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**GUIDANCE ON SELECTING A STRATEGY FOR ASSESSING THE ECOLOGICAL RISK OF  
ORGANOMETALLIC AND ORGANIC METAL SALT SUBSTANCES BASED ON THEIR  
ENVIRONMENTAL FATE**

Series on Testing & Assessment  
No. 212

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ENVIRONMENTAL FATE**

**IOMC**

**INTER-ORGANIZATION PROGRAMME FOR THE SOUND MANAGEMENT OF CHEMICALS**

A cooperative agreement among **FAO, ILO, UNDP, UNEP, UNIDO, UNITAR, WHO, World Bank and OECD**

**Environment Directorate**

**ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT**

Paris 2015

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## FOREWORD

The OECD Workshop on Metals Specificities in Environmental Risk Assessment was held on 7-8 September 2011 in Paris. A number of conclusions and recommendations were agreed upon by workshop participants. Some of the recommendations required further development for discussion and consideration by the OECD Task Force on Hazard Assessment to become eligible for acceptance. To this end, the OECD Secretariat, on behalf of the OECD Environment, Health and Safety Division, sent a request in January 2012 to members of the Task Force, workshop participants and experts groups inviting them to submit proposals concerning the further development of these recommendations. Canada responded to this invitation by submitting a proposal that addresses three of the recommendations from the workshop pertaining to the development of approaches/guidance for the hazard and/or risk assessment of metal compounds.

The present document endeavours to fill this need for specific ecological assessment guidance regarding organometallic compounds (OM) and organic metal salts (OMS). A strategy is presented to facilitate the ecological risk assessment of OM and OMS, outlining key steps that are based on elucidation of the fate of these substances in the environment. Reference has been made in various other guidance documents regarding the importance of considering fate, however, this document puts forth the recommendation that the initial determination of their fate in the environment is a primary factor for deciding how these substances should be assessed. The reader should be aware that this document is not intended to provide full ecological assessment guidance for OM or OMS, and it is recognized that regulatory and program requirements will vary with each jurisdiction. In addition, the proposed strategy encompasses the ecological component of a risk assessment only.

The step-by-step strategy presented in this document begins with the determination of the fate of OM and OMS in the environment, with subsequent identification of the moieties to consider for ecological risk assessment. These moieties may be the compound itself and/or any transformation products that may have been formed in the environment. This strategy may also be used to contribute to the effective prioritization of groups of chemicals for ecological risk assessment. Section 2 of the document provides relevant concepts, definitions related to OM and OMS, and an overview of the strategy. Section 3 provides the technical details to support the evaluation of environmental fate and ecotoxicity of OM, OMS and/or their transformation products in relation to the various steps outlined in the strategy. This process ultimately leads to the determination of the moieties that are most relevant for ecological risk assessment. Data selection and evaluation are also briefly considered in Section 4. Worked examples are provided in an appendix, representing the proposed outcomes of the step-by-step strategy.

This document was prepared by Environment Canada. The Joint Meeting of the Chemicals Committee and Working Party on Chemicals, Pesticides and Biotechnology agreed to its declassification on 26<sup>th</sup> January, 2015. It is published under the responsibility of the Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology.

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## INTRODUCTION

Metals occur naturally in the environment. The fate and toxicological effects of a metal or metal-containing substance are strongly dependent upon its chemical speciation, which is dictated by environmental chemistry that can vary across geographic regions and over time.

Guidance documents on the ecological risk assessment of organic substances have been developed by multiple jurisdictions (e.g., European Union, United States and Canada). Additional guidance has been developed in recent years to address metal-specific characteristics that are pertinent for risk assessment. For example, the US EPA Framework for Metals Risk Assessment (US EPA, 2007) effectively documents key principles for the risk assessment of metals. The Metal Environmental Risk Assessment Guidance (MERAG) (ICMM, 2007) also consolidates metal-specific risk assessment concepts into prescriptive guidance.

Although existing guidance documents on the assessment of metals have been published, there remains a specific need for approaches pertaining to the ecological risk assessment of organometallic compounds (OM) and organic metal salts (OMS). OM and OMS compounds are two diverse classes of chemicals, which consequently exhibit differences in reactivity, fate and toxicity in the environment depending on their structures. Existing guidance does appropriately suggest that the fate of an OM determines how it should be assessed, more specifically, whether it should be considered individually or as a source of an inorganic moiety. For example, the *European Chemicals Agency (ECHA)* states that unless an OM acts as a significant source of the metal ion (as a result of degradation processes), the organic moieties and the inorganic components should be assessed individually in accordance with the general procedures laid out in the guidance on information requirements and chemical safety assessment (ECHA, 2008a). Other examples including the *US EPA Framework for Metals Risk Assessment*, the *MERAG* and the *OECD Guidance on Grouping of Chemicals*, similarly suggest that both the inorganic and organic components of an OM compound merit consideration.

This document aims to further develop this concept by providing a strategy that would facilitate the ecological risk assessment of OM and OMS, and builds on the experience gained from the OECD Workshop on Metals Specificities in Environmental Risk Assessment (OECD, 2011). The strategy is based on key steps that first consider the fate of these substances in the environment, the identification of moieties of concern, and subsequently the selection of an appropriate path forward to either assess the inorganic moiety and/or the individual substance. This process may indicate that a particular OM or OMS may merit assessment as an individual substance. However, it is important to consider the possibility of assessing the individual substance as part of a group of substances. Guidance on the grouping of chemicals has recently been published by the OECD (OECD 2014), with some specific considerations for metal-containing substances being highlighted. It is noted that the grouping of most inorganic compounds and some metal-containing organic compounds (e.g., metal salts of some organic acids) for read-across purposes is based on the assumption that properties are likely to be similar as a result of the presence of a common metal ion (or ion complex).

Ultimately, the ecological risk assessment conducted for these chemicals should focus on the most significant moieties of concern likely to be present in the environment, and may include the OM, the OMS, or one or more of their transformation products. These moieties are evaluated or quantified in terms of

their relative potential for occurrence (exposure concentrations) and relative potential for effects. To accomplish this, the potential for transformation (e.g. degradation, dissociation) of the OM or OMS must first be considered, as it will lead to identification of the potential moieties present in the environment (e.g., the OM or the OMS as a result of no transformation, an inorganic moiety or one or more new OM moieties representing the transformation products). The relative potential for toxicity among these moieties is then considered. The moieties of concern are identified with respect to causing harm to the environment. Finally, an appropriate strategy can be selected for the ecological risk assessment of the moieties, whether the focus is on an individual substance or a group of substances. This will ultimately inform risk characterization. When empirical data and/or a reliable prediction technique are not available for a moiety and prediction techniques are not applicable (e.g., OM), a category approach may be needed (OECD, 2007; OECD, 2014). The present strategy may provide additional considerations specific to OM / OMS for grouping and prioritizing for present or future ecological risk assessment initiatives.

## CONCEPTS AND OVERVIEW

### 2.1 Terminology and Definitions

**Organic metal salts (OMS):** Compounds that contain a metal or metalloid moiety and an organic moiety generally linked by an ionic-character single bond. Dissociation of the metal is likely, following solubilization of the compound. The metal may alternatively be liberated by another transformation process (e.g., degradation). Two examples are provided below, cobalt acetate and copper oxalate (ethanedioic acid, copper salt) respectively:

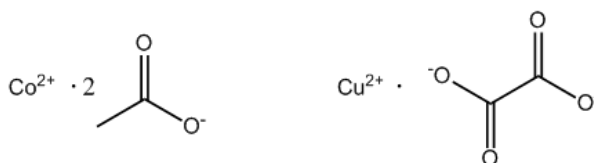


Figure 1: OMS examples

**Organometallics (OM):** Organometallics are often strictly defined as compounds that contain at least one metal (e.g., aluminium, cobalt) or metalloid (e.g., antimony, arsenic, boron, germanium, silicon, selenium) covalently bonded to a carbon. However, for regulatory purposes, the definition of OM will include all other compounds identified as coordination complexes where the metal or metalloid has covalent-character bonds with oxygen, nitrogen, sulphur and/or phosphorus belonging to an organic moiety. Therefore, coordination complexes are considered to be an OM in this document<sup>1</sup>. Dissociation of the metal or metalloid is generally considered to be negligible; however, the metal or metalloid may be liberated by other transformation processes (e.g., ligand exchange or degradation). Two examples are provided below, n-butyllithium, and phenylarsonic acid respectively:

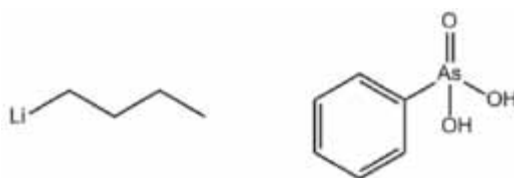


Figure 2: OM examples

**Coordination complex:** An “assembly consisting of a central atom (usually metallic) to which is attached a surrounding array of other groups of atoms (ligands)” (IUPAC, 2007). Metal ions that are coordinated with ligands containing donor groups such as nitrogen, oxygen, phosphorus or sulfur and contain no metal or metalloid-carbon bond:

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<sup>1</sup> In addition, three scientific journals: “*Applied Organometallic Chemistry*”; “*Journal of Organometallics chemistry*”; “*Organometallics*” include compounds consistent with the regulatory definition of “organometallics” presented in this document.

Examples of categories of coordination complexes:

- Azo dye complexes
- Chelate complexes
- Macrocyclic complexes

Examples of subclasses of organometallic compounds include the following:

- Organoaluminum compounds
- Organolead compounds
- Organomercury compounds
- Organotin compounds
- Organo-transition metal compounds
- Organo-alkali/alkali earth metal compounds
- Organoarsenic compounds
- Organoboron compounds
- Carbonyls compounds
- Azo dye complexes
- Chelate complexes
- Macrocyclic complexes

**Transformation product:** Any new distinct molecule or ion issued from the conversion of an original molecule or compound via any type of transformation pathway, such as species transformation, ionization, abiotic degradation, microbial degradation, photodegradation or metabolism.

**Moiety of concern:** A moiety or form of concern is a discrete chemical entity that is expected to have toxicological significance in terms of relative presence and toxicity. In the context of OM or OMS compounds, the relevant moieties would be the original OM or OMS compound and/or any potential inorganic and organic transformation products.

**Chemical category:** A chemical category is a group of chemicals whose physicochemical properties, toxicological (human health/environmental) effects and/or environmental fate properties are likely to be similar or follow a regular pattern as a result of structural similarity (or other similarity characteristic). The similarities may be based on common functional group(s) (e.g., aldehyde, epoxide, ester, specific metal ion), common constituents or chemical classes, similar number of carbons range, an incremental and constant change across the category (e.g., a chain-length category) or common precursors and/or breakdown products (OECD, 2014).

**Chemical species:** Chemical species are “chemical compounds that differ in isotopic composition, conformation, oxidation or electronic state, or that in the nature of their complexed or covalently bound substituents, can be regarded as distinct chemical species” (IUPAC, 2007; as cited in US EPA, 2007).

**Ligand:** a ligand is “an inorganic or organic coordination entity, the atoms or groups joined to the central atom.” (IUPAC 2007),

**Speciation:** speciation is the “distribution of an element amongst defined chemical species in a system.” (IUPAC 2007).

## 2.2 Overview of the Approach

This document aims to provide an approach for selecting a strategy for the ecological risk assessments of OM and OMS compounds based on an examination of predominant environmental fate processes and transformation products. More specifically, whether an OM or OMS is assessed as part of an inorganic moiety assessment or separately as an individual substance will depend on the predominant moieties of concern identified in considering persistence, bioavailability and toxicity of the OM or OMS compound and/or its transformation products. In addition, this strategy may also be used to form groups and prioritize OM /OMS chemicals for ecological risk assessments (e.g. grouping copper-containing substances prior to a copper moiety assessment to determine extent of upcoming work and possible sub-groups, see also OECD (2014)).

This strategy should be applicable to complex substances, or substances of unknown or variable composition, complex reaction products and biological extracts or materials (UVCBs) depending if representative structures are identified and selected according to approaches stated in the *Guidance on Grouping of Chemicals* (OECD, 2014).

The overall strategy and associated decision logic for the evaluation of OM and OMS compounds are illustrated in Figure 3 and briefly described below. The subsequent sections of this document provide further elaboration and detail on considerations associated with each of the steps, as well as how to deal with different levels of data availability.

