Bioaccumulation Assessment of Medium Chain Chlorinated Paraffins (MCCPs)

Prepared for The Regulatory Network Inc.

Summary Report

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Summary

This document provides summary information for the bioaccumulation (B) assessment of medium chain chlorinated paraffins (MCCPs) including (i) a review key B terminology and concepts, (ii) current scientific methods recommended for B hazard assessment, and (iii) the application of these methods using available relevant and acceptable quality B data for MCCP constituents.

Substances are generally considered B hazards because concentrations in higher trophic level organisms (at or near the top of food webs) may become high, even though concentrations in the environment are comparatively low. It has been recommended that the overarching objective of B assessment is to identify chemicals that biomagnify in food webs. Chemicals that biomagnify are those that increase in concentration with increasing trophic levels, i.e., chemical concentrations in an organism are greater than chemical concentrations in its diet.

There are various B assessment measurements (data) and criteria. Some B measurements are from laboratory models and some data are obtained from the environment. Academic, government and industry scientists have developed a weight of evidence B assessment framework for interpreting the seemingly disparate sources of B data to identify chemicals that biomagnify in the environment. In this framework different sources of B data are converted into a "common currency" and compared against a single criterion (a value of "1") to answer the question "Does the chemical biomagnify?". Data points greater than 1 indicate biomagnification and bioaccumulation in the environment.

This B assessment framework was applied for MCCP constituents using relevant and reliable (acceptable) quality B data included in the REACH substance evaluation (SEV) document and the peer-reviewed literature. A total of 97 measured data points are compared against the B assessment criterion; 92% of these data are highly relevant because they are measured from the environment. Of the 97 measured data points, 7 (7.2%) met or exceeded the threshold criterion of 1 and 90 (92.8%) were lower than the threshold criterion. The median value (estimate of central tendency) is 0.27. The current weight of evidence indicates that MCCP constituents are not likely to biomagnify in fish and in aquatic food webs.

Previous analyses have shown that the key determinant in assessing the B potential of MCCP constituents is the metabolic biotransformation rate constant. These analyses showed that estimates of the biotransformation rate constants are approximately the same for a range of MCCP constituents. Thus additional animal testing is not expected to provide value added information for the B hazard assessment of MCCP constituents.

Introduction

This document provides summary information regarding the bioaccumulation (B) hazard assessment of medium chain chlorinated paraffins (MCCPs). MCCPs are a mixture of chemicals, considered a UVCB substance (unknown or variable composition, complex reaction products or biological materials), registered for evaluation under a single CAS No (85535-85-9). The range of chemical properties for the MCCP constituents is large. For example, measurements and predictions for the octanol-water partition coefficient (K_{OW}) for MCCP constituents span a few orders of magnitude (log K_{OW}s from ~7 to >9.0 [1] or ~5.5 to 8.2 [2]). The very high K_{OW}s reflect the fact that these chemicals are very hydrophobic ("water-hating") and hence partition from water to biological phases. This summary includes (i) a review of key bioaccumulation terminology and concepts and (ii) current scientific methods recommended for B hazard assessment, and (iii) the application of these methods using available relevant and acceptable quality bioaccumulation data for MCCP constituents. The data used include data in the REACH substance evaluation (SEV) document and associated studies including recent peer-reviewed literature related to the B assessment of MCCP constituents.

Terminology and key concepts

Bioaccumulation is broadly defined as a process by which the concentration of a chemical in an organism exceeds that in the respiratory medium (e.g., water for fish, air for mammals), or in the diet, or both [3]. Bioaccumulation is the net result of competing rates of chemical uptake and elimination in an organism under a defined set of exposure conditions [3-5]. Fish are commonly used as a model organism for B assessment. In the environment fish are exposed to chemical in the water and food. Key routes of chemical elimination include gill elimination, fecal egestion and biotransformation (metabolism). Bioaccumulation is the result of bioconcentration (exposure from the surrounding environment, i.e., water) and biomagnification (exposure from food). Biomagnification is fundamentally different from the bioconcentration process in that it involves chemical transport against the thermodynamic gradient (i.e., from a low fugacity in the prey to a higher fugacity in the predator), whereas bioconcentration involves equilibrium partitioning in which the fugacity in the organism can at the most achieve that in the water [3, 6]. For chemicals with log K_{OW} > ~ 4.5 the biotransformation rate constant is a critical parameter determining whether or not a chemical bioaccumulates and biomagnifies [7-10].

