No-Effect Concentration), and ends with the input of available, measured data to establish a set of materials for further testing, if necessary.

This screening level assessment is revised with each new volume of use survey performed by the fragrance industry (minimally every five years) and as new fate and effects data become available. The initial screening resulted in greater than 92% of the materials being found to have an aquatic risk quotient less than 1 (minimal risk). Through the use of structure-activity groups and read-across, and data that have been generated as a result of regulatory programs and industry sponsored studies, this set of priority materials has been continuously reduced.

Fragrance materials and the environment

Clearly, an aquatic screening level assessment does not answer all the questions that may arise regarding these materials and the environment. The fragrance material industry, through RIFM, has funded research in the areas of soil fate, biotransformation, and, presently, bioavailability from sediment exposures. Other research groups have looked at the atmospheric chemistry of key fragrance ingredients and the potential for endocrine effects. Monitoring of these materials in various environmental compartments and biota is also on-going. A broader review of the issue of fragrance material use and their potential environmental impact is provided by Salvito et al. (2004).

While more data are always desired, the existing information available, and considering current use levels, indicates that fragrance materials present a minimal environmental risk. The fragrance industry has voluntarily committed to continue to study these materials in various environmental compartments and publish their findings in the peer-reviewed literature. The issue as to whether or not fragrance materials pose a risk to the environment has not yet been fully answered, but data available to date would argue against it.

References

- SCCNFP. 2002a. Opinion of the Scientific Committee on Cosmetic Products and Non-Food Products Intended for Consumers Concerning 6-Acetyl-1,1,2,4,47-Hexamethyltetraline (AHTN). SCCNFP/0609/02
- SCCNFP. 2002b. Opinion of the Scientific Committee on Cosmetic Products and Non-Food Products Intended for Consumers Concerning Hexahydro-Hexamethyl-Cyclopenta (γ)-2-Benzopyran (HHCB). SCCNFP/0610/02
- HERA, 2004. Human and Environmental Risk Assessment on Ingredients of Household Cleaning Products: Polycyclic musks AHTN (CAS 1506-02-1) and HHCB (CAS 1222-05-05) Environmental Section Ver. 2.0 (http://www.heraproject.com/ RiskAssessment.cfm)
- Salvito DT, Senna RJ, Federle TW. 2002. A Framework for prioritizing fragrance materials for aquatic risk assessment. Environ Toxicol Chem 21: 1301-1308.
- Salvito DT, Vey MGH, Senna RJ. 2004. Fragrance materials and their environmental impact. Flav Frag J 19:105-108.

Ecotoxicology of Nanoparticles (NPs)

T. F. Fernandes, P. Rosenkranz, A. Ford, N. Christofi, and V. Stone *Napier University, Edinburgh, UK.*, *<t.fernandes@napier.ac.uk>*

Introduction

Nanotechnology is a rapidly developing field of science, technology and innovation. It involves the development and manufacture of materials in the nanometer size range and includes the production and use of nanoparticles (NPs; particles with at least one dimension of less than 100 nm). Due to their small size a relatively large proportion of the atoms and molecules making up the particles are exposed at the particle surface compared to larger particles. This structural difference coupled with the relatively large surface area per unit mass of NP allows such materials to exhibit properties that differ from bulk chemicals, making them useful in a wide variety of applications including electronics, paints, cosmetics, medicines, foods, textiles and environmental remediation. This means that the potential for exposure to NPs both in an occupational setting and as consumers is large.

NP Toxicology

There is a general lack of information regarding the human health and environmental implications of engineered NP. Some toxicological studies have been conducted and results demonstrate that the toxicity of these materials is related to their ability to induce oxidative stress and inflammation in the lung leading to impacts on lung and cardiovascular health. Studies which investigate the ability of NPs made from low toxicity materials to generate oxidative stress and inflammation suggest that potency is dependent upon their surface area (Duffin et al. 2002). Furthermore, studies that compare low toxicity materials and particles made from more noxious substances, such as nickel or alpha-quartz, demonstrate that biological reactivity is a function of both surface reactivity and surface area (Duffin et al. 2002).

Ecotoxicology of NPs

Many of the current and intended uses of NPs are 'environmental' including remediation (removal of contaminants from contaminated water or soil where large quantities are used in e.g. permeable reactive barriers), water treatment filters and control of algal growth in water systems. The rapid growth of nanotechnologies will also lead to increased accidental and purposeful release of NPs into the environment. NPs are released into the environment via air, water or soil, which means that they have access to a wide range of organisms, from microorganisms such as bacteria and algae, through to more complex organisms including terrestrial and aquatic vertebrates. It is important to assess the fate and distribution of NPs that are released into the environment to determine which environments and organisms are most exposed, and what the consequences may be.