Step 1. The first step is to identify and evaluate the solubility and dissociation processes for the OM or OMS to determine the extent of dissolution/dissociation in the relevant environmental media. Both processes may co-occur, however, dissolution is not always accompanied by dissociation. See section 3.1 for more details. There are two possible outcomes:

Outcome 1: the OM/OMS readily dissolves and dissociates into O (organic moiety) and M (metal/metalloid or metal/metalloid free inorganic moiety). “Readily” is suggested to be consistent with the “minutes-hours” time duration based upon the screening test of the OECD Transformation Dissolution (T/D) protocol maximum duration of 24 hours (OECD, 2001).

For OMS compounds from Outcome 1, the risk assessment is based upon one molar equivalent of the metal that will follow inorganic guidance for assessment such as MERAG, (ICMM, 2007), see sections 3.3.1 and 3.3.4. For this outcome, the fraction of the salt (OMS) is considered to be negligible. Because dissociation also releases the organic ligand that may further transform, co-exposure to one or more organic component(s) might take place. Dissociated organic components of the OMS compound, as well as organic transformation products from Outcomes 3 and 4 (described below), if significant enough in terms of proportion, residence time and ecotoxicity, should be considered as part of an organic assessment or in an individual substance assessment if warranted.

- Outcome 2: the OM/OMS is insoluble and does not dissociate, or the OM/OMS dissolves but does not dissociate or dissociate only partially. All or a significant portion of the OMS or OM remains in its original form (proceed to Step 2).

Step 2. The second step is to: a) in addition to products identified through any partial dissolution/dissociation identified in step 1 (e.g., hydrolytic pathways), identify other relevant transformation processes (e.g., biotic degradation transformation, photolysis, transmetallation) and possible new products and/or increased contribution to products identified in step 1, as well as b) estimate the half-life of predominant processes and the resulting overall proportions (steps 1 & 2) of the moieties.

Step 2a. For OM or OMS compounds that do not undergo complete dissolution and dissociation (or for which these processes are not applicable), the next step is to examine and evaluate all available stability and persistence information of the OM/OMS in air or the aqueous medium of interest (water column, sediment or soil porewater) and identify the potential transformation pathways. The moieties (original compounds and/or transformation products) that will likely exist in the environment and require consideration for ecological risk assessment are thus identified.

Step 2b. Determine the extent and relative importance (predominance) of transformation potential in terms of half-life for each reaction pathway of the OM/OMS in order to determine the proportions (in terms of relative presence) of each moiety that will need to be considered for ecological risk assessment.

For transformation processes that can liberate an inorganic moiety of concern (M) from the OM<sup>2</sup> compound under environmental conditions, the OM compound is assigned to one of the three outcomes in the flowchart:

- Outcome 3: Short half-life (e.g. seconds to days: up to ~14 days): the OM transforms (e.g. degrades) instantaneously or relatively quickly into M and O (which could be changed as a result of the transformation or may itself further transform).
- Outcome 4: Intermediate half-life (e.g. weeks to months: from ~14 up to ~60 days) or the half-life is unknown and cannot readily be estimated: the OM partially transforms into M and/or a new organometallic (nOM) and/or any O (proceed to Step 3).
- Outcome 5: Long half-life (e.g. months to years: >~60 days): the OM is recalcitrant/persistent.

Exposure scenarios for ecological risk assessment are based upon the most significant moieties in terms of both relative presence in the environment and relative ecotoxicities. Assumptions that give the most weight may be taken. Transformation products that are OM compounds (Outcome 4) may re-enter step 2 of the flowchart as new OM compounds, while those that are organic compounds (Outcomes 1, 3 and 4) are assessed as part of organic assessment(s) or in the individual substance assessment if warranted. In the case of an individual substance assessment, the soluble metal ion and the organic fraction should be assessed separately based on relevant ecotoxicity data sets for soluble metal and the organic fraction. As a precautionary approach, a toxicity-additivity approach can be followed to address potential combined effects of both fractions.

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<sup>2</sup> To simplify text and flowchart (figure 3), only OM is mentioned in the Outcomes 3-4-5. However, OMS may also be subject to further transformation to the M moiety and could also be assigned to Outcomes 3 and 4. As well, OMS may also be determined as recalcitrant/persistent (Outcome 5).

For chemicals assigned to Outcome 3, 100% of the OM is expected to be degraded and so all of the inorganic metal moiety (M) is released. As a result, there will be negligible presence or exposure of the OM in the environment compared to M, and so the OM will have a negligible contribution to the overall risk. Therefore, the assessment will focus on M and the OM does not require further consideration in the assessment. As such, the OM compound can also be included in a group M moiety assessment as a contributor to the risk posed by M in the environment.

Assessment of some moieties may be considered under existing or future assessment initiatives for the appropriate chemical grouping, also refer to OECD (2014).

Step 3. For chemicals assigned to Outcome 4, the degree of toxicity of the transformation product(s) containing an inorganic moiety (M) is compared to that of the original OM on a molar basis in order to select the critical moieties for further consideration for the development of exposure scenarios in the ecological risk assessment(s). If sufficiently detailed information is available, then refined proportions of the OM and the base inorganic moiety to which environmental exposure could occur should be calculated. However, data are unlikely to be available for all compartments (environmental media) and conditions for the majority of cases. Thus, the following three options should be considered in order to determine the moiety or moieties of concern for consideration in the assessment(s):

- (1) If the toxicity of the inorganic moiety (M) is much greater than that of its OM (e.g. 2 orders of magnitude or more), then the OM is considered unlikely to cause concern. In this case, the risk assessment focusses solely upon the inorganic moiety (M).
- (2) If the toxicity of the OM is much greater than that of the inorganic moiety (M) (e.g. 2 orders of magnitude or more), then the risk assessment focusses solely upon the OM.
- (3) If the toxicity of the inorganic moiety (M) and the OM are similar (e.g., do not differ by 2 orders of magnitude or more) or if data is unavailable for one or both of the moieties, then one molar equivalent of each moiety should be considered to contribute to risk in each assessment type (M and OM), resulting in a conservative assessment that addresses the additive toxicity potential of each individual moiety. Depending if risks are found or not, assumptions may be taken to refine the moiety proportions depending on data availability. When empirical, modelled or category data are not available, the evaluator applies their best professional judgment to decide whether a certain level of precaution should be applied to the outcome of the assessment(s). See section 4 for additional details.

For chemicals assigned to Outcome 5, since the OM is not expected to degrade to any significant extent in the environment, the contribution to the risk posed by the inorganic metal moiety (M) in the environment is considered negligible. In this case, the assessment focusses on the risk posed by the OM in its original form including specific attention to bioaccumulation/biomagnification properties. In addition, these properties should be evaluated for OM from Outcome 4 (2) above.

The assessment of the environmental partitioning (relative presence) of moieties of interest may be important to determine the transformation process(es) that may apply as well to seek for adequate ecotoxicity data for comparison purposes.

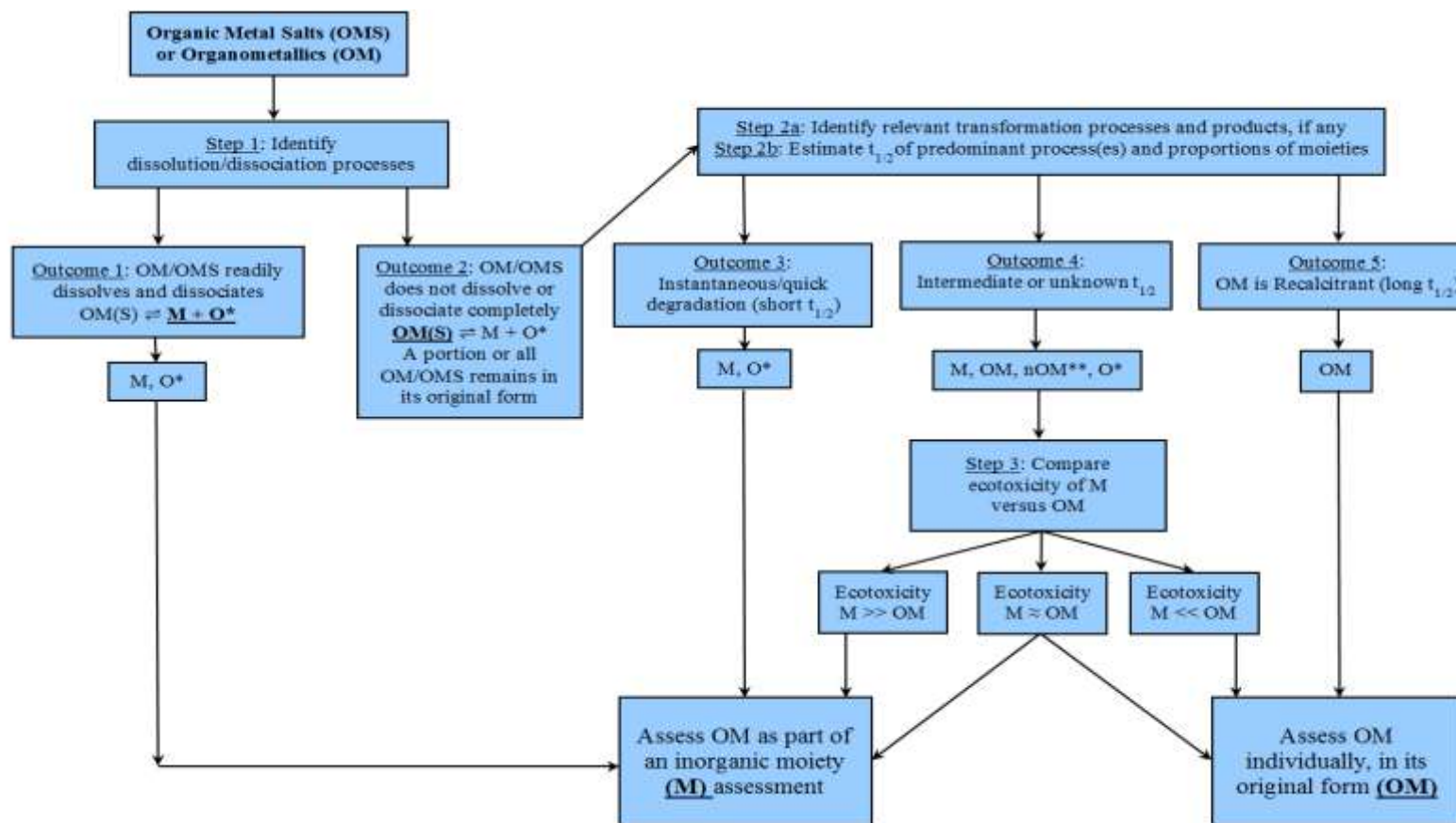


Figure 3: Overview of approach for selecting an ecological assessment strategy for organic metal salts and organometallics

OMS = organic metal salt; OM = organometallic; M = metal/metalloid (e.g. cation, oxyanion, free ion) or metal/metalloid free inorganic moiety; O\* = organic moiety; nOM\*\* = transformation product that is a new organometallic;  $t_{1/2}$  = half-life;

\*Any O released as a product upon dissociation or other transformation process, should be assessed as part of an organic assessment (e.g., matched to an organic moiety or group assessment, or considered immediately if the OM/OMS is being addressed on a substance-by-substance basis) if warranted (option not illustrated in flowchart); \*\*Any nOM released as a product upon transformation of the original OM or OMS should re-enter Step 2

### **2.3 Data availability**

Because limited empirical fate and ecotoxicity data are available for most OM compounds, the evaluator may consider alternative approaches (e.g. using the category/read-across approach). The category/read-across approach considers closely related chemicals as a group, or chemical category, rather than individual compounds. A chemical category is comprised of chemicals whose physicochemical, toxicological (human health/environmental) and/or environmental fate properties are similar or follow a regular pattern as a result of structural similarity (or other similarity characteristics) (OECD 2014). Therefore, this approach allows for the data for one or more chemicals within a category to be interpolated or extrapolated to other category members that are lacking data. Section 4 below provides more details on data consideration.

## CONSIDERATIONS FOR THE APPLICATION OF THE APPROACH

OM and OMS compounds may undergo a variety of chemical transformations under environmental conditions. Chemicals under evaluation should be assessed for reactivity in all relevant environmental compartments in order to identify potential transformation products. It is important to keep in mind that multiple chemical reactions will likely occur under environmental conditions, either sequentially or simultaneously. Rarely does a chemical degrade in the environment by a single mechanism to produce a single product.

There are two components to assessing the environmental fate of OM and OMS compounds: assessment of the persistence of the original compound and determination of the presence of the original compound and its stable transformation products in the environment. As part of the process of determining persistence, the relevant transformation processes must first be identified for the OM or OMS compound.