Bioaccumulation hazard assessment metrics include K_{OW}, the bioconcentration factor (BCF; L/kg), the bioaccumulation factor (BAF; L/kg), the biomagnification factor (BMF; kg-lipid/kg-lipid) and the trophic magnification factor (TMF) [3, 6]. By definition, K_{OW}, BCF, BAF, BMF and TMF are steady-state metrics, i.e., there are no significant changes in chemical concentrations over time. K_{OW} is used as a surrogate for lipid-water equilibrium partitioning and has recognized limitations for B assessment, primarily because it is only a chemical property and ignores biological processes such as biomagnification and biotransformation [7, 9, 11]. The BCF is the ratio of the chemical concentration in a fish to the chemical concentration in the water following chemical exposure from the water only. The BCF is measured under controlled laboratory conditions; there is no dietary exposure. The BAF is the ratio of the chemical concentration in a fish to the chemical concentration in the water as a result of all routes of exposure (i.e. water and food). The BMF is the ratio of the chemical concentration in an organism to the chemical concentration in its diet. The BMF can be determined through laboratory (model) testing *or* field measurements. Field BMFs include all routes of exposure, whereas laboratory BMFs only include dietary exposures under controlled conditions in which there is no exposure to chemical in the water. The TMF is the average factor by which the chemical concentration in biota of a food web increases per trophic level and is determined from environmental monitoring data, i.e.,

organisms are exposed to chemical from the environment and diet. Obtaining accurate BCFs and BAFs for very hydrophobic chemicals like MCCP constituents is challenging because of technical difficulties and a general lack of extensive scientific knowledge on the actual dissolved (bioavailable) chemical concentration in the water for such hydrophobic ("water-hating") chemicals. Rationales for lipid correction (normalizing) for neutral organic chemicals and growth correction of the measured data are provided elsewhere [3, 6, 10, 12-14]. It is noted that growth correction methods have not historically been applied in B assessments, i.e., pre-2012. Thus hydrophobic chemicals being evaluated now are not being evaluated to the same historical standards.

Bioaccumulation assessment

Most regulations define persistent, bioaccumulative and toxic (PBT) chemicals and persistent organic pollutants (POPs) in terms of fairly strict bright-line or "pass/fail" criteria based on the state of the science in the late 1970s and early 1980s [15, 16]. The science of environmental chemistry and toxicology has evolved and produced new insights and an assortment of new methods to identify PBT chemicals. Regulatory programs and criteria strive to evolve with this pace; however, this is typically not the case. As a result, current scientific guidance on PBT and POPs criteria is limited and sometimes out of date [15, 16]. To address these issues workshops are commonly organized to bring together experts from academia, industry, and government to reach consensus on current scientific understanding and to promote the best available scientific methods for regulatory decision-making. Two recent and notable workshops related to B assessment and consensus building were (i) the "Science-Based Guidance and Framework for the Evaluation and Identification of PBTs and POPs" (Jan 28–Feb 1, 2008) Pellston Workshop organized by the Society of Environmental Toxicology and Chemistry (SETAC) and (ii) the "Laboratory–Field Bioaccumulation Workshop'' (November 18–19, 2009) sponsored by the International Life Sciences Institute, Health and Environmental Sciences Institute (ILSI-HESI), US EPA, and SETAC. These, and other similar workshops, have led to the publication of "state of the science" papers and guidance for PBT assessment including some cited in this summary.

The general objective of B hazard-based screening assessment is to identify chemicals with a high potential to accumulate in organisms. Bioaccumulative substances are considered hazardous because concentrations in higher trophic level organisms (at or near the top of food webs) may become high, even though concentrations in the environment are comparatively low. Regulatory frameworks for B screening include criteria to identify bioaccumulative substances but do not contain a definition for a bioaccumulative substance [3]. This anomaly contributes to inconsistencies in chemical evaluations between countries and limits the use of high-quality scientific data in assessments [16, 17]. To address the absence of a recognized definition, experts at the SETAC PBT/POP Workshop have defined a B substance as one that biomagnifies in the food-web, that is, increases in normalized concentration (or fugacity) with increasing trophic position [3]. While there is still some debate, the growing consensus in the scientific community is that the overarching objective of B screening is to identify chemicals that biomagnify in food webs [3, 6]. The most relevant metrics for assessing biomagnification are the TMF and the BMF in aquatic (water-breathing, i.e., fish) and terrestrial (air-breathing) species. Chemicals with TMFs > 1 are considered "confirmed B" and chemicals with BMFs > 1 are considered "probable B" [3]. The BCF and K_{OW} are not directly relevant because they do not explicitly include dietary exposures, and hence cannot explicitly quantify chemical biomagnification, although BCF data can be used to model (predict) BMFs, BAFs and TMFs [18]. Chemicals with BCFs or BAFs > 5,000 are considered "possible B" and chemicals with log K_{OW} > 4 are considered "potential B" [3]. Comprehensive reviews further detail the limitations and uncertainties in using BCF and K_{OW} data for B assessment [3, 5, 19-21].