Assessment of Effects to Biota

One of the main problems encountered in animal testing of NP ecotoxicology has been the protocol used to prepare the NPs. Many NPs tend to form large aggregates, and it is not currently clear whether the NPs in the aggregates possess the same toxic potential and bioavailability as single NPs. What is important to consider, however, is the form of nanoparticle that is found in the environment, which is likely to depend upon the formulation of the released nanoparticle along with the substances with which the nanoparticle interacts with once released. For example, release of NPs via waste water suggests that NPs will be mixed with significant quantities of household and industrial detergents that could help to disaggregate the particles. Furthermore, naturally occurring surfactants, such as humic acids, may help to disaggregate particles.

A number of published ecotoxicology studies have used the organic solvent tetrahydrofuran (THF) to disaggregate NPs such as C_{60} prior to treatment of organisms. However THF is not representative of materials widely found naturally or via

contamination in the environment. Brant et al. (2005) have demonstrated that, even after filtration and evaporation, THF remains trapped between the aggregated C_{60} particles, suggesting that the studies by Oberdorster (2004) and by Lovern and Klaper (2006), outlined below, have investigated the effects of C_{60} combined with THF rather than the effects of C₆₀ per se. THF is classified by many regulatory bodies as a neurotoxin and so could in part explain some of the effects observed in fish. For these reasons it is worth considering some of the following information with caution. We could not find any evidence in the literature that THF per se is able to induce oxidative stress.

Lovern and Klaper (2006) exposed *Daphnia magna* to C_{60} or TiO₂ (Degussa P25, 25nm diameter). The particles were treated to break up the aggregates by either sonicating in medium for 30 minutes, or by solubilisation in the organic solvent THF. The TiO₂ and the C_{60} particles were both more potent at killing the organisms when prepared in THF than when prepared by sonication, and the C_{60} was more potent than the TiO₂. The question remains as to whether the particles prepared in THF were more toxic because they were better dispersed or because of THF induced toxicity.

Oberdorster et al. (2006) tried to overcome the preparation-linked problems by stirring the fullerenes in water. They exposed the aquatic crustaceans *D. magna* and *Hyalella azteca*, and marine harpacticoid copepods to a range of fullerene concentrations. These could not be prepared at high enough concentration levels to cause 50% mortality of the invertebrate species tested at 48 or 96 hrs. The maximum concentrations tested were 35 ppm for freshwater and 22.5 ppm for full-strength (35 ppt) seawater, since at higher concentrations the fullerene precipitated out of solution. *D. magna* exposures for 21 days to 2.5 and 5 ppm concentrations, respectively resulted in a significant delay in moulting and significantly reduced offspring production, which could have negative impacts at the population level (Oberdorster et al. 2006).

Work in our own laboratory has assessed the effects of exposing a range of aquatic crustaceans (D. magna and Gammarids) to several NPs (TiO₂, ultra-fine carbon black, C₆₀). Results indicate that particles are rapidly ingested, resulting in accumulation in the gastrointestinal tract within 30 minutes of exposure. The particles also adhere to the exoskeleton surfaces of the exposed organisms, suggesting multiple routes of exposure and absorption. Exposures of D. magna to negatively charged carboxylated fluorescent polystyrene NPs resulted in a rapid uptake by the neonates and adults. These particles translocated from the gastrointestinal tract to lipid storage droplets. In addition, LC50 (48 hr) results ranged between 5-20 ppm. Subtoxic doses of carbon black and TiO2 NPs were also found to be associated with increased moulting by neonates. Pilot data suggest CB may induce oxidative stress at 4h and 24h, at the tested concentrations. In these studies, the methodology employed involved sonication but not the use of a solvent such as THF.