Some considerations:

- Reaction equation constants such as the formation constant describe systems in equilibrium. Although conditions may favor one outcome or set of products, the complete conversion from original compound to product is often not observed in nature.
- Ambient conditions can and do influence product formation. A compound may not behave the same way in the environment as it does in controlled laboratory settings.
- Although a reaction may be thermodynamically favorable, it may proceed slowly or not at all, if the reaction kinetics are unfavorable; therefore, Outcomes 1, 3, 4 and 5 designations are kinetic-based.
- Metals and metalloids that are released as a consequence of dissociation or chemical reaction of an OM compound or an OMS may undergo further reaction in the environment, but they cannot be degraded, and are considered to be persistent.

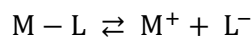
Quantitative kinetic data for the reactions described in this document are often unavailable. In the absence of degradation data such as half-lives, the evaluator must estimate the likely persistence of the original OM compound based on the nature of the chemical under review and the conditions present in the environment. For the approach presented in this document, compounds that are air- or moisture-sensitive, readily hydrolyze or dissociate in water are not considered to be persistent. Metal complexes that contain labile metal ions are also not considered to be persistent, since they may be expected to undergo rapid dissociation and/or ligand exchange. Soluble OMS compounds are assessed as fully dissociated species in solution and are not considered persistent. Further information about the chemical attributes and environmental conditions that influence the rate and extent of degradation is included in Sections 3.2.6 and 3.2.7, respectively.

The next sections provide brief descriptions of the transformation processes, mechanisms and equilibria relevant to several common types of reactions involving OM compounds and OMS compounds.

### 3.1 Step 1. Identify dissociation / dissolution processes

Dissolution and dissociation are often described together, and in many cases occur simultaneously. Dissolution is the complete integration of a substance into a mobile phase, or solvent. A completely

dissolved material in solution forms a single phase rather than a dispersed biphasic (solid in liquid or liquid in liquid) system. Upon dissolution, a coordination complex or an OMS can dissociate to release the constituent metal and ligand(s) as discrete, solvated species, as described in the generalized equilibrium equation:



The equilibrium constant  $K_d$  describes the dissociation reaction:

$$K_d = \frac{[M^+][L^-]}{[ML]}$$

The formation constant  $K_f$  describes the reverse reaction, the formation of an associated complex from freely circulating metal (or metalloid) atoms and ligands:

$$K_f = \frac{[ML]}{[M^+][L^-]}$$

Higher values of  $K_d$  indicate a greater tendency for a complex to dissociate, while higher values of  $K_f$  indicate a more stable and less dissociable compound.

Typically, a substance must dissolve in order to dissociate, but not all soluble substances are necessarily dissociable. Coordination complexes having ligands that are stable anionic species in water (such as halides, carboxylates or hydroxide) or are neutral molecules (such as carbon monoxide or amines) are able to undergo dissociation. Coordination complexes having metal-ligand bonds with significant covalent-character are less likely to dissociate but may nonetheless dissolve. Water-reactive compounds do not typically dissociate, but instead undergo hydrolysis.

The screening test of the OECD T/D protocol is suggested to be used as a key empirical tool to determine the extent of dissolution/dissociation (OECD, 2001) in association with adequate analytical techniques. For instance, if there is dissolution but no dissociation, a total measure of the dissolved metal concentration may not suffice to estimate the extent of dissociation. A measurement of the free ion concentration by Ion selective electrode (ISE) or by Ion-Exchange Technique (IET) or other method would be needed. Other moieties (O or OMS) could also be measured by other available techniques to estimate proportions in solution and estimate extent of dissociation and  $K_d$ .

The qualitative terms ‘labile’ and ‘inert’ are used to describe the relative rate at which a compound undergoes dissociation. Complexes that undergo rapid ligand exchange are considered labile, while complexes that undergo slower ligand exchange are considered inert. It is important to remember, however, that these terms provide only a relative estimate of the kinetic stability of a metal-ligand bond. For the purposes of the topic at hand, lability and inertness should be discussed within the context of exposure and toxicity durations.

The relative labilities of selected aqua metal ions are presented in Table 1. In general, lower charge and larger ionic radius are associated with greater lability than a higher charge and smaller ionic radius.

**Table 1: Relative lability of selected metal ions**

<b>Metal ions that are generally considered labile</b>	Group 1, 2 and 13 metal ions; cadmium(II); chromium (II); cobalt(II); copper(II); iron(II); mercury(II); manganese(II); nickel(II); zinc(II); europium(III)
<b>Metal ions that are generally considered inert</b>	Chromium(III); cobalt(III); iron(III); ruthenium(II)

Source: Atkins et al., 2010

Further information on the factors affecting the strength of metal-ligand bonds is found in Section 3.2.6.

### 3.2 Step 2. Identify relevant transformation processes, half-lives and products

This section covers some common transformation pathways (e.g. degradation) of OM compounds in the environment. The outcomes of these reactions can include displacement of ligands, formation of bonds with new ligands and changes in the oxidation state of the metal. Factors related to the substances and to the environment that may influence these transformations pathways are also presented.

#### 3.2.1 Ligand-exchange

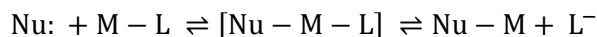
Water bodies and saturated soils contain abundant ionic and neutral species that can form compounds and coordination complexes with metal ions. Dissociated metals and ligands can therefore participate in multiple equilibria. The most stable and abundant products formed depend upon environmental conditions, but tend to have favorable formation constants, or are protected from further reaction (e.g., an insoluble product that precipitates out of solution). Ligands that are abundant in the environment include humic acids, fulvic acids and dissolved organic compounds (both naturally-occurring and anthropogenic).

OM can also react to form new complexes in the environment through the process of transmetallation involving the transfer of ligands from one metal to another. Formation of stable new complexes via transmetallation (usually, but not always, involving alkyl, aryl, alkynyl, allyl, halogen, or pseudo-halogen group ligands) can inhibit re-formation of the original OM complex in solution. This may be an important fate process to consider if the ligand is known to form stable complexes with metals of concern in the environment. Abundant metals include Na, K, Ca and Mg. Hydrogen ions ( $H^+$ ) can also compete with metals for ligands. Increasing acidity therefore tends to increase the degree of dissociation of OM complexes.

The transformation pathway applies to OM and is covered in the flowchart by the creation of new OM (nOM). Unless thermodynamic data exist for a particular compound, existing data on ligand-exchange is likely more qualitative in nature, so that assumptions would have to be made on a case by case basis as environmental conditions may be complex and variable. The outcome of the ligand exchange transformation pathway is to increase or reduce the proportion/concentration of the free metal in the environment (M) or of the OM.

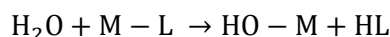
### 3.2.2 Nucleophilic substitution and hydrolysis

Metal-ligand bonds are typically polarized, with the partial positive charge residing with the metal ( $M^{\delta+}-L^{\delta-}$ ). This decreased electron density increases the susceptibility of the ligand-bound metal to attack by other nucleophilic reagents. A nucleophilic agent (Nu:) attacks the electrophilic metal atom, initially forming an intermediate. Either the nucleophile or the ligand is then eliminated from the intermediate.



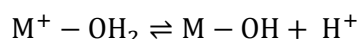
A net change occurs if the new bond to the nucleophile is more stable than the bond to the original ligand and if the released ligand is less nucleophilic than the reacting species. In order for the reaction to proceed, the nucleophilic agent must be able to access an appropriate unoccupied orbital on the metal. The rate and progression of the reaction are therefore sensitive to interference by bulky ligands. Common environmental nucleophiles include water, hydroxide ion and HS-.

Hydrolysis of OM compounds proceeds via nucleophilic attack by either water or hydroxide ion. The net reaction is depicted below.



The rate of hydrolysis of an OM compound can be sensitive to pH. Under basic conditions, the predominant nucleophile is hydroxide ion, which is more nucleophilic than water. Under acidic conditions, the predominant nucleophile is water. Protonation of the ligand can weaken the M-L bond, increasing the rate of elimination of the neutralized ligand (HL). Whether or not the rate of hydrolysis of an OM compound is accelerated under either acidic or basic conditions (or both) depends on the nature of the M-L bond, the accessibility of the metal to nucleophilic attack and the ability of the ligand to become protonated while bound to the metal.

OM/OMS compounds and dissociated metal ions with coordinated water molecules may also undergo hydrolysis. A water molecule coordinated to a metal has increased acidity relative to an un-coordinated water molecule. Upon release of a hydrogen ion, a metal hydroxide species is formed.



This is an acid/base reaction, and the equilibrium concentrations of hydrates and hydroxides are dependent on the acid dissociation constants ( $pK_a$ ) of the metal-aquo complex and the pH of the surrounding environment.

### 3.2.3 Oxidation-reduction (redox reactions)

Redox reactions result from the net transfer of electrons from one element to another. The element that loses electrons (i.e., reducing agent) is oxidized, while the element that accepts the electrons (i.e., oxidizing agent) is reduced. Both the oxidizing and reducing agents experience a change in oxidation state. Every element has preferred oxidation states based upon its unique electron configuration. The ability of a given element to accept electrons is expressed as its reduction potential ( $E^0$ ). The more positive the value of  $E^0$ , the more likely the species will be reduced. Reduction potentials for some common reactions in water are shown in Table 2 (Weast, 1989).

**Table 2: Reduction potentials for selected reactions**

Reaction	E <sup>0</sup> , volts
$O_2 + 4H^+ + 4e^- \rightleftharpoons 2H_2O$	1.229
$MnO_2 + 4H^+ + 2e^- \rightleftharpoons Mn^{2+} + 2H_2O$	1.224
$Fe^{3+} + e^- \rightleftharpoons Fe^{2+}$	0.771
$NO_3^- + H_2O + 2e^- \rightleftharpoons NO_2^- + 2OH^-$	0.01
$CO_2 + 2H^+ + 2e^- \rightleftharpoons HCO_2H$	-0.199
$S + H_2O + 2e^- \rightleftharpoons HS^- + OH^-$	-0.478
$Fe(OH)_3 + e^- \rightleftharpoons Fe(OH)_2 + OH^-$	-0.56

Source: Weast, 1989

Commonly occurring oxidizing agents in aqueous environmental compartments include dissolved O<sub>2</sub>, manganese oxides and metal oxyanions (e.g., chromate). Commonly occurring reducing agents include S and H<sub>2</sub>S. Reduction potentials can be used as guides for predicting reactivity, but many substances can act as either oxidizing agents or reducing agents depending on the conditions. For example, consider the difference between the reduction potential for Fe<sup>3+</sup>/Fe<sup>2+</sup> as solvated cations and the reduction potential for Fe(OH)<sub>3</sub>/Fe(OH)<sub>2</sub>, included in the table above. Changing the nature of the ligands (coordinated water molecules vs. -OH) significantly decreases the reduction potential. Competing reactions can also complicate efforts to predict chemical reactions based on reduction potentials alone. Some general observations include the following:

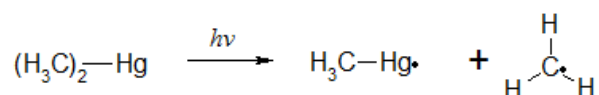
- Zero-valent metals are often prone to oxidation. OM compounds having metals in the zero-valent state are likely to be oxidized.
- OM and OMS compounds having metals in non-preferred oxidation states, if not stabilized, are likely to produce transformation products in which the metal is either oxidized or reduced to attain more stable or more preferred oxidation states.
- OM and OMS compounds having metal ions with noble gas electron configurations are unlikely to produce transformation products in which the metal is either oxidized or reduced under environmental conditions.

Redox reactions are important in the context of aqueous solutions, but water is not the only medium in which redox reactions can occur. Many OM compounds react readily with atmospheric oxygen and other airborne oxidants such as ozone and photochemically generated radical species. Such reactions typically produce metal oxides and can degrade the organic ligand. Although volatile compounds can receive the most exposure to airborne reactants, compounds need not volatilize to be susceptible to air oxidation.

Further information on determining the speciation of metals under various environmental conditions is discussed in Section 3.2.7.

### 3.2.4 Photolysis

Direct photolysis is a decomposition process relevant for OM compounds that have stable metal-carbon bonds. Upon absorption of photons, the metal-carbon bond is cleaved, yielding radical intermediates. For example, dimethyl mercury photolyzes to produce methyl radical and a mercury-centered radical, as shown in the reaction below.



The radical species (i.e.,  $\text{Hg}\cdot$ ) formed by this process undergo further reactions, such as radical combination and hydrogen abstraction, to form stable products.