To a first approximation, exposure via the water and diet for a typical fish in the environment is about equal when log K_{OW} ~ 5.6 [18]. When log K_{OW} is lower, exposure from the water (bioconcentration) dominates and when log K_{OW} is higher exposure from the diet (biomagnification) dominates [18]. Relative dietary exposure increases as K_{OW} increases accounting for approximately 85% of the body burden for very hydrophobic chemicals, i.e., log K_{OW} ~8 [22]. The key point is that environmental exposures to MCCP constituents (log K_{OW} > 5.5) are predominantly from the diet (food), not from the water. Hence the most appropriate B metrics are those that address and include dietary exposure pathways such as the BMF, BAF and TMF and not the BCF because it does not include dietary exposures.

Weight of evidence for MCCP B assessment

Following the bioaccumulation expert workshop co-sponsored by the US EPA, SETAC and ILSI-HESI, Burkhard and colleagues [6] proposed a framework to assess bioaccumulation and biomagnification in food webs using a weight of evidence approach that maximizes the application of various available B assessment metrics (i.e., BCFs, BAFs, BMFs, TMFs). Briefly, the approach converts measurements of laboratory and field B assessment metrics (i.e., BCFs, BAFs, BMFs, TMFs) into a "common currency" (fugacity ratios) enabling direct comparisons of different data for B assessment [6]. In this manner the data can be compared against a single B-hazard criterion of 1. Data points > 1 indicate biomagnification, data points < 1 indicate no biomagnification. The additional benefit of the approach is that it can be conveniently displayed in a picture. It is important to recognize that all B data are uncertain due to errors and practical limitations to measurements. Therefore the weight of evidence approach also provides some indication of error in the data in terms of the frequency of data points above or below the threshold criterion of 1.

Figure 1 illustrates the application of this B assessment framework with available measured B data for MCCP constituents from various aquatic species (plankton, invertebrates, fish) from laboratory testing (BCF, BMF) and environmental monitoring (BMF, BAF, TMF). A total of 97 measured data points are compared against the B assessment criterion of 1 (red horizontal line). Data derived from field studies, and in particular TMF values, are considered to be the ultimate indicator of a compound's potential to bioaccumulate in the natural environment [3]. 93% of the data in Figure 1 are from environmental (field) studies and are thus considered highly relevant ("real world") B assessment data. Of these 97 measured data points, 7 (7.2%) met or exceeded the threshold criterion and 93 (92.8%) were lower than the threshold criterion. The median value (central tendency) is 0.27 (black dashed line). The SETAC POP/PBT expert workshop experts considered that a TMF >1 represented the most conclusive evidence of the bioaccumulative nature of a chemical [3]. Figure 1 shows that all of the TMFs for the MCCP constituents < 1. The current weight of evidence indicates that MCCP constituents are not likely to biomagnify in fish and in aquatic food webs.