The results so far obtained from the acute tests conducted on *D. magna* indicate that the lethality of the NPs tested is relatively low, but that they are still a cause for concern. Preliminary results indicate increased oxidative stress in *D. magna* with increased ultrafine carbon black concentrations. Therefore,

Strategic Priorities for Ecotoxicology

Considering the rapid expansion of nanotechnologies, and the potential for nanomaterials to be released into the environment, it is essential that regulatory authorities and ecotoxicologists prioritise their research. It is beyond the scope of this Learned Discourse to list fully the studies required; however, development of such a strategy will require the establishment of a panel of well-characterised NPs that vary in size, shape, durability, composition and surface reactivity, as well as varying the presence of potential contaminants such as metals. In addition, tests should also include natural and man-made materials, which may interact with such materials. The toxicity tests conducted will require both acute and chronic exposures, preferably using standard laboratory models. It might be appropriate to use endpoints that have been identified as relevant in mammalian and human toxicological studies using NPs; for example, oxidative stress appears to be an important process driving particle toxicity. Finally, it will be necessary to develop standard methodologies for the assessment of nanomaterial toxicity or hazard that are relevant to the full life-cycle of NPs.

effects on these species, the indication of accumulation within

body compartments suggests that such research is essential.

References

- Brant J, Lecoanet H, Hotze M, Wiesner M. 2005. Comparison of electrokinetic properties of colloidal fullerenes (n-C₆₀) formed using two procedures. Environ Sci Technol 39: 6343-6351.
- Duffin R, Tran CL, Clouter A, Brown DM, MacNee W, Stone V, Donaldson K. 2002. The importance of surface area and specific reactivity in the acute pulmonary inflammatory response to particles. Ann Occup Hyg 46(Suppl. 1): 242-245.
- Lovern SB, Klaper RD. 2006. Daphia magna mortality when exposed to titanium dioxide and fullerene (C_{60}) nanoparticles. EnvironToxicol Chem 25: 1132–1137.
- Oberdorster E. 2004. Manufactured nanomaterials (Fullerenes, C_{60}) induce oxidative stress in the brain of juvenile largemouth bass. Environ Health Perspect 112: 1058-1062.
- Oberdorster E, Zhu S, Blickley TM, McClellan-Green P, Haasch ML. 2006. Ecotoxicology of carbon-based engineered NPs: Effects of fullerene (C₆₀) on aquatic organisms. Carbon 44: 1112-1120.

Science and Politics: SETAC and the 'Untreated Sewage' Issue in Western Canada

Peter M. Chapman

Golder Associates, North Vancouver, BC, Canada, <pmchapman@golder.com>

There has been a great deal of debate over the years (cf Chapman 2006 or simply Google "Victoria sewage") regarding the need to treat sewage discharged from the City of Victoria and surrounding municipalities (British Columbia, Canada). In brief, the sewage is presently untreated other than by fine screening. Extensive scientific studies have indicated an absence of major environmental or human health impacts due to a combination of relatively low industrial inputs, strong tidal currents with net movement to the open ocean, substantial vertical mixing, substantial oxygenation, and naturally high abundance of nitrogen. However, there has been increasing public and political pressure to treat the effluent 'because it is the right thing to do'.

The Capital Regional District (CRD), which manages the City of Victoria and surrounding municipalities' water and wastewater services, retained the Society of Environmental Toxicology and Chemistry (SETAC) to establish and manage an independent scientific panel to provide the CRD with technical advice: the Scientific and Technical Review Panel (the Panel). Their report (Stubblefield et al. 2006), a separate report (Mac-Donald and Smorong 2006), and subsequent political actions are the subject of this Learned Discourse.

The Panel report noted that the CRD's source control program is well developed and in fact represents the current "state of the science"; however, source control will only reduce concentrations of targeted contaminants. Stormwater, sanitary and combined overflows, and other discharges, particularly into Victoria's harbours, are a more pressing issue than the present deep, offshore submarine sewage discharges. Although the available evidence does not indicate immediate concern for human health from the outfall discharges, limited exposures to sewage could occur if individuals were in the water (well over a km offshore) during certain periods in the fall and winter when the sewage plume can surface. These exposures could result in gastrointestinal illness and / or ear infections. Similarly, the available evidence does not indicate immediate concern for environmental health from the outfall discharges or that concentrations of measured contaminants are changing over time. In fact, there is evidence that environmental conditions near the outfall may be improving. However, uncertainties remain, particularly in the long-term given that discharges are expected to increase with population growth. Uncertainties also remain regarding emerging contaminants of concern such as estrogens, pharmaceuticals, personal care products, surfactants, nanotechnology products, etc. As a result, the Panel was unable to predict future risks ("the larger problem is with estimating the likelihood of events that have not yet and might never, occur"). Although the report stated "There is no reason to believe that serious human health effects or severe ecological consequences not yet in evidence will arise in the near future", it was also noted that "such consequences remain a possibility."