This reaction process is important for volatile OM compounds that can partition to the vapor phase, but it can also occur in other environmental compartments that receive sunlight, including shallow surface waters, organic-rich films that form at the surface of natural waters and soil surfaces. The overall rate of reaction varies with sunlight intensity. In the air compartment, direct photolysis competes with indirect photolytic processes. Indirect photolysis is the reaction of an airborne substance with photochemically-generated reactants in the atmosphere. Hydroxyl radicals are important atmospheric reactants that are generated by photolytic cleavage of ozone in the presence of water vapor. Hydroxyl radicals can react with the organic ligand(s) of an OM compound, or may combine with radical transformation products generated from the original OM compound to produce new products. Depending on the chemical and the conditions, degradation by combined direct and indirect photochemical pathways in the air can range from hours to days (Craig et al., 2003).

### 3.2.5 Methylation/alkylation of inorganic metal forms

An important environmental transformation for certain metals is the addition of alkyl groups to metals, creating new OM compounds. While alkylation involving larger alkyl groups is possible, methyl groups are the most commonly transferred groups by this process. Methylation reactions can proceed via both abiotic and biotic pathways, but this transformation is considered to be predominantly biologically mediated. Biotic methylation can occur in the water column, but it most often occurs in sediments under anoxic conditions (Craig et al. 2003). Metals and metalloids that are subject to alkylation in the environment are those that can form stable metal-carbon bonds, including Si, Ge, Sn, Pb, Hg, As, Sb and Se (Bodek et al. 1988). The transformation pathway applies to OM and is covered in the flowchart by the creation of new OM (nOM) from (M).

Stable alkyl-metal compounds can also undergo bio-mediated dealkylation in oxygenated environments. In this process, the metal-carbon bonds are cleaved sequentially, ultimately yielding the

organic ligands as neutral molecules and the metal in an inorganic form. This is an important pathway for the environmental degradation of alkyltin species (Maguire, 1992).

### 3.2.6 Influence of intensive properties of the OM/OMS substance on fate

The strength of metal-ligand bonds depends on the chemical and electronic character of both the metal and the ligand. The following subsections provide information on the chemical considerations that are useful in assessing the stabilities of OM substances and predicting likely reaction products.

#### *Hard and soft acids and bases*

Cationic species (Lewis acids) and anionic ligands (Lewis bases) are classified as either hard or soft depending on the polarizability of their outer electron clouds. Hard acids and bases have relatively compact electron clouds, with the electrons bound tightly. In complexes, hard species retain ionic character and do not readily share electrons. Soft acids and bases have larger, more diffuse and polarizable electron clouds. In complexes, soft species have a greater tendency to share electrons and form bonds with covalent character. Hard acids tend to have higher oxidation states than softer acids, particularly for elements with multiple stable oxidation states. Within groups of the periodic table, elements placed higher in the group tend to form harder cations than those occupying lower positions. Hard bases tend to be based on oxygen or carbon ligands. Softer bases tend to be based on nitrogen and sulfur ligands (Craig et al., 2003; Cowan, 1993).

*Classifications for selected metals and ligands include (where "R" refers to an organic molecule; US EPA, 2007):*

- Hard acids:  $\text{Al}^{3+}$ ,  $\text{Ba}^{2+}$ ,  $\text{Be}^{2+}$ ,  $\text{Co}^{3+}$ ,  $\text{Cr}^{3+}$ ,  $\text{Fe}^{3+}$ ,  $\text{Mn}^{2+}$ ,  $\text{Sr}^{2+}$ ,  $\text{U}^{4+}$ ,  $\text{UO}_2^{2+}$ ,  $\text{VO}^{2+}$
- Borderline acids (between hard and soft):  $\text{Co}^{2+}$ ,  $\text{Cu}^{2+}$ ,  $\text{Fe}^{2+}$ ,  $\text{Ni}^{2+}$ ,  $\text{Pb}^{2+}$ ,  $\text{Zn}^{2+}$
- Soft acids:  $\text{Ag}^+$ ,  $\text{Cd}^{2+}$ ,  $\text{Cu}^+$ ,  $\text{Hg}^{2+}$ ,  $\text{Hg}^+$ ,  $\text{CH}_3\text{Hg}^+$ ,  $\text{Tl}^{3+}$ ,  $\text{Tl}^+$
- Hard bases:  $\text{F}^-$ ,  $\text{H}_2\text{O}$ , oxyanions:  $\text{OH}^-$ ,  $\text{SO}_4^{2-}$ ,  $\text{CO}_3^{2-}$ ,  $\text{HCO}_3^-$ ,  $\text{C}_2\text{O}_4^{2-}$ ,  $\text{CrO}_4^{2-}$ ,  $\text{MoO}_4^{2-}$ ,  $\text{H}_n\text{PO}_4^{n-3}$ ,  $\text{H}_n\text{AsO}_4^{n-3}$ ,  $\text{SeO}_4^{2-}$ ,  $\text{H}_2\text{VO}_4^-$ ,  $\text{NH}_3$ ,  $\text{RNH}_2$ ,  $\text{N}_2\text{H}_4\text{ROH}$ ,  $\text{RO}^-$ ,  $\text{R}_2\text{O}$ ,  $\text{CH}_3\text{COO}^-$
- Borderline bases (between hard and soft):  $\text{Cl}^-$ ,  $\text{Br}^-$ ,  $\text{NO}_2^-$ ,  $\text{SO}_3^{2-}$ ,  $\text{H}_n\text{AsO}_3^{n-3}$ ,  $\text{C}_6\text{H}_5\text{NH}_2$ ,  $\text{C}_5\text{H}_5\text{N}$ ,  $\text{N}_3^-$
- Soft bases:  $\text{I}^-$ ,  $\text{HS}^-$ ,  $\text{S}^{2-}$ ,  $\text{CN}^-$ ,  $\text{SCN}^-$ ,  $\text{Se}^{2-}$ ,  $\text{S}_2\text{O}_3^{2-}$ ,  $-\text{SH}$ ,  $-\text{SCH}_3$ ,  $\text{C}_2\text{H}_4$ ,  $\text{C}_6\text{H}_6$ ,  $\text{RNC}$ ,  $\text{CO}$ ,  $\text{R}_3\text{P}$ ,  $(\text{RO})_3\text{P}$ ,  $\text{R}_3\text{As}$ ,  $\text{R}_2\text{S}$ ,  $\text{RSH}$ ,  $\text{RS}^-$

Hard acids form strong, mostly ionic bonds with hard bases, and soft acids form strong, mostly covalent bonds with soft bases. Mixed pairs (hard acids with soft bases or soft acids with hard bases) tend to form less stable complexes.

#### *Polarization of the metal-ligand bond*

OM complexes in which the metal-ligand bond is highly polarized tend to be more reactive than those with less polarized bonds (Craig et al., 2003). Elements with electronegativities less than approximately 1.7 form highly reactive bonds with organic ligands (US EPA, 2007). These compounds do not persist.

With the exception of stable metal-alkyl compounds, OM compounds containing ligands that are strong bases compared to hydroxide ion, such as  $\text{R}^-$ ,  $\text{RO}^-$  and  $\text{R}_2\text{N}^-$ , tend to react readily with water,

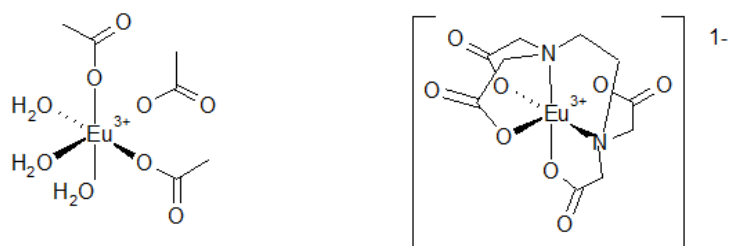
yielding metal hydroxides and the neutralized organic ligands. The rate of reaction varies depending on the electronegativity of the metal and the  $pK_a$  of the ligand, but for practical purposes, these compounds are not persistent under environmental conditions. Increasing the steric bulk of the ligand can increase persistence times by restricting the access of water to the metal.

#### *Other ligand considerations*

As a general rule, the rate of reaction of OM compounds in the environment is related to the accessibility of the metal to reactants. OM compounds in which the coordination sphere of the metal is fully occupied by ligands or the coordinated ligands are prevented from rapid dissociation, as well as OM compounds that contain bulky or hydrophobic ligands that isolate the metal from reactive species in the environment, tend to persist relative to compounds with more accessible metals (Craig et al., 2003).

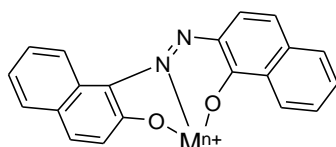
OM compounds containing ligands with greater hydrophobicity have lesser lability and reactivity. OM compounds and metal-organic salts containing insoluble or poorly soluble ligands tend to be insoluble themselves. Poor solubility in water diminishes reactivity by isolation of the metal center from water and waterborne reactants.

Ligands with multiple coordination sites (polydentate ligands) tend to form more stable complexes with metals than those possessing a single coordination site (monodentate ligands). Dissociation of individual metal-ligand bonds for coordinated polydentate ligands occurs sequentially, rather than simultaneously. Coordination to multiple sites prevents a partially dissociated ligand from diffusing away from the metal, increasing the potential for re-association and re-formation of the metal ligand bond. In addition, coordination of a polydentate ligand to multiple sites on the metal inhibits approach by competing ligands. Complexation by a monodentate and polydentate ligand is illustrated by the europium complexes (acetate and ethylenediamine tetraacetic acid [EDTA], respectively) in Figure 4.



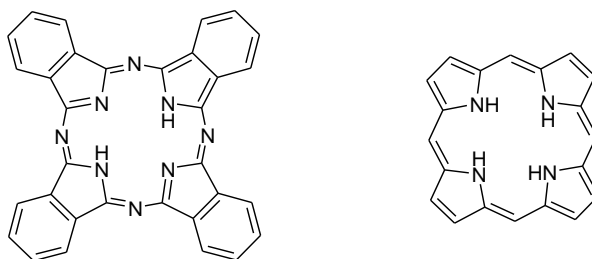
**Figure 4: Europium complexes with acetate and EDTA**

Special classes of polydentate ligands include chelating agents, azo dyes and macrocyclic compounds. Chelating agents are organic molecules that can act as polydentate ligands and form stable complexes with metals. Some common chelating agents include citrate, EDTA and other amine-polycarboxylate compounds. Complexes with these ligands tend to have high formation constants, but may undergo ligand exchange with labile cations. Azo dyes typically contain multiple functionalized aromatic subunits joined by diazo (-N=N-) linkages, and are sometimes complexed to transition metals to achieve the desired color. Azo ligands coordinate to metals via a combination of oxygen and nitrogen donors, as illustrated in Figure 5.



**Figure 5: Subunit of an azo dye coordinating center**

The size and functionalization the azo dye ligand can vary considerably, affecting its solubility and the strength of the metal-ligand bonding. The lability of metals coordinated to these dyes is potentially also variable, and both labile and inert compounds may exist. Macrocyclic molecules containing electron-donating groups such as amines or ethers also form strong complexes with metals. Two examples of macrocyclic ligands are shown in Figure 6: a phthalocyanine (left) and a porphyrin (right). The lone pairs of electrons on the nitrogen donors in these examples align with four of the six octahedral coordination sites on most metals. Because the rings surround the coordinated metal and are not deformable, dissociation is inhibited. These ligands have high formation constants compared with acyclic ligands (Cotton et al., 1999). Metal complexes with such ligands are generally considered to be inert.



**Figure 6: A phthalocyanine and a porphyrin**

#### *Physical and chemical properties relevant to the fate of the OM compound*

Whenever available, the following physicochemical properties are useful for evaluating the potential reactivity and environmental partitioning of OM compounds.

**Thermal stability:** Thermal decomposition temperature is a measure of the overall stability of a compound. Decomposition at low temperatures indicates instability. Thermal decomposition may also contribute to, or accelerate the rate of, degradation of an OM compound.

**Volatility/vapor pressure:** Many OM compounds and nearly all OMS compounds have negligible volatilities. However, vapor pressure data are important for identifying volatile compounds and determining their potential to partition to the vapor phase.

**Water solubility:** The solubility of the original OM compound and the solubilities of the potential products in water affect their reactivity, bioavailability and mobility in soils and surface waters.

**Octanol-water partition coefficient ( $K_{ow}$ ):** For stable compounds,  $K_{ow}$  is essential for assessing bioavailability and environmental partitioning, including potential for bioaccumulation.