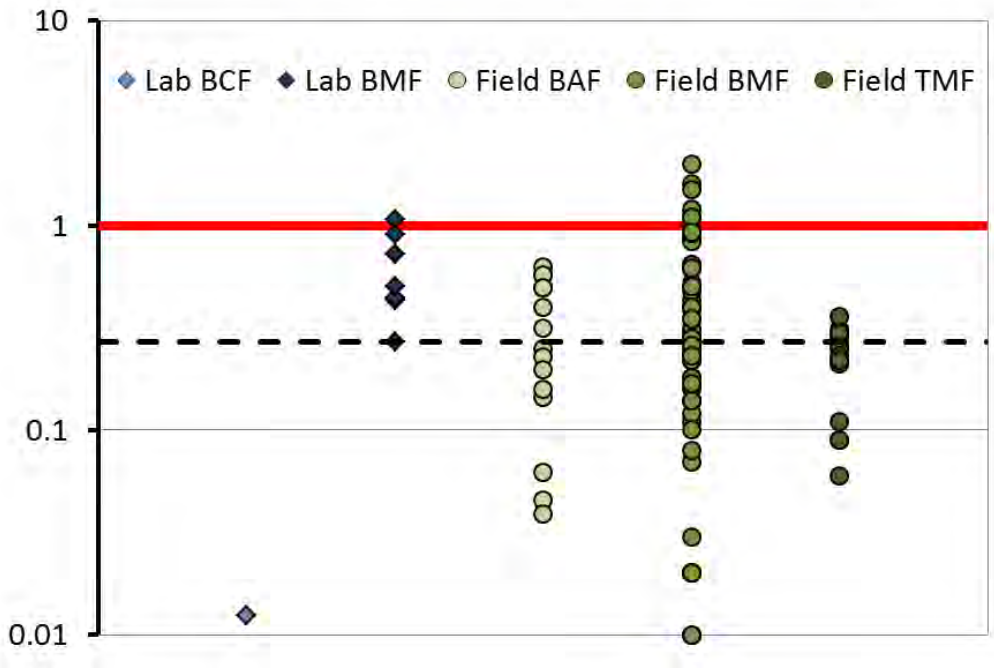

Figure 1. Fugacity ratios calculated using the recommended methods [6] for available relevant and reliable bioaccumulation data for MCCP constituents. Values > 1 (red line) indicate biomagnification (bioaccumulation) hazard. 93% of the data points are < 1 and the median value = 0.27.

The data displayed in Figure 1 are the same data included in the SEV, except as follows:

- A data quality evaluation conducted earlier highlighted that the BCF data from Thompson (2000) are more uncertain (less reliable) than the BCF data from Hurd and Vaughn (2010); therefore, the better quality BCF data were used. The better quality BCF is higher (more conservative) then the poorer quality BCF. The laboratory BCF and BMF tests were conducted with radiolabelled test chemical and hence in this context are considered "conservative" B estimates [5, 23]. The BCF cannot in and of itself be used to assess biomagnification potential because the laboratory test model does not include dietary exposure (required for biomagnification to occur); however, it is included here to combine to the weight of evidence.
- Of note, the laboratory BMFs in Table 26 of the SEV are growth corrected and lipid (corrected) normalized as indicated in the original papers by Fisk and colleagues; however, B data for predominantly SCCPs and LCCPs are not considered relevant and not included here.
- Toxicity testing considered conducted by Cooley et al. (2001) used in the SEV B assessment are less relevant (i.e., not B testing) and also more uncertain than specific laboratory testing that targeted dietary B assessment endpoints (Fisk et al. 1996; Fisk et al. 2000). When existing, reliable quality bioaccumulation (relevant) data exist it does not seem necessary to use data from other types of tests (i.e., toxicity) such as the Cooley et al. (2001) test;

however, it is worth mentioning that all of the BMF data derived from the Cooley et al. (2001) toxicity testing are < 1, thus supporting the general findings of this B assessment.

- Dietary bioaccumulation testing data for terminal Cl-substituted chlorinated alkanes (Fisk et al. 1998) are not considered representative of MCCP constituents and were not included.
- Field BMFs calculated from 1 dietary sample (i.e., some Sculpin-Diporeia data) are considered highly uncertain (as discussed elsewhere [24, 25]) and not included here.

Uncertainty and data gaps

A previous report [10] highlighted the key role of the metabolic biotransformation rate constant for MCCP constituent B assessment. The previous analyses [10] showed that in vivo estimates of the biotransformation rate constants calculated from the existing laboratory BCF and BMF testing data are approximately the same for the range of MCCP constituents tested. Thus additional animal testing is not expected to provide value added information for the B hazard assessment of MCCP constituents. As discussed in the B expert workshops and related publications, e.g., [3], data from a range of species and trophic positions should be considered for B assessment. The current analysis presented in Figure 1 includes a range of aquatic species (plankton, invertebrates and various species and trophic levels of fish) from two different lakes (ecosystems). Data gaps in the overall B analysis include limited (no) information for terrestrial and air-breathing species. If desirable, available measured data could be used to parameterize models to predict BMFs and TMFs for representative terrestrial and air-breathing species if this data gap is considered relevant and until it can be addressed with reliable quality measured data.

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