The Panel did not recommend sewage treatment, they simply assessed the available evidence. They did note that a decision to treat current sewage discharges will result in other environmental issues including sludges that must be treated and managed ("Part of the risk is therefore diverted to a different environment rather than being eliminated."). They also emphasized the importance of a comparative assessment of risk versus benefit in decision-making. And they provided specific recommendations regarding additional studies that should be conducted as well as improvements to the CRD's current approach to responding to emerging issues to continue to protect human and ecosystem health.

The Panel recognized the importance of perception: "Certainly part of the reason some CRD citizens favour sewage treatment in Victoria is the sense that this is a reasonable expectation of cities in advanced industrial nations". And they noted the potential impact on the important tourism industry of "bad publicity". But they also noted "...it can be argued that other policies would provide a greater return per dollar of expenditure."

Two prophetic statements were made at the end of the report: "People can reach different conclusions based on their own interpretation of the available evidence..." and "...many people would decide the issue on grounds other than an absence of currently demonstrated health and ecological effects." The same day as the release of the Panel's Report (July 12, 2006), the CRD Board Chair released a statement that the Panel's report would be reviewed over a 5 month period, together with public input, following which a decision would be made how to proceed. However, this review period was obviated two days later when the provincial Minister of the Environment directed the CRD to develop a detailed schedule for the provision of sewage treatment, in other words, 'just do it'.

The abrupt decision by the Minister of Environment was apparently related to a separate report that, although submitted to the BC Ministry of Environment (BCMoE) in May 2006, was not made available to the SETAC Panel. This report (MacDonald and Smorong 2006) evaluated sediment quality around the two outfalls compared to provincial regulations and determined that these areas could be considered contaminated sites. The report curiously did not consider or cite the published findings of a SETAC Pellston workshop regarding limitations of sediment chemistry data that render them generally inappropriate for sole use in decision-making (Wenning et al. 2005). Further, despite the SETAC Panel's clear conclusions as noted above, the senior author of the report to the BCMoE told a reporter from the local newspaper a different story (Times Colonist July 26, 2006): "The best way to stop the environmental damage is to start sewage treatment, MacDonald said in an interview.'

The Minister of Environment's decision ignored the Panel's recommendations that politics, like science, is only one of several factors that should be considered in the risk benefit decision. His decision also ignored the proper decision-making strategy initially advocated by the CRD Board Chair; there was no apparent consideration of, for instance, social or economic factors or of the magnitude (arguably relatively small) of any potential future environmental or public health risks. There was no apparent consideration of whether the money required for sewage treatment would be better spent obviating more important environmental concerns identified by the Panel such as stormwater and contaminated harbours. There was no consideration given to the magnitude of different risks, time frames, costs, etc. before the final decision was made.

So did the scientific review process work? Yes and no. Yes because an independent group managed by SETAC provided necessary input to a process that had become increasingly polarized (cf Chapman 2006). No because the SETAC Panel was not provided with a key report (political games?), and because a political decision was made before the SETAC report could be fully evaluated and the science (or other factors) truly incorporated into the final decision.

Should such scientific reviews continue to be done by SETAC? Absolutely. Although science is only one part of the decision-making process, it provides the basis for good decision-making – politicians and other stakeholders taking advan-

tage of the information provided and individuals playing political games are a different issue. Science did not have as large a role in this decision as could and should have been the case, but it did have a role.

Hopefully politicians and the public will come to realize that there are no simple solutions to environmental problems, and that a "holistic watershed viewpoint" as advocated by the Panel is necessary to ensure that the environment and human health are adequately protected within available, limited resources. Hopefully also the CRD's new directed focus on relatively expensive sewage treatment will not reduce or even eliminate their very useful programs to address stormwater and other overflows, watersheds and landfills. However, only time will tell...

References

- Chapman PM. 2006. Science, politics and ideology the Victoria (BC, Canada) sewage issue. *Mar Pollut Bull.*
- MacDonald DD, Smorong DE. 2006. An evaluation of sediment quality conditions in the vicinity of the Macaulay Point and Clover Point outfalls. Report prepared for the BC Ministry of Environment, Victoria, BC, Canada.
- Stubblefield WA, Servos M, Gersberg RM, Riley C, Simpson D, Smith D, Wells P. 2006. Scientific and technical review. Capital Regional Core Area Liquid Waste Management Plan. Available at www.crd. bc.ca
- Wenning R, Ingersoll C, Batley G, Moore M (eds). 2005. Use of Sediment Quality Guidelines (SQGs) and Related Tools for the Assessment of Contaminated Sediments. SETAC Press, Pensacola, FL, USA.