### 3.2.7 Influence of extensive properties on fate of the OM/OMS substance

In addition to the intensive properties of the compound, the ambient conditions in the environment play an important role in influencing the reactivity, persistence and partitioning of OM compounds and their transformation products. The following sections describe some of the ways in which changes in environmental conditions affect the environmental fate of OM compounds.

#### *Media consideration*

The fate processes that occur in the water, soil and sediment compartments are influenced by similar agents, although the conditions in each of these environments are different. The important fate processes in these compartments include dissociation, sorption and complexation, redox reactions and biomediated degradation. These processes are affected by the redox potential of the medium, the pH and the presence of inorganic and organic substances that can compete for metal binding sites.

Little information is available about the effects of air quality on the fate of OM compounds. Increased concentrations of reactive species, including ozone, hydroxyl radicals and smog components, as well as the concentration of airborne particulates, are likely to influence reactions with OM compounds. However, even the most stable OM compounds are not expected to persist in the atmosphere for more than a few days, and the effects of air quality on persistence do not appear to have been examined (Craig et al., 2003). Also see last paragraph of section 3.2.4.

#### *Oxidation-reduction (redox) reactions and potentials*

The oxidation potential (Eh) and pH of the ambient environment mutually influence the speciation of metals, whether they are present as dissociated metal ions or incorporated into OM/OMS compounds. More specific information about common chemical transformations that occur under various oxic and anoxic conditions are discussed in other sections, notably redox reactions and methylation/demethylation reactions. In general, increasing pH and decreasing Eh in combination leads to the ultimate formation of insoluble species, often sulfides. Increasing pH, while maintaining oxygenated conditions, commonly leads to the formation of insoluble oxide and carbonate compounds. However, translating this information to real environmental conditions is not always simple. One useful tool for visualizing how these properties work together under real conditions is an Eh vs. pH diagram, provided that there are no kinetic limitations and that chemical equilibrium is established. (see Figure 3-1 in US EPA, 2007).

#### *Water chemistry*

The majority of the processes affecting the fate and transformation of OM/OMS compounds and their degradation products occur in water. Water quality in various environments affects the stability of metal complexes, the speciation of metal-containing transformation products, the bioavailability of metals and mobility of metals in the environment. Very limited data are available concerning how changes in water chemistry affect the persistence and transformation chemistry of OM and OMS in the environment, but based on the chemistry of inorganic metal species, some general observations can be made regarding the potential effects of some essential water parameters, including pH, hardness, salinity and dissolved organic carbon (DOC).

*pH*

pH influences the complexation equilibria of OM, OMS and free dissociated metal ions, as well as metal speciation and the fraction of a metal that is present in a bioavailable (and toxic) form (US EPA, 2007). Increasing the pH reduces the concentration of free protons available to compete for ligand complexation sites, and tends to increase the stability of some metal complexes. Increased alkalinity also reduces metal bioavailability by increasing the tendency for dissociated metals to form insoluble carbonate complexes and insoluble oxides. However, at a constant free ion concentration, a pH increase will increase metal bioavailability because of the reduced free protons competition as mentioned above.

Acidification can affect metal complexation equilibria of OM/OMS in solution as well as interactions of the metal ion at organic and/or biological surfaces (ICMM, 2007). Increased dissociation of metal complexes under acidic conditions increases the free metal ion concentration in solution. The strength of metal-ligand complexation is decreased by competition between bound metal ions and free protons ( $H^+$ ) for binding sites on organic and inorganic ligands. Competition with free protons can promote dissociation of the original OM/OMS, as well as influence the complexation of the dissociated metal ions with DOC, humic acids and other potential ligands in the environment.

Hydrolysis reactions of OM compounds can also be sensitive to pH, and may be either acid- or base-catalyzed. If hydrolysis of the OM or OMS compound is not an important fate process, then the overall concentration of the free metal typically decreases with increasing pH, due to increasing complexation strength and the formation of poorly soluble transformation products.

*Hardness*

As described in earlier sections, OM and OMS compounds can undergo transmetallation reactions with ambient metal ions. Increased concentrations of metal ions, such as calcium, magnesium or iron, that can compete for ligand binding sites and form strong complexes can increase dissociation of metals from the original OM or OMS compounds and inhibit re-formation of the original complexes. If transmetallation was to occur, it could potentially increase the toxicity associated with the OM or OMS by liberating a metal of concern that may otherwise be sequestered within the complex and incapable of exerting toxic effects<sup>3</sup>.

*Salinity*

Specific information on how salinity or ionic strength affects the stability and transformation of OM and OMS compounds is lacking. In general, increasing ionic strength of the aqueous environment may decrease the solubility of the original OM/OMS and complexation strength, but the magnitude and relevance of this effect may be uncertain and needs to be addressed specifically for each case under consideration. Any change in the type and concentration of ionic species present in the local environment will affect the complexation and dissociation equilibria in which the original compound participates. If an OM/OMS undergoes dissociation, the ionic species naturally found in marine and estuarine waters may

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<sup>3</sup> The presence of major cations ( $K^+$ ,  $Na^+$ ,  $Ca^{2+}$ ,  $Mg^{2+}$ ) in natural waters may reduce the potential toxicity of the dissociated metals by competition for binding to the site(s) of toxic action; as hardness increases, bioavailability is decreased. Several metals that are significantly affected by hardness ( $Ca^{2+}$  and  $Mg^{2+}$ ) include cadmium, chromium, cobalt, copper, manganese, nickel and zinc (ICMM, 2007).

compete for abiotic or biotic uptake with the dissociated ionic metal species, or may influence the thermodynamic equilibria, thus altering the ratios of metal species in solution (Stumm and Morgan, 1981).

### *DOC*

Dissolved and suspended organic carbon (DOC) can undergo ligand exchange reactions with OM and OMS compounds in solution. Active DOC substances include proteins, carbohydrates, amino acids, humic substances and other chemicals of biological or anthropological origin. Metal complexes to humic acids in particular typically have high formation constants, and binding of the metal in the complex can become stronger over time as it ages. In environments with high DOC content, transformation of OM and OMS compounds may therefore release relatively low levels of freely dissolved metal ions compared to free ligands. Complexation to DOC can potentially increase the mobility of the metal in the environment by reducing sorption and reaction to form insoluble species. However, complexation with DOC can also decrease the bioavailability of a metal relative to the corresponding un-complexed dissolved ion by inhibiting its uptake by organisms and interactions with reactive sites.

### **3.3 Step 3: Determining the relative ecotoxicity of moieties of concern**

OM compounds that are stable (kinetically inert, Outcome 5 OM, see section 2 and Table 1) may have intensive properties that differ from those of the constituent metal and the free or dissociated ligand(s) and these OM compounds should therefore be assessed as unique substances. In contrast, unstable OM or OMS compounds may undergo a variety of transformations that could result in the release of the liberated free ion, neutral or charged organic moieties and/or new OM compounds (nOM), each of which has potential toxicological significance (Outcomes 1, 3 and 4). Any nOM released as a product upon transformation of the original OM or OMS should re-enter step 2. An important consideration in the risk assessment of OM and OMS compounds is a comparison of the level of toxicities among the moieties resulting from such transformations (which may also include the original OM/OMS). The risk assessment should be based on the most significant moieties in terms of relative presence and toxic effects.

The moieties of concern should be determined from among the stable OM compounds and the potential transformation products based upon their potential bioavailability. The bioavailability of the candidate moieties can be determined by assessing their physicochemical properties and the ways in which they interact with, and partition in, the environment including biota. Specifically, the bioavailability and toxicological effects of a compound depend on the interaction of physicochemical properties (e.g., solubility, oxidation state), environmental conditions (e.g., DOC, pH) and abiotic and biotic processes (e.g., sorption, competition with other chemical species, microbial activity) that affect metal speciation. In addition, interaction with uptake sites on animals/plants is also a very important consideration regarding bioavailability. It is therefore important that the ecological assessment process address the bioavailability of each moiety of concern in each environmental compartment (if applicable). For OM compounds assigned to Outcome 4 (intermediate half-life), the toxicity of the inorganic metal moiety should be compared to that of the original OM compound. Although toxicity and bioavailability data may be limited for the original OM compound, predicted no effect concentrations (PNECs) have been established for a number of inorganic metals in various jurisdictions. Therefore, the risk evaluator may consider using existing PNECs when assessing the inorganic metal moiety.

#### ***3.3.1 Inorganic metal***

For OM compounds that degrade instantaneously (Outcome 3), the inorganic metal is considered to be the moiety of concern; the assessment is therefore based on the inorganic moiety, and no further consideration is required in the assessment of the original OM. For many dissolved metals, the toxic response of aquatic organisms is usually a function of the free metal ion concentration (Campbell, 1995).

In other words, the concentration of free ion can be used to predict bioavailability and toxicity of the metal to aquatic organisms when all other factors are kept constant. Current guidance for the assessment of inorganic metals has been established by the United States (US EPA, 2007) and the European Union (ICMM, 2007; ECHA, 2008a). Additional tools such as the TICKET-Unit World Model and MeCLAS are also being developed to assess fate, bioavailability and ecotoxicity of a number of metals or metal-containing compounds (Farley et al. 2011; MeCLAS 2014).

### ***3.3.2 Original OM/OMS compound***

For OM compounds that are recalcitrant (long half-life), the original OM or OMS is the focus of the assessment. Data describing the bioavailability and toxicity of the original OM or OMS may be obtained from laboratory experiments, field studies, predictive models and comparison to analogs. See Section 4 for a discussion of these sources of data and the level of confidence associated with each.

### ***3.3.3 Organic transformation product/salt component***

Organic transformation products and dissociated organic components of OMS should be considered as part of an organic assessment if warranted. Established evaluation processes and guidance include the US EPA Guidelines for Ecological Risk Assessment (US EPA, 1998) and ECHA Guidance on Information Requirements and Chemical Safety Assessment (ECHA, 2011).

### ***3.3.4 Biotic Ligand Model (BLM) considerations***

To account for the water quality parameters (pH, hardness and DOC) described above, the risk evaluator may be able to utilize the BLM (Di Toro et al., 2001; Santore et al., 2001), which is a mechanistic-based approach for addressing the bioavailability and toxicity of metals on the basis of physical and chemical factors affecting speciation, complexation and competition of metals for interaction at the biotic ligand (i.e., the gill in the case of fish). The BLM has been most extensively developed for copper and is also being developed for use with other metals, including silver and cobalt (see ECHA 2008a for more details). Specifically, the biotic ligand model (BLM) (Di Toro et al., 2001; Paquin et al., 1999; Santore et al., 2001) takes into account the influences of both speciation (e.g., free metal ion, DOC complexation) and cationic competition (e.g.,  $K^+$ ,  $Na^+$ ,  $Ca^{2+}$ ,  $Mg^{2+}$ ) for binding sites on biological surfaces (e.g., gills) on bioavailability and toxicity of metals to aquatic organisms. The BLM cannot be used to predict OM bioavailability and toxicity properties (stable/recalcitrant: Outcome 5; intermediate half-life: Outcome 4) that may well be different compared to the released dissolved inorganic metal fraction (Outcomes 1 and 3). In fact, the BLM considers the OM as sole ligands (i.e. a constituent of DOC) that may reduce the dissolved inorganic metal concentration and thus bioavailability and toxicity related to the inorganic metal fraction, which is the case. However, it does not consider the bioavailability and toxicity of the OM itself. See Appendix AI.4 for an illustrative example case study where an OM containing Zn (Ziram) is showing more bioavailability and toxicity than inorganic Zn (M) and, thus, does not behave in a manner consistent with the BLM. The application of the BLM is not suitable in that case. In other instances, for example in the presence of EDTA (chelate), the BLM would apply as EDTA-metal complexes, because of their hydrophilic properties, are not bioavailable to organisms and are limited to a complexation role (Campbell, 1995).

## DATA CONSIDERATION AND SUMMARY

There are many widely known and accepted approaches across jurisdictions for determining the reliability and quality of study data (e.g., European Union, 1995; ECHA, 2011; OECD, 2005; Klimisch et al. 1997; Kollig, 1998; Rand 1995). However, study data is sparse for a large proportion of OM and OMS. In the absence of empirical data, quantitative structure activity relationship (QSAR) models may predict values for physical-chemical properties, toxicity, fate, and bioavailability. However, few and very limited QSAR models have been published for OM and OMS. Developing and validating QSARs applicable to OM and OMS is challenging due to issues associated of speciation, complexation and interactions within biological systems, stability of the metal-ligand bond, kinetics of metal-ligand bond formation and degradation, and the medium used to study these interactions (Walker et al., 2003).

An additional option when empirical data are unavailable is the implementation of read-across and grouping approaches. As noted in the OECD Guidance on Grouping of Chemicals, care is needed when applying these approaches, as metals can occur in a range of various substances (e.g., inorganic metal compounds, OMS compounds, OM compounds, metals, metal-metal compounds, alloys and complex substances). Categories of metals and metal-containing compounds should therefore be comprised of compounds that potentially lead to exposure to the same metal moiety (OECD, 2014). Due to the common importance of fate, the approach and concepts presented in this guidance can therefore also assist the inclusion of OM and OMS in category formation. A third option, anticipated to be very important, is the use of professional/expert judgment.

### 4.1 Professional/expert judgment

Input from experienced chemists and toxicologists is valuable in every step of the risk assessment process. Since data are sparse for many OM and OMS compounds, the use of professional and expert judgment is particularly important in this evaluation. Given the lack of data, many compounds will require estimation of fate, bioavailability and toxicity parameters through modeling or read-across to analogs. Selection of appropriate QSAR models and analogs for estimation of fate, bioavailability and toxicity will require careful analysis, as will interpretation of modeled and analog data. Where applicable, general trends and first principles for assessing the reactivity, bioavailability and toxicity of metals and OM compounds are included in the earlier sections of this document. While these trends and principles cannot replace measured data, they do provide a context for interpreting modeled and estimated data, and can be helpful for predicting a chemical's activity in the absence of data.

Expert judgment may be necessary in the comparison of functional groups of OM/OMS compounds with those of other compounds and subsequent identification of analogs that have similar functional groups. Evaluation of the location of functional groups on a molecule may provide insight into the fate, bioavailability and toxicity of the compound (e.g., functional groups that appear close to each other in the molecule or that are positioned in a certain way may trigger specific [receptor] interactions) (ECHA, 2008b). Interactions between and among functional groups should also be considered.

Experienced scientists may be able to provide insight in the evaluation of the various factors that are present in the environmental matrix of the compartment being evaluated in the risk assessment and identify the specific factors that are most likely to influence bioavailability and toxicity. Antagonistic, additive or potentiated effects of extensive/intensive factors on bioavailability/toxicity may also be a consideration (Phinney and Bruland, 1997).

Data should be compiled from all available sources (including empirically derived laboratory and field data, QSAR predictions and values estimated using read-across strategies). A trained eye will be able to identify patterns in these data and determine whether outlying data points should be discarded to increase the potential of selecting the most reliable data. Integration of the entire body of knowledge that is available, including evaluation of all available data from various sources as well as the influence of extensive factors on bioavailability and toxicity, can best be achieved by professionals with experience in evaluating interactions among physicochemical and toxicological parameters.

#### **4.2 Summary and needs**

Most OM compounds lack sufficient empirical data to allow for a quantitative assessment to be conducted, and until additional information becomes available, specific properties may need to be addressed initially on a qualitative basis using expert and professional judgment based on physicochemical principles, read-across and QSARs.

Although numerous fate and toxicity models exist for nonionic organic chemicals based on simple chemical properties, analogous models for OM and OMS compounds are either not available or are not sufficiently validated. One factor that complicates the development of models for assessing metals, as well as OM compounds, is the high degree of specificity exhibited by the mechanisms and processes underlying the behavior of metals (e.g., speciation, exposure conditions and organism physiology) (US EPA 2007). As a result, OM/OMS ecological risk assessments may be limited to the use of empirical data to address and predict specific endpoints (e.g., ecotoxicity).

When sufficient empirical data are not available for the OM/OMS of interest, the use of acceptable models in combination with professional/expert judgment should be incorporated into the assessment and the reduced confidence in the outcome recognized. In the absence of data and acceptable models a high degree of uncertainty will be inherent and the limitations of this uncertainty should be communicated in the assessments. These limitations can also be used to prioritize the generation of new data under specific protocols/methods. The application of the approach could be facilitated with the availability of: (i) data relevant to the fate or transformation of OM/OMS in the environment; (ii) short or long term toxicity (aquatic, soil, or sediment) for an OM found to be stable and kinetically inert.

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**APPENDIX I:  
REPRESENTATIVE CASE STUDIES FROM SELECTED CLASSES OF OM AND OMS**

**AI.1 Introduction**

The first step in the assessment of an OM/OMS compound is to determine the extent of dissolution/dissociation in the aqueous medium of interest (water column, sediment or soil porewater). The second step (2a) consists in examining and evaluating all available stability and persistence information of the OM/OMS in air or the aqueous medium of interest and determining potential transformation pathways. Potential organometallic transformation products may re-enter the flowchart (step 2), whereas any organic transformation products are set aside for current or future consideration. The second step (2b) to be considered is the extent and relative importance (predominance) of transformation potential in terms of half-life for each reaction pathway to determine the proportions (in terms of relative presence) of each moiety to be assessed. The third step for consideration in risk assessment of an OM compound is the comparative level of toxicities among moieties. The consideration for development of exposure scenarios in the risk assessment will thus be based on the most significant moieties in terms of relative presence and effects.

The following section contains representative case studies for OM compounds assigned to Outcomes 3, 4 and 5 (short, intermediate and long half-lives, respectively) as well as for an OMS that readily dissolves and dissociates (Outcome 1).

**AI.2 Case study on Outcome 1 OMS compound: Chromium (III) acetate (CASRN: 1066-30-4)**

Considerations	Relevant information/ Outcome
<b>STEP 1</b> <b>Determine the extent of dissolution/dissociation of original OMS</b>	
Solubility and other physicochemical properties	<p><b>Solubility:</b></p> <ul style="list-style-type: none"> <li>• For the monohydrate: soluble in water at 20 °C (quantitative data were not located); 45.4 g/L in methanol at 15 °C; 2 g/L in acetone at 15 °C (ATSDR, 2012)</li> </ul> <p><b>Boiling point:</b> No data (ATSDR, 2012).</p> <ul style="list-style-type: none"> <li>• Chromium triacetate is a salt and will not volatilize.</li> </ul> <p><b>Log K<sub>ow</sub>, log K<sub>oc</sub>:</b></p> <ul style="list-style-type: none"> <li>• No data (ATSDR, 2012).</li> </ul>
Dissociation	Dissociation of the chromium-acetate bonds, forming mixed aquo- and acetate complexes, and eventually solvated Cr <sup>3+</sup>

Considerations	Relevant information/ Outcome
	(Predominant transformation pathway).
Other types of transformation pathways in the environment	Solvated Cr <sup>3+</sup> ion may undergo hydrolysis (conversion to Cr-OH species) and oxidation reactions.
Influence of intensive properties of the original compound on fate	<p><b>Key consideration:</b> The fate of the original compound is determined by the coordination chemistry of Cr<sup>3+</sup>. Cr<sup>3+</sup> is kinetically inert to ligand exchange reactions compared to other metal ions.</p> <ul style="list-style-type: none"> <li>• Dissociation of chromium-acetate bonds is relatively slow (hours) for an organic-metal salt (Cotton and Wilkinson, 1980).</li> <li>• The coordination chemistry of Cr<sup>3+</sup> is complex. Commercial chromium triacetate may consist of a variety of bridged, condensed and polynuclear complexes (Eshel and Bino, 2001).</li> <li>• The complex [Cr(H<sub>2</sub>O)<sub>6</sub>](O<sub>2</sub>CCH<sub>3</sub>)<sub>3</sub> readily decomposes under ambient conditions (Eshel and Bino, 2001).</li> </ul> <p><b>Other reaction pathways:</b></p> <ul style="list-style-type: none"> <li>• Cr(III) is a stable oxidation state for chromium. It may also be oxidized to Cr(VI).</li> <li>• Chromium-aquo species may be converted to hydroxides.</li> </ul> <p>(Bodek et al. 1988)</p>

Considerations	Relevant information/ Outcome
Influence of extensive properties on fate of the original compound	<p><b>Media considerations:</b> The fate of the original compound and the degradation product distribution will be most affected by ligand availability and pH.</p> <p><b>Air composition/quality:</b> No effect expected.</p> <p><b>Water chemistry:</b></p> <ul style="list-style-type: none"> <li>• Polydentate organic ligands (e.g., citrate, tartrate or humic acids) may displace the acetate ligands on chromium. The resulting complexes are expected to be more stable than the original compound (Page and Loar, 2001; ATSDR, 2012).</li> <li>• Upon dissociation, the low concentration of acetate relative to water/hydroxide in the environment will inhibit re-formation of chromium-acetate bonds.</li> <li>• Dissociated Cr<sup>3+</sup> will exist as the solvated ion at low pH (&lt; 2.5) and as Cr(OH)<sub>3</sub> at pH ≥ 3 (Bodek et al., 1988).</li> </ul> <p>Oxidation from Cr(III) to Cr(VI) occurs only under highly oxidizing conditions (Bodek et al., 1988; ATSDR, 2012).</p> <p><b>Sediments and soils:</b></p> <ul style="list-style-type: none"> <li>• Factors affecting chromium speciation in soils and sediments are similar to those in the water column (ATSDR, 2012).</li> </ul>
Environmental partitioning	<p><b>Chromium(III) species:</b></p> <ul style="list-style-type: none"> <li>• Volatilization is negligible for ionic species.</li> <li>• In the water column, Cr<sup>3+</sup> sorbs to suspended solids and forms complexes with humic ligands. Sorption, precipitation and settling are the main removal processes.</li> <li>• In river waters, chromium is found predominantly in the suspended particulate phase, rather than as dissolved species.</li> <li>• Cr(III) species have low solubility and low mobility in soils. In leaching studies, Cr(III) was found to form insoluble and immobile complexes with soil components.</li> </ul>
Extent of transformation (half-life)	Dissociation of chromium-acetate bonds (hours)

Considerations	Relevant information/ Outcome
	Oxidation of Cr(III) to Cr(VI) (2-9 years) (Cotton and Wilkinson, 1980; ATSDR, 2012)
Moiety to be evaluated/moiety of concern	Cr <sup>3+</sup> ; Cr(OH) <sub>3</sub>
Organic/inorganic transformation products/salt component	Acetates. It should be considered for assessment according to other (current or future) frameworks for organic substances.
Original compound	The original OMS is considered to be negligible in this assessment because it transforms relatively rapidly (hours) to generate the above transformation products.

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## AI.3 Case study on Outcome 3 OM compound: Dicobalt octacarbonyl (CASRN: 10210-68-1)

Considerations	Relevant information/ Outcome
<b>STEP 1</b> <b>Determine the extent of dissolution/dissociation of original OM</b>	
Solubility and other physicochemical properties	<p><b>Solubility:</b> Generally described to be insoluble in water and soluble in organic solvents; quantitative solubility data were not located (NOAA, 2013; HSDB, 2005).</p> <ul style="list-style-type: none"> <li>• Significant concentrations in water are not expected.</li> <li>• Migration of the original compound to water from solution in organic solvents is expected to be relatively slow.</li> </ul> <p><b>Thermal decomposition:</b> Decomposition temperature = 52 °C (NOAA, 2013).</p> <ul style="list-style-type: none"> <li>• In the absence of oxygen, the expected products are carbon monoxide and cobalt metal.</li> <li>• Thermal decomposition is not expected to influence the overall persistence of the original compound for practical purposes.</li> </ul> <p><b>Volatility:</b> Vapor pressure = 0.07 torr at 15 °C (NOAA, 2013).</p> <ul style="list-style-type: none"> <li>• The original compound will partially vaporize at ambient temperature.</li> <li>• Transport of the original compound in the vapor phase is unlikely due to rapid decomposition.</li> <li>• Reaction with air proceeds whether or not the compound has volatilized.</li> </ul>
Dissociation	<ul style="list-style-type: none"> <li>• Dissociation of the CO ligands (not predominant)</li> </ul>
<b>STEP 2a</b> <b>Examine and evaluate stability and persistence information of original OM</b>	
Types of transformation pathways in the environment	<p><b>Predominant transformation pathway:</b> Dicobalt octacarbonyl is pyrophoric and decomposes instantaneously to generate carbon monoxide and cobalt oxides on contact with air or water (NOAA, 2013; Gelest, 2005).</p>

Considerations	Relevant information/ Outcome
	<p><b>Other pathways:</b></p> <ul style="list-style-type: none"> <li>• Oxidation of <math>\text{Co}^0</math> to <math>\text{Co(II)}</math> compounds and/or cobalt oxides</li> </ul>
Influence of intensive properties of the original compound on fate	<p><b>Key consideration:</b> The environmental fate of dicobalt octacarbonyl is primarily influenced by its reactivity with oxygen.</p> <ul style="list-style-type: none"> <li>• The original compound will decompose immediately on exposure to air.</li> <li>• Elemental cobalt (<math>\text{Co}^0</math>) is susceptible to oxidation.</li> <li>• The expected cobalt oxide reaction products in air include <math>\text{Co}_3\text{O}_4</math> and <math>\text{CoO}</math> (Donaldson and Beyersmann, 2012).</li> <li>• In water and wet soils, the original compound readily decomposes to generate carbon monoxide and <math>\text{Co(II)}</math> compounds.</li> <li>• Under oxidizing and moderately reducing conditions, the dominant cobalt aqueous species at pH values less than 9.5, the predominant form of cobalt will be <math>\text{Co}^{2+}</math> species either as a dissolved ion species or insoluble cobalt oxides. Typically, <math>\text{Co}^{3+}</math> is not favored under environmental conditions.</li> </ul> <p>(Krupka and Serne, 2002; HSDB, 2006)</p>
Influence of extensive properties on fate of the original compound	<p><b>Media considerations:</b> Elemental cobalt is subject to oxidation under all environmentally relevant conditions. Ionic cobalt exists as <math>\text{Co}^{2+}</math> in the environment (US EPA, 2005a). Speciation and solubility of <math>\text{Co}^{2+}</math> compounds vary with the pH and oxidation/reduction potential of the local environment, as well as the availability of organic ligands.</p> <p><b>Air composition/quality:</b> Reaction with air occurs so rapidly that variations in air quality will not affect the rate or extent of reaction.</p> <p><b>Water chemistry:</b></p> <ul style="list-style-type: none"> <li>• In oxygenated waters, the original compound will be converted to dissolved <math>\text{Co}^{2+}</math> species that will speciate to various forms, including insoluble forms depending on factors such as pH, redox potential, and presence of dissolved and dispersed organic matter.</li> </ul> <p>(ATSDR, 2004; WHO, 2006; US EPA, 2005a; Krupka and Serne, 2002)</p> <p><b>Sediments and soils:</b> Speciation of the cobalt reaction products as a function of pH, water chemistry and oxidation/reduction potential is expected to be similar to that observed in aqueous systems.</p>

<b>Considerations</b>	<b>Relevant information/ Outcome</b>
Environmental partitioning	<p><b>Dicobalt octacarbonyl:</b> Due to its reactivity, unreacted dicobalt octacarbonyl is not expected to persist in any environmental compartment, and its partitioning behavior cannot be described. Partitioning and mobility of the expected oxidation products, cobalt oxides and soluble <math>\text{Co}^{2+}</math>, are discussed below.</p> <p><b>Cobalt oxides (<math>\text{Co}_3\text{O}_4</math>):</b> Cobalt oxides are formed upon the reaction of dicobalt octacarbonyl in air. Ultimately, cobalt oxides partition to soils and sediments via wet and dry deposition, sorption and settling.</p> <p><b>Ionic cobalt (<math>\text{Co}^{2+}</math>):</b> Ionic cobalt (<math>\text{Co}^{2+}</math>) is soluble in water, sorbs to soils and suspended particulates, and forms coordinate complexes with dissolved organic compounds. It partitions to the water, soil and sediment compartments, but ultimately deposits in soil and sediment.</p> <p>(ATSDR, 2004, WHO, 2006)</p>
<p><b>STEP 2b</b></p> <p><b>Extent of transformation and relative presence of moieties</b></p>	
Extent of transformation (half-life)	Instantaneous (seconds)
Moiety to be evaluated/moiety of concern	<p>Cobalt(II, III) oxide (<math>\text{Co}_3\text{O}_4</math>)</p> <p>Soluble <math>\text{Co}^{2+}</math> ionic compounds</p> <p>Because dicobalt octacarbonyl reacts instantly with air, it is assigned to Outcome 3, and 100% of the metal is therefore considered to be the moiety of concern for the ecological risk assessment; the original OM is considered to be negligible. The inorganic transformation product, carbon monoxide, should be addressed immediately if the OM is being addressed on a substance-by-substance basis or under a moiety assessment as needed..</p>
original compound	The original OM is considered to be negligible in this assessment because it decomposes instantaneously to generate carbon monoxide and cobalt oxides on contact with air or water.

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## AI.4 Case study on Outcome 4 OM compound: Ziram (CASRN: 137-30-4)

Considerations	Relevant information/ Outcome
<b>STEP 1</b> <b>Determine the extent of dissolution/dissociation of original OM</b>	
Solubility and other physicochemical properties	<p><b>Solubility:</b> Water solubility = 65 mg/L at 25 °C (HSDB, 2003)</p> <ul style="list-style-type: none"> <li>Ziram has low but significant solubility in water, and is described to be lipophilic (Phinney and Bruland, 1997).</li> </ul> <p><b>Thermal decomposition:</b> No decomposition reported, melting point = 246 °C (HSDB, 2003).</p> <ul style="list-style-type: none"> <li>Thermal decomposition is not expected to influence the overall persistence of the original compound.</li> </ul> <p><b>Volatility:</b> Vapor pressure = <math>7.5 \times 10^{-9}</math> Torr at 0 °C (HSDB, 2003).</p> <ul style="list-style-type: none"> <li>Volatilization is not important for this compound.</li> </ul> <p><b>Partition coefficient:</b> Log <math>K_{ow}</math> = 1.23 at 20 °C (HSDB, 2003)</p>
Dissociation	Not expected, negligible
<b>STEP 2a</b> <b>Examine and evaluate stability and persistence information of original OM</b>	
Types of transformation pathways in the environment	<p><b>Predominant transformation pathways:</b> Dissociation of the zinc-ligand bond and hydrolysis of the dimethyldithiocarbamate ligand to produce CS<sub>2</sub> and dimethylamine.</p> <p><b>Other reported pathways include:</b></p> <ul style="list-style-type: none"> <li>Transmetalation, especially with Cu<sup>2+</sup>, Hg<sup>2+</sup>, Cd<sup>2+</sup>, Ni<sup>2+</sup> or Pb<sup>2+</sup>, forming new dithiocarbamate complexes (Sachidinis and Grant, 1981; Phinney and Bruland, 1997).</li> <li>Photolytic degradation of the dimethyldithiocarbamate ligand in surface water and soil (US EPA, 2001).</li> </ul>

Considerations	Relevant information/ Outcome
	<ul style="list-style-type: none"> <li>• Biodegradation of the dimethyldithiocarbamate ligand in soil under both aerobic and anaerobic conditions (US EPA, 2001).</li> </ul>
Influence of intensive properties of the original compound on fate	<p><b>Key consideration:</b> Lability of the zinc-dithiocarbamate bond</p> <ul style="list-style-type: none"> <li>• Literature data indicate that <math>Zn^{2+}</math> is more labile in dithiocarbamate complexes than <math>Hg^{2+}</math>, <math>Cu^{2+}</math>, <math>Ni^{2+}</math>, <math>Pb^{2+}</math> or <math>Cd^{2+}</math>.</li> </ul> <p><b>Other reaction pathways:</b></p> <ul style="list-style-type: none"> <li>• The dimethyldithiocarbamate ligand is reactive under environmental conditions.</li> <li>• <math>Zn^{2+}</math> is a stable oxidation state for zinc; it is not expected to undergo oxidation or reduction under environmental conditions.</li> <li>• <math>Zn^{2+}</math> does not form stable bonds to carbon; therefore, methylation is not expected to be important.</li> </ul>
Influence of extensive properties on fate of the original compound	<p><b>Media considerations:</b> The fate of ziram in the environment is most influenced by conditions in surface waters and soils.</p> <p><b>Water chemistry:</b></p> <ul style="list-style-type: none"> <li>• Divalent cations in solution, including <math>Hg^{2+}</math>, <math>Cu^{2+}</math>, <math>Ni^{2+}</math>, <math>Pb^{2+}</math> and <math>Cd^{2+}</math>, compete with <math>Zn^{2+}</math> in binding to the dimethyldithiocarbamate ligand.</li> <li>• The rate of hydrolysis of the dimethyldithiocarbamate ligand increases with increasing acidity. Little hydrolysis is reported at pH 9 (US EPA, 2001).</li> <li>• Photolysis of the dimethyldithiocarbamate ligand is expected to be dependent on light intensity.</li> <li>• Solvated <math>Zn^{2+}</math> is expected to be the predominant zinc species in acidic to neutral oxygenated waters. As the pH increases, zinc carbonates and oxides are formed. The predominant species in low oxygen environments is <math>ZnS</math> (US EPA, 2005).</li> </ul> <p><b>Soils:</b></p> <ul style="list-style-type: none"> <li>• As in aqueous solution, the rate of hydrolysis of the ligand increases with increasing acidity.</li> <li>• Photolysis of the ligand is expected to be dependent on light intensity.</li> <li>• Ziram degraded faster under aerobic conditions than under anaerobic conditions in soil metabolism studies.(US EPA, 2001)</li> </ul>

<p align="center"><b>Considerations</b></p>	<p align="center"><b>Relevant information/ Outcome</b></p>
<p>Environmental partitioning</p>	<p><b>Ziram:</b></p> <ul style="list-style-type: none"> <li>• The low vapor pressure indicates negligible volatilization.</li> <li>• Ziram is reported to have slight to moderate mobility in suspended solids and sediments.</li> <li>• Ziram is reported to be less mobile in a clay soil than in sand, silt loam and sandy loam soils.</li> <li>• Sorption to soils was found to be independent of organic content.</li> <li>• A similar substance Cadmium diethyldithiocarbamate was found to be significantly associated with natural organic matter (Suwannee River humic acid) (Boullemant et al. 2007). Thus, Ziram could behave similarly. Association with natural organic matter likely decreases the bioavailability of the substance to organisms. (US EPA, 2001)</li> </ul> <p><b>Zinc ion (Zn<sup>2+</sup>):</b> Zinc ion is liberated upon dissociation of ziram or degradation of the dimethyldithiocarbamate ligand.</p> <ul style="list-style-type: none"> <li>• Zinc strongly sorbs to soils at pH ≥ 5.</li> </ul> <p>(HSDB, 2006)</p>
<p align="center"><b>STEP 2b</b></p> <p align="center"><b>Extent of transformation and relative presence of moieties</b></p>	
<p>Extent of transformation (half-life)</p>	<p>Dissociation of Zn<sup>2+</sup>: ≤ hours</p> <p>Transmetallation of the ligand: ≤ hours</p> <p>Hydrolysis: 0.173 hours (pH 5); 17.7 hours (pH 7); 151 hours (pH 9).</p> <p>Photolysis: ~8-9 hours in water and soil</p> <p>Aerobic metabolism (soil): 42 hours</p> <p>Anaerobic metabolism (soil): 14.1 days</p>
<p>Moiety to be evaluated/moiety of concern</p>	<p>Ziram</p>

<b>Considerations</b>	<b>Relevant information/ Outcome</b>
	<p>Zn<sup>2+</sup> ion</p> <p>Ziram transforms under environmental conditions at a rate such that both the original compound (OM) and the transformation product (M) are relevant for assessment.</p>
Organic/inorganic transformation products/salt component	<p>Carbon disulfide (CASRN 75-15-0) and dimethylamine (CASRN 124-40-3).</p> <p>Dimethylamine should be considered for assessment according to other (current or future) frameworks for organic substances. Carbon disulfide should be assessed as part of a M assessment.</p>
<p><b>STEP 3</b></p> <p><b>Ecological effects of moieties or forms of concern liberated</b></p>	
Bioavailability, mode of action	<p>Zinc is an essential element in the environment. The possibility exists for both a deficiency and an excess of this metal in organisms.</p> <p>Toxicity of Zn<sup>2+</sup> to terrestrial plants occurs when Zn<sup>2+</sup> replaces other metals (e.g., iron, manganese) in metalloproteins (e.g., hydrolases and heme enzymes) (WHO, 2001).</p> <p>Because ziram is susceptible to degradation, especially in neutral and acidic environments, the probability of prolonged exposure to the chemical is reduced (US EPA, 2001).</p> <p>Phinney and Bruland (1997) demonstrated that ziram is able to complex toxic trace metals such as copper, which promotes passive uptake of lipophilic organic copper complexes across the plasmalemma of the cell and into the cytosol. It is suggested that a synergistic toxic effect of copper and ziram is related mainly to the alkyl- or the ethylene bis-dithiocarbamate structure (Bonnemain and Dive, 1990; HSDB, 2003).</p>
Toxicity: Inorganic metal	<p><b>Aquatic:</b></p> <p>Acute toxicity values for microorganism in the aquatic environment ranged from 0.25 to 50 mg/L (WHO, 2001).</p> <p>The LC<sub>50</sub> values for fish ranged from 1.27 to 2.6 mg/L for</p>

Considerations	Relevant information/ Outcome
	<p>freshwater species and from 21.5 to 176.6 mg/L for marine species. Chronic NOEC values for freshwater fish were <math>\leq 50</math> mg/L when water hardness was <math>\leq 100</math> mg/L CaCO<sub>3</sub>; however, when the water hardness was <math>\geq 100</math> mg/L CaCO<sub>3</sub>, all NOEC values were <math>\geq 500</math> mg/L, except in one behavior study that reported a NOEC of 60 mg/L (WHO, 2001).</p> <p>The LC<sub>50</sub> values for invertebrates ranged from 0.5 to 10 mg/L for freshwater species and from 0.191 to 0.586 mg/L for marine species. Chronic threshold values for freshwater invertebrates ranged from 25 to 225 <math>\mu</math>g/L (WHO, 2001).</p> <p>Acute toxicity values for algae ranged from 0.03 to 10 mg/L for freshwater species and from 0.058 to 0.271 mg/L for marine species. EC<sub>50</sub> values for freshwater aquatic plants ranged from 10 to 67.7 mg/L and NOEC values ranged from 0.654 to 32.7 mg/L (WHO, 2001).</p> <p>Dissolved Zn PNEC based on Species Sensitivity Distribution, Hazardous Concentration for 5% of species (SSD HC<sub>5</sub>) and application factor of 2 = 0.0031 mg/L, for low water hardness &lt; 24 mg/L as CaCO<sub>3</sub> (European Union 2006)</p> <p><b>Terrestrial:</b> The toxicity of zinc to terrestrial organisms also depends on bioavailability. The bioavailable fraction of zinc in soil has been calculated to range from &lt; 1% to 10% of the total zinc concentration (WHO, 2001).</p> <p>Earthworms (<i>Eisenia andrei</i>) and woodlice (<i>Porcellio scaber</i>) show adverse effects on reproduction starting at total zinc concentrations of 560 and 1,600 mg/kg dry weight, respectively (WHO, 2001).</p> <p>Soil Zn PNEC based on SSD HC<sub>5</sub> and application factor of 2 = 26 mg/kg dry weight (European Union 2006)</p>
<p>Toxicity: Original compound</p>	<p><b>Aquatic:</b></p> <p>According to the US EPA Registration Eligibility Decision (RED) for ziram (US EPA, 2001), the acute toxicity to freshwater and marine fish is high with 96-hour LC<sub>50</sub> values of 0.008-1.7 and 0.84 mg/L, respectively. A 33-day NOEC of 0.094 mg/L was reported for fathead minnows (US EPA, 2013).</p> <p>The acute toxicity to freshwater and marine invertebrates is also high, with toxicity values ranging from 0.014 to 0.077 mg/L. A 21-day no-observed-adverse-effect concentration (NOAEC) of</p>

Considerations	Relevant information/ Outcome
	<p>0.039 mg/L was reported for <i>Daphnia magna</i> (US EPA, 2013).</p> <p>Acute and chronic toxicity data to aquatic plants are limited. A green algae EC<sub>50</sub> value of 0.067 mg/L was reported (US EPA, 2001).</p> <p>Ziram has relatively high solubility in lipids and is highly toxic to aquatic organisms; therefore, there is potential that ziram may cause adverse effects to amphibians via dermal exposure from broadcast spray applications (US EPA, 2001).</p> <p><b>Terrestrial:</b> The acute and chronic toxicity of ziram to terrestrial mammals (rats) is low, with an acute oral LD<sub>50</sub> of 320 mg/kg and a 2-generation dietary reproductive NOAEL of 207 mg/kg. Ziram is practically nontoxic to honeybees; the LD<sub>50</sub> is &gt; 100 µg/bee (US EPA, 2001). The reported toxicity values for terrestrial plants are all &gt; 6 lbs/A. Fourteen-day LC<sub>50</sub> and NOEC values of 140 and 100 mg/kg soil dry weight were reported for earthworms (<i>Eisenia foetida</i>), respectively (European Commission, 2000).</p> <p>Ziram is moderately toxic to avian species. An acute avian LD<sub>50</sub> value of 5,156 mg/kg was reported. A 1-generation reproductive study in mallard ducks reported a NOAEC of 29 mg active ingredient/kg diet (US EPA, 2001).</p> <p>Dietary ingestion of ziram has been reported to cause ovarian atrophy and cessation of egg laying in hens, which is most likely attributed to inhibition of dopamine beta-hydroxylase (Shore and Rattner, 2001; HSDB, 2003).</p>
<p>Comparative toxicities<sup>4</sup>: original OM vs. M</p>	<p>Lowest aquatic M value 0.0031 mg/L = 47 nM (based on 65.4 g/mol for Zn) (European Union 2006):</p> <p>Lowest aquatic OM value (fish): 0.008 mg/L = 26 nM (based on a molecular weight of Ziram of 305.8 g/mol)</p>

<sup>4</sup> Provided as example only and are considered approximate comparisons. More detailed comparisons taking more factors into consideration should ideally be made in full assessments (e.g. additional SSD HC5s, species similarity, exposure conditions, studies conducting both tests in parallel M and OM, speciation measurements/calculations).

Considerations	Relevant information/ Outcome
	<p>Factor difference = M is 1.8 times less toxic than OM</p> <p>Lowest terrestrial M value 26 mg/kg = 398 µM/kg (European Union 2006):</p> <p>Lowest terrestrial OM value (diet, bird): 29 mg/kg = 95 µM/kg</p> <p>Factor difference = 4.2 times</p> <p>M ≈ original OM (see Figure 3)</p> <p>The ecotoxicity of the OM is likely greater than that of M. In other words, the bioavailability of Zn is greater in the form of the OM rather than in the form of the M assuming an equal mode of action. However, the difference in ecotoxicity is less than 2 orders of magnitude therefore, each moiety should be considered to contribute to risk in each assessment type (M and OM) or a toxicity-additivity approach can be followed if the OM is being addressed on a substance-by-substance basis. In addition, bioavailability and toxicity of the OM is greater than predicted based upon the BLM which would solely consider Ziram as a ligand exerting no bioavailability/toxicity on its own. See section 3.3.4 for more information on BLM.</p>

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## AI.5 Case study on Outcome 5 OM compound: Tributyltin chloride (CASRN: 1461-22-9)

Considerations	Relevant information / Outcome
<b>STEP 1</b>  <b>Determine the extent of dissolution/dissociation of original OM</b>	
Solubility and other physicochemical properties	<p><b>Solubility:</b> 17 mg/L in water at 20 °C (Blunden et al., 1984).</p> <ul style="list-style-type: none"> <li>• Low, but significant solubility in water.</li> </ul> <p><b>Boiling point:</b> 171-173 °C at 25 torr (HSDB, 2002).</p> <ul style="list-style-type: none"> <li>• The original compound is minimally volatile, and is unlikely to partition to the vapor phase.</li> <li>• Cleavage of the tin-chlorine bond yields cationic tributyltin. Ionic tributyltin compounds will not volatilize.</li> </ul> <p><b>Log K<sub>ow</sub>:</b> 4.76 (HSDB, 2002); 2.07 (OECD 2007)</p> <ul style="list-style-type: none"> <li>• Tributyltin chloride is moderately hydrophobic.</li> <li>• The hydrophobic nature of this compound and its transformation products will promote partitioning of alkyltin compounds to the sediment compartment, where degradation processes are typically slower than in the water column.</li> <li>• This log K<sub>ow</sub> value indicates a potential for bioconcentration.</li> </ul> <p><b>K<sub>oc</sub>:</b> K<sub>oc</sub> values up to 90,800 have been reported for tributyltin species (HSDB, 2002)</p> <ul style="list-style-type: none"> <li>• Sorption to soils, particulates and sediment is expected to be strong.</li> </ul>
Dissociation	Partial dissociation of the tin-chlorine bond
<b>STEP 2a</b>  <b>Examine and evaluate stability and persistence information of original OM</b>	
Types of transformation pathways in the environment	<p><b>Predominant transformation pathway:</b> Marine scenario: partial dissociation of the tin-chlorine bond, yielding persistent tributyltin<sup>+</sup> and Cl<sup>-</sup> species is likely. Tributyltin<sup>+</sup> can undergo species transformation leading to different forms depending on environmental conditions. Tributyltins are present in seawater as</p>

Considerations	Relevant information / Outcome
	<p>three main species (chloride, hydroxide and carbonate).</p> <p><b>Other transformation pathways:</b></p> <ul style="list-style-type: none"> <li>• Bio-mediated cleavage of Sn-Bu bonds</li> <li>• Biomethylation of tin</li> <li>• Photolytic cleavage of Sn-Bu bonds</li> </ul> <p>(GDCh, 1988; WHO, 1990; ECB, 2008)</p>
Influence of intensive properties of the original compound on fate	<p><b>Key consideration:</b> The tin-chlorine bond is labile, but tin-carbon bonds are stable under most conditions. Cationic trialkyltin species are stable.</p> <ul style="list-style-type: none"> <li>• While tributyltin chloride will partially dissociate, persistent alkyltin transformation products are formed in the environment.</li> </ul> <p><b>Other reaction pathways:</b></p> <ul style="list-style-type: none"> <li>• Tin(IV) is a stable oxidation state for tin. Tributyltin chloride and its transformation products are unlikely to participate in redox reactions under environmental conditions.</li> </ul>
Influence of extensive properties on fate of the original compound	<p><b>Media considerations:</b> Environmental degradation of tributyltin species occurs primarily by bio-mediated processes, with some contribution by photolysis. Conditions affecting the microbial population will therefore affect the rate of destruction of tributyltin.</p> <p><b>Air composition/quality:</b> No effect expected.</p> <p><b>Water chemistry:</b></p> <ul style="list-style-type: none"> <li>• Aerobic conditions promote biodegradation in the water column.</li> <li>• Photolysis is dependent on sunlight intensity.</li> <li>• pH and ionic strength (e.g. concentration of Cl<sup>-</sup>) of the aqueous environment can influence the dissociation of the tin-chlorine bond; however, the equilibrium favors dissociation in both fresh and saline water (Eng et al. 1986).</li> <li>• pH and major anion concentrations may also influence the proportions of the tributyltin species present. Tributyltin chloride predominates in waters with high concentrations of Cl<sup>-</sup>, such as seawater (OECD 2007).</li> </ul>

<b>Considerations</b>	<b>Relevant information / Outcome</b>
	<p><b>Sediments and soils:</b></p> <ul style="list-style-type: none"> <li>• The rate of biodegradation in soils and sediments is faster under aerobic conditions than under anaerobic conditions.</li> <li>• Methylation of tin species occurs under anaerobic conditions.</li> </ul> <p>(Environment Canada, 2009; HSDB, 2002)</p>
Environmental partitioning	<p><b>Tributyltin species:</b></p> <ul style="list-style-type: none"> <li>• Volatilization is negligible for ionic species.</li> <li>• Tributyltin species sorb strongly to soils and sediments, and are removed from the water column by sorption and settling.</li> <li>• Sorbed tributyltin species do not leach from soils or sediments.</li> </ul>
<p><b>STEP 2b</b></p> <p><b>Extent of transformation and relative presence of moieties</b></p>	
Extent of transformation (half-life)	<p>Initial Sn-Cl cleavage (&lt; minutes)</p> <p>Biodegradation in water (6 days to 35 weeks)</p> <p>Photolysis in water (&gt; 89 days)</p> <p>Biodegradation in soil (15-20 weeks)</p> <p>Biodegradation in sediment (0.9-15 years)</p> <p>Biodegradation in deep anoxic sediment (87 years)</p> <p>(HSDB, 2002; Environment Canada, 2009)</p>
Moiety to be evaluated/moiety of concern	<p>Tributyltin species: original compound: tributyltin chloride; new OM (nOM): tributyltin hydroxide and tributyltin carbonate.</p> <p>Tributyltins can persist in the water column, in soils and sediments and thus assigned to Outcome 5 (as original compound or nOM), and 100% of the OM (as total tributyltins) is considered to be the moiety of concern for the ecological risk assessment, the metal M is considered to be negligible and remains strongly bonded to the</p>

Considerations	Relevant information / Outcome
	alkyl groups.
Organometallic transformation product/salt component	The additional expected transformation products are dibutyltin and monobutyltin. However, their proportions in the environment are considered negligible considering the very long half-lives. Therefore, no further consideration is given to these moieties for the purposes of ecological risk assessment.